Chapter 18
Radiation Therapy

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18.1 Introduction

It has been long established that postsurgical radiotherapy reduces the risk of locoregional failure. A survival advantage, however, has recently also been demonstrated [1, 2]. Therefore, some women with breast cancer will need radiation therapy, in addition to other treatments, as summarized below:

- After breast-conserving surgery (BCS) to reduce locoregional failure in the same breast or nearby lymph nodes. Breast radiotherapy is recommended in patients with invasive breast cancer treated with breast-conserving surgery where complete microscopic excision has been achieved, unless life expectancy is less than 3 years due to comorbidities.
- This approach has enormously improved the quality of life and cosmetic outcome for appropriately selected and treated patients while achieving excellent long-term survival rates.
- After a mastectomy, especially if the cancer was large (T3/T4), if cancer is found in many lymph nodes, or if certain surgical margins have cancer such as the skin or muscle.
- The need for radiotherapy in patients with ductal carcinoma in situ (CDIS) can be guided by use of the Van Nuys Prognostic Index (VNPI) score that accounts for tumor size, grade, margin, presence of necrosis, and patient age.
- If cancer has spread to other parts of the body, such as the bones or brain.

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18.2 Imaging Findings

Before addressing the findings expected after radiotherapy, it is important to reinforce that since radiotherapy generally follows surgical treatment, the findings of these two procedures often overlap. Besides that, imaging the treated breast presents challenges due to its limited compressibility and the overlapping features of benign posttreatment alterations and tumor recurrence, as described below.

18.2.1 Mastectomy

After any type of mastectomy procedure, most of the breast cells are removed. However, there is a chance of a small amount of breast tissue remaining, and therefore the chance of recurrence exists. The rate of recurrence at the chest wall following mastectomy is between 5% and 27%.

Recurrence involving the chest wall or skin can frequently be detected on clinical or breast self-exam, as they are often obvious changes such as palpable masses, skin thickening, retraction, edema, and redness. The addition of US to clinical exams may prove to be more accurate than mammography when evaluating a palpable or visible abnormality, as recurrence tends to be small and close to the skin surface. Magnetic resonance imaging (MRI) is another imaging tool that can be used to evaluate the mastectomy site and plays an important role in detecting recurrent lesions.

For the asymptomatic patients, there is a continuing debate concerning imaging following mastectomy, because it is said that imaging modalities may not be helpful after this kind of surgery. So the findings commonly associated with this type of surgical procedure, followed or not by radiation therapy, will not be addressed in this chapter.

18.2.2 Breast Conservation Surgery

Breast conservation treatment achieves local tumor control by the surgical removal of the cancer with margins and is usually followed by radiation therapy. The combination of conservative surgery and radiation therapy offers the advantage of preserving the breast, usually with a satisfactory cosmetic result. Given equivalent survival rates for breast conservation therapy and mastectomy, breast conservation therapy has become the treatment of choice for early-stage breast cancer.

However, radiologists are faced with increased imaging and diagnostic challenges when dealing with the conservative treated breast. The treated breasts may be difficult to position adequately and to compress sufficiently due to surgical deformities, pain, or radiation changes. Also, the interpretation of imaging findings can be difficult because imaging features after treatment may mimic or hide tumor recurrence [3, 4].

The findings after lumpectomy and radiation therapy often overlap, and it is important to recognize that radiation therapy often intensifies and delays resolution of postsurgical changes [3, 4].

Although certain posttreatment alterations may persist, most changes after breast conservation therapy diminish and regress over time and then remain stable. Stability, defined as the lack of interval change on two successive studies, usually occurs at 2–3 years after the completion of radiation therapy, which is around the same time tumor recurrences typically begin to appear [5]. After stability has been achieved, any increase in the changes, development of new asymmetries, or calcifications should raise suspicion for tumor recurrence [4].

