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Second opinion interpretation of breast ultrasound images-is it worth another look?

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Abstract

Purpose: To determine if real-time breast ultrasound (RTUR) after second opinion reinterpretation of submitted static ultrasound images at a comprehensive cancer center impacts clinical management, specifically by detecting additional cancer and preventing unnecessary biopsy.

Materials and Methods: In this IRB-approved and HIPAA-compliant retrospective study, 209 patients were included who had breast ultrasound studies from outside facilities submitted for second opinion review between January 2013 and May 2014, and who subsequently underwent RTUR at our institution within three months of the outside study. Findings on submitted exams were compared with those on RTUR and disagreements between them were annotated to indicate the presence or absence of suspicious lesions and recommendation for biopsy. Changes in management were defined as any additional biopsies performed or biopsies averted after RTUR and reported as frequencies and percentages using 95% confidence intervals.

Results: Following RTUR, 49 additional biopsies were performed in 43/209 patients (20.6%; 95% CI 15.1–26.1%). Additional cancer was found in 12/49 (24.5%) biopsies in 11/209 patients (5.3%; 95% CI 2.2–8.2%). Forty biopsies in 31/209 (14.8%; CI 10.0–19.7%) patients originally recommended were canceled after RTUR. Overall, a change in management after RTUR was observed in 68/209 patients (32.5%; 95% CI 26.1–38.9%), including patients with either additional biopsies performed or biopsies averted.

Conclusion: RTUR was found to be an important tool in the management of patients at our comprehensive cancer center. Although additional false-positive lesions may be detected on RTUR, a great number of patients will benefit from RTUR in finding additional cancers or avoiding unnecessary biopsies.

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Conflicts of interest

None.

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Keywords

Diagnostic Imaging; Ultrasonography; Breast Neoplasms; Image-Guided Biopsy; Patient Care Management

Introduction

Second opinion review of breast imaging studies is currently widely performed in many specialized cancer centers throughout the United States [1]. As part of their care, patients from non-tertiary medical centers with suspicious imaging findings or diagnosed malignancies may be referred for or seek second opinion consultations at comprehensive cancer centers for specialized management and treatment [2, 3]. These consultations often include second opinion review of imaging studies where specialty radiologists assess the diagnostic accuracy of the studies performed, address questions raised by referring surgeons or clinical oncologists, and help improve the management of these patients [4].

The added value of second opinion review has been demonstrated by multiple studies [1–11]. Re-evaluation of outside studies at comprehensive cancer centers frequently leads to a change in management [3–5, 7, 8, 11]. However, while re-evaluation may detect new cancers, an increase in the number of false positive lesions is also expected [9, 10]. Second opinion review may lead to an elevation in costs, anxiety, and prolonged time between diagnosis and treatment [12].

Ultrasound (US) of the breast is used as a complementary modality to mammography and as an adjunct tool for breast cancer screening, particularly in women with dense breasts [13]. US examinations are performed in the diagnostic setting to characterize lesions and evaluate the surrounding parenchyma in real time. These examinations are operator-dependent and the training and experience of the operator, either that of a technologist or a radiologist, is of paramount importance [14]. Overlooked tumors or misinterpretation of lesion features may lead to undiagnosed cancers [15–17].

Second opinion review of breast US studies involves evaluating static images of studies performed at a different time and institution. The US images reviewed are a screenshot of what the technologist or radiologist noted during an US exam originally performed in real time. The true real-time features of a lesion are not available to the reviewing radiologist and may lead to uncertainty in characterizing lesions on static US images. As such, radiologists reviewing static breast US images as part of a second opinion consultation often recommend a real-time US re-evaluation (RTUR) in order better to characterize lesions depicted on the static images and potentially avoid misdiagnosis.

In this context, this study aims to assess change in management brought by RTUR after second opinion review of outside studies at a comprehensive cancer center, particularly by detecting additional cancers and avoiding unnecessary biopsies.

Materials and Methods

The Institutional Review Board approved this single-center Health Insurance Portability and Accountability Act compliant retrospective study and waived the requirement for patient informed consent.

Study Population

We queried our institutional database to include consecutive patients with breast US studies from outside facilities whose studies were submitted for second opinion review between January 2013 and May 2014 and who subsequently underwent real-time breast US performed at our institution within three months of the outside study. Ultrasound studies submitted for second opinion review included screening and diagnostic studies. The exclusion criteria were (a) outside US images or reports unavailable on Picture Archiving and Communication System (PACS), (b) no recommendation for RTUR on the second opinion consultation report, (c) RTUR performed in the contralateral breast when the outside exam was solely unilateral, and (d) RTUR intended to evaluate magnetic resonance imaging (MRI) findings. The final study population consisted of 209 patients. Patient accrual is demonstrated in Fig. 1.

