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THE ROLE OF IMAGING IN SCREENING SPECIAL FEATURE: FULL PAPER

Retroareolar masses and intraductal abnormalities detected on screening ultrasound: can biopsy be avoided?

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To investigate the malignancy rate of retroareolar masses and intraductal abnormalities discovered in asymptomatic females during screening whole breast ultrasound (US-S) and determine if biopsy can be avoided.

Methods: This is a HIPAA compliant retrospective study. Our radiology electronic medical records were searched for the phrases “retroareolar mass” or “intraductal mass” combined with “screening whole breast ultrasound” performed between 10/1/2009 and 5/30/2015. Inclusion criteria included retroareolar masses in asymptomatic females with normal mammography, mammographically dense breast tissue and imaging or biopsy follow-up.

Results: 1136 charts were reviewed. 87 BI-RADS 3 and 4 retroareolar findings were included in final analysis. The average lesion size was 9.5 mm (range 4–28 mm). 47/87 lesions were classified as BI-RADS 3 and 40/87

BI-RADS 4. Of the 47 BI-RADS 3 lesions, 36 were stable on follow-up; 6 benign lesions were biopsied at patients’ request; and 5 biopsied due to suspicious interval change on follow-up imaging, including 4 benign lesions and a 5 mm Grade 2 ductal carcinoma *in situ*. 3/40 BI-RADS 4 lesions were not biopsied and stable at follow-up; 37/40 lesions underwent benign biopsy. The malignancy rate of BI-RADS 3 and 4 lesions was 2.1% [CI (0.4–11.1)] and 0% [CI (0.0–8.8)], respectively. The overall combined malignancy rate was 1/87 [1.1%, CI (0.2–6.2)].

Conclusion: The malignancy rate for BI-RADS 3 and 4 retroareolar masses and intraductal abnormalities detected on US-S is low (<2%).

Advances in knowledge: Careful imaging surveillance in lieu of biopsy of these lesions may be appropriate in asymptomatic females with negative mammography.

INTRODUCTION

Approximately 40–50% of all females in the United States have dense breast tissue on mammography,^{1,2} which is known to decrease the sensitivity of mammography and increase breast cancer risk.³ Females with dense breast tissue also tend to have higher interval cancer rates,⁴ as well as worse prognosis for subsequent clinically detected cancers.^{5,6} The first breast density notification law went into effect in 2009 and, as of this writing, 30 states have breast density inform laws.⁷ The goal of breast density legislation is to notify females women about breast density based on mammography and to raise awareness of the effect of breast density on mammographic accuracy.

As a result of breast density awareness, patients may seek supplemental screening, including ultrasound. The benefits of screening whole breast ultrasound (US-S) include easy access and wide availability, relatively low cost, no

ionizing radiation and no intravenous contrast requirement. Previous studies have shown that the supplemental cancer detection rate of US-S is 2.7–4.6 per 1000 females screened, with greater than 90% of cancers being invasive, less than 1 cm and low grade.^{8–11} However, compared to mammography, the specificity and the positive predictive value (PPV) of US-S may be low, with a reported PPV for biopsies (PPV3) performed of 10% or less.^{9,10,12,13} False positive US-S findings result in increased patient anxiety and increased healthcare costs due to additional follow-up testing and/or biopsies for lesions that are ultimately proven to be benign.

Standard US-S scanning protocol includes full evaluation of the entire breasts with documentation of all four quadrants and the retroareolar regions bilaterally, plus optional documentation of the axilla.^{9,14} Ultrasound evaluation of the retroareolar region can be complex as there are frequently

mildly dilated benign ducts, often containing internal debris and associated with artifact related to the nipple areolar complex. Artifact can be reduced and often avoided by scanning around the areola and angling the ultrasound transducer to scan the area immediately below the nipple.¹⁵ Proper scanning of the retroareolar region during US-S may result in the incidental discovery of asymptomatic retroareolar masses (non-intraductal) and intraductal abnormalities, which may represent a variety of benign entities, including fibroadenomas, fibrocystic changes (FCCs), intraductal debris, benign papillomas, as well as malignant invasive or *in situ* ductal carcinoma.¹⁶

