Digital Mammographic Features of Breast Cancer Recurrences and Benign Lesions Mimicking Malignancy Following Breast-Conserving Surgery and Radiation Therapy

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Summary: Mammography after breast-conserving surgery and radiation therapy is an important tool for follow-up. Early diagnosis of local recurrence enables prompt treatment decisions, which may affect patient prognosis. For complicated post-treatment changes, radiologists sometimes have difficulties in interpreting follow-up mammography. Fat necrosis, dystrophic calcifications, suture calcification features, breast edema, seroma and distorted breast are benign changes related to treatment. These findings may mimic or hide tumor recurrence making it difficult to diagnose recurrences or prevent inappropriate biopsies. Recurrent tumors in follow-up mammography show several typical findings such as increasing asymmetric density, enlarging mass, reappearance of breast edema, and micro-calcifications. The purpose of this pictorial review is to demonstrate and discuss mammographic findings of recurrent tumors and important post-treatment changes that may mimic benign or malignant lesions, also using breast ultrasound images or breast magnetic resonance images. Recognizing post-treatment changes may help radiologists to more effectively identify candidates for suspected local recurrences.

Key words breast cancer, breast-conserving surgery, radiation therapy, digital mammography, recurrence

INTRODUCTION

Mammography after breast-conserving surgery (BCS) and radiation therapy (RT) is an important surveillance tool for assessment of local control. In Japanese populations, the 3- to 4-year local recurrence rate is only around 3% in patients with BCS and RT [1, 2], but early detection of local recurrences with post-treatment mammography (PTMG) may lead to successful salvage therapy and improved outcomes [3-10]. The clinical guidelines of various cancer committees recommend annual routine mammography after BCS (Table 1) [7,11,12]. The most recent recommendation from the American Society of Clinical Oncology and National Comprehensive Cancer Network suggests that patients should receive their first PTMG at least 6 months after completion of RT [13,14]. Thereafter, they recommend subsequent PTMG to be obtained every 6 to 12 months. The Italian Group for Mammography Screening and the Italian College of Breast Radiologists recommend that
women previously treated for breast cancer should receive annual mammography for dedicated sessions starting from the year after completion of treatment for 10 years and more [15]. The Japanese Breast Cancer Society also recommends PTMG, but adequate timing and intervals of PTMG are not indicated. On the other hand, the European Society for Medical Oncology (ESMO) [16] recommends receiving annual mammography with ultrasound. However, there are no data to indicate that the use of other imaging modalities, including ultrasound, CT, FDG-PET, and breast MR, yields a survival benefit [13-17]. Therefore, PTMG may be a singular useful imaging modality for follow-up.

However, complicated changes of the breast occur and evolve over time in PTMG. Radiologists sometimes face difficulty in interpreting benign changes which may mimic and hide tumor recurrence in PTMG [18,19]. Identifying post-treatment changes more efficiently will improve the interpretation of PTMG and make it easier to identify recurrent lesions and prevent inappropriate biopsies for benign lesions. This pictorial review shows both benign mammographic findings and recurrences by comparing serial mammography, US, and MR images.

### TABLE 1.

*Mammographic guidelines of surveillance after breast conserving surgery and radiation therapy for primary breast cancer patients.*

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Year</th>
<th>Initial mammography</th>
<th>Mammography after 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Society of Clinical Oncology</td>
<td>2012</td>
<td>6 months after completion of RT</td>
<td>Annual mammography</td>
</tr>
<tr>
<td>National Comprehensive Cancer Network</td>
<td>2015</td>
<td>6 to 12 months after completion of breast conserving therapy</td>
<td>Annual mammography</td>
</tr>
<tr>
<td>Italian Group for Mammography Screening and Italian College of Breast Radiologists</td>
<td>2016</td>
<td>The year after completion of treatment</td>
<td>Annual mammography with possible addition of supplemental mammographic views, digital breast tomosynthesis, clinical breast examination, breast ultrasound and prompt planning of possible further workup</td>
</tr>
<tr>
<td>European Society of Medical Oncology</td>
<td>2015</td>
<td></td>
<td>Annual ipsilateral (after breast conserving therapy) and/or contralateral mammography with ultrasound recommended</td>
</tr>
<tr>
<td>Canadian Medical Association</td>
<td>2005</td>
<td></td>
<td>Annual mammography</td>
</tr>
<tr>
<td>National Institute for Clinical Excellence</td>
<td>2009</td>
<td></td>
<td>Annual mammography</td>
</tr>
</tbody>
</table>

