



**Breast Imaging** Original Research

## Imaging Surveillance of the Reconstructed Breast in a Subset of Patients May Aid in Early Detection of Breast Cancer Recurrence

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### ABSTRACT

**Objectives:** The purpose of this study is to determine the biological markers more frequently associated with recurrence in the reconstructed breast, to evaluate the detection method, and to correlate recurrent breast cancers with the detection method.

**Material and Methods:** An institutional review board-approved retrospective study was conducted at a single institution on 131 patients treated with mastectomy for primary breast cancer followed by breast reconstruction between 2005 and 2012. Imaging features were correlated with clinical and pathologic findings.

**Results:** Of the 131 patients who met our inclusion criteria, 40 patients presented with breast cancer recurrence. The most common histopathologic type of primary breast cancer was invasive ductal carcinoma in 82.5% (33/40) of patients. Triple-negative breast cancer was the most common biological marker with 42.1% (16/38) of cases. Clinically, 70% (28/40) of the recurrences presented as palpable abnormalities. Of nine patients who underwent mammography, a mass was seen in eight patients. Of the 35 patients who underwent ultrasound evaluation, an irregular mass was found in 48.6% (17/35) of patients. Nine patients with recurrent breast cancer underwent breast MRI, and MRI showed an irregular enhancing mass in four patients, an oval mass in four patients, and skin and trabecular thickening in one patient. About 55% of patients with recurrent breast cancer were found to have distant metastases.

**Conclusion:** Patients at higher risk for locoregional recurrence may benefit from imaging surveillance in order to detect early local recurrences.

**Keywords:** Breast cancer recurrence, Reconstructive surgery, Biological markers, Deep recurrences

### INTRODUCTION

Breast cancer is the most common malignancy among women worldwide. In 2021, an estimated 281,550 women will be diagnosed with invasive carcinoma and 49,290 within situ carcinoma.<sup>[1]</sup> Breast conserving surgery and mastectomy are two equally suitable surgical options for breast cancer treatment. However, rates of bilateral mastectomies have progressively increased by 14% in the past decade, and nearly 40% of mastectomies are accompanied by breast reconstruction.<sup>[2]</sup> As a result of the increasing trend of mastectomies followed by either implant-based or autologous

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breast reconstructions, imaging surveillance of reconstructed breasts may be necessary to detect early recurrence.

Local recurrence after modified radical mastectomy ranges between 2% and 7.5% of cases and reported rates of recurrences in reconstructed breasts are lower, ranging between 2% and 4%.<sup>[3,4]</sup> Local recurrence implies a worse prognosis with associated distant metastases in half of the patients.<sup>[4]</sup> Current guidelines do not support surveillance of patients with reconstructed breasts, and there is limited evidence that suggests some benefit for screening mammography in patients with autologous breast reconstructions.<sup>[5]</sup>

The purpose of this study is to assess what type of biological markers are more frequently associated with recurrence in the reconstructed breast and to correlate the detection method (palpation versus imaging) with recurrent cancer.

## MATERIAL AND METHODS

One hundred thirty-one patients treated with mastectomy for primary breast cancer followed by breast reconstruction at a single institution between 2005 and 2012 were reviewed to be included in the study. This study was approved by our institutional review board, which granted a waiver of informed consent. A retrospective review of the medical records for demographic data, clinical history, and clinical outcomes was performed. Imaging studies were reviewed.

Primary and recurrent breast cancers were reviewed for the histological and intrinsic subtypes. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor 2 (HER2) were extracted from pathology reports. ER+ and PR+ were defined as a nuclear staining  $\geq 10\%$ . HER2 status was defined as 3+ by IHC or 2+ by IHC with a FISH ratio of  $\geq 2.0$  for HER2:CEP17 (chromosome 17 centromere) or single probe copy number of  $\geq 6$  per cell.

At the study institution, breast cancer patients treated with mastectomy followed by reconstruction with either implants or autologous flaps are not routinely screened with imaging. Physical examination is routinely performed by the clinician. If there is a palpable abnormality, sonographic evaluation is the preferred modality to evaluate the reconstructed breast.

The location of tumor recurrences in the transverse rectus abdominis myocutaneous flap reconstructed breast were categorized as superficial if the recurrence was localized in the skin or the subcutaneous tissues and deep if the recurrence was adjacent to or involving the pectoralis major or the chest wall muscles. In the breast reconstructed with implants, lesions anterior to the pectoralis muscle were defined as superficial and lesions within the pectoralis muscle or the deeper structures were defined as deep.