Prior to the increased utilization of US-S, retroareolar masses and intraductal abnormalities were typically encountered on ultrasound during the diagnostic imaging workup of symptomatic females with a new mammographic finding or worrisome nipple discharge, often requiring tissue sampling performed with ultrasound-guided core needle biopsy (CNB). A diagnosis of a papillary lesion with or without associated atypia on CNB frequently requires surgical excision and histopathological confirmation because these are typically considered high-risk lesions, which may be upgraded to ductal carcinoma *in situ* (DCIS) or invasive carcinoma, with reported malignant upgrade rates > 2%.^{17,18}

The BI-RADS 5th edition states that most intraductal masses discovered in women with bloody nipple discharge require biopsy.¹⁴ However, little data and guidance are available regarding optimal management of retroareolar abnormalities detected on US-S. The purpose of this study was to investigate the malignancy rate of retroareolar masses (non-intraductal) and intraductal abnormalities detected on US-S in asymptomatic women with negative screening mammography and determine if biopsy can be avoided.

METHODS AND MATERIALS

This retrospective study was approved by our institutional review board and was Health Insurance Portability and Accountability Act-compliant. Informed consent was waived.

Patient selection

The breastimaging electronic medical record was searched for “screening whole breast ultrasound” or “bilateral screening breast ultrasound” to determine the total number of US-S examinations performed at our institution between October 1, 2009 and May 30, 2015. Similarly, the EMR was also searched for the phrases “retroareolar mass” or “intraductal mass” reported in US-S examinations performed during this time. The inclusion criteria included US-S performed in asymptomatic females with dense breast tissue and normal mammography; retroareolar masses or retroareolar intraductal lesions located within 2 cm of the nipple areolar complex discovered only on US-S,¹⁹ and available reference standard, either histopathology findings or follow-up mammography and/or ultrasound to establish stability. Breast density determination was assessed visually by the radiologist at the time of the most recent mammography interpretation, using BI-RADS criteria.²⁰

Patient age and breast cancer risk were recorded in our database. The patient's breast cancer risk was assessed following the National Cancer Institute guidelines²¹ at the time of examination by the mammography or ultrasound technologist, and was manually entered into our mammography reporting system (Penrad Technologies, Minnetonka, MN) as described previously.¹⁰ Risk was defined as unknown, none or weak, intermediate (postmenopausal mother or sister with breast cancer) and high (premenopausal mother or sister, multiple premenopausal first-degree relatives with breast cancer, or BRCA positive). Remote personal history of breast cancer (*i.e.* breast cancer diagnosis and treatment >1 year prior to US-S date) was considered to be of intermediate risk. Overall, patients with elevated cancer risk were defined as patients with intermediate or high risk.

Screening whole breast ultrasound

An experienced mammography technologist trained in breast ultrasound or a dedicated ultrasound technologist performed each US-S and a subspecialist breastimaging radiologist was available to scan any lesion in realtime at their discretion. All scans were obtained with an ultrasound unit (IU22; Philips, Bothell Wash) and a handheld high-resolution linear-array broadband transducer with a frequency of 12.5–17.5 MHz. Standardized scanning protocol was utilized.^{9,14} Bilateral breasts were scanned in multiple planes, including the radial and anti-radial planes, extending from the nipple to the posterior breast tissue. Images were documented in all four quadrants and the retroareolar region, and sometimes the axilla. Each lesion was evaluated using greyscale plus colour Doppler imaging and documented with three-dimensional measurements. All scans were immediately reviewed and reported by one of eight dedicated breast radiologists with 2–32 years of experience in breast imaging, who also had access to the patients' screening mammogram images and results.

Each US-S report and associated images were retrospectively reviewed. The date of US-S, the frequency of multiple bilateral masses (defined as a minimum of three masses with at least one mass in each breast), number of retroareolar lesions in each patient, BI-RADS category for each lesion and the lesion size (maximal dimension) were recorded. Subsequently, prospective consensus review of recorded US-S images of each lesion was also performed. Each lesion was classified as either an intraductal abnormality or retroareolar mass, depending on the visual assessment of the presence or absence of lactiferous duct involvement. Imaging features were also reviewed and recorded (Table 1), including shape (oval, irregular and round), margin (circumscribed, microlobulated, angular, indistinct and spiculated), orientation (parallel and non-parallel), echogenicity (hypoechoic, heterogeneous, anechoic, hyperechoic, isoechoic and complex), vascularity (internal, rim and absent), posterior acoustic features (none, enhancement, shadowing and combined), duct (partial fill, complete fill and beyond the duct) and frequency of multiple bilateral masses. All imaging data were reviewed and collected together by both a resident in radiology with 1 year of radiology training (YG) and a fellowship trained breast radiologist with 20 years of experience (RJH) with knowledge of the original radiology report.

