Clinical Radiology 74 (2019) 569.e9–569.e17

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Imaging features of pure mucinous breast carcinoma: correlation with extracellular mucus content

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ARTICLE INFORMATION

Article history:
Received 10 September 2018
Accepted 24 January 2019

AIM: To analyse the correlation between imaging features using multiple techniques and extracellular mucus content in pure mucinous breast carcinoma (PMBC).

MATERIALS AND METHODS: A retrospective review of available images from 25 patients with 25 PMBC tumours was conducted, with ultrasonography (US), ultrasonic elastography (USE), mammography, and breast-specific gamma imaging (BSGI) available for 25, 15, 11, and eight patients, respectively. Microscopic slides from each tumour were evaluated for extracellular mucus content. The correlation between imaging features and mucus content was analysed using linear-by-linear association chi-square tests or Spearman's rank correlation analyses.

RESULTS: On US images, a significant correlation was found between mucus content and echo pattern (p=0.042) and colour Doppler blood flow (p=0.032), with a trend that the lower mucus content present in tumours, the more likely they were detected with isoechoic echo and high blood flow. On USE images, a moderate negative correlation (r=−0.60, p=0.029) was observed between mucus content and tumour stiffness. On BSGI images, a strong negative correlation (r=−0.92, p=0.001) was shown between mucus content and lesion to non-lesion ratio (L/N) values of radioactivity counts. No significant correlation was found between mucus content and mammography imaging features (all p>0.05).

CONCLUSION: Imaging features at US, USE, and BSGI correlated with extracellular mucus content in PMBC tumours, among which the L/N value using BSGI imaging is the most relevant feature.

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Introduction

Mucinous breast carcinoma (MBC) is an uncommon subtype of breast malignancy, characterised by aggregates of tumour cells floating in pools of extracellular mucus.[1] Histologically, MBC is further divided into pure mucinous

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https://doi.org/10.1016/j.crad.2019.01.031
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breast carcinoma (PMBC) and mixed mucinous breast carcinoma (MMBC) by different proportions of tumour components. PMBC consists of clusters of mucinous cancer cells embedded in extracellular mucus and displays no other type of infiltrating carcinoma; MMBC contains a component of any other type of infiltrating carcinoma, which is not surrounded by extracellular mucus.[2–4] Such subclassification is necessitated by the fact that mixed and pure forms of MBC present distinct pathological and clinical manifestations, with PMBC showing a slower tumour growth rate, a lower frequency of axillary lymph node metastasis, and a lower recurrence rate compared with MMBC.[3,5] Generally, PMBC tends to have a better prognosis than MMBC and other subtypes of breast carcinoma.[1,6,7] Consistent with its indolent behaviour, PMBC typically presents with less aggressive imaging appearances mammographically and sonographically: smaller size, circumscribed margin, round or lobular shape, and isoechogenicity.[8–10]

It is believed that the existence of abundant mucus in PMBC may act as a mechanical barrier and diminish the tumour cell invasion at the tumour margin, thus playing an important role in the mechanism of tumour progress.[10] Furthermore, a high proportion of mucus in PMBC has been suggested to be a favourable prognostic factor.[3,10] As such, it is of prime significance to investigate the correlation between mucus content and different imaging features of PMBC. Although several previous studies have made efforts in related fields, the results were discordant.[10–12] The inconsistency between different studies may be due to either a small sample size or a lack of mucus quantification. Hence, additional studies focusing on the correlation between mucus content and imaging findings by multiple imaging techniques are warranted to further increase our understanding of this special subtype of breast carcinoma.

This study depicts the imaging appearances of PMBC tumours using multiple imaging technologies, including ultrasonography (US), ultrasonic elastography (USE), mammography, and breast specific gamma imaging (BSGI), and aims to correlate mucus content with different imaging findings of PMBC tumours. To the authors' knowledge, no literature has yet reported BSGI findings of PMBC tumours and this is the first study exploring the relationship between mucus content in PMBC and imaging features by multiple imaging techniques including BSGI.

Materials and methods

Patients

This retrospective study was approved by the Institutional Review Board. Informed consent was waived as all data were collected retrospectively from routine practice. The electronic medical records of patients who underwent preoperative breast US examinations for tumour localisation between May 2012 and August 2017 were reviewed, and all PMBC patients were enrolled. Twenty-eight female patients were diagnosed with PMBC at surgical pathology, among which three had a history of breast mastectomy and/or chemotherapy and thus were excluded from the study. A total of 25 patients with 25 PMBC tumours were recruited to the study. Among them, 12 patients were enrolled by US and/or mammography screen with no clinical symptoms; 13 patients presented with a palpable breast mass and four with nipple discharge, with two displaying both symptoms. All patients underwent US examinations within 2 days prior to surgery. In addition, USE, mammography, and BSGI were performed for 13, 11, and eight patients within 2 weeks before surgery, respectively.

US and USE

Bilateral breasts of all enrolled patients were scanned by one of the two radiologists who had 8 and 20 years of experience in breast ultrasonography, respectively. Suspicious lesions were recorded comprehensively with respect to B-mode features and colour Doppler information, and representative images were saved. USE was performed for 13 patients after US examinations by the senior radiologist. The stiffness of the tumour was evaluated according to the colour pattern of the tumour on USE images, with increasing hardness presented in the ascending order of red, yellow, green, and blue. A HITACHI ecom EUB-8500 (7.5–13 MHz, Hitachi Medical Corporation, Tokyo, Japan) was used for US and USE examinations, and ACUSON S2000 (6–18 MHz, Siemens Medical Solutions, Mountain View, CA, USA) was used for US examinations.

