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Original Article

Sonoelastography of retroareolar carcinomas

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ABSTRACT

Purpose. – To review the sonographic and elastographic features of retroareolar carcinomas.

Materials. – Institutional review board approval was obtained. Among 967 sonographically guided biopsies (2013–2014) (14-gauge cores), 53 yielded the diagnosis of retroareolar carcinoma (located less than 2 cm from the nipple on mammograms). Out of these 53 lesions, 30 were assessed additionally with strain elastography prior to the biopsy in addition to conventional sonographic analysis. Imaging features were analyzed in consensus by two radiologists. Elasticity score was evaluated by the score defined by Itoh (Tsukuba score). Descriptive analysis was performed.

Results. – A total of 30 lesions were included (30 patients; mean age, 66.03 (± 12.88)). The mean size of the lesions at diagnosis was 23.97 mm (± 13.64). Sonographically, most of lesions appeared as hypochoic masses (96.5%, 28/29) displaying an irregular shape (75.9%, 22/29), non parallel orientation (58.6%, 17/29), non circumscribed margins (86.2%, 25/29), posterior attenuation (93.3%, 28/29). Among the 30 lesions, 3.3% (1/30) of lesions appeared as an attenuation and distortion without discrete mass. Most of the lesions were categorized as BI-RADS category 5 (76.7%, 23/30). Approximately half of lesions (53.3%, 16/30) appeared as firm and larger than 2D mode with strain elastography according to the Tsukuba score.

Conclusion. – Retroareolar carcinoma displayed malignant features at US and elastographic examination. In our study population, the addition of elastography to breast US in this location did not improve diagnostic accuracy.

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Introduction

Elastography has become a complimentary technique in breast imaging in addition to conventional US during the last decade. Elastography is now included in the latest edition of the BI-RADS lexicon [1]. Strain elastography with freehand compression was demonstrated as being useful for differentiating breast masses with a sensitivity of 79–98% and a specificity of 72–88% [2,3].

Retroareolar carcinomas are often underdiagnosed on imaging (mammograms and US) due essentially to the geometry of the nipple [4,5]. Masses might be subtle and missed by breast imagers [6]. The objective of this study was to analyze the added value of strain elastography in the categorization of retroareolar carcinomas to the BI-RADS lexicon.

Materials and methods

Patients

This retrospective study was approved by the Institutional Review Board. The goal was to identify all retroareolar breast carcinomas, biopsied under US guidance, for which elastography was performed.

Mammographic protocol

From 2007 to 2012, all film-mammograms were performed using the LORAD MIV mammographic unit (LORAD, Danbury, CT). Standard craniocaudal and mediolateral oblique views were routinely obtained and additional mammographic views were obtained as needed. After 2012, all mammograms were performed using a full-field digital mammography (FFDM) system (Selenia Dimensions, Hologic Inc.).

US technique

In our practice, breast sonography is performed to evaluate specific abnormalities discovered either at clinical examination, on

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mammography or on breast MRI, as part of the initial work-up of patients diagnosed with breast carcinoma, or as an adjunct to screening mammography in women with dense breasts (heterogeneously dense or extremely dense). The entire breast is usually scanned. All the ultrasounds were performed with high-resolution ultrasound scanners using high frequency linear array transducers (High frequency matrix transducer PLT1204AX, Aplio, Toshiba Medical Systems, Calif). B-mode, Doppler and strain elastography were routinely used during US examinations, particularly in order to help in identifying subtle lesions prior to biopsy.

US guided biopsy

The core needle biopsies were performed under sonographic guidance by one of five radiologists with fellowship training ($n = 3$) or extensive experience in breast imaging ($n = 2$) using high-frequency linear-array transducers (CA; high frequency Matrix transducer PLT1204AX, Aplio™, Toshiba Medical Systems, Tustin, CA) and a free-hand technique with the patient in the supine position. An automated gun (Bard Magnum, Bard Urological, Covington, GA) fitted with a standard 14-gauge, 22-mm throw Tru-Cut needle (Core Biopsy Needles 14G, Bard Urological, Covington, GA) was used and a minimum of three cores were obtained from each lesion.