It is important to acknowledge that both surgery and radiotherapy alter the appearance of the breasts and sometimes distinguishing between recurrence and benign postsurgical changes can be challenging due to overlapping features. Despite this, differentiation between these two entities is usually possible by recognizing characteristic features of posttreatment sequelae and the evolution of the appearance of the conservatively treated breast by comparing interval findings on serial studies. There is an expected chronological appearance for these findings on the conservatively treated breast, as described below (Fig. 18.1).

The most common posttreatment findings that include breast edema, skin thickening, fluid collections, fat necrosis, architectural distortion, and calcifications [3, 6] will be revised and illustrated.

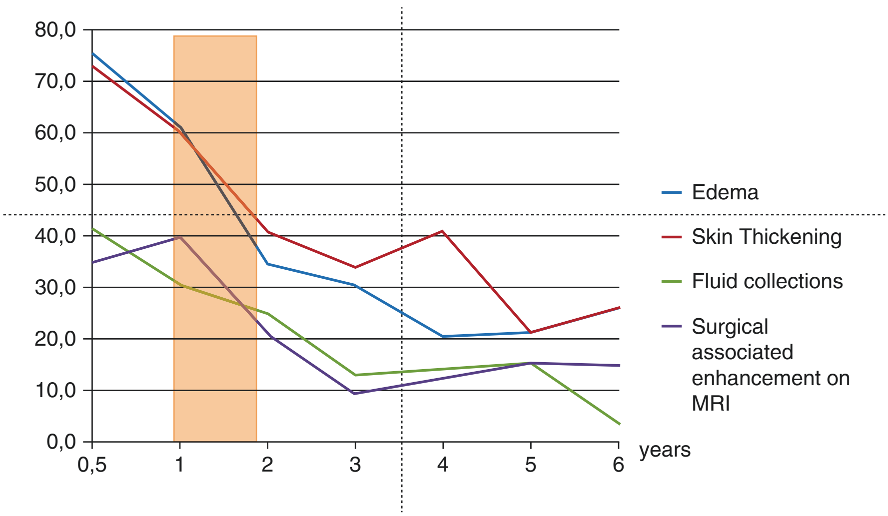

Fig. 18.1 Expected chronological appearance of the surgical findings on the conservatively treated breast

18.2.2.1 Fluid Collections

A common finding on posttreatment mammography is fluid collections at the lumpectomy site. Dead space is often intentionally left at surgery of a malignant breast neoplasm to allow fluid to fill in the space and, in this way, achieve better cosmesis [3].

Fluid with or without blood which collects in the postoperative cavity appears on mammography as an oval or round circumscribed or obscured mass that is most commonly seen within the surgical bed and should not be confused with recurrent tumor (Figs. 18.2 and 18.3).

Sonography of these collections often reveals a complex cystic mass with septations, loculations, thick walls, or a combination of these findings (Figs. 18.2 and 18.3).

Approximately half of breast cancer patients have fluid collections at the surgical site at 4 weeks after surgery and about 25% at 6 months. Over subsequent months, postoperative seromas, and hematomas are gradually resorbed and are replaced by scarring and fibrosis.

Fluid collections generally diminish in size over time and resolve completely by 12–18 months after surgery, although they may persist in a minority of patients. Any increase in the size of a fluid collection over time should alert the radiologist to a possible recurrence.

18.2.2.2 Breast Edema and Skin Thickening

Breast edema and skin thickening are posttreatment findings with similar time courses for appearance and regression. Typically, post-lumpectomy edema is localized to the area of the incision, and breast edema from radiation therapy usually encompasses the entire breast.

Breast edema may present as more of an accentuated trabecular pattern or as overall increased breast density depending on the degree of the edema (Figs. 18.4 and 18.5). The perceived increased density in the irradiated breast may also be explained by suboptimal exposure because the treated breast often is swollen and less compressible.

Skin thickening during the period after radiation is secondary to breast edema from the damage of small vessels. Skin thickening is the most common finding after breast-conserving therapy, reported in up to 90% of patients. Normal skin thickness of the breast as seen on mammograms is 2 mm. The skin thickness after radiation therapy may reach 1 cm or more (Figs. 18.4 and 18.5).