Four fellowship-trained breast radiologists (1–10 years of experience) individually analyzed and compared the imaging findings when available according to the BI-RADS imaging lexicon 5th edition.<sup>[6]</sup>

## RESULTS

### Demographics

From 2005 to 2012, 131 patients who underwent mastectomy followed by reconstruction with implants or autologous flaps had images available for review. Among them, 40 had a recurrence in the reconstructed breast [Table 1]. The median age at the time of diagnosis of the primary cancer was 43-years-old (range, 24–70 years). Of these 40 patients, 26 women had undergone modified radical mastectomy, nine had skin sparing mastectomies, and five had simple mastectomies. Ninety-five percent (38/40) of the patients had immediate reconstruction and 5% (2/40) had delayed reconstruction, 45% (18/40) with implants, and 55% (22/40) with an autologous flap. Of the 40 recurrences, the most common histology type was invasive ductal carcinoma (IDC) in 82%. The clinical and pathologic features are listed in [Table 1].

The median time between the mastectomy and the recurrence in the reconstructed breast was 19.1 months (range, 1.6–63 months). The median size of the recurrence was 1.5 cm.

**Table 1:** Characteristics of 40 primary breast cancers in patients who developed recurrences in the reconstructed breast.

Histopathologic finding (40 patients)	Number of patients (%)
IDC	33 (82.5)
DCIS	3 (7.5)
Angiosarcoma	1 (2.5)
Metaplastic carcinoma	1 (2.5)
Myoepithelial carcinoma	2 (5)
Cancer clinical stage (39 patients)	
0	3 (7.7)
I	14 (35.9)
II	15 (38.5)
III	7 (17.9)
Biological markers (38 patients)	
Luminal A	10 (26.3)
Luminal B	7 (18.4)
HER2+	5 (13.2)
ER–PR–HER2–	16 (42.1)
Type of surgery (40 patients)	
Modified radical mastectomy	26 (65)
Simple mastectomy	5 (12.5)
Skin sparing mastectomy	9 (22.5)

IDC: Invasive ductal carcinoma, DCIS: Ductal carcinoma *in situ*, HER2: Human epidermal growth factor receptor 2, ER: Estrogen receptor, PR: Progesterone receptor

### Method of detection of local breast recurrence and imaging findings

The most common method of detection was self-palpation or palpation by the clinician in 70% (28/40) of the recurrences, 5% (2/40) with redness, and 3% (1/40) with pain. The recurrences were clinically occult in 22.5% of patients (9/40). In these nine patients, six recurrent cancers were detected on ultrasound, two on MRI, and one on mammography.

Mammography in nine patients with recurrence after reconstruction revealed a mass in eight patients, [Figure 1] and a focal asymmetry in one patient. None of the recurrent cancers had calcifications on mammography.

The majority of patients (35/40) underwent ultrasound. Imaging findings associated with recurrences on ultrasound included irregular masses in 48.6% (17/35) with non-circumscribed margins in 80% (28/35) and hypoechogenicity in 82.8% (29/35) of the cases [Table 2].

### Sites of local recurrence

Sixty percent (24/40) of patients had superficial recurrences [Figure 1] and the remaining patients presented with either deep (32.5% [13/40]) [Figure 2] or combined superficial and deep recurrences (7.5% [3/40]). Among the 40 patients with recurrence, one case presented with inflammatory carcinoma.