US images of the 25 PMBC tumours were reviewed to evaluate lesion shape (round/oval, lobulate, irregular), margin (well-defined, ill-defined), echo pattern (isoechoic, hypoechoic, mixed echogenicity), and posterior echo (shadowing, normal, enhancement). Angular and spiculate margins were classified as ill-defined margins. Tumour echo pattern was assessed with comparison to surrounding fat tissue. Colour Doppler blood flow was evaluated according to Adler's semi-quantitative analysis (grades 0, I, II, and III)[13]; grade I was considered as low levels of blood flow, and grades II–III were considered as high levels of blood flow. USE images were analysed according to Tsukuba elasticity criterion, whereby the hardness of lesions was classified on a five-point scale.[14] Tumours with elasticity scores of 1–3 were regarded as soft, whereas those with scores of 4–5 were regarded as stiff.

Mammography

Mammography examinations were performed for bilateral breasts and axillaries in11 patients using a GE Senographe DS mammography X-ray machine (GE Medical Systems, Fairfield, CT, USA). Standard craniocaudal (CC) and mediolateral oblique (MLO) views were obtained routinely. Mammograms were reviewed to evaluate lesion shape (round/oval, lobulate, irregular) and margin (well-defined, ill-defined).

BSGI

BSGI was performed in eight patients using high-resolution breast-specific gamma imaging (Dilon 6800;

Dilon Technologies, Newport News, Virginia, USA) equipped with a low-energy collimator with an energy window of 140 keV ±10%. Imaging agent, Tc-99m-MIBI (Shanghai GMS Pharmaceutical, Shanghai, China), was administered 10 minutes prior to BSGI examinations as described in an earlier study.[15] Similar to mammography, bilateral breasts and axillaries were imaged by CC and MLO views. A visual analysis of BSGI images was graded according to the 2010 guideline of the Society of Nuclear Medicine and Molecular Imaging[16]; grades 1 to 3 were considered to be low uptake and indicate benign lesions, and grades 4 to 5 were considered to be high uptake and indicate malignant lesions. A semi-quantitative analysis of the lesion to non-lesion ratio (L/N) was carried out as depicted in a previous study.[15] Briefly, the radioactivity count of the lesion area was divided by that of the non-lesion area, and the ratio calculated was regarded as the value of L/N.

All retrospective reviews and evaluation of the above multi-imaging features were independently performed by two experienced radiologists who were unaware of the purpose of this study and patients' medical history. Any discrepancies were resolved in consensus.

Histopathological analysis

Microscopic slides stained with haematoxylin and eosin (H&E) were available for all the PMBC tumours in this study and were re-evaluated by an experienced pathologist with 7 years of breast pathology experience. PMBC diagnosis was reconfirmed by evaluating all available H&E slides (8–10 slides/lesion) under both low- and high-power fields. Stringent criteria were used to diagnose PMBC: every cluster of tumour cells was partially or completely embedded within the extracellular mucus and the tumour displayed no other type of invasive carcinoma.[3,4] Tumours containing areas of ductal carcinoma in situ were not placed in this group. Tumour size was determined by the maximum diameter measured on fresh specimens after surgical resection.

Three representative slides from each tumour were chosen to estimate the percentage of extracellular mucus under low power fields. For this purpose, the area ratio of extracellular mucus and tumour clusters were calculated and stratified as follows: low content, ≤30% of mucus (1+); moderate content, >30% and <80% of mucus (2+); and high content, ≥80% of mucus (3+). Information of the expression of oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2), and lymph node metastasis was noted by reviewing histopathology reports. HER-2 status was classified as negative (0/1+), positive (3+), and borderline (2+). Fluorescence in situ hybridisation was performed on HER-2 2+ tumours to make a final determination on status. The HER-2 gene was considered amplified if the gene-to-chromosome ratio was >2.[17]

Statistical analysis

SPSS 23.0 software package (SPSS, Chicago IL, USA) was used for statistical analysis. Continuous variables were expressed as mean ± standard deviation. The correlation between mucus content (graded as 1+, 2+, 3+) and imaging features of US and mammography was analysed by linear-by-linear association chi-square tests, while Spearman's rank correlation analyses were used to correlate mucus content (percentage) with L/N values, elasticity scores, and tumour size, respectively. Correlation coefficients (r) were further calculated for data with statistically significant results in above Spearman's rank correlation analyses. $|r| \geq 0.7$ indicates a high degree of correlation; $0.4 \leq |r| < 0.7$ indicates a moderate degree of correlation; $|r| < 0.4$ indicates a low degree of correlation. In all cases, $p<0.05$ was considered statistically significant.

Results

Clinicopathological findings

The average age at diagnosis in patients with PMBC was 64.2±15.3 years (32–89 years) and the average tumour size was 2.6±1.2 cm (1.2–7 cm). Most of the tumours detected were ER (25/25, 100%) and PR (23/25, 92%) positive, whereas only two were Her-2 positive (8%). Axillary lymph node metastasis presented in two patients (8%). For the estimation of extracellular mucus content, three (12%) tumours had low content (1+), 13 (52%) had moderate content (2+), and nine (36%) had high content (3+). The correlation between tumour size and mucus content was analysed, but no significant results were found ($p>0.05$).