Breast edema and skin thickening are best appreciated when compared with the contralateral breast or with pretreatment mammograms (Figs. 18.4 and 18.5).

At mammography, maximal breast edema and skin thickening are usually seen during the first 6 months after completion of radiation therapy. These alterations then diminish and attain stability within 2–3 years.

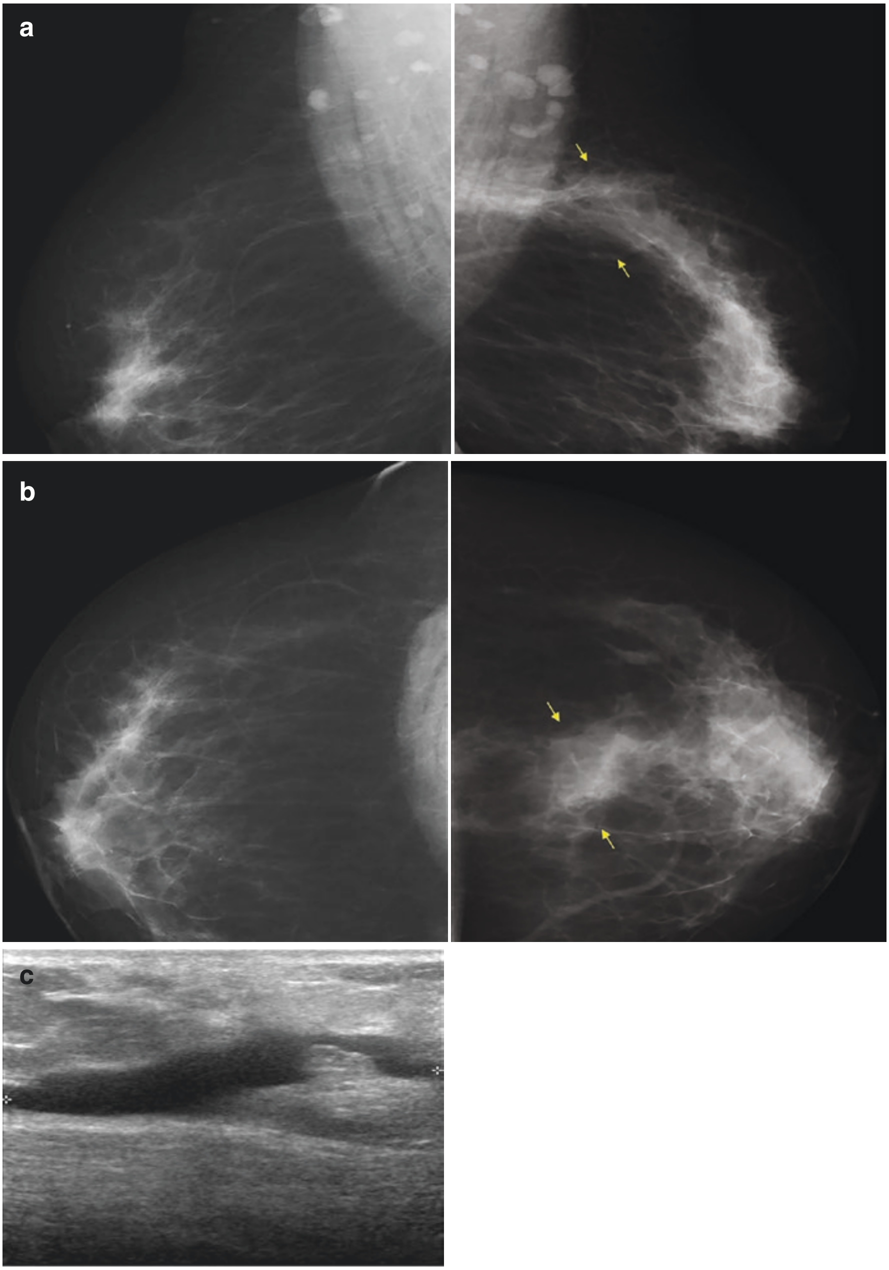

Fig. 18.2 Postoperative seroma in a 62-year-old woman with history of invasive left breast carcinoma. Mediolateral oblique (**a**) and craniocaudal (**b**) mammograms obtained 6 months after radiation therapy show an ill-defined mass in upper outer left breast consistent with postoperative seroma (arrows). The ultrasound image (**c**) shows a complex solid-cystic mass. These findings are consistent with postoperative seroma given history of breast conservation therapy in this area