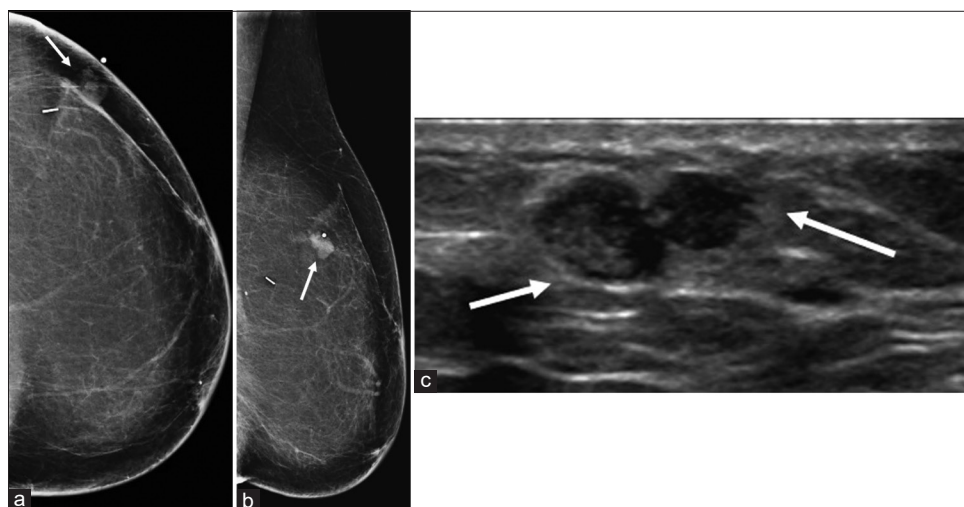
### Distant metastases

Fifty-five percent (22/40) of the cases were found to have distant metastases on average 15 days after the diagnoses of

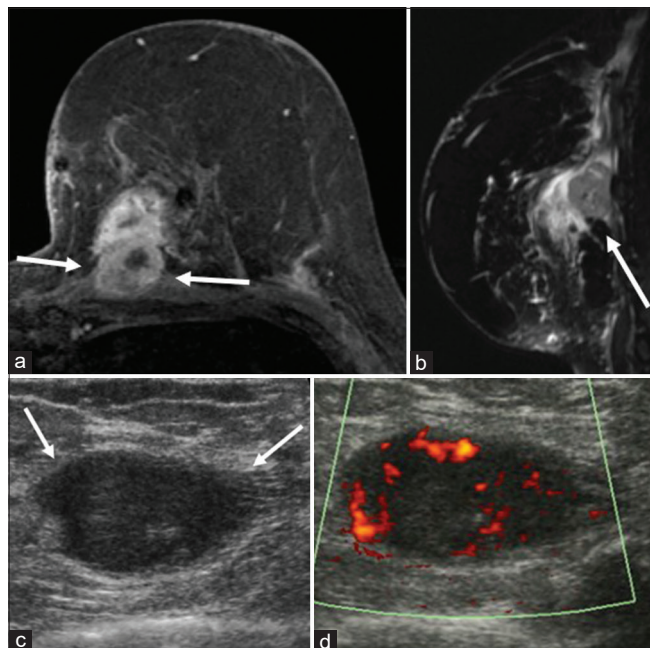
their locoregional recurrence. In our study, 77% (10/13) of the deep recurrences were associated with distant metastases, and 32% (8/25) of the superficial recurrences were associated with distant metastases. Two cases were diagnosed with distant metastases prior to developing locoregional relapse. Bone, liver, and lung were the most common sites of distant relapse.

**Table 2:** Imaging findings of 40 primary breast cancers in patients who developed recurrences in the reconstructed breast.

Imaging findings	Number of patients (%)
Mammography	9
Masses	6 (66.7%)
Focal asymmetry	2 (22.2%)
Occult	1 (11.1%)
Masses shape	
Oval/Round	3 (50%)
Irregular	3 (50%)
Ultrasound	35
Masses shape	
Round/Oval	17 (48.6)
Irregular	18 (51.4)
Masses margins	
Circumscribed	7 (20)
Non-circumscribed	28 (80)
Echogenicity	
Hypochoic	29 (82.8)
Heterogeneous	3 (8.6)
Complex cystic and solid	3 (8.6)
Breast MRI	9
Masses	8 (88.9)
Skin thickening	1 (11.1)



**Figure 1:** A 70-year-old woman with a history of left breast IDC (ER-, PR-, HER2-), status post mastectomy with TRAM reconstruction. She presented with a palpable abnormality in the upper outer left breast. (a and b) CC and MLO mammograms show an oval hyperdense mass with circumscribed margins correlating with the palpable abnormality (white arrows). (c) Longitudinal gray scale ultrasound shows a superficial oval bilobed hypochoic mass (arrows) correlating with the palpable abnormality. Ultrasound-guided core biopsy showed recurrent IDC.



**Figure 2:** A 57-year-old woman with a history of myoepithelial cancer (ER-, PR-, HER2-) who underwent mastectomy and reconstruction with deep inferior epigastric artery perforator (DIEP) flap. She presented with thickening and pain in the right reconstructed breast. (a) Axial T1-weighted MRI with contrast shows a bilobed rim enhancing mass involving the pectoralis major muscle and the chest wall muscles (arrows). (b) Sagittal T2-weighted MRI shows that the mass is hypointense (arrow) and associated with marked peritumoral edema. (c) Longitudinal gray-scale ultrasound shows that the mass is oval and hypoechoic (arrows). (d) Power Doppler ultrasound shows internal vascularity in the mass. Ultrasound-guided core biopsy showed a recurrent myoepithelial cancer.