Conventional US analysis

Conventional US images were analyzed by two radiologists in consensus, and classified into appropriate categories according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) to indicate probability of malignancy: BI-RADS Category 3 indicated probably benign; Category 4A/4B/4C, low/moderate/high suspicion for malignancy; Category 5, highly suggestive of malignancy. For areas of abnormal tissues displaying attenuation or distortion without associated masses, they were defined as non-masses [7].

Strain elastography analysis

Elasticity score was evaluated by the Tsukuba score (five-point scale grading the stiffness of a mass) [8–14]. A score from 1 to 5 is assigned based on the color (balance of green and blue) inside the tumor and the surrounding area, with a higher score indicating a higher diagnostic confidence of malignancy. A soft lesion is classified with a score of 1. A lesion with mixed pattern is given a score of 2. A lesion that is hard but smaller on the elastogram is given a score of 3. A hard lesion displaying the same size on elastography than in B-mode, is given a score of 4. A hard lesion larger on elastography is classified as 5.

Post biopsy mammograms

All post biopsy mammograms of these patients were reviewed by a breast radiologist in order to determine the location of the lesion in relation to the nipple. The distance between the clip marker of the biopsied structure and the nipple was measured: a lesion was considered to be retroareolar if the distance between the clip marker of the biopsied lesion and the nipple was 2 cm or less than 2 cm on the mammogram as defined by Gies [4]. If the distance was greater than 2 cm, the case was not included. Out of the 967 diagnosed cancers, 5.5% (53 lesions, 53 patients) were considered as retroareolar location. Cases without elastography were excluded. Finally only 30 cases were performed with strain elastography to perform this retrospective study.

Statistical analysis

Data were entered in a spreadsheet program (Excel, Microsoft). Statistical analyses were performed using SPSS, version 19.0 (SPSS, Chicago, IL, USA). Descriptive analysis was performed. We considered BI-RADS score and Tsukuba scores as qualitative values given they were not either continuous for BIRADS score and Tsukuba score was considered as a categorical variable instead of group.

The Fisher exact test was used to compare independent groups for categorical variables. $P < 0.05$ was considered to indicate a statistically significant difference. Data analysis was conducted with SAS software, version 9.2.

Results

We reviewed 967 diagnosed cases of carcinomas biopsied under US guidance from December 2012 to December 2013.

Clinical data

A total of 30 lesions were included (30 patients; mean age, 66.03 (± 12.88)). Among 30 patients, 96.67% (29/30) had no previous history of breast carcinoma.

53% (16/30) of the masses were palpable and clinically suspicious. Among the 14 asymptomatic masses (47%; 14/30), 13 (92.9%) were detected with mammograms and 1 (7.1%) with ultrasound. Findings are summarized in Table 1.

Pathologic findings

Out of the 30 cases of ultrasound-guided core biopsies, 27 (90%) corresponded to invasive ductal carcinoma at final pathology whereas 3 corresponded to DCIS (10%), one DCIS being associated with IDC. Findings are summarized in Table 1.

Mammographic findings

Mammograms were all available for all patients. Among the 30 lesions, only 1 (3.3%) was not visible on mammogram. When visible (29/30), they presented as a mass in 56.8% (17/30), as masses associated with calcifications in 30% (9/30), as suspicious pleomorphic calcifications in 3.3% (1/30), as a distortion (3.3%, 1/30) and as a focal asymmetry (3.3%, 1/30). Most masses displayed

Table 1
Descriptive statistics on epidemiological and pathologic variables.