Table 1. Ultrasound features of BI-RADS 3 and BI-RADS 4 findings

		BI-RADS 3		BI-RADS 4		<i>p</i> value
		Intraductal lesions (1)	Retroareolar masses (2)	Intraductal lesions (3)	Retroareolar masses (4)	
		<i>N</i> = 13 (%)	<i>N</i> = 34 (%)	<i>N</i> = 21 (%)	<i>N</i> = 19 (%)	
Shape	Oval	11 (84.6)	31 (91.2)	19 (90.4)	12 (63.2)	≥0.15
	Irregular	1 (7.7)	1 (2.9)	1 (4.8)	5 (26.3)	≥0.11
	Round	1 (7.7)	2 (5.9)	1 (4.8)	2 (10.5)	=1.0
Margin	Circumscribed	12 (92.3)	32 (94.1)	18 (85.7)	10 (52.6)	(2) vs (4), 0.004 ^{a,b}
	Micro-lobulated	0 (0)	1 (2.9)	3 (14.3)	1 (5.3)	>0.9
	Angular	0 (0)	0 (0)	0 (0)	1 (5.3)	=1.0
	Indistinct	1 (7.7)	1 (2.9)	0 (0)	7 (36.8)	(2) vs (4), 0.01 ^{a, b} (3) vs (4), 0.01 ^{a, b}
	Spiculated	0 (0)	0 (0)	0 (0)	0 (0)	All 1.0
Orientation	Parallel	13 (100)	31 (91.2)	21 (100)	15 (78.9)	≥0.25
	Non-parallel	0 (0)	3 (8.8)	0 (0)	4 (21.1)	≥0.25
Echogenicity	Hypoechoic	6 (46.1)	15 (44.1)	4 (19.0)	12 (63.2)	≥0.053
	Heterogeneous	0 (0)	0 (0)	0 (0)	0 (0)	=1.0
	Anechoic	0 (0)	3 (8.8)	0 (0)	0 (0)	=1.0
	Hyperechoic	0 (0)	0 (0)	4 (19.0)	0 (0)	≥0.11
	Isoechoic	5 (38.5)	10 (29.4)	13 (61.9)	4 (21.0)	≥0.07
	Complex	2 (15.4)	6 (17.6)	0 (0)	3 (15.8)	≥0.43
Vascularity	Internal	1 (7.7)	3 (8.8)	6 (28.6)	1 (5.3)	≥0.42
	Rim	0 (0)	1 (2.9)	0 (0)	0 (0)	=1.0
	Absent	12 (92.3)	30 (88.2)	15 (71.4)	18 (94.7)	≥0.57
Posterior acoustic features	None	7 (53.8)	19 (55.9)	16 (76.2)	13 (68.4)	>0.95
	Enhancement	6 (46.2)	14 (41.2)	5 (23.8)	3 (15.8)	≥0.43
	Shadowing	0 (0)	0 (0)	0 (0)	3 (15.8)	≥0.25
	Combined	0 (0)	1 (2.9)	0 (0)	0 (0)	=1.0
Duct	Partial fill	7 (53.8)	n/a	11 (52.4)	n/a	=1.0
	Complete fill	6 (46.2)	n/a	10 (47.6)	n/a	=1.0
	Beyond the duct	0 (0)	n/a	0 (0)	n/a	=1.0
Frequency of multiple bilateral masses		4 (30.8)	16 (47.1)	4 (19.0)	11 (57.9)	≥0.13

^aStatistically significant.^bAdditional *p* values across subgroups were not significant, *p* > 0.05.

Reference standard

The reference standard was either follow-up imaging or histopathology results of biopsy, if performed. Imaging documented stability was established using subsequent follow-up ultrasound and/or mammography. The interval follow-up imaging report was reviewed and the final assessment was recorded for 2 years after the initial US-S examination.