## DISCUSSION

Although breast conservation surgery has comparable outcomes to mastectomy, in the past decade, patients with breast cancer have increasingly chosen to undergo mastectomy followed by breast reconstruction.<sup>[7]</sup> Immediate reconstruction with either autologous flaps, implants or a combination of the two has been shown to be effective and reliable with good cosmetic outcomes. Implant-based reconstruction is the preferred option for breast reconstruction nationwide due to the simplicity of the procedure, the shorter recovery time and no additional donor site morbidity, whereas autologous breast reconstruction is a labor-intensive surgery with a longer recovery time and additional donor site morbidities.<sup>[8,9]</sup> Nevertheless, known advantages of autologous breast reconstruction are greater patient satisfaction with a more natural-looking reconstructed breast and long-lasting results.<sup>[10]</sup> At our institution, 55% of the patients underwent autologous breast reconstruction in our series. The higher rate of autologous

breast reconstruction at our center is likely due to more available resources at a tertiary academic center as well as patient preferences.

While mastectomy removes most of the tissue in the breast, breast cancer may recur in the remaining tissue. Accordingly to Sharma *et al.*, significant predictors for local recurrence among patients who underwent breast reconstruction were patients younger than 40 years and larger tumor size.<sup>[11]</sup> In our study, 72.5% (29/40) of the patients were younger than 50-years-old at the time of the primary cancer diagnosis with 55% (22/40) of the cancers being stage II–III. Another factor reported to increase the risk for local-regional recurrence is the molecular subtype of breast cancer. Triple-negative breast cancers, which lack of ER, PR, and HER2 expression, have been reported to be at a higher risk of recurrence.<sup>[12–14]</sup> In our study, triple-negative breast cancer had the highest risk of recurrence, accounting for 42% of the recurrences.

Regarding the patterns and the locations of recurrence, 60% of the recurrences in our study were superficial, 32.5% were in a deep location and 7.5% were in a combined superficial and deep location. This compares with the literature in which superficial recurrences in autologous breast reconstructions comprised between 72% and 88% of the recurrences and deep recurrences occurred in 13–28% of patients.<sup>[15,16]</sup> Langstein *et al.* stated that superficial recurrences are recurrences with a better overall survival rate, whereas deep recurrences oftentimes have an ominous prognosis.<sup>[16]</sup> In our study, 77% of the deep recurrences were associated with distant metastases, whereas 32% of the superficial recurrences were associated with distant metastases. Since deep recurrences have a worse prognosis, imaging may be beneficial in the early identification of deep recurrences.

Most surgeons and plastic surgeons believe breast cancer recurrences in patients with reconstructed breasts can be easily detected by physical examination.<sup>[17–19]</sup> Although most of the breast cancer recurrences after reconstruction occur in the skin or in the subcutaneous tissues, where they are easily identified by palpation, the second most common site of relapse is deep, adjacent to the pectoralis muscle, where the autologous tissue or the pre-pectoral implant may conceal the recurrence. These more deeply situated recurrences require imaging to detect them at an early stage. In our study, 70% of recurrences were detected by palpation, 8% with redness/pain and 22% were clinically occult. The use of mammography has not been routinely advocated as a screening imaging modality for reconstructed breasts. In the subset of patients who have undergone implant-based reconstruction, mammography is of limited value as the implant might obscure small masses. According to the American College of Radiology appropriateness criteria, mammography might be beneficial in patients reconstructed with autologous reconstructions due to the transposed fatty flap that provides an excellent