| | | |
|---------------------------|-----------|-----------------|
| Epidemiological variables | | |
| Age mean (\pm SD) | 66.03 | (± 12.88) |
| Family history N (%) | | |
| N | 29 | (96.67) |
| Y | 1 | (3.33) |
| Total | 30 | (100.00) |
| History N (%) | | |
| Clinical suspicious mass | 15 | (50) |
| Mammo | 13 | (43.33) |
| Redness | 1 | (3.33) |
| US | 1 | (3.33) |
| Total | 30 | (100.00) |
| Pathologic variables | | |
| BX path N (%) | | |
| DCIS | 1 | (3.33) |
| IDC | 21 | (70) |
| IDC + DCIS | 1 | (3.33) |
| ILS | 1 | (3.33) |
| IMC | 6 | (20) |
| Total | 30 | (100.00) |

Table 2
Conventional US features of the 29 retroareolar masses.

| Biopsy variables | | |
|--------------------------|-------|----------|
| Mammo N (%) | | |
| Asymmetric density | 1 | (3.45) |
| Calcs | 1 | (3.45) |
| Distorsion | 1 | (3.45) |
| Mass | 16 | (55.17) |
| Mass+ calcs | 9 | (31.03) |
| No | 1 | (3.45) |
| Total | 29 | (100.00) |
| Echographic variables | | |
| Size mean (±SD) | 23.97 | (±13.64) |
| US N (%) | | |
| Mass | 29 | (96.67) |
| Non mass | 1 | (3.33) |
| Total | 30 | (100.00) |
| SHAPE N (%) | | |
| Irregular | 22 | (75.86) |
| Oval | 6 | (20.69) |
| Round | 1 | (3.45) |
| Total | 29 | (100.00) |
| Orientation N (%) | | |
| Non parallel | 17 | (58.62) |
| Parallel | 12 | (41.38) |
| Total | 29 | (100.00) |
| Margins N (%) | | |
| Circumscribed | 4 | (13.79) |
| Not circumscribed | 25 | (86.21) |
| Total | 29 | (100.00) |
| Posterior features N (%) | | |
| Attenuation | 28 | (93.33) |
| Enhancement | 1 | (3.33) |
| None | 1 | (3.33) |
| Total | 30 | (100.00) |
| Cals N (%) | | |
| In the non mas | 1 | (3.33) |
| In a mass | 7 | (23.33) |
| No | 22 | (73.33) |
| Total | 30 | (100.00) |
| BI-RADS N (%) | | |
| BIRADS=4b | 3 | (10) |
| BIRADS=4c | 4 | (13.33) |
| BIRADS=5 | 23 | (76.67) |
| Total | 30 | (100.00) |

an irregular shape (80%, 20/25) with non-circumscribed margins (92%, 23/25). Findings are detailed in Table 2.

Breast sonography indication

Breast sonography was performed to evaluate specific abnormalities found initially identified on physical examination (53.4%, 16/30), mammogram (43.3%, 13/30). One lesion (3.3%; 1/30) was incidentally detected on ultrasound, as part of screening breast ultrasound.

Sonographic findings

Among the 30 retroareolar lesions identified sonographically visualized and biopsied under US guidance, 96.7%, appeared as a mass (29/30) and one a non-mass (3.3%, 1/30). The mean size of the

Table 3
Descriptive statistics on Elastography variables.

| TSUKUBA N (%) | | |
|----------------|-------|----------|
| TSUKUBA=1 | 1 | (3.3) |
| TSUKUBA=2 | 7 | (23.4) |
| TSUKUBA=3 | 2 | (6.7) |
| TSUKUBA=4 | 4 | (13.3) |
| TSUKUBA=5 | 16 | (53.3) |
| Total | 30 | (100.00) |
| FLR mean (±SD) | 14.43 | (±11.05) |