Tissue sampling was achieved by ultrasound-guided CNB (ultrasound-CNB) and/or surgical excisional biopsy. For ultrasound-CNB, a 14-gauge automated core biopsy (Achieve, Cardinal Health, Dublin, OH; or Monopty, Bard, Tempe, AZ) or a 12-gauge

vacuum-assisted core needle biopsy (Celero, Hologic, Bedford, MA) was utilized. Vacuum-assisted biopsy was preferred for intraductal lesions. The pathology report was reviewed and the final diagnosis recorded. The concordance of US-S and biopsy was assessed at the time of the biopsy by the performing breast radiologist and confirmed by an experienced fellowship trained breast radiologist (RJH) during both retrospective review of the radiology report (which included the pathology results) and US-S images.

Statistical analysis

Each lesion was assigned to a group based on the final BI-RADS assessment as stated in the US-S report and subsequently each

Figure 1. Study flow chart.

group was assigned into either intraductal or retroareolar subgroups (subgroup 1: BI-RADS 3 intraductal lesions; subgroup 2: BI-RADS 3 retroareolar masses; subgroup 3: BI-RADS 4 intraductal lesions; and subgroup 4: BI-RADS 4 retroareolar masses). Average patient age, percentage of females at elevated risk, average and mean lesion size, percentage of intraductal abnormalities and retroareolar masses, plus malignancy rate for each group were calculated and compared using standard statistical tests (SPSS, v. 23, Chicago, IL). Confidence intervals (CIs) proportions were computed with the method of Wilson²² using the implementation in R (The R Foundation for Statistical Computing, www.r-project.org, The ultrasound features among four subgroups were compared using a pairwise Fisher test in R. The test was considered statistically significant with a *p* value of less than 0.05.

RESULTS

Study population

1136 patient charts were reviewed and 1020 were excluded including: 184 duplications (*e.g.* the same lesion imaged multiple times during the study period); 487 with *no* retroareolar mass or intraductal abnormalities; 349 with lesions identified on bilateral diagnostic/targeted ultrasound. The initial study population included 116 retroareolar masses or intraductal abnormalities in 107 females, including 27 BI-RADS 2, 48 BI-RADS 3 and 41 BI-RADS 4 findings (Figure 1). There were no BI-RADS 5 lesions. A total of 9116 US-S examinations were performed at our institution during the study period. Thus, the overall incidence of retroareolar masses and intraductal lesions detected on US-S was 1.3% (116/9116) and the incidence of these lesions requiring short interval follow-up or biopsy was 1.0% (89/9116).

After excluding the 27 lesions assessed as BI-RADS 2 (including 20 simple cysts, 4 duct ectasia, 2 proven fibroadenomas and 1 lymph node) and additional 2 lesions found in 2 patients lost to follow-up (1 patient with BI-RADS 3 lesion also diagnosed with

Figure 2. Study population and management based on US-S assessment.

ovarian cancer and 1 patient with BI-RADS 4 lesion also diagnosed with multiple myeloma), a total of 87 BI-RADS 3 probably benign or BI-RADS 4 suspicious retroareolar lesions in 78 patients were included in our final analysis. The average patient age was 53 years (range 36–81 years) and the average and median lesion size were 9.5 and 8 mm, respectively (range 4–28 mm). Of the 87 included lesions, 47 (54%) were classified as BI-RADS 3 lesions and 40 (46%) were BI-RADS 4 lesions on initial US-S examination; management of these lesions is shown in Figure 2.

BI-RADS 3

Of the 47 BI-RADS 3 findings, 13 were intraductal (27.7%) and 34 were solid-appearing retroareolar masses (72.3%). Representative intraductal and retroareolar mass lesions are shown in Figure 3. The average patient age was 52.8 ± 11.2 and 5 lesions (10.6%) were found in women at elevated breast cancer risk. The average lesion size was 1.02 ± 0.47 cm, 5 lesions (10.6%) demonstrated internal vascularity on initial US-S. 20/47 (42.5%) of the lesions were associated with multiple bilateral masses on US-S and no malignancy was detected in these lesions.

36 lesions (76.6%) were not biopsied and were stable on follow-up imaging. 6 BI-RADS 3 lesions (12.8%) underwent biopsies all at the patients' request: one intraductal abnormality which was a sclerotic papilloma *vs* fibroadenoma on pathology (stable for 2 years on follow-up ultrasound); and five retroareolar masses four of which were FCCs on pathology and one complicated cyst which was aspirated and fluid discarded.