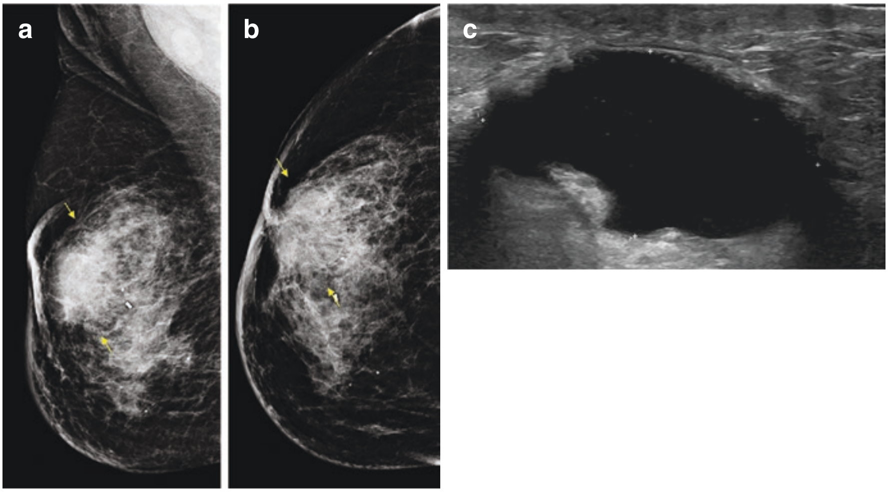

Fig. 18.3 Postoperative seroma in a 44-year-old woman with history of in situ right breast carcinoma. Mediolateral (**a**) and craniocaudal (**b**) mammograms obtained 6 months after radiation therapy show an obscured oval mass in upper outer right breast consistent with postoperative seroma (arrows). Increased breast density and skin thickening can also be seen. The ultrasound image (**c**) shows a complex solid-cystic mass with thick walls. These findings are consistent with postoperative seroma given history of breast conservation therapy in this area

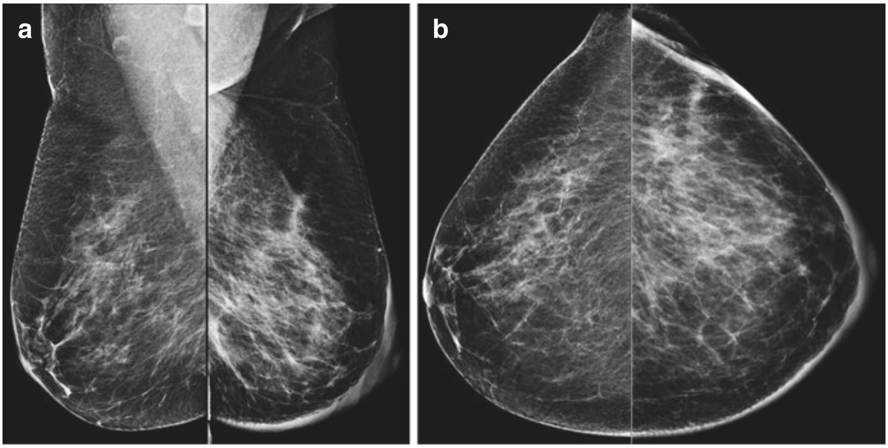

Fig. 18.4 Breast edema and skin thickening due to radiation therapy in a 74-year-old woman with history of invasive left breast carcinoma. Mediolateral oblique (**a**) and craniocaudal (**b**) mammograms of the right and left breasts obtained 1 year after radiation therapy show increased breast density and skin thickening of the left breast

Edema or skin thickening that increases after stability has been achieved should alert radiologists to the need for further investigation. The differential diagnoses of recurrent or worsening breast edema include lymphatic spread of cancer, obstructed venous drainage, congestive heart failure, and infection.

