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

Beatriz Elena Adrada¹, Niloofar Karbasian², Monica Huang¹, Gaiane Maia Rauch³, Piyanoot Woodtichartpreecha⁴, Gary Whitman¹

¹Department of Breast Imaging, MD Anderson, Houston, Texas, United States, ²Department of Radiology and Biomedical Imaging, Yale School of Medicine, New Haven, Connecticut, ³Department of Breast and Abdominal Imaging, MD Anderson, Houston, Texas, United States, ⁴Department of Diagnostic Radiology, The Prince of Songkla University, Hat Yai, Songkhla, Thailand.

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. 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. As a result of the increasing trend of mastectomies followed by either implant-based or autologous...
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%.\textsuperscript{[1,4]} Local recurrence implies a worse prognosis with associated distant metastases in half of the patients.\textsuperscript{[4]} 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.\textsuperscript{[5]}

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 ≥10%. HER2 status was defined as 3+ by IHC or 2+ by IHC with a FISH ratio of ≥2.0 for HER2:CEP17 (chromosome 17 centromere) or single probe copy number of ≥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.\textsuperscript{[6]}

**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 margins       |                        |
| Circumscribed        | 7 (20)                 |
| Non-circumscribed    | 28 (80)                |
| Echogenicity         |                        |
| Hypoechoic           | 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 hypoechoic mass (arrows) correlating with the palpable abnormality. Ultrasound-guided core biopsy showed recurrent IDC.
In our study, significant predictors for local recurrence among patients who underwent breast reconstruction were patients younger than 40 years and larger tumor size. 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. 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. Langstein et al. stated that superficial recurrences are recurrences with a better overall survival rate, whereas deep recurrences oftentimes have an ominous prognosis. 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. 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 patient satisfaction with a more natural-looking reconstructed breast and long-lasting results.
contrast to detect an early abnormality in the reconstructed breast.\textsuperscript{[20]} 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.\textsuperscript{[20]} Of the 485 women, 390 (80.4\%) underwent three rounds of screening mammography, and breast cancer recurred in 13 of the 485 patients.\textsuperscript{[21]} 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) (\textit{P} = 0.001) in the non-screened group.\textsuperscript{[21]} 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.\textsuperscript{[21]} The mammographic appearances of the recurrences were masses in 86\% of the cases and masses associated with calcifications in 14\% of the cases.\textsuperscript{[21]} 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.\textsuperscript{[22]}

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 \textit{et al.}, where 50\% of the masses had a benign appearance.\textsuperscript{[23]}

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 \textit{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.\textsuperscript{[23]} 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.\textsuperscript{[24]}

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.\textsuperscript{[25,26]} 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.\textsuperscript{[27]} 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,\textsuperscript{[28]} 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.

\textbf{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.