Second Opinion Consultation

All second opinion consultations during the study period were performed by one of 21 radiologists specializing in breast imaging with 5 to 30 years of experience. The majority of the outside studies were also reviewed by a fellow training in breast imaging interpretation. Radiologists re-evaluated images of outside studies in conjunction with the outside reports and patient medical records. Outside images were retrieved for second opinion review through our breast imaging consultation service with patients either self referred or referred through the breast surgery service. They were electronically processed and transformed into digital files in the institutional PACS. Breast US images were evaluated in conjunction with mammography and MRI when available. For each patient undergoing a second opinion consultation, the interpreting radiologist issued a single report containing his or her findings and recommendations including recommendations for biopsy or additional imaging. If the patient was referred by a referring physician, these were discussed with the referring physician. Additional biopsies were performed at our institution when recommended.

Data Analysis

Patient clinical information was retrospectively obtained and compiled from a detailed electronic medical record review using a standardized form. Data collected included: (a) patient demographic data, (b) breast imaging studies performed at outside facilities, (c) breast imaging studies performed at our institution, (d) biopsy procedures, (e) pathological results, and (f) follow-up breast studies.

Outside US reports and images were analyzed for exam date, institution, extent of examination (classified as bilateral or unilateral), and imaging findings. Findings on submitted exams were compared with those on RTUR—regarding size, location, morphological features, BI-RADS descriptors, final assessment, and recommendation.

Disagreements between outside studies and RTUR were annotated to indicate the presence or absence of suspicious lesions and recommendation for biopsy.

Change in management was defined as any additional biopsies performed or biopsies averted after RTUR. The number of additional biopsies was determined by procedures performed for lesions recommended for biopsy on the RTUR report but not on the outside report. The number of biopsies averted was determined by lesions recommended for biopsy on the outside report but not on the RTUR report. If available, one or two-year follow-up breast imaging studies were assessed for stability of the RTUR findings for patients with biopsies averted.

Pathology results were classified into benign, malignant, and high-risk lesions, using histopathology from breast biopsy as the reference standard.

Statistical Analysis

Descriptive and comparative statistics were performed. Summary statistics were performed for the overall study population and summarized using frequencies and percentages for categorical variables. Continuous variables were summarized using medians and ranges. 95% binomial proportion confidence intervals were estimated for each parameter. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Second Opinion Consultation

Two hundred and nine patients had outside US studies submitted for second opinion consultation from 134 different institutions. Outside imaging studies were performed in the private practice setting, community hospital centers, and academic centers. The mean patient age was 57 years (range, 17–91).

Outside breast US exams were bilateral in 114/209 (54.5%) of cases and unilateral in 95/209 (45.5%). Outside US studies included screening and diagnostic breast US exams. Outside US reports had a BI-RADS 4 or 5 assessment in 172/209 (82.3%) of cases. The average time between outside US and RTUR studies was 31 days (range, 2–90). Radiologists on second opinion reports recommended RTUR for one or more reasons. 163/209 (78.0%) RTUR were recommended to better characterize a finding demonstrated on submitted static US images to determine whether a lesion was a true lesion and/or needed biopsy. 46/209 (22.0%) RTUR were recommended to re-assess a finding on outside mammography and evaluate for possible sonographic correlate.

Change in Management on RTUR

Following RTUR, 49 additional biopsies of lesions not originally recommended for biopsy were performed in 43/209 patients (20.6%; 95% CI 15.1–26.1%). Of the 49 additional biopsies performed, additional cancer was found in 12/49 (24.5%) biopsies in 11/209 patients (5.3%; 95% CI 2.2–8.2%). Biopsy of 4/49 (8.2%) lesions yielded high-risk lesions in 4/209 patients (1.9%; 95% CI 0–3.8%). Table 1 summarizes malignancies and high-risk

lesions detected on the additional biopsies performed. Examples illustrating cases recommended for additional biopsy are shown in Fig. 2–4.

Forty biopsies in 31/209 (14.8%; CI 10.0–19.7%) patients originally recommended were canceled after RTUR. Among patients with biopsies averted, 11/31 (35.5%) had no follow-up, 20/31 (64.5%) had 1-year breast imaging follow-up including US, and 17/31 (54.8%) had 2-year follow-up showing stability of the RTUR findings.

Overall, a change in management after RTUR was observed in 68/209 patients (32.5%; 95% CI 26.1–38.9%), including patients with either additional biopsies performed or biopsies averted. The results per patient are demonstrated in Fig. 5. Example cases illustrating change in management after RTUR are shown in Fig. 6 and 7.

Discussion

RTUR after second opinion review of submitted static US images was found to be an important tool in the management of patients at our comprehensive cancer center. RTUR led to additional biopsies being performed, and approximately 25% of the biopsies were positive for cancer. Biopsies were averted in a number of patients with US findings remaining stable on long term follow up.

Multiple studies report inconsistent interobserver agreement on many of the descriptors used in the BI-RADS lexicon [13, 18–20]. This alone could explain why changes in the impression and recommendation of breast imaging exams are not rare on second opinion evaluation. On US, the misinterpretation of a suspicious feature has been reported as a leading cause of undetected malignancies [16]. Lesions may also be overlooked, especially when they are small, deep in the breast or among multiple distracting lesions [15, 21].