Five ultrasound-CNBs (10.6%) were performed on BI-RADS 3 findings which were reclassified as BI-RADS 4 because of suspicious interval change at 6-month follow-up imaging, including three intraductal abnormalities and two retroareolar masses (Table 2). Documented interval changes on ultrasound included increase in size or changes in internal vascularity. Two were proven FCCs on ultrasound-CNB pathology and both lesions subsequently demonstrated imaging stability for over 1 year. The remaining three lesions were found to be atypical ductal hyperplasia (ADH, *n* = 1), radial sclerosing lesion with low risk ductal intraepithelial neoplasia 1 (DIN, *n* = 1) and DCIS (*n* = 1) on US-CNB histopathology; all three

Figure 3. BI-RADS 3 US-S detected retroareolar masses in two separate asymptomatic patients with negative mammography. (a) Intraductal 5.0 mm mass in a 50-year-old female demonstrates an isoechoic avascular mass within a duct, BI-RADS 3. (b) Oval retroareolar, circumscribed mixed echogenic mass without an associated dilated duct (arrow) in a 48-year-old female, BI-RADS 3. Both masses were stable on follow-up ultrasound.

lesions underwent subsequent surgical excision and no upgrades were found. The single case of DCIS was a solitary 5 mm in size, Grade 2, papillary subtype diagnosed in a 67-year-old female with intermediate breast cancer risk. The US-S and follow-up images are shown in Figure 4. The malignancy rate for BI-RADS 3 findings was 2.1% [CI (0.4–11.1)].

BI-RADS 4

Of the 40 BI-RADS 4 abnormalities, 21 were intraductal abnormalities (52.5%) and 19 were solid retroareolar masses (47.5%). Representative images for intraductal and mass lesions are shown in Figure 5. The average patient age was 53.7 ± 11.1 and 4 lesions (10%) were found in females at elevated breast cancer risk. The average lesion size was 0.86 ± 0.43 cm, 6 lesions (15%) demonstrated internal vascularity on initial US-S. 15/40 (37.5%) of lesions were associated with multiple bilateral masses on US-S and no malignancy was found in these lesions.

3 intraductal abnormalities (7.5%) were not biopsied for the following reasons: one patient underwent breast MRI in lieu of ultrasound-CNB biopsy and MRI did not reveal the retroareolar lesion as seen on US-S; one lesion could not be identified at the time of ultrasound-CNB and was reclassified as BI-RADS 2; the third lesion was identified but thought to be stable on prior ultrasound imaging for over 2 years at the time of the biopsy and thus biopsy was cancelled. All three findings were stable on subsequent follow-up ultrasound performed at 12 and 24 months.

37/40 (92.5%) BI-RADS 4 findings were biopsied and all benign on pathology as shown in Table 3. One patient proceeded directly to surgery without ultrasound-CNB for an intraductal

abnormality, which was a fibroadenoma on pathology. 36 lesions including 19 retroareolar masses and 17 intraductal abnormalities underwent US-CNB. Of these 36 lesions, 10 lesions were fibroadenomata, 13 were FCCs and all were stable on follow-up. The remaining 13 lesions required surgical excision including 12 cases with high-risk pathology on ultrasound-CNB and one case of FCCs that was discordant with imaging findings. High-risk lesions on ultrasound-CNB histopathology were papillary lesions without atypia ($n = 9$), papillary lesion with atypia ($n = 1$), ADH ($n = 1$) and mixed papillary and ADH lesion ($n = 1$). There were no histopathological upgrades and all 13 excised lesions were proven to be benign with the following findings on surgical pathology: papilloma with atypia ($n = 1$), papillary lesion without atypia ($n = 8$), mixed papillary and ADH lesions ($n = 3$) and fibroadenoma ($n = 1$). The malignancy rate for BI-RADS 4 lesions was 0% [CI (0.0–8.8)].

Sonographic features

There was no significant difference between BI-RADS 3 and 4 lesions in regards to size, patient demographics or the presence of multiple bilateral masses. However, intraductal findings were more likely to be assessed as BI-RADS 4 as shown in Table 4. Overall, compared to BI-RADS 3 retroareolar masses, BI-RADS 4 masses were significantly more likely to have indistinct margins and less likely to be circumscribed. The sonographic features of all lesions included in this study are reported in Table 1.