**FAT NECROSIS**

Fat necrosis is known to develop as a result of accidental breast trauma [20]. After the spread of BCS and RT for breast cancer patients, fat necrosis has become commonly seen in PTMG [21-27]. Lovey et al. [23] reported that the 4-year actuarial rate of fat necrosis was 31.9, 36.5, and 17.7% after BCS with conventional whole breast irradiation, interstitial high-dose-rate brachytherapy, and external beam partial breast irradiation with electrons, respectively. Radiological and histopathological appearances of fat necrosis differ between early and late periods [28]. Fat necrosis appears early as an area of hemorrhage within fat. Fibrosis forms a rim surrounding the fat necrosis with fibroblasts in the following months or years [21,26,28]. In the late period, it shows various appearances caused by differences in the degree of histiocytic infiltration, hemorrhage, fibrosis, and calcification [21]. In PTMG, oil cysts and dystrophic calcifications reflecting fat necrosis are diagnosed as typically benign lesions. On the other hand, fat necrosis shown as focal asymmetric densities, micro-calcifications, or spiculated masses mimicking recurrences [28] may be diagnosed as probably benign, suspicious of recurrences, or highly suggestive of recurrences.

Oil cysts show a radiolucent low-density mass
with a circumscribed margin (Fig. 1a). This low-density area is caused by necrotic fat [21]. The circumscribed rim is formed by minimal fibrosis [26,28] and some oil cysts show rims with linear, curvilinear, or egg-shell-like calcifications along the fibrosis (Fig. 1b) [18,21]. These oil cysts lead to diagnosis of typically benign lesions [29].

Dystrophic calcifications may occur in older fat necrosis [21]. These coarse dystrophic calcifications (Fig. 2a) are judged as typically benign lesions [29]. In the course of the completion of the coarse calcifications, fat necrosis uncommonly forms a group of clustered micro-calcifications (Fig. 2b, arrows) with amorphous, pleomorphic, or fine linear branching.

**Fig. 1.** Fat necrosis as a typically benign finding.
(a) Nine months after completion of radiation therapy, a lobular circumscribed low-density mass (arrowheads) was seen in mammography.
(b) Five years after treatment, mammography revealed an oval circumscribed low-density mass with peripheral coarse calcifications (arrowheads).
(c) Two years and 6 months after treatment, a US image showed a lobular indistinct hypoechoic mass.
(d) A US image 5 years after treatment shows a cystic area (arrow) in the lobular indistinct hypoechoic mass.
(e) A T1-weighted axial unenhanced MR image shows a round circumscribed high-intensity mass (arrow) beside the surgical scar.
(f) The mass is suppressed similarly to fat on a T1-weighted fat suppressed MR image.
(g) A subtracted Gd-enhanced image shows a thin rim enhancement (arrow).

**Fig. 2.** Dystrophic calcification as a typically benign finding.
(a) Six years after treatment, mammography showed coarse lucent centered calcifications as a typically benign lesion on and around the skin.
(b) Four years before Figure 2a, mammography showed a group of micro-calcifications (arrowheads) and coarse calcifications (arrow). These calcifications surround the thickened skin, and the focal high-density area suggests fluid collection.

**Fig. 3.** Suture calcifications as a typically benign finding.
Thirteen years after treatment, mammography showed regional curved-linear calcifications in the post-breast conserving surgery bed.
morphologies [18,21,29,30]. Reviewing previous successive PTMG images and detecting oil cysts with typically benign appearances may help to diagnose fat necrosis in cases of suspicious malignant calcifications.

When the fat necrosis is diagnosed as oil cysts or dystrophic calcifications, simple observation is recommended. In cases without obvious indication of fat necrosis, further precise imaging examinations, like US and MR, are needed. In US, fat necrosis shows variable findings which reflect the degree of fibrosis [26]. Specifically, fat necrosis is shown to be a mass with echogenic internal bands that shift in orientation with changes in patient position. These internal bands may reflect the interface between the lipid and serous-hemorrhagic components of fat necrosis. We also found that fat necrosis may be a solid mass (Fig. 1c), a complex of cystic and solid mass (Fig. 1d), an anechoic cystic mass with posterior features, or an isoechoic mass [26]. In MR, the most common appearance of fat necrosis is a round or oval mass with central hypointensity in T1-weighted fat-saturated images (Fig. 1f, arrow) and short inversion time inversion recovery images [31,32]. A thin rim of enhancement (Fig. 1g, arrow) is common [31,33]. A correlation between PTMG, US, and MR may often be helpful to diagnose fat necrosis [33,34]. However, fat necrosis shows a wide spectrum of findings, and biopsy may be required if typical fat necrosis is not identified in any imaging modality.