The accuracy of cancer detection can vary among healthcare facilities [22]. Radiologists practicing at tertiary centers or those who have more experience and training in breast imaging may have a greater sensitivity for detecting cancer than general radiologists [7, 14, 17]. On the other hand, it has been demonstrated that a higher sensitivity will frequently result in a lower specificity [23]. In our study, RTUR led to additional biopsies for 20.6% patients, while biopsies were averted in 14.8%. Although the number of additional biopsies performed was higher, these biopsies detected additional cancer in 24.5% of biopsies performed and 5.3% of the total individuals included. These data demonstrate that although additional false-positive lesions may be found on RTUR, a great number of patients can benefit from RTUR in finding additional cancers or avoiding unnecessary biopsies.

Previous studies have reported the role of second opinion review in breast imaging. Coffey et al evaluated second opinion review in different breast imaging modalities, including mammography, US, and magnetic resonance imaging [4]. They demonstrated a change in image interpretation in approximately 28% of patients, while a significant change in management was achieved in 13%, including additional cancers in 5% of cases. Spivey et al reported a change in management in 53.5%, including recommendation for additional imaging or biopsy [7]. In their study, the additional biopsies performed yielded malignancy in 2.1% of all patients. Mallory et al likewise observed additional cancers in 4.5% of patients

after second opinion review [9]. In our study, additional cancers were found in 5.3% of cases. This demonstrates that disagreement may be even higher in US, and that RTUR performed in comprehensive cancer centers may be more beneficial than second opinion review of static images.

There were some limitations in our retrospective study. First, only a fraction of patients at our institution undergoes second opinion consultation, self-referred or referred through the breast surgery service, which could have caused a selection bias. Additionally, a number of patients were excluded from our study, as outside US images were not available in our database. Finally, some patients with biopsies averted were lost to follow-up with two-year follow-up available only in approximately half of these patients. Prospective studies are necessary to overcome these limitations and better evaluate the role of RTUR.

Conclusion

In conclusion, RTUR after second opinion review of outside breast US studies led to a change in management in 32.5% of patients, and detection of additional cancers in 5.3%. Additional biopsies were performed in one fifth of cases, while unnecessary biopsies were averted in one sixth of patients.

Acknowledgments

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Abbreviations

MRI	Magnetic resonance imaging
PACS	Picture Archiving and Communication System
RTUR	Real-time ultrasound re-evaluation
US	Ultrasound

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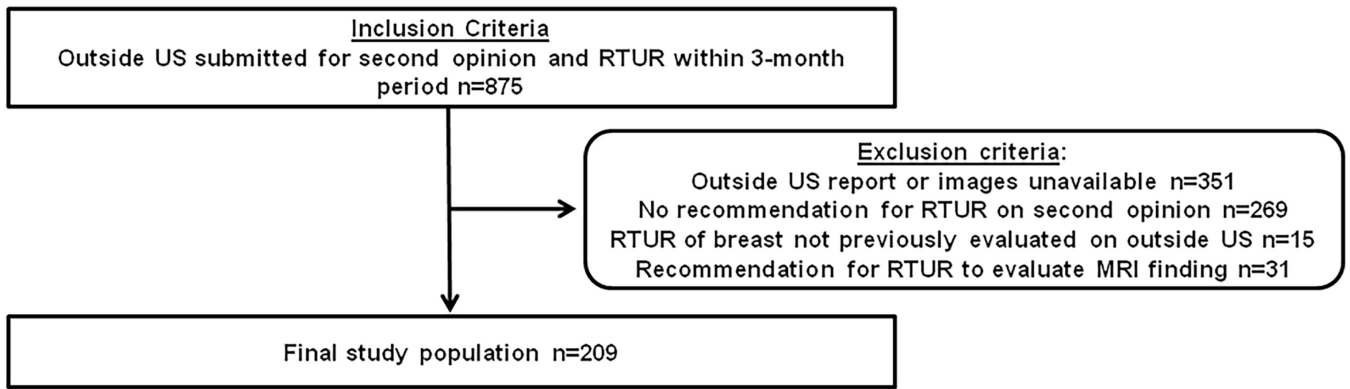


Fig. 1 -
Flowchart of patient accrual.