\textbf{Declaration of patient consent}

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

\textbf{Financial support and sponsorship}

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

REFERENCES

1. US. Breast Cancer Statistics; 2021. Available from: https://www.breastcancer.org/symptoms/understand_bc/statistics [Last accessed on 2021 May 20].
2. Champaneria MC, Wong WW, Hill ME, Gupta SC. The evolution of breast reconstruction: A historical perspective. World J Surg 2012;36:730-42.
3. Fersis N, Hoening A, Relakis K, Pinis S, Wallwiener D. Skin-sparing mastectomy and immediate breast reconstruction: Incidence of recurrence in patients with invasive breast cancer. Breast 2004;13:488-93.
4. Romics L Jr., Chew BK, Weiler-Mithoff E, Doughty JC, Brown IM, Stallard S, et al. Ten-year follow-up of skin-sparing mastectomy followed by immediate breast reconstruction. Br J Surg 2012;99:799-806.
5. ACR Appropriateness Criteria® Imaging after Mastectomy and Breast Reconstruction. American College of Radiology; 2021. Available from: https://www.acsearch.acr.org/docs/3155410/ narrative [Last accessed on 2020 Jul 21].
6. D’Orsi CJ, Sickles EA, Mendelson EB, Morris EA. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston, VA: American College of Radiology; 2013.
7. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg 2015;150:9-16.
8. Gurunluoglu R, Gurunluoglu A, Williams SA, Tebockhorst S. Current trends in breast reconstruction: Survey of American society of plastic surgeons 2010. Ann Plast Surg 2013;70:103-10.
9. Lee GK, Sheckter CC. Breast reconstruction following breast cancer treatment-2018. JAMA 2018;320:1277-8.
10. Pusic AL, Matros E, Fine N, Buchel E, Gordillo GM, Hamill JB, et al. Patient-reported outcomes 1 year after immediate breast reconstruction: Results of the mastectomy reconstruction outcomes consortium study. J Clin Oncol 2017;35:2499-506.
11. Sharma R, Rourke LL, Kronowitz SJ, Oh JL, Lucci A, Litton JK, et al. Management of local-regional recurrence following immediate breast reconstruction in patients with early breast cancer treated without postmastectomy radiotherapy. Plast Reconstr Surg 2011;127:1763-72.
12. Casey WJ 3rd, Rebecca AM, Silverman A, Macias LH, Kreymerman PA, Pockaj BA, et al. Etiology of breast masses after autologous breast reconstruction. Ann Surg Oncol 2013;20:607-14.
13. Tsoutsou PG, Vozeni MC, Durham AD, Bourhis J. How could breast cancer molecular features contribute to locoregional treatment decision making? Crit Rev Oncol Hematol 2017;110:43-8.
14. Gabos Z, Thoms J, Ghosh S, Hanson J, Deschênes J, Sabri S, et al. The association between biological subtype and locoregional recurrence in newly diagnosed breast cancer. Breast Cancer Res Treat 2010;124:187-94.
15. Yoo H, Kim BH, Kim HH, Cha JH, Shin HJ, Lee TJ. Local recurrence of breast cancer in reconstructed breasts using TRAM flap after skin-sparing mastectomy: Clinical and imaging features. Eur Radiol 2014;24:2220-6.
16. Langstein HN, Cheng MH, Singletary SE, Robb GL, Hoy E, Smith TL, et al. Breast cancer recurrence after immediate reconstruction: Patterns and significance. Plast Reconstr Surg 2003;111:712-20; discussion 721-2.
17. Freyvogel M, Padia S, Larson K, Dietz J, Grobmyer S, O’Rourke C, et al. Screening mammography following autologous breast reconstruction: An unnecessary effort. Ann Surg Oncol 2014;21:3256-60.
18. Patterson SG, Teller P, Yengar R, Carlson GW, Gabram-Mendola SG, Losken A, et al. Locoregional recurrence after mastectomy with immediate transverse rectus abdominis myocutaneous (TRAM) flap reconstruction. Ann Surg Oncol 2012;19:2679-84.
19. Reddy S, Colakoglu S, Curtis MS, Yueh JH, Ogunleye A, Tobias AM, et al. Breast cancer recurrence following postmastectomy reconstruction compared to mastectomy with no reconstruction. Ann Plast Surg 2011;66:466-71.
20. Expert Panel on Breast Imaging. Heller SL, Lourenco AP, Niell BL, Ajkay N, Brown A, et al. ACR appropriateness criteria® imaging after mastectomy and breast reconstruction. J Am Coll Radiol 2020;17:S403-14.
21. Noroozian M, Carlson LW, Savage JL, Jeffries DO, Joe AL, Neal CH, et al. Use of screening mammography to detect occult malignancy in autologous breast reconstructions: A 15-year experience. Radiology 2018;289:39-48.
22. Adrada BE, Whitman GJ, Crosby MA, Carkaci S, Dryen DJ, Dogan BE. Multimodality imaging of the reconstructed breast. Curr Probl Diagn Radiol 2015;44:487-95.
23. Edeiken BS, Fornage BD, Bedi DG, Sniege N, Parulekar SG, Pleasure J. Recurrence in autogenous myocutaneous flap reconstruction after mastectomy for primary breast cancer: US diagnosis. Radiology 2003;227:542-8.
24. Peng C, Chang CB, Tso HH, Flowers CI, Hylton NM, Joe BN. MRI appearance of tumor recurrence in myocutaneous flap reconstruction after mastectomy. AJR Am J Roentgenol 2011;196:W471-5.
25. Medina- Franco H, Vasconez LO, Fix RJ, Heslin MJ, Beenken SW, Bland KI, et al. Factors associated with local recurrence after skin-sparing mastectomy and immediate breast reconstruction for invasive breast cancer. Ann Surg 2002;235:814-9.
26. Pinel-Groux FM, El Khoury MM, Trop I, Bernier C, David J, Losken A, et al. Outcome of patients with previous breast reconstruction following re-reconstruction. Plast Reconstr Surg 2013;132:322-30.
27. National Comprehensive Cancer Network, Incorporated; 2021. Available from: https://www2.tri-kobe.org/nccn/guideline/breast/english/breast.pdf [Last accessed on 2021 Sep 21].

How to cite this article: Adrada BE, Kurbasian N, Huang M, Rauch GM, Woodichartpreecha P, Whitman G. Imaging surveillance of the reconstructed breast in a subset of patients may aid in early detection of breast cancer recurrence. J Clin Imaging Sci 2021;11:58.