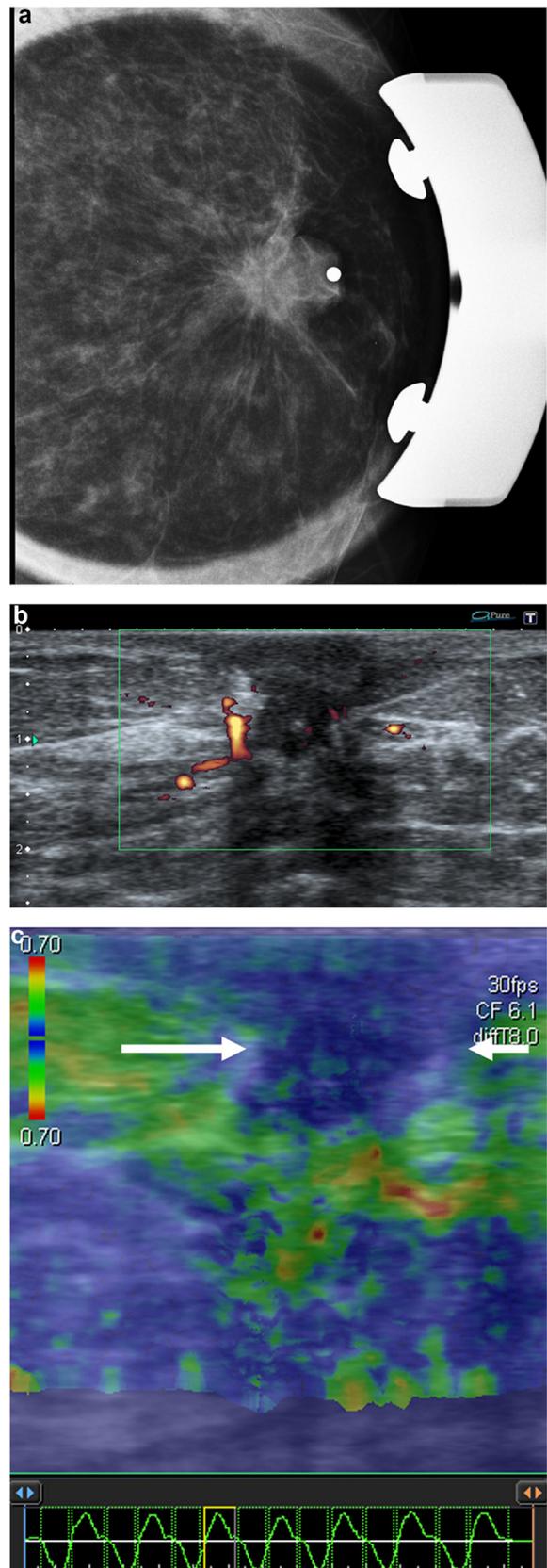


Figure 1. 61 year old patient presenting with a suspicious spiculated dense retroareolar mass associated to nipple retraction (a). It corresponds on ultrasound (b) to a non parallel hypoechoic hypervascular mass. Strain elastography shows no strain appearing either in the hypoechoic area or in surrounding areas (the lesion and surrounding areas are shown in blue corresponding to a Tsukuba elasticity score 5) (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

lesions at diagnosis was 23.97 mm (± 13.64). Sonographic features of the 29 masses are summarized in Table 2. Sonographically, most of lesions appeared as hypoechoic masses (96.5%, 28/29) displaying an irregular shape (75.9%, 22/29), non parallel orientation (58.6%, 17/29), non circumscribed margins (86.2%, 25/29), posterior attenuation (93.3%, 28/29). Among the 30 lesions, 3.3% (1/30) of lesions appeared as an attenuation and distortion without discrete mass (non-mass lesion). Color power Doppler interrogation was performed in 93.3% (28/30) of cases. A positive signal was seen in 89.3% cases (25/28). Calcifications were seen in the mass in 27.6%, (8/29). According to the

final BI-RADS assessment, most of the lesions were categorized as BI-RADS category 5 (76.7%, 23/30).

Elastography findings

Elastographic features of the 30 lesions are described in Table 3. Half of lesions appeared as firm and larger than 2D mode (53.3% 16/30) with a score of 5 (Fig. 1). However 26.7% of lesions showed Tsukuba scores 1 and 2 in favor of soft and benign lesions (8 false negative cases) (Figs. 2 and 3).