The majority of BI-RADS 4 intraductal masses were oval (19/21, 90.4%), circumscribed (18/21, 85.7%), demonstrated a parallel orientation (21/21, 100%) and were avascular (15/21, 71.4%), with no or enhanced posterior acoustic features (21/21, 100%), although these features were not significantly different compared

Table 2. BI-RADS 3 findings reclassified as BI-RADS 4 on follow-up

Lesions	Type	Interval Change (3–6 months)	Core needle biopsy	Surgical resection
No.1	Intraductal	Increase in size	Benign FCC	NA
No.2	Intraductal	New indistinct margin	Benign FCC	NA
No.3	Intraductal	Increase in size	Radical sclerosing lesion	Radical sclerosing lesion
No.4	Mass	Increase in size	ADH	ADH
No.5	Mass	New Vascularity	DCIS	DCIS, 5 mm, Grade 2

ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma *in situ*; FCC, fibrocystic change.

Figure 4. Initial US-S image (a) and 6-month follow-up image (b and c) for the BI-RADS 3 retroareolar mass in a 67-year-old patient, which was proven to be a 5 mm, Grade 2 DCIS. Although the mass did not change significantly in size, internal vascularity was noted at the 6-month follow-up examination. Because this was a new finding and represented a change, this lesion was assessed as BI-RADS 4.

to intraductal masses assessed as BI-RADS 3. No BI-RADS 3 or 4 intraductal mass demonstrated growth beyond the duct.

The majority of BI-RADS 4 retroareolar masses were oval (12/19, 63.2%), circumscribed (10/19, 52.6%), demonstrated a parallel orientation (15/19, 78.9%), hypoechoic (12/19, 63.2%), avascular (18/19, 94.7%) and with no or enhanced posterior acoustic features (16/19, 84.2%). 24/40 (60%) of BI-RADS 4 lesions including 17 intraductal lesions and 7 retroareolar masses not associated with a dilated duct demonstrated all the combination of benign ultrasound features. 7/24 of these benign-appearing lesions were associated with multiple bilateral masses.

DISCUSSION

Our study demonstrates that the overall incidence of retroareolar masses and intraductal lesions detected on US-S is very low at 1.3%. The incidence of retroareolar lesions categorized as BI-RADS 3 or 4 requiring short interval follow-up or biopsy respectively was also infrequent at 1%. Although masses assessed as BI-RADS 4 were significantly more likely to be irregularly shaped and not exhibit circumscribed margins, the ultrasound features across BI-RADS 3 and 4 intraductal lesions were not significantly different. This suggests that better management guidelines regarding these infrequent findings are needed for radiologists interpreting US-S examinations.

Figure 5. BI-RADS 4 US-S detected retroareolar masses in two separate asymptomatic patients with negative mammography. (a) Isoechoic intraductal retroareolar mass in a 49-year-old female. Because there was internal vascularity (arrows), this lesion was assessed as BI-RADS 4. Ultrasound-guided CNB revealed a benign papilloma without atypia. Surgical excision was performed and showed a sclerosing papillary lesion with atypical intraductal hyperplasia. (b) Oval hypoechoic retroareolar mass in a 41-year-old female. This lesion was assessed as BI-RADS 4 and ultrasound-guided CNB showed benign fibroadenoma. CNB.

Both retroareolar solid masses and intraductal abnormalities are uncommon findings seen on ultrasound, but are better characterized with the use of high frequency linear ultrasound transducers due to improved spatial resolution and image quality.²³ Management of intraductal lesions found on ultrasound can be challenging. Typically, these lesions are found in patients presenting with bloody, clear, or serosanguinous unilateral spontaneous nipple discharge or a new retroareolar mass, dilated duct, or asymmetry initially seen on routine mammography. High resolution ultrasound is the imaging modality of choice in females with a normal mammogram and worrisome spontaneous, bloody or clear unilateral nipple discharge.²⁴ MRI and ductography may be also used to identify intraductal masses in these symptomatic females if ultrasound is normal. Lesions detected on diagnostic workup may represent benign papillomas, ductal carcinoma *in situ* or invasive ductal carcinoma and, therefore, biopsy is often advised. If a papilloma is diagnosed at CNB, many institutions follow a protocol proceeding to surgical excision because a minority of such lesions will be associated with malignancy.¹⁶ Even if the diagnosis of a benign papilloma without atypia is made with ultrasound-guided core needle biopsy, surgical consultation is often advised and excision may be performed as these are considered high risk lesions, with a malignant upgrade rate in two recent studies of approximately 3–5%.^{25,26}