Correlation between US imaging features and mucus content in PMBC

US imaging features stratified by different mucus content in PMBC are presented in Table 1. Mucus content was found to be significantly correlated with echo pattern ($p=0.042$) and colour Doppler blood flow ($p=0.032$), with a trend that the lower mucus content the tumours contained, the more likely they were detected with isoechoic echo and high blood flow levels (Fig 1). No correlation was found between mucus content and lesion shape, margin, or posterior echo features (all $p>0.05$). In addition, three PMBC tumours with low mucus content demonstrated lobulate shape, well-defined margin, isoechoic echo, posterior enhancement, and high levels of blood flow.

Correlation between USE findings and mucus content in PMBC

Of the 13 tumours with USE examinations, more than half (8/13, 62%) had an elasticity score of 4 or 5, among which six tumours had moderate mucus content, one had a low content, and one had high content. Of the five tumours with a score ≤3, four had a high mucus content and one had a moderate content. Spearman's rank correlation analyses were used to correlate mucus content with elasticity scores, and a moderate negative correlation ($r=-0.60$, $p=0.029$) was observed between them (Figs 2 and 3).

Table 1
Correlation between ultrasound imaging features and mucus content in pure mucinous breast carcinoma.

Characteristic	Extracellular mucus content			X^2	*p*-Value
	1+	2+	3+		
No. of tumours	3 (12%)	13 (52%)	9 (36%)	—	—
Shape				0.25	0.614
Round/oval	0 (0%)	5 (38.5%)	4 (44.4%)		
Lobulate	3 (100%)	4 (30.8%)	3 (33.3%)		
Irregular	0 (0%)	4 (30.8%)	2 (22.2%)		
Margin				0.49	0.485
Well-defined	3 (100%)	8 (61.5%)	6 (66.7%)		
Ill-defined	0 (0%)	5 (38.5%)	3 (33.3%)		
Echo pattern				4.14	0.042
Isoechoic	3 (100%)	9 (69.2%)	3 (33.3%)		
Hypoechoic	0 (0%)	2 (15.4%)	3 (33.3%)		
Mixed	0 (0%)	2 (15.4%)	3 (33.3%)		
Posterior echoic				1.00	0.318
Shadowing	0 (0%)	1 (7.7%)	1 (11.1%)		
normal	0 (0%)	5 (38.5%)	3 (33.3%)		
Enhancement	3 (100%)	7 (53.8%)	5 (55.6%)		
Blood flow level				4.62	0.032
0	0 (0%)	2 (15.4%)	3 (33.3%)		
I	0 (0%)	5 (38.5%)	4 (44.4%)		
II-III	3 (100%)	6 (46.1%)	2 (22.3%)		

Correlation between mammography imaging features and mucus content in PMBC

A total of 10 PMBC tumours were examined using mammography and nine presented as a mass of high density. One tumour with 90% mucus content could not be detected in a dense breast both preoperatively and retrospectively. Mammography imaging features are showed in Table 2. Two tumours with low mucus content manifested with round/oval shape and well-defined margin, which was consistent with their corresponding US findings (Fig 1a). Two tumours with high mucus content showed ill-defined margins (Fig 4a). No statistically significant correlation was found between mucus content and mammography imaging features (all $p>0.05$).

Correlation between BSGI findings and mucus content in PMBC

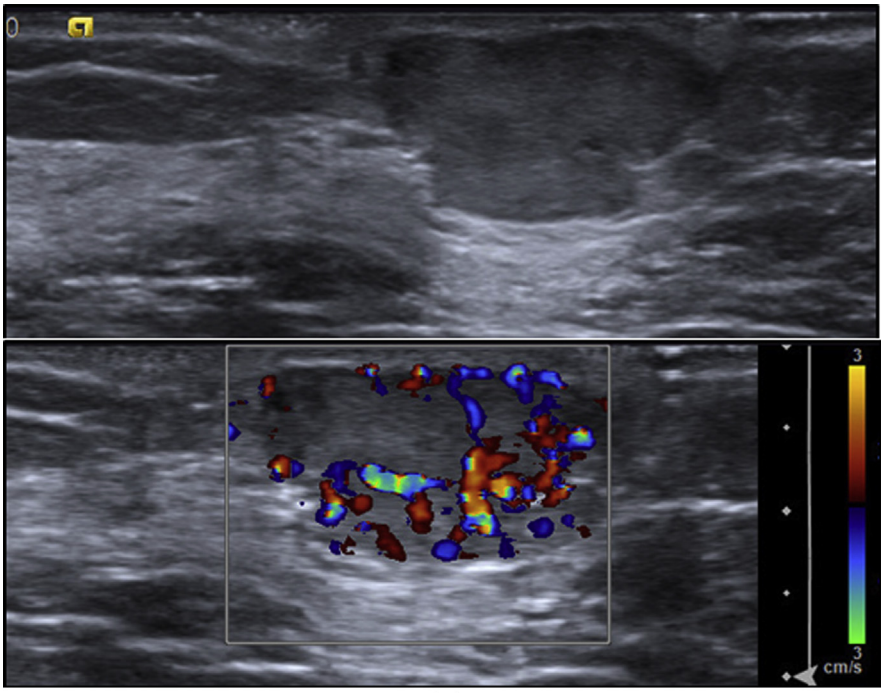
Of the eight PMBC tumours examined by BSGI, only three (38%) with low or moderate mucus content showed high uptake in the CC and/or MLO views (Fig 4b and c); five (62%) with high mucus content showed low uptake. L/N values were calculated for all the tumours and the mean value was 2.3±1.3. A strong negative correlation was revealed between mucus content and L/N values ($r=-0.92$, $p=0.001$; Fig 5).