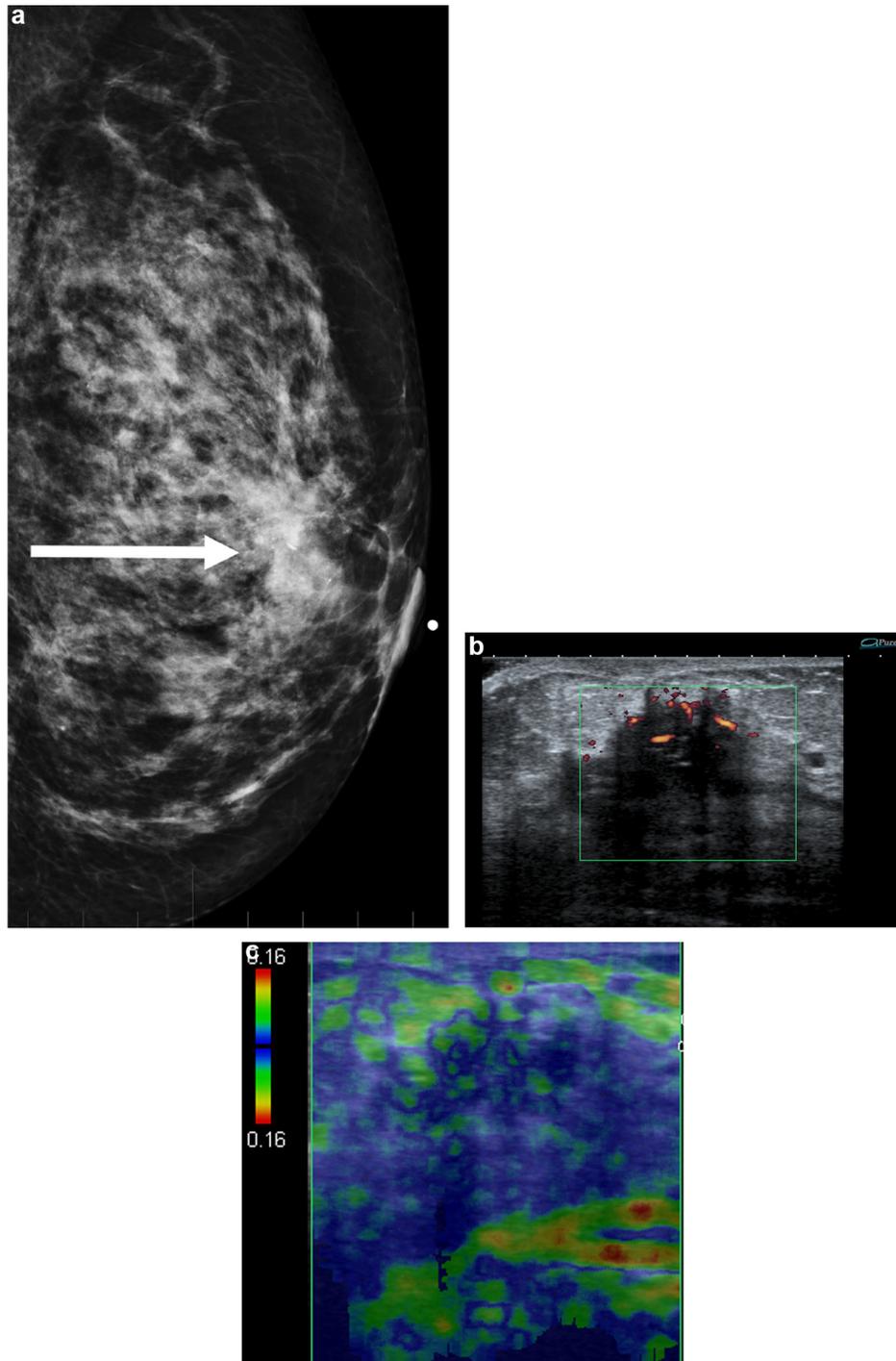


Figure 2. 45 year old patient presenting a suspicious lump in the retroareolar region of the left breast. Mammogram (a) shows a retroareolar irregular mass associated some calcifications. Ultrasound shows a non parallel hypoechoic mass associated to some calcifications. Strain (c) appears only in the peripheral areas and not in the center of the hypoechoic area (the center of the lesion is shown in blue while the peripheral areas in green). The Tsukuba score is 3 (For interpretation of the references to color in text/this figure legend, the reader is referred to the web version of the article.).