contrast to detect an early abnormality in the reconstructed breast.<sup>[20]</sup> This is especially true if the abnormality is deeply located and clinically occult. In a recent study, screening mammograms were performed in autologous reconstructed breasts.<sup>[20]</sup> Of the 485 women, 390 (80.4%) underwent three rounds of screening mammography, and breast cancer recurred in 13 of the 485 patients.<sup>[21]</sup> Mammography detected five occult cancers, and the median size of the cancers in the screened group was 0.8 cm (range, 0.5–1.6 cm) versus 2.2 cm (range, 1.3–3.0 cm) ( $P = 0.001$ ) in the non-screened group.<sup>[21]</sup> The cancer detection rate was 1.5 cancers/1000 patients, with a sensitivity of 42% and a specificity of 99.4% in the screening mammography group.<sup>[21]</sup> The mammographic appearances of the recurrences were masses in 86% of the cases and masses associated with calcifications in 14% of the cases.<sup>[21]</sup> Although screening mammography is not advocated for surveillance of patients with breast reconstruction, mammography may be a useful screening modality in the subset of patients at high risk for local recurrence who have undergone autologous breast reconstruction. Additionally, mammography can be helpful in the work-up of masses with worrisome features on ultrasound to exclude fat necrosis, as mammography will depict typical features of fat necrosis.<sup>[22]</sup>

The mammographic features of breast recurrences in the reconstructed breast in our study were oval masses in 50% (3/6) and irregular masses in 50% (3/6). These findings are similar to the results reported by Yoo *et al.*, where 50% of the masses had a benign appearance.<sup>[15]</sup>

Ultrasound is often the imaging modality of choice for the work-up of palpable masses in patients with reconstructed breasts. In our study, ultrasound was performed in 35 patients with recurrences. Of those 35, 48.6% (17/35) of the masses were oval in shape and 51.4% (18/35) were irregular. About 82.8% of the masses (29/35) were hypoechoic, 8.6% (3/35) were heterogeneous, and 8.6% (3/35) were complex cystic and solid in echotexture. Edeiken *et al.*, in a study of recurrences noted on ultrasound, found that 87% of the masses were hypoechoic, 3% were heterogeneous and 2% were hyperechoic.<sup>[23]</sup> Ultrasound is a valuable and affordable imaging modality to detect and sample suspicious lesions for recurrence regardless of the type of breast reconstruction. It should be emphasized that the ultrasound appearance of many recurrent breast cancers may simulate benign lesions.

Breast MRI is the most sensitive modality to detect superficial and deep breast recurrences regardless of whether the patient has undergone implant-based or autologous reconstruction. Nine out of forty patients underwent breast MRI, and 56% (5/9) showed oval homogeneously enhancing masses, and 44% (4/9) showed irregular masses. Breast MRI is a valuable imaging modality in symptomatic patients where deep recurrence is suspected. In addition, breast MRI is critical in

the evaluation of deep recurrences to determine involvement of the pectoralis major muscle and the chest wall muscles.<sup>[24]</sup>

The median time in our study between the mastectomy and the recurrence in the reconstructed breast was 19.1 months (range, 1.6–63 months). The frequency of breast recurrence was similar to that noted in the published literature.<sup>[25,26]</sup> It is important to detect the recurrences earlier, as the smaller the size of the detected recurrence, the higher the probability of salvaging the reconstructed breast.<sup>[27]</sup> In our study, nine of 40 patients had recurrent cancer that was occult on physical exam; of those nine, seven patients with recurrent cancers are alive and two are dead. This highlights the importance of imaging surveillance besides a meticulous physical examination in patients with a high risk for recurrence. Although the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology guidelines do not recommend any imaging of the reconstructed breast,<sup>[28]</sup> mammography should be considered in autologous reconstructed breasts, and ultrasound can be performed in implant reconstructed breasts. Breast MRI is costly, and breast MRI can be reserved for women who carry multiple risks factors for recurrence such as young age, triple-negative histology, larger size of the primary breast cancer, or multicentricity. Breast MRI is also suggested in deep recurrences as the only imaging modality that can exclude invasion of the chest wall muscles. With advancing breast MRI technology, abbreviated breast MRI might be an option to offer as a cost-effective imaging modality to closely monitor these patients.

Limitations of this study include its retrospective nature and the small number of cases. In addition, we were unable to determine the total number of patients who had mastectomies followed by immediate or delayed reconstruction.

## CONCLUSION

Young and triple-negative breast cancer patients are at a higher risk of recurrence. This subset of patients likely requires imaging surveillance to detect early recurrences in the reconstructed breast. Although most recurrences in the reconstructed breast are superficial and detected by physical exam, deep recurrences are likely to be occult with a worse prognosis for the patient. The type of breast imaging modality selected to survey these patients may depend on the type of breast reconstruction and patient characteristics.

## Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

## Conflicts of interest

Gary Whitman is a member of the Editorial Board of the Journal of Clinical Imaging Science.

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