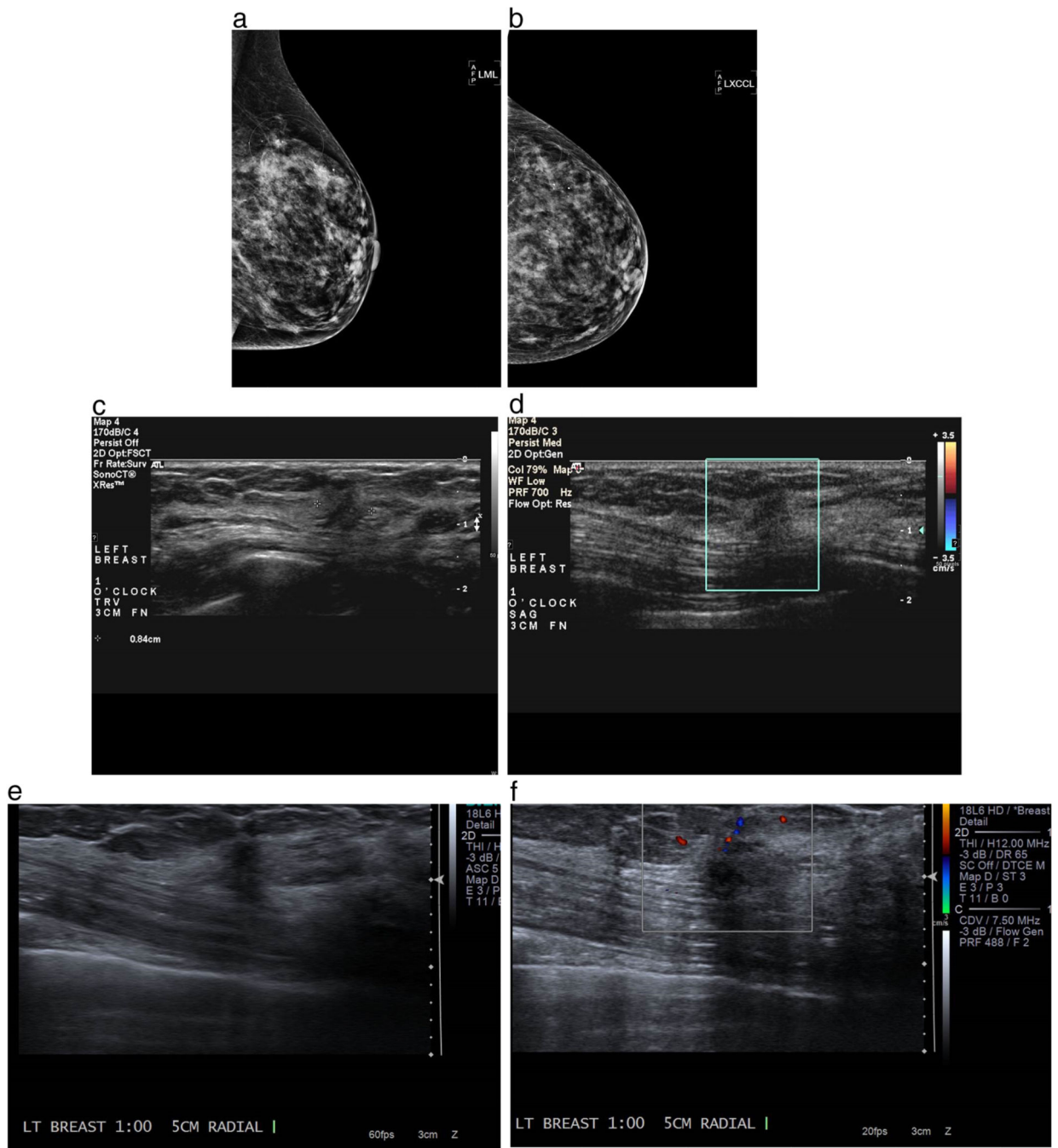


Fig. 2 -
 66 yo woman with outside mammogram ML and XCCL views (a,b) read as BI-RADS 2, benign findings. Original ultrasound performed (c,d) interpreted as heterogeneous questioned mass or calcifications for which MRI was recommended. RTUR (e,f) demonstrates irregular shadowing mass with associated vascularity. Biopsy yielded invasive ductal carcinoma.