Discussion

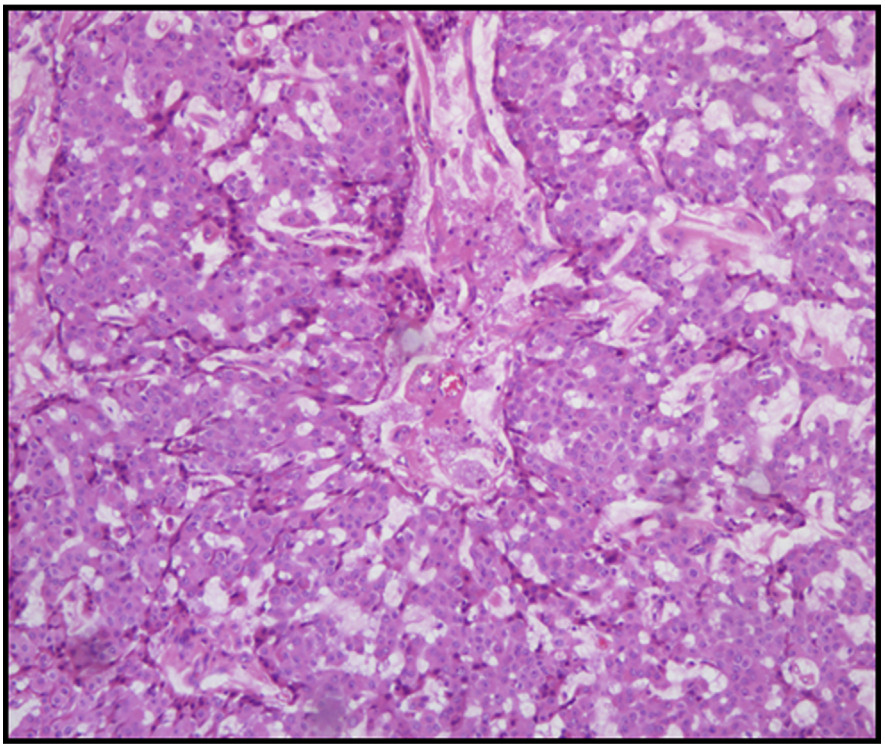
PMBC is a rare type of breast malignancy accounting for up to 2% of all breast cancers.[18] In this series, elderly women (average 64.2 years) were the major population of patients with PMBC, with an age range similar to that of earlier studies.[7,9] In accordance with previously reported findings,[18,19] PMBC tumours consistently expressed ER (100%) and PR (92%), but lacked Her-2 expression (8%) and axillary lymph node involvement (8%), indicating a favourable prognosis. In addition, no correlation was detected between tumour size and mucus content in this study.

Consistent with previous studies,[8–10] US imaging features of PMBC tumours in the present study tend to be less aggressive, with round/oval and lobulate shape, well-defined margin, and posterior enhancement more frequently detected; however, no significant relationship was found between mucus content and these imaging features. Interestingly, internal echogenicity was found to be moderately correlated with mucus content in the present study, with a trend that the lower levels of the mucus content, the greater possibilities of the tumours with isoechoic echo; however, discrepancies exist between the results from this study and previous ones. Memis *et al.*[10] reported that most PMBC tumours (5/6, 83%) with high mucus content showed isoechoic echo, while only 50% (4/8) with low or moderate content did. Liu *et al.*[12] found no correlation between sonographic features and mucus content in PMBC. The discrepancies between the different studies may be explained by varying proportions of mucus, stroma, and tumour cells in the tumour entity. It was noted that internal echo of PMBC correlated with reflection and back-scattering were caused mainly by the interface between mucus and stroma.[20] In addition, differences in acoustic impedance, which are associated with interfaces, rely on frequency; therefore, the internal echo may vary slightly with different probes and equipment.[20] To the authors' knowledge, only one previous study depicted colour Doppler information of PMBC tumours,[9] reporting that 35% (7/20) of PMBC tumours demonstrated colour Doppler blood flow lower than that (80%) in the present study. The inconsistency may be caused by different equipment used with a VST Master's Series (Diasonics) and a 10 MHz linear array transducer used in that study. A negative correlation was observed between mucus content and blood flow levels; lower levels of mucus content correlated with higher levels of blood flow. Such a finding is not surprising considering that tumours with lower mucus content contain more tumour cells as well as more feeding vessels. Similar to the present observation, using contrast-enhanced MRI, strong rim or heterogeneous enhancement was observed in hypercellular PMBC tumours with prominent proliferated epithelial tumour cells and large tumour cell clusters.[4]