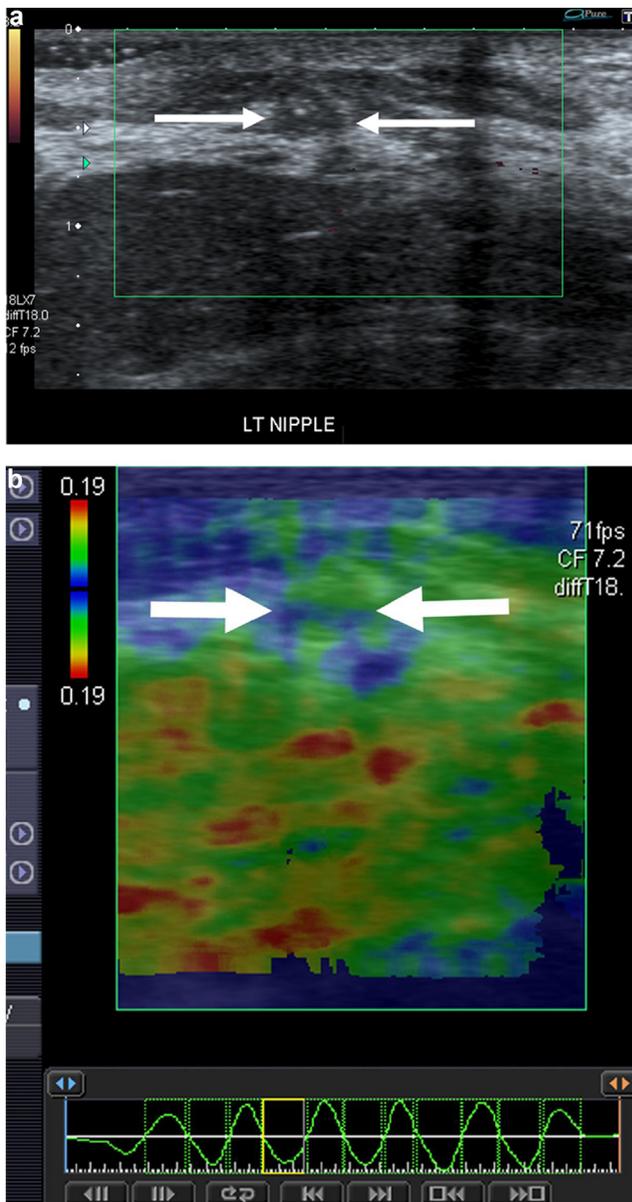


Figure 3. 70 year patient presenting with suspicious microlobulated retroareolar mass. Clinical examination and mammograms were normal. US (a) shows a microlobulated mass with posterior reinforcement. It is avascular on Doppler imaging. Strain (b) is not seen in part of the hypoechoic area (the lesion is shown as a mosaic of green and blue) corresponding to a Tsukuba score 2 (For interpretation of the references to color in text/this figure legend, the reader is referred to the web version of the article.).

Hypothetical effect of strain elastography on BI-RADS Assessment

BI-RADS score and elastographic score were linked to assess if strain elastography would increase the detection of retroareolar carcinomas in addition to the BI-RADS assessment. We linked

BI-RADS score with Tsukuba score to determine if this would aid the radiologist to find out a malignancy in addition to B mode and Doppler findings. Findings are evaluated in Table 4. According to the Fisher exact test, strain elastography doesn't increase the benefit to the BI-RADS lexicon.