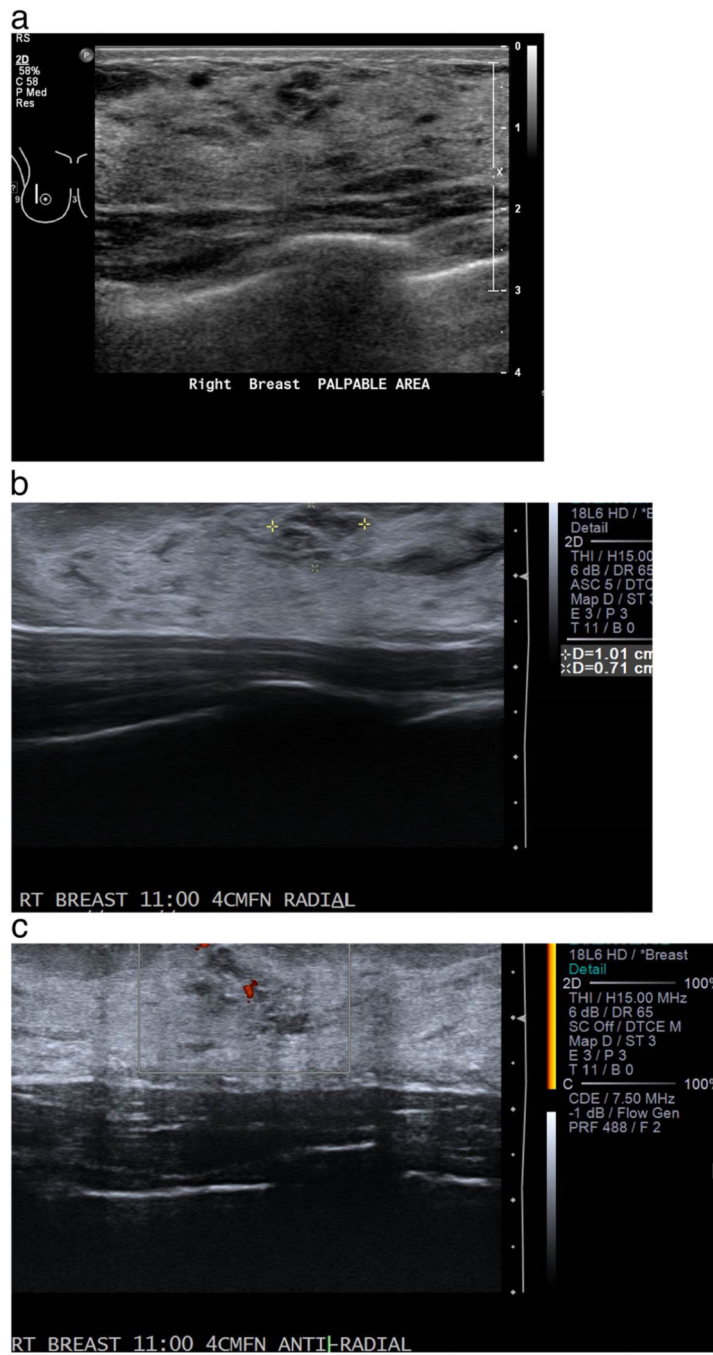


Fig 3. -
 42 yo woman presented to outside facility with palpable area of concern in the right breast. Original ultrasound (a) targeted to the area of concern interpreted as benign. RTUR performed for characterization of the single submitted image of the palpable area of concern (c,d) interpreted as suspicious and biopsy was recommended. Biopsy yielded DCIS.