Literature regarding the correlation between mucus content and USE findings is limited. PMBC is thought to be soft due to the presence of mucus components within the tumour. Paradoxically, more than half the PMBC tumours (8/13, 62%) in the present series were stiff with elasticity scores ≥4. Consistent with this finding, an earlier study documented a similar rate (9/13, 69%) of PMBC tumours and a higher rate (12/16, 75%) of MBC tumours with elasticity scores ≥4.[21] Nevertheless, a negative correlation was observed between mucus content and elasticity scores; in other words, tumours with higher mucus content tend to be softer. A lower proportion (5/13, 38%) of PMBC with high



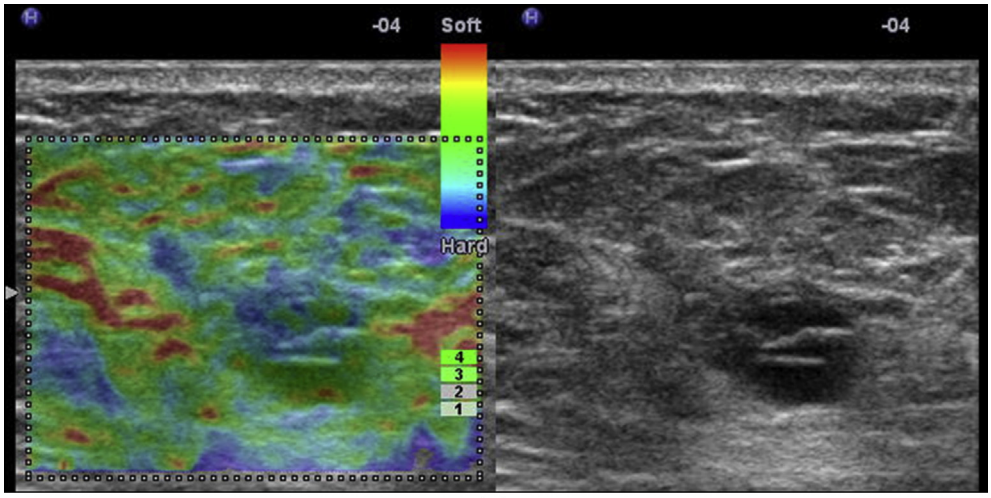
(a)



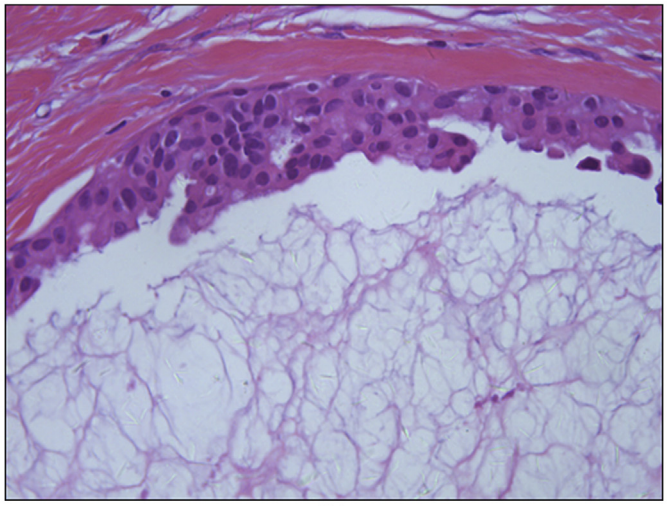
(b)

Figure 1 Ultrasonography and histology of a PMBC tumour with low extracellular mucus content in an 81-year-old woman. (a) Ultrasonogram shows a tumour with lobulate shape, well-defined margin, isoechoic echo, and posterior enhancement. Colour Doppler flow imaging shows high levels of blood flow in the tumour. (b) Photomicrograph (H&E, ×100) shows large amounts of tumour cell clusters mixed with sparse extracellular mucus indicating a mucus content of 10%.

mucus content in this study may explain the present finding that more tumours were found to be stiff. In addition, one tumour with high mucus content had an elasticity score of 5, indicating that the mucus content is not the only factor that affects PMBC stiffness. Several studies have considered factors determining tumour elastography and have demonstrated that tumour stiffness is not only affected by tumour components, but also by tumour size, location, and breast density.[22–25] Given the various factors affecting USE and the small sample size in the present study, it is



(a)



(b)

Figure 2 Elastography and histology of a PMBC tumour with high extracellular mucus content in a 69-year-old woman. (a) Ultrasonogram shows a tumour with round shape, ill-defined margin, mixed echogenicity, and posterior enhancement. Elastography shows the tumour elasticity score was score 2. (b) Photomicrograph (H&E, ×100) shows few tumour cell clusters in a large pool of extracellular mucus, indicating a mucus content of 90%.