Discussion

Retroareolar carcinomas are often missed on breast ultrasound [15]. Contributing factors leading to missing retroareolar carcinomas on ultrasound are often explained by the geometry of the nipple [4]. A perfect positioning of the probe is difficult and consequently scanning the retroareolar area is technically more difficult to scan than other areas. Understanding of the nipple-areolar complex anatomy and physiology is important to avoid misinterpretation and misdiagnosis. The ability of breast imager to manage difficulties related to the retroareolar area is paramount by adjusting settings (Compounding, Tissue Harmonic Imaging, frequency, Doppler) or some specific manoeuvres described by Stavros [16,17]. Familiarity with the typical normal and abnormal ultrasound imaging appearance for radiologist or technologist is crucial to differentiate abnormal subtle findings from normal features.

Retroareolar carcinomas are rare tumors accounting for less than 10% of locations [18]. They often present with large palpable masses diagnosed on clinical examination concordant with our data [6]. The larger average size of retroareolar carcinomas had been already demonstrated because they are often missed on breast imaging [6]. A majority of the retroareolar tumors we reviewed presented with pejorative features on mammograms and ultrasound. Consequently their BI-RADS score was high and was concordant with the expected pathology [1].

Strain elastography is a new method of ultrasound imaging providing tissue deformability information relying on stress applied. Diagnostic performance of Shear Wave Color Patterns had been demonstrated useful in breast lesions. However some studies have demonstrated interobserver variability occurring data acquisition and interpretation [19]. Technical errors, particularly probe compression can lead to inaccurate results. To the best of our knowledge, this is the first publication about retroareolar carcinomas and strain elastography to our knowledge.

Consequently, considering that the retroareolar area is more difficult to scan than other areas, we evaluated role of strain elastography on retroareolar suspicious masses and compared to the BIRADS lexicon. Interestingly, we noted that strain elastography wasn't helpful for radiologists in diagnosing retro areolar breast carcinoma in complementary to the BI-RADS mammography and echo graphic features. The majority of retroareolar breast carcinomas were appropriately classified using the BIRADS lexicon, whereas, eight of these lesions were undercategorized with elastography.

A possible explanation is the difficulties encountered in performing a strain elastography in case of retroareolar lesions. The triangular shape of the nipple doesn't facilitate the performance of strain elastography. Even with a correct placement of the

Table 4
Link between BI-RADS and Tsukuba scores.

| Variable | BIRADS = 4b | BIRADS = 4c | BIRADS = 5 | Test | P value |
|---------------|-------------|-------------|------------|---------------|-----------------|
| TSUKUBA N (%) | | | | F. Exact test | P value = 0.018 |
| TSUKUBA = 1 | 1 (33.4) | 0 (0) | 0 (0) | | |
| TSUKUBA = 2 | 1 (33.3) | 3 (75) | 3 (13.0) | | |
| TSUKUBA = 3 | 0 (0) | 0 (0) | 2 (8.7) | | |
| TSUKUBA = 4 | 1 (33.3) | 0 (0) | 3 (13.0) | | |
| TSUKUBA = 5 | 0 (0) | 1 (25) | 15 (65.3) | | |

probe with a sufficient amount of gel, strain elastography is probably technically limited in this specific location.

This study had several limitations. First, selection bias may exist because it is a retrospective study. Second, large masses were not excluded in our study, when there was discrepancy between lesion size and elastography. If correlation exists, the exclusion of large masses may cause selection bias to study cohort. Third, benign retroareolar lesions have not been included. Fourth, the definition of retroareolar lesions is unclear to our knowledge. This is why we defined a retroareolar lesion on the post biopsy mammogram if it was located less than two centimeters from the nipple.

Retroareolar carcinoma display malignant features at US and elastographic examination. Although doable in this location, the addition of elastography to breast US is limited. Further prospective studies of large sample size including benign retroareolar masses would be needed for validation of our results.

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