In a prior study of 163 intraductal masses identified on ultrasound, the overall malignancy rate was 8%, with asymptomatic lesions demonstrating a malignancy rate of 4.2%.²³ Although this study did not specifically investigate lesions detected only on US-S, two cancers were found within a subset of 70 intraductal masses among asymptomatic females with negative mammography, resulting in an overall malignancy rate of 2.8%; both cancers were low grade DCIS. The authors concluded that malignant intraductal masses are more often associated with symptoms, a personal history of breast cancer, large size (>1 cm) and masses completely filling the duct or extending beyond the duct.²³ Our study shows similar findings as no malignancies were found among 34 intraductal lesions discovered on US-S in asymptomatic females with a negative mammogram, an average size of 7.9 mm and none extending beyond the duct.

Ultrasound BI-RADS criteria are based on lesions initially detected on diagnostic targeted ultrasound, typically performed

Table 3. BI-RADS 4 lesions histopathology

Initial biopsy method	Ultrasound-CNB pathology	Ultrasound-CNB ^a (n = 36)	Surgery ^a (n = 14)	Surgical pathology
Ultrasound-CNB (n = 36)	FCC	n = 14 (7)	n = 1 (1) Discordant	Papilloma with atypia
	Fibroadenoma	n = 10 (2)	n/a	n/a
	Papillary w/o atypia	n = 9 (7)	n = 9 (7)	8 Papillary w/o atypia 1 Papillary/ADH
	Papillary/ADH ADH Papillary w atypia	n = 1 (0) n = 1 (0) n = 1 (1)	n = 3 (1)	Papillary/ADH FCC Papillary/ADH
Surgery (n = 1)	n/a	n/a	n = 1 (1)	Fibroadenoma

ADH, atypical ductal hyperplasia; CNB, core needle biopsy; FCC, fibrocystic change.

^aNumber in parentheses = number of intraductal lesions.

to evaluate an abnormal finding on mammography or physical examination.²⁷⁻²⁹ The pre-test probability of malignancy for lesions detected on US-S is lower compared to that of lesions detected on a diagnostic ultrasound examination. Therefore, optimal management of lesions discovered on US-S may differ from similar lesions detected on diagnostic ultrasound so that specificity can be improved while also maintaining sensitivity. Previous studies support different management algorithms for US-S detected masses. For example, non-solitary complicated cysts in average risk females discovered on US-S do not require short interval follow-up.^{10,30} Likewise, data derived from ACRIN 6666 showed that BI-RADS 3 findings, including solitary oval and parallel circumscribed solid masses as well as bilateral circumscribed masses may be safely followed with repeat imaging at 12 months.^{31,32} Although elastography is not commonly used to evaluate masses on US-S, a study by Lee et al also revealed that masses detected on US-S may require different criteria when using shear wave elastography as these masses are usually softer and smaller than masses detected on targeted ultrasound.³³

Retroareolar masses discovered on ultrasound are typically encountered in the diagnostic setting and biopsy is often advised because of the possibility of DCIS or an intracystic papillary carcinoma, particularly if located with a dilated duct.¹⁴ In our study no malignancy was found in either BI-RADS 3 or BI-RADS 4 lesions associated with multiple bilateral masses. 24/40 (60%) of BI-RADS 4 masses, including 7 masses not associated with

a dilated duct and 17 intraductal masses demonstrated all the combination of benign features including oval shape, circumscribed margins and parallel orientation fitting the criteria for BI-RADS 3, if not located within a duct¹⁴ or 4a final assessment, if located within a duct.²³ If these 24 US-S detected lesions initially assessed as BI-RADS 4, despite benign ultrasound features, were to be reclassified as BI-RADS 3, the biopsy rate would decrease by 60% and the BI-RADS 3 malignancy rate would be 1.4% without a loss in sensitivity. Furthermore, if the 7/24 BI-RADS 4 lesions with benign ultrasound features and 20/47 BI-RADS 3 lesions also associated with multiple bilateral circumscribed masses were downgraded to BI-RADS 2, the BI-RADS 3 rate would decrease by 38%. The variable management of these findings in our study may be the result of limited radiologist experience with these uncommon retroareolar findings in asymptomatic females with a negative mammogram.