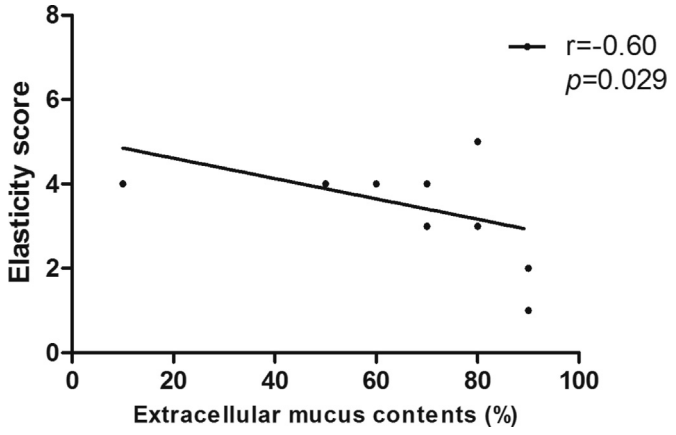


Figure 3 Scatter plot depicting a moderate correlation between elasticity scores and extracellular mucus content in PMBC.

reasonable that only a moderate correlation (r=−0.60) was observed between mucus content and tumour stiffness. A definitive conclusion remains to be derived by further studies on a larger scale.

Table 2
Correlation between mammography imaging features and mucus content in pure mucinous breast carcinoma.

Characteristic	Extracellular mucus content			X^2	p-Value
	1+	2+	3+		
No. of tumours	2 (20%)	6 (60%)	2 (20%)	—	—
Shape				3.32	0.070
Round/oval	2 (100%)	3 (50%)	0 (0%)		
Lobulate	0 (0%)	2 (33.3%)	1 (50%)		
Irregular	0 (0%)	1 (16.7%)	1 (50%)		
Margin				3.75	0.053
Well-defined	2 (100%)	2 (33.3%)	0 (0%)		
Ill-defined	0 (0%)	4 (66.7%)	2 (100%)		

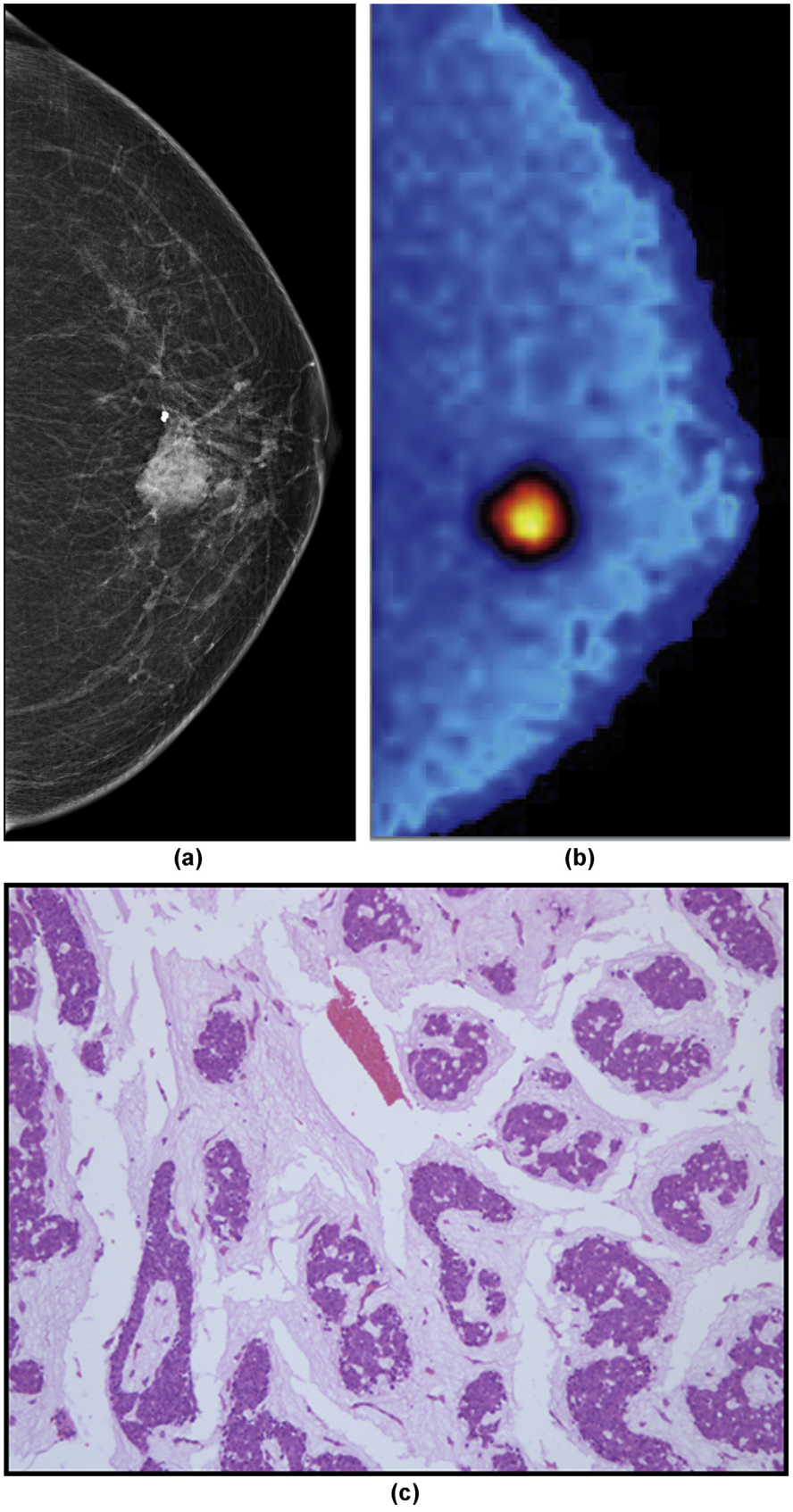


Figure 4 Mammography, BSGI and histology of PMBC tumour with moderate extracellular mucus content. (a) Mammogram shows the tumour with irregular shape, ill-defined margin, and high density. (b) BSGI shows the tumour with high radioactive concentration. (c) Photomicrograph (H&E, ×100) shows a few tumour cell clusters surrounded by a pool of extracellular mucus, indicating a mucus content of 50%.