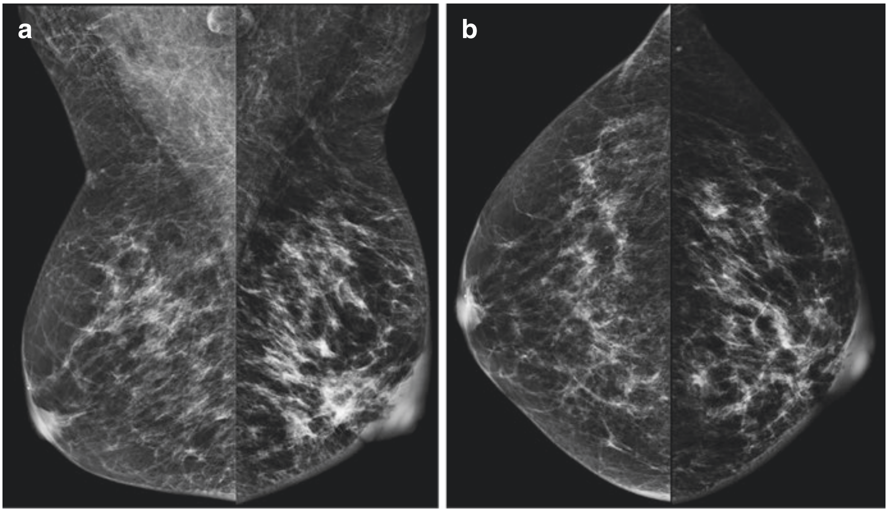

Fig. 18.5 Breast edema and skin thickening due to radiation therapy in an 80-year-old woman with history of invasive left breast carcinoma. Mediolateral oblique (**a**) and craniocaudal (**b**) mammograms of right and left breasts obtained 3 years after radiation therapy show increased breast density and skin thickening of the left breast, which is most prominent in the periareolar area

18.2.2.3 Fat Necrosis

Fat necrosis of the breast is a benign entity which may be seen after trauma, surgery, and radiotherapy, among other conditions [6–8]. Clinically, the patients may be asymptomatic or may present with a palpable lump, skin tethering, and induration.

In imaging studies, the appearance of fat necrosis ranges from typically benign to worrisome for malignancy, depending on the time at which diagnostic imaging is performed. This is directly related to whether inflammation or fibrosis is predominating within the lesion, and correlation with clinical history is very important for the correct evaluation of these lesions [6].

The classically benign appearing mammographic findings for fat necrosis are the oil cysts, which are masses with central lucency. These oil cysts may be accompanied by peripheral rim or "eggshell" calcifications (Fig. 18.6).

The presence of calcifications on mammography suggests that most of the calcifications will evolve to a dystrophic morphology as the lesions become older. At the beginning of the calcification process, sometimes we can intercept pleomorphic or amorphous appearing calcifications on mammography.

Fat necrosis appearing as suspicious noncalcified masses may demonstrate increased density due to progressive parenchymal fibrosis resulting in an ill-defined, spiculated mass on mammography, and biopsy may be warranted for the adequate diagnosis.

Fat necrosis ranges from simple cyst to complex cystic or solid masses on sonography (Fig. 18.7). As the appearance of fat necrosis can be undetermined