Based on the ACRIN 6666 data, the malignancy rate of BI-RADS 3 lesions discovered on US-S was 0.8%, including six malignancies of which five were invasive with an average size of 10 mm.³² Similarly, Chae et al showed a malignancy rate of 0.7% among BI-RADS 3 lesions detected among 12,187 US-S examinations.³⁴ In our series, the BI-RADS 3 malignancy rate was slightly higher at 2.1%. The single malignancy was a solitary 5 mm Grade 2 DCIS which initially presented as an oval circumscribed mass and was upgraded to BI-RADS 4 at 6-month follow-up ultrasound due to a subtle change with new internal vascularity identified on colour Doppler evaluation. Internal vascularity is not specific for malignancy, but can be sometimes helpful to exclude the possibility of an intraductal pseudo-mass secondary to debris. Nevertheless, any change in the appearance of a breast mass on follow-up imaging, including subtle changes in shape, margin and/or vascularity may prompt a biopsy recommendation.

To our knowledge, our study represents the only series investigating US-S detected retroareolar masses and intraductal abnormalities. Although the overall incidence is low at 1.3%, optimal patient management is essential. In our series, intraductal abnormalities were more likely to be classified as BI-RADS 4 compared to retroareolar masses not definitely associated with a duct, which were more likely to be classified as BI-RADS 3. 36 BI-RADS 4

Table 4. Comparison of BI-RADS 3 and BI-RADS 4 findings

	BI-RADS 3 (n = 47)	BI-RADS 4 (n = 40)	p value
Size (mm)	10.2 ± 0.47	8.6 ± 0.43	0.811
Age (years)	52.8 ± 11.2	53.7 ± 11.1	0.605
Elevated risk	5 (10.6%)	4 (10%)	1.0
Intraductal	27.7%	52.5%	0.018 ^a
Mass	72.3%	47.5%	0.018 ^a
Malignancy rate	2%	0%	1.0

^aStatistically significant.

lesions were found to be benign at ultrasound-guided CNB, but 39% (14/36) still required surgical excision although no upgrades to malignancy were found. Similar to benign-appearing solid lesions identified elsewhere in the breast, in our practice biopsy is no longer routinely recommended for oval, circumscribed retroareolar masses and intraductal lesions discovered on US-S and these findings may often be assessed as BI-RADS 3 if the mass does not have any malignant ultrasound features and, if located within a duct, does not extend beyond the duct wall. The signs and symptoms of worrisome nipple discharge are also reviewed with these patients, who are instructed to return sooner for repeat ultrasound if spontaneous, unilateral, bloody, clear or serosanguineous nipple discharge occurs. Immediate biopsy should be considered for retroareolar masses without typical benign ultrasound features, as well as intraductal masses extending beyond the duct.

This study is limited because it is a retrospective study performed at a single academic medical centre. Because intraductal lesions and retroareolar masses are uncommon findings on US-S, the study sample size is small. Further prospective and multicentre studies are warranted for further validation before generalization of our results can be made. Only lesions detected and documented on the radiology report were included in our data set. BI-RADS 4 final assessment subclassification was not consistently reported and therefore not included in our data analysis, even though such stratification could reduce the false positive findings on US-S. We included masses in our analysis

of retroareolar findings as it may be difficult to differentiate an intraductal mass completely filling the duct from a mass that is truly separate from the adjacent duct. All studies were performed using handheld ultrasound and the results may not be applicable to lesions detected on automated US-S. Conclusions regarding the role of breast cancer risk in the management decisions cannot be made. Two patients were lost to follow-up and were not included in our analysis.

In conclusion, our study demonstrates that a low malignancy rate among retroareolar masses and intraductal abnormalities identified on US-S performed in the general population. Careful imaging surveillance with symptom monitoring of incidentally detected, oval, circumscribed retroareolar masses, including masses located within a duct on US-S in lieu of biopsy may be appropriate in asymptomatic females with negative mammography. Future prospective studies are needed to define and validate improved management criteria for US-S detected retroareolar and intraductal masses.

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