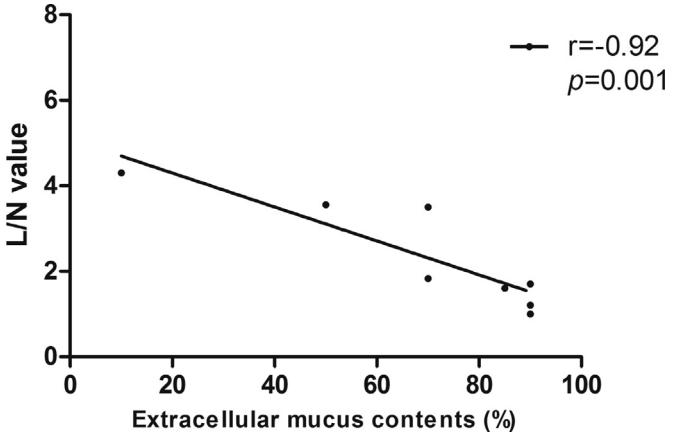


Figure 5 Scatter plot depicting a strong correlation between L/N values and extracellular mucus content in PMBC.

According to previous studies, there was a trend that PMBC tumours with high mucus content were more likely to have a well-defined margin at mammography.[10,11] In contrast to this trend, two tumours with low mucus content showed a well-defined margin, while two tumours with high mucus content showed an ill-defined margin in the present study. One reason for this inconsistency may be that MMBC was included in previous studies. In addition, Liu *et al.* reported that the mammographic margin had no relation to mucus content, but was correlated with breast density and patient age.[12] In support of the results of Liu *et al.*, one tumour with high mucus content in the present study could not even be detected because of the density of the surrounding breast tissue. Similarly, another study also reported that as many as 21.2% MBC tumours could not be detected by mammography.[9] In addition, no correlation was found between mucus content and mammography features. Therefore, the correlation between mucus content and mammography findings may be affected by breast density and needs further study.

BSGI is an emerging nuclear medicine technique and has been increasingly applied in clinic. As a functional imaging method, BSGI has been proven useful as a complementary technique to US and mammography by improving the sensitivity of breast cancer diagnosis. Surprisingly, only 38% (3/8) of the PMBC tumours in this series showing high uptake were considered as breast malignancy, and the others with low uptake were mistaken for benign lesions. In contradiction to its high sensitivity in diagnosing other types of breast cancers, BSGI seemed to have limited sensitivity in diagnosing PMBC tumours; however, a strong negative correlation (r=−0.92) was found between mucus content and L/N values; that is to say, tumours with higher L/N values had lower mucus content and in turn, higher percentages of tumour cells and/or stromal components including blood vessels. This observation in part supports the rationale that increased uptake of Tc-99m-MIBI in cancers is proportional to the neovascularisation/blood volume in the cancer and the mitochondrial density in the cancer cells.[16] Recently, a study reported seven MBC cases treated with neoadjuvant chemotherapy and observed a specific pathological response pattern characterised by abundant mucus pools in tumours with sparse residual tumour cells. Persistent mucus pools result in a continued mass effect, and thus conventional imaging methods, such as US and mammography, may suggest a minimal response or even a progressive disease despite an excellent pathological response.[26] Notably, L/N values were found strongly correlated with mucus content in the present study; in other words, L/N values can reflect tumour cellularity to some extent. Although it shows compromised sensitivity in diagnosing PMBC tumours, BSGI may hold great promise in evaluating therapeutic responses of PMBC or MBC tumours to neoadjuvant chemotherapy.

Several limitations of this study need to be mentioned. Firstly, the sample size was relatively small due to the rarity of PMBC tumours, especially in the analysis of the relationship between BSGI and extracellular mucus content; therefore, more cases should be accumulated for future studies. Secondly, all data were obtained from patients scheduled to undergo preoperative US examinations, which may cause sample selection bias. Lastly, the definition of PMBC has not been unified, whereby attention should be payed to the results from studies using different definitions to make a reasonable analysis.

In conclusion, the imaging features of PMBC using US, USE, and BSGI were correlated with extracellular mucus content in PMBC tumours. Lower mucus content was associated with isoechoic echo, higher blood flow levels, higher tumour stiffness, and higher L/N values. L/N values from BSGI imaging are the most correlated with mucus content in PMBC and may be used to assess therapeutic responses to neoadjuvant chemotherapy. Although lacking pathognomonic imaging features for PMBC, the combination of multi-imaging features can provide more information about mucus content within PMBC.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

This study was supported by grant no. 16ZR1433200 from the Shanghai Natural Science Foundation.