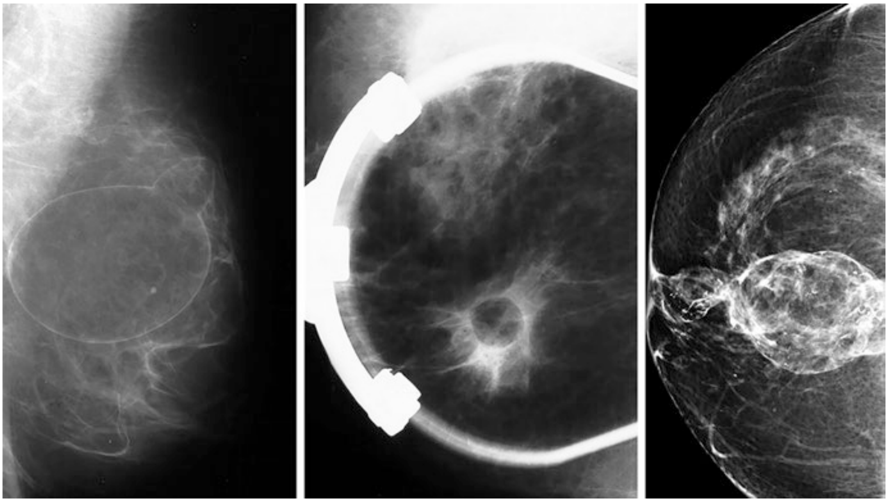

Fig. 18.6 Different examples of fat necrosis on mammography

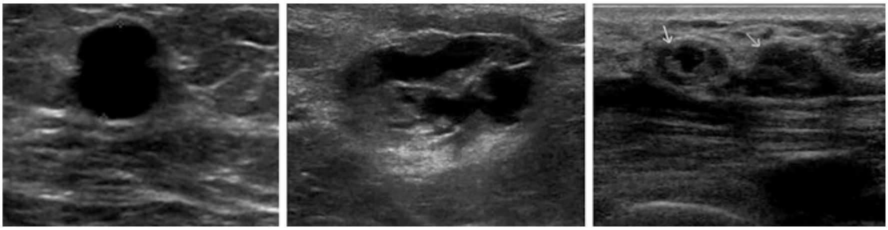

Fig. 18.7 Different examples of fat necrosis on ultrasound

on ultrasound, whenever we are faced with complex or inconclusive masses in a posttreated breast, mammographic correlation is essential for their proper evaluation.

The amount of inflammatory reaction, presence of liquefied fat, and the degree of fibrosis determine the varying findings of fat necrosis on MRI (Fig. 18.8). Administration of contrast may result in enhancement, particularly during the early stages of the inflammatory process. The presence of fat signal on MRI findings usually suggests its benignity.

Nonfatty signal intensity irregular masses with variable enhancement patterns are likely a reflection of the later stages of fat necrosis, when the fibrotic chances are more prominent.

In summary, mammography is more specific than sonography, and emphasis should be placed on mammography in making the diagnosis of fat necrosis. In selected cases, MRI may be helpful in showing findings consistent with fat necrosis, especially when fat signal can be detected inside the imaging findings.