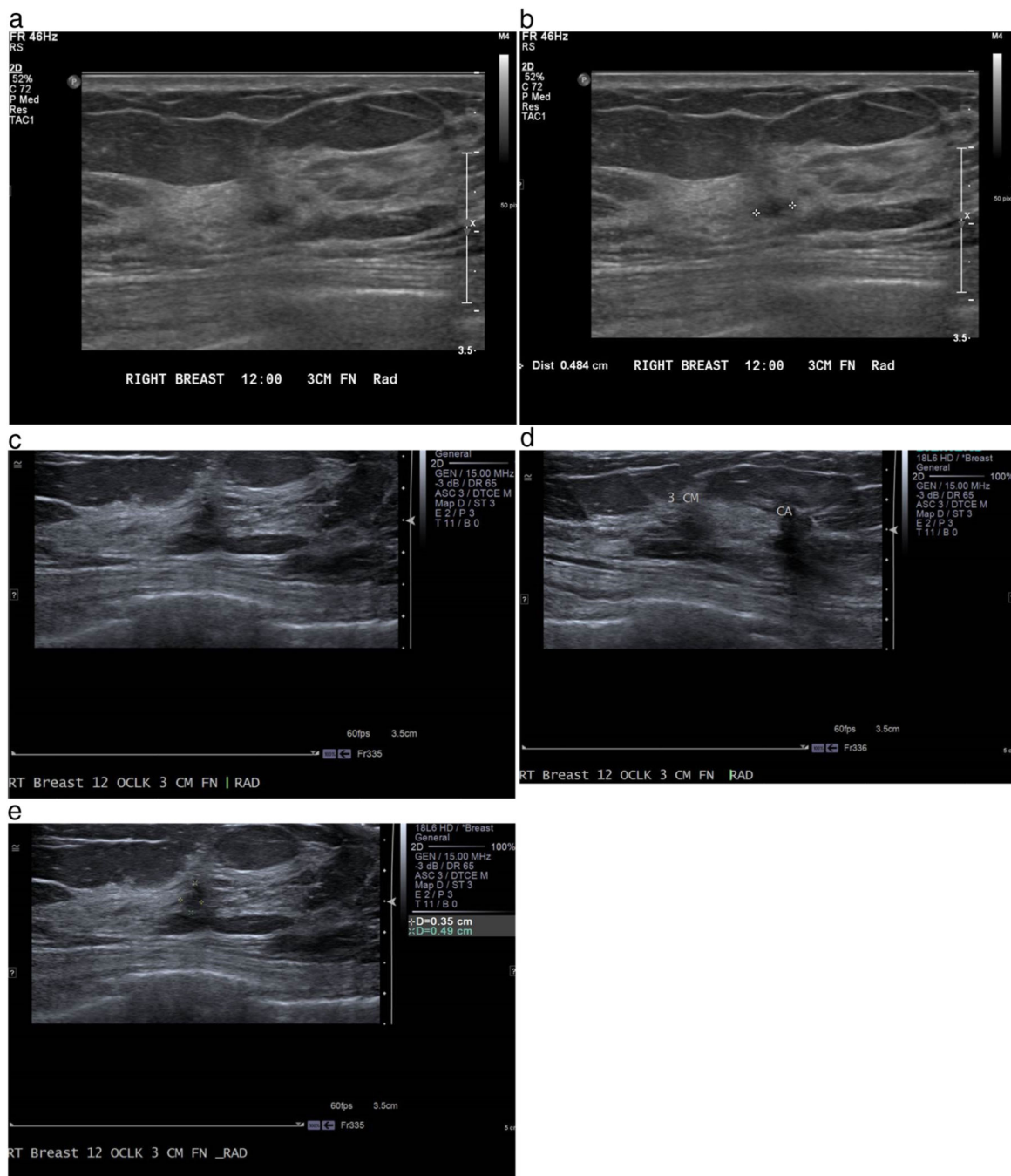


Fig. 4 - 62 yo woman with recent diagnosis of right breast cancer. Original ultrasound (a, b) interpretation of additional 12:00 axis 3CMFN lesion was probably benign and 6 months follow up ultrasound was originally recommended. RTUR (c,d,e) demonstrates suspicious sonographic features of this mass at the 12:00 axis 3CMFN and the relationship to the biopsy proven cancer suspicious for satellite lesion. Lumpectomy confirmed two morphologically similar adjacent invasive ductal cancers.

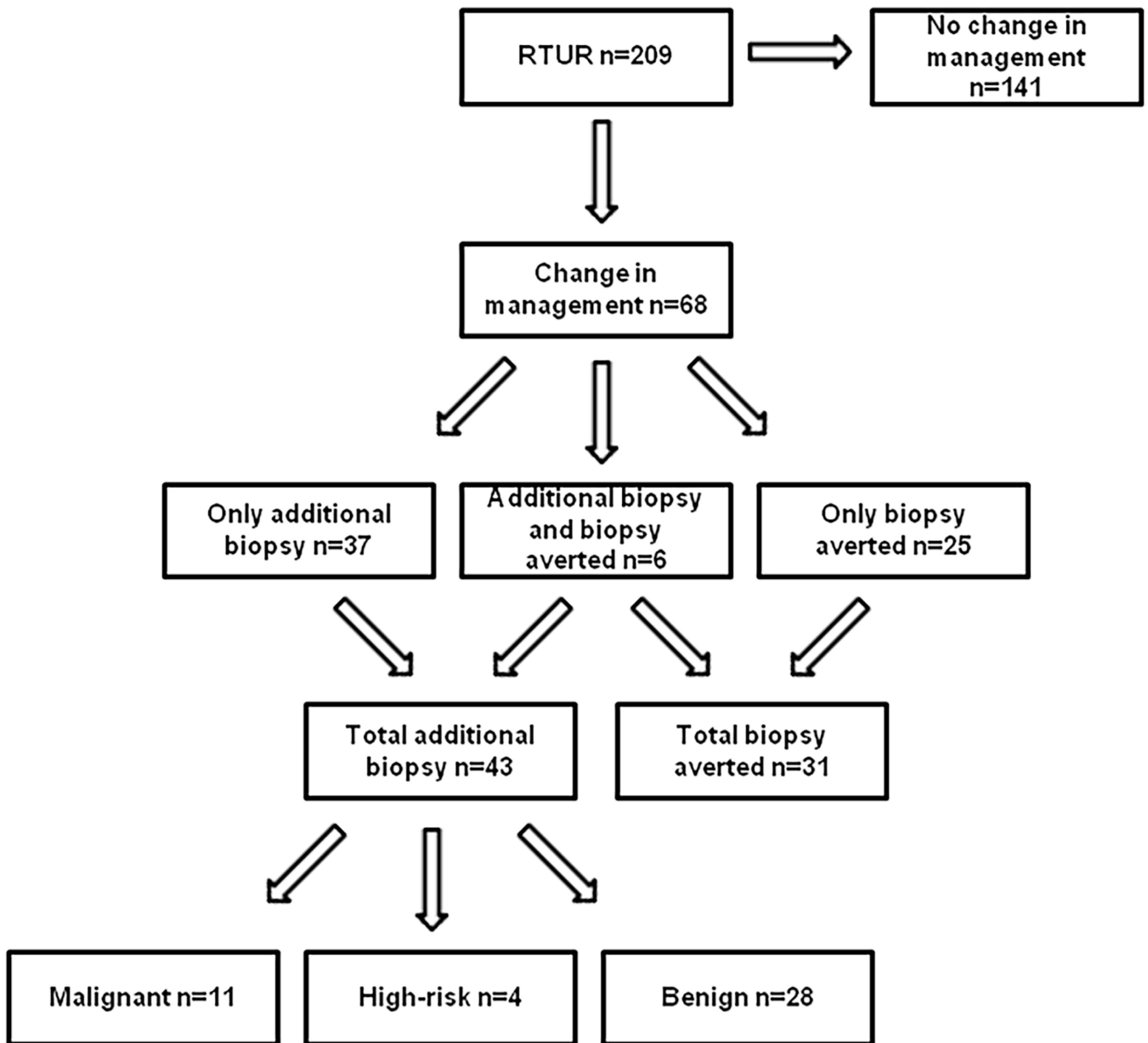


Fig. 5 - Chart demonstrating results after RTUR per patient.