References

1. Zhang M, Teng XD, Guo XX, *et al.* Clinicopathological characteristics and prognosis of mucinous breast carcinoma. *J Cancer Res Clin Oncol* 2014;**140**(2):265–9.
2. Zhang L, Jia N, Han L, *et al.* Comparative analysis of imaging and pathology features of mucinous carcinoma of the breast. *Clin Breast Cancer* 2015;**15**(2):e147–54.
3. Kashiwagi S, Onoda N, Asano Y, *et al.* Clinical significance of the subclassification of 71 cases mucinous breast carcinoma. *Springerplus* 2013;**2**:481.
4. Monzawa S, Yokokawa M, Sakuma T, *et al.* Mucinous carcinoma of the breast: MRI features of pure and mixed forms with histopathologic correlation. *AJR Am J Roentgenol* 2009;**192**(3):W125–31.

5. Skotnicki P, Sas-Korczynska B, Strzepek L, *et al*. Pure and mixed mucinous carcinoma of the breast: a comparison of clinical outcomes and treatment results. *Breast J* 2016;**22**(5):529–34.
6. Ranade A, Batra R, Sandhu G, *et al*. Clinicopathological evaluation of 100 cases of mucinous carcinoma of breast with emphasis on axillary staging and special reference to a micropapillary pattern. *J Clin Pathol* 2010;**63**(12):1043–7.
7. Komenaka IK, El-Tamer MB, Troxel A, *et al*. Pure mucinous carcinoma of the breast. *Am J Surg* 2004;**187**(4):528–32.
8. Tan JZ, Waugh J, Kumar B, *et al*. Mucinous carcinomas of the breast: imaging features and potential for misdiagnosis. *J Med Imaging Radiat Oncol* 2013;**57**(1):25–31.
9. Lam WW, Chu WC, Tse GM, *et al*. Sonographic appearance of mucinous carcinoma of the breast. *AJR Am J Roentgenol* 2004;**182**(4):1069–74.
10. Memis A, Ozdemir N, Parildar M, *et al*. Mucinous (colloid) breast cancer: mammographic and US features with histologic correlation. *Eur J Radiol* 2000;**35**(1):39–43.
11. Conant EF, Dillon RL, Palazzo J, *et al*. Imaging findings in mucin-containing carcinomas of the breast: correlation with pathologic features. *AJR Am J Roentgenol* 1994;**163**(4):821–4.
12. Liu H, Tan H, Cheng Y, *et al*. Imaging findings in mucinous breast carcinoma and correlating factors. *Eur J Radiol* 2011;**80**(3):706–12.
13. Adler DD, Carson PL, Rubin JM, *et al*. Doppler ultrasound colour flow imaging in the study of breast cancer: preliminary findings. *Ultrasound Med Biol* 1990;**16**(6):553–9.
14. Itoh A, Ueno E, Tohno E, *et al*. Breast disease: clinical application of US elastography for diagnosis. *Radiology* 2006;**239**(2):341–50.
15. Tan H, Zhang H, Yang W, *et al*. Breast-specific gamma imaging with Tc-99m-sestamibi in the diagnosis of breast cancer and its semiquantitative index correlation with tumour biologic markers, subtypes, and clinicopathologic characteristics. *Nucl Med Commun* 2016;**37**(8):792–9.
16. Goldsmith SJ, Parsons W, Guiberteau MJ, *et al*. SNM practice guideline for breast scintigraphy with breast-specific gamma-cameras 1.0. *J Nucl Med Technol* 2010;**38**(4):219–24.
17. Bartlett JM, Starczynski J, Atkey N, *et al*. HER2 testing in the UK: recommendations for breast and gastric in-situ hybridisation methods. *J Clin Pathol* 2011;**64**(8):649–53.
18. Lacroix-Triki M, Suarez PH, MacKay A, *et al*. Mucinous carcinoma of the breast is genomically distinct from invasive ductal carcinomas of no special type. *J Pathol* 2010;**222**(3):282–98.
19. Paramo JC, Wilson C, Velarde D, *et al*. Pure mucinous carcinoma of the breast: is axillary staging necessary? *Ann Surg Oncol* 2002;**9**(2):161–4.
20. Kaoku S, Konishi E, Fujimoto Y, *et al*. Sonographic and pathologic image analysis of pure mucinous carcinoma of the breast. *Ultrasound Med Biol* 2013;**39**(7):1158–67.
21. Mori M, Tsunoda H, Kawauchi N, *et al*. Elastographic evaluation of mucinous carcinoma of the breast. *Breast Cancer* 2012;**19**(1):60–3.
22. Evans A, Sim YT, Thomson K, *et al*. Shear wave elastography of breast cancer: sensitivity according to histological type in a large cohort. *Breast* 2016;**26**:115–8.
23. Chang JM, Moon WK, Cho N, *et al*. Clinical application of shear wave elastography (SWE) in the diagnosis of benign and malignant breast diseases. *Breast Cancer Res Treat* 2011;**129**(1):89–97.
24. Chang JM, Moon WK, Cho N, *et al*. Breast mass evaluation: factors influencing the quality of US elastography. *Radiology* 2011;**259**(1):59–64.
25. Chamming'S F, Latorre-Ossa H, Le Frere-Belda MA, *et al*. Shear wave elastography of tumour growth in a human breast cancer model with pathological correlation. *Eur Radiol* 2013;**23**(8):2079–86.
26. Didonato R, Shapiro N, Koenigsberg T, *et al*. Invasive mucinous carcinoma of the breast and response patterns after neoadjuvant chemotherapy (NAC). *Histopathology* 2018;**72**(6):965–73.