SUTURE CALCIFICATIONS

Suture calcifications represent calcium deposited on suture materials and show a curved-linear, tubular, or knot-like shape (Fig. 3) as final forms on or around sutures [18,27,29,35,36]. They may form a group of amorphous, fine pleomorphic, or fine linear microcalcifications to mimic malignancy. There are currently no reports of suture calcifications in other imaging modalities including US and MR. Typical suture calcifications need no additional image examinations.

BREAST EDEMA, SKIN THICKENING, AND TRABECULAR THICKENING

Nearly all patients have breast edema after BCS and RT. PTMG shows a global asymmetry-like high density area caused by edema in the early period [27]. Skin thickening and linear trabecular thickening (Fig. 4a) also appear to be related to breast edema caused by postoperative and radiation-induced damage of the

Fig. 4. Skin thickening as a typically benign lesion. (a) Three months after the completion of radiation therapy, mammography showed skin thickening and linear trabecular thickening. (b) The skin returned to near-normal thickness. Trabecular thickening improved 3 years after Figure 4a. (c) Skin thickening and edema changes were seen in a US image 3 months after the completion of radiation therapy. (d) Skin thickening and edema changes were seen in an MR image 4 months after the completion of radiation therapy.
small vessels [18]. Thereafter, these findings gradually diminish and disappear within 2 years after treatment [27]. The skin returns to near-normal thickness (Fig. 4b) within a few years, although mild thickening persists in some patients [27]. These findings return to normal and are typically benign findings with no need for any additional imaging examinations. On follow-up breast US (Fig. 4c) or MR (Fig. 4d) after BCS, skin thickening and edema changes are shown as posttreatment findings progressively decreasing over time [37].

SEROMA

Seroma is a serous fluid collection within the breast parenchyma after BCS [38] seen in the early period. The etiology is suggested to be multifactorial, including surgically-created dead spaces, extended axillary surgery, disorder of lymphatic and vascular flows, and delayed wound healing [39, 40]. Seroma occurs in 9–15% of patients after BCS with RT [41, 42]. They show an oval or round circumscribed non-calcified solid mass (Fig. 5a) [18] in PTMG. They may be diagnosed as benign. MR images 6–12 months after treatment show seroma in 31.6% [37]. The signal pattern of the seroma is simple fluid, hematoma, fat, or a mixture of these components (Fig. 5b–d). Enhancement related to the seroma cavity was seen in 59.6% of seromas in the early period [37]. US is a helpful tool to diagnose seroma (Fig. 5e) [40, 43]. It shows a complex cystic mass with a solid mass in an anechoic cyst, which represents resolving postoperative hematomas [18, 44]. Seromas usually tend to diminish in size and density over time and are replaced by scarring and fibrosis to mimic breast cancer. Seroma may reaccumulate or remain [45]. Follow-up to confirm shrinkage or stability of seroma using US is desirable (Fig. 5f).

Fig. 5. Seroma as a probably benign lesion
(a) Mammography 1 year after treatment showed an oval circumscribed non-calcified solid mass.
(b) A short inversion time inversion recovery MR image shows high signal intensity with partial septa (arrow)
(c) A T1-weighted fat-saturated unenhanced MR image shows a focal high signal intensity consistent with blood.
(d) A T1-weighted fat-saturated enhanced MR image with subtraction shows homogeneous rim enhancement around a seroma cavity.
(e) A US image shows a well circumscribed complex mass with a hypo-echogenic septated cystic part and a hyper-echogenic solid part.
(f) A US image shows a shrunken cystic mass with a hyper-echogenic solid nodule.
DISTORTION, SCAR AND SKIN RETRACTION

Architectural distortion develops secondary to postsurgical scars due to diminished seroma or fat necrosis [18,43]. Complexes of the skin, parenchyma, and fat tissue are distorted by cicatrical contracture around the resected tissues. These changes appear as distortions, scars, or skin retractions (Fig. 6) in PTMG. A feature of postsurgical distortion is the absence of a central mass, with changed forms in different projections [18,27,43]. These are typically benign findings that differ from recurrences. Distortion usually relaxes or stabilizes over a 2-year period [18], and observation

![Figure 6](image6.png)

**Fig. 6.** Distortions and skin retractions as typically benign lesions.
(a) Three years after treatment, distortion and skin retraction were seen in mammography. (b, c) A short inversion time inversion recovery MR image (b) and a T1-weighted MR image (c) show linear low signal intensity (arrows) with skin and nipple retraction without mass.