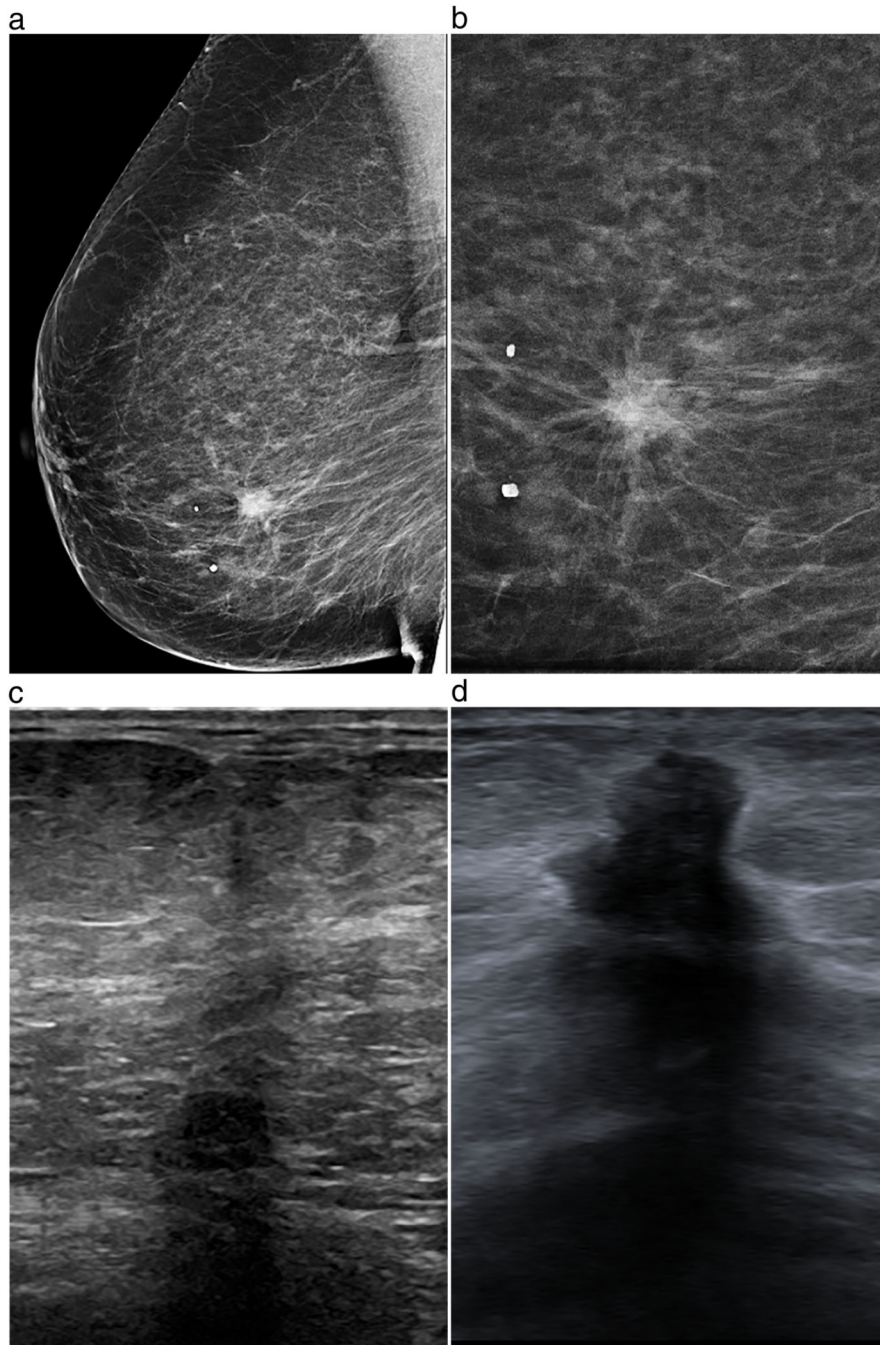


Fig. 6 - 69-year-old woman with a spiculated mass in the right breast on outside mammography (a,b). Outside US demonstrates an area of shadowing deep in the breast thought to be correlated (c). RTUR in our institution demonstrates that the spiculated lesion was in a different location, right below the skin (d). Histopathology results yielded invasive ductal carcinoma. The lesion seen on the outside US was not visible on RTUR.