![Figure 7](image7.png)

**Fig. 7.** Local recurrence as a suspicious recurrent lesion.
(a) Four years after treatment, mammography revealed an asymmetric high-density area.
(b) A US image showed a round indistinct hypo-echoic mass. Re-operation was performed. Histopathologic analysis revealed the recurrence of invasive ductal carcinoma.

![Figure 8](image8.png)

**Fig. 8.** Local recurrence as a suspicious recurrent lesion.
(a) One year after treatment of mucinous carcinoma, thickened skin (arrow) was shown as a benign change in mammography.
(b) Two years after treatment, further thickened skin (arrow) was seen and misdiagnosed as benign changes. This finding continued for 2 years.
(c) A short inversion time recovery MR image shows a very high signal intensity mass.
(d) A T1-weighted fat-saturated enhanced MR image shows a rim enhancement and slight internal heterogeneous enhancement. Re-operation was performed. Histopathologic analysis revealed recurrence of mucinous carcinoma.

![Figure 9](image9.png)

**Fig. 9.** Skin metastases spread with lymphatic invasion from primary breast cancer.
(a) One year after treatment, trabecular thickening was shown as a suspicious recurrent lesion in the affected breast (triangle) with erythema and ulcers on the skin (not shown).
(b) A US image shows skin thickening, subcutaneous multiple echogenic foci with posterior acoustic shadow (arrows), and breast edema with tubular and reticular anechoic structures.
is recommended. In US, scars show irregular or spiculated margined hypoechoic structures with posterior echo enhancements and architectural distortion [46]. In MR, scars show distorted parenchyma and skin retraction without mass (Fig. 6) [33].

**RECURRENCES**

Recurrences in or around the post-BCS bed may be caused by failure to eradicate the primary tumor and represent residual lesions within a few years after treatment. Recurrences more than 10 years after treatment are more likely to occur outside the postoperative bed and likely represent new metachronous cancer [19]. Approximately 50% of recurrences are detected by mammography, while the rest are detected by clinical examination or reported by the patient [47]. Benign changes may cause misdiagnoses as recurrences, and Houssami et al. [48] reported that the sensitivity of ipsilateral recurrence after BCS with radiation therapy was 64% in PTMG.

Recent tumors show several typical findings including increasing asymmetric density (Fig. 7), enlarging mass (Fig. 8), reappearance of breast edema-related change (Fig. 9), and micro-calcifications [19]. The morphology of micro-calcification in recurrences appear on mammography as amorphous, pleomorphic, or linear calcifications (Fig. 10) [49,50]. Recurrences may or may not have similar mammographic features as the original lesion. Guenhan-Bilgen et al. [50] reported that 66% of recurrences showed mammographic findings similar to those of primary tumors. Pinsky et al. [49] reported that 94% of recurrences had calcifications similar to those in the initial DCIS. Comparison of MGs of the unaffected and previously affected breasts may help detect recurrences [50].

US did not yield a higher detection rate than mammography, although combined surveillance with US and mammography detected metachronous ipsilateral recurrence slightly earlier than mammography alone [51]. To our knowledge, there have been no studies comparing the accuracy of mammography and MR for surveillance of ipsilateral recurrences in patients after BCS with RT. Some studies indicate the superiority of MR over mammography for early detection, although these study populations included ipsilateral recurrences and/or contralateral primary tumors in patients who received mastectomy or BCS with or without RT [7, 52-54]. Biopsy is required when mammography shows suspicious or highly suggestive findings of recurrence [19,50,55]. When mammography shows indeterminate findings, MR may distinguish posttreatment changes from recurrences [19].

**CONCLUSION**

PTMG sometimes shows complicated benign changes that mimic local recurrence and diagnosis can be a challenge in daily practice. Awareness of typical benign changes will help to appropriately identify recurrences to improve outcomes and avoid unnecessary biopsy.
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