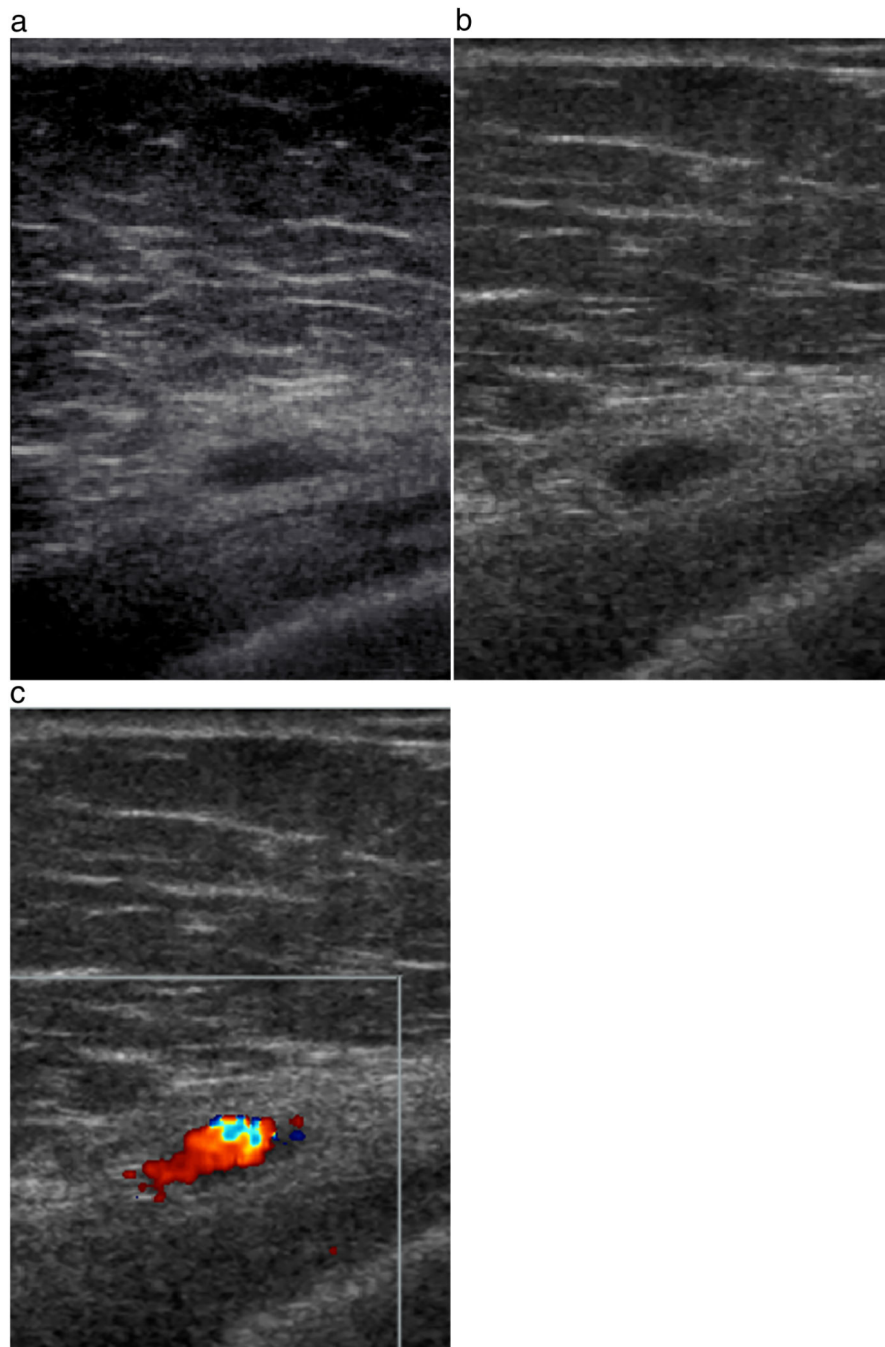


Fig. 7 - 56-year-old woman with a hypoechoic lesion deep in the right breast on the outside screening US study (a) and on RTUR (b). Outside report recommended biopsy of the lesion. On RTUR, color Doppler evaluation (c) demonstrates it was a vessel.

Table 1.

Malignancies and high-risk lesions detected on additional biopsies performed.

Case #	Lesion #	Detected on Outside US	Change in Management after RTUR	Pathological Result
1	1	Yes	New recommendation for biopsy	IDC
2	2	No	New lesion detected	IDC
3	3	No	New lesion detected	IDC
4	4	No	New lesion detected	MALT lymphoma
5	5	No	New lesion detected	IDC
6	6	No	New lesion detected	IDC
7	7	No	New lesion detected	DCIS
8	8	No	New lesion detected	IDC
9	9	No	New lesion detected	IDC
9	10	No	New lesion detected	IDC
10	11	No	New lesion detected	IDC
11	12	Yes	New recommendation for biopsy	IDC
12	13	Yes	New recommendation for biopsy	Papilloma
13	14	Yes	New recommendation for biopsy	LCIS and ALH
14	15	No	New lesion detected	Fibroadenoma and LCIS
15	16	Yes	New recommendation for biopsy	Papilloma and ALH

ALH: atypical lobular hyperplasia; IDC: invasive ductal carcinoma; DCIS: Ductal carcinoma in situ; LCIS: Lobular carcinoma in situ; MALT: mucosa-associated lymphoid tissue; US: ultrasound; RTUR: real-time US re-evaluation.