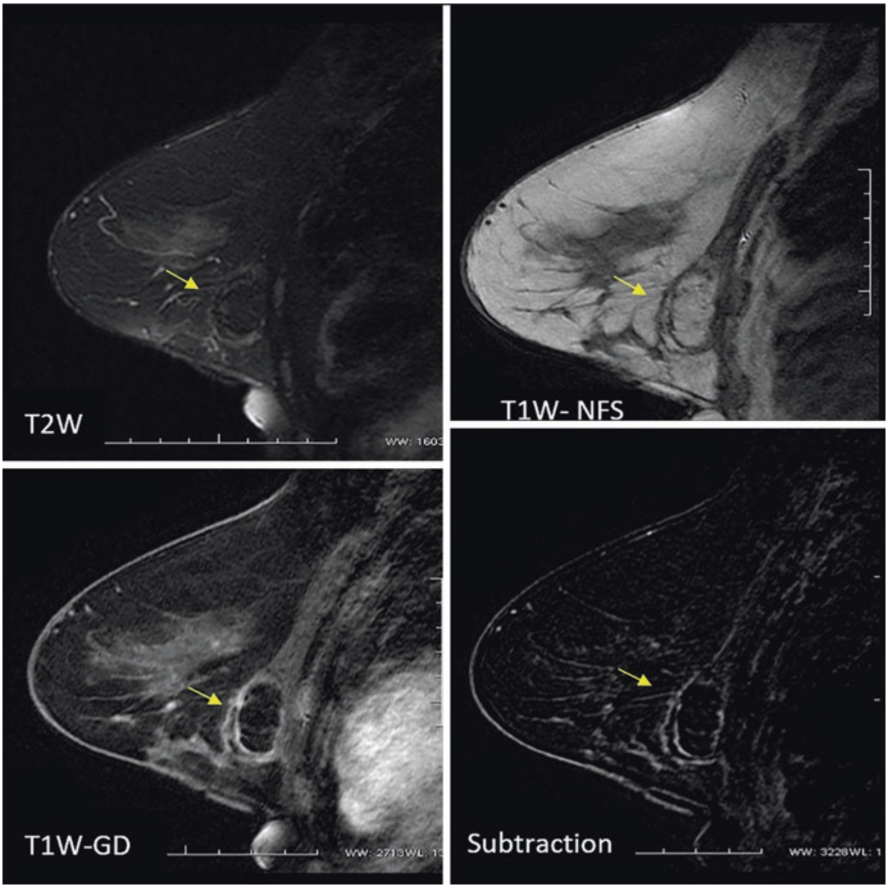

Fig. 18.8 Fat necrosis on MRI. T1-weighted nonfat-saturated image (NFS) shows a hyperintense circumscribed mass with a hypointense rim (arrow). The mass signal is similar to the adjacent fat, characteristic of fat necrosis. Sagittal T1-enhanced and fat-suppressed and subtraction images show the fat-containing mass with a non-enhancing thin fibrous rim (arrow)

18.2.2.4 Architectural Distortion

Architectural distortion in the treated breast develops secondary to scar formation and fat necrosis. Architectural distortion is commonly seen in the lumpectomy bed and within the lower axilla if sentinel node biopsy or axillary node dissection was performed (Fig. 18.9).

Parenchymal scarring and fat necrosis can cause an irregular spiculated or indistinct mass, associated with skin retraction that mimics recurrent malignancy.

However, the presence of the following mammographic features is more likely to suggest benign architectural distortion rather than tumor recurrence: the presence of

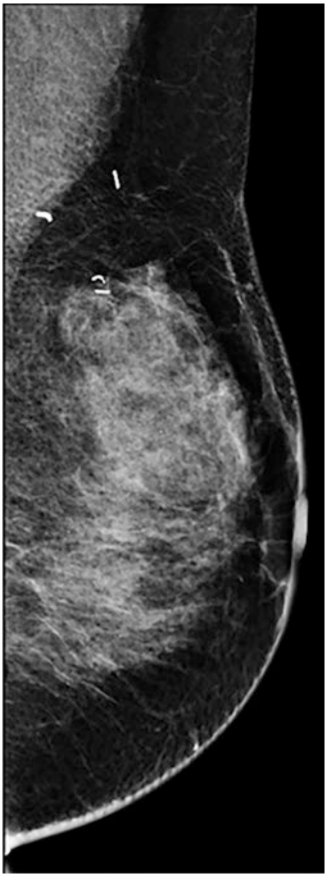

Fig. 18.9 Mediolateral oblique mammogram of the left breast shows post lumpectomy site as an area of architectural distortion in the upper quadrant. Surgical clips delineate site of tumor removal

central lucencies; a changing appearance on different projections; and thick, curvilinear spiculations [3] (Fig. 18.10).

Central lucencies suggest scarring because they represent fat trapped by fibrous stranding in the scar. These differentiating features can often be helpful, although they are not always reliable. For instance, some breast carcinomas, notably, infiltrating lobular, may contain central lucencies and may not have a central mass.

Architectural distortion usually diminishes in conspicuity and stabilizes over a 2-year period. In evaluating suspicious lesions, spot compression, magnification, and tomosynthesis views are helpful in showing the features of scarring and in excluding recurrent tumors.

Annual follow-up mammograms are necessary to show the sequential decrease in the size and prominence of the density to ensure its benignity. If the scar grows in size or if it becomes denser or more mass like, recurrent tumor should be suspected and should prompt biopsy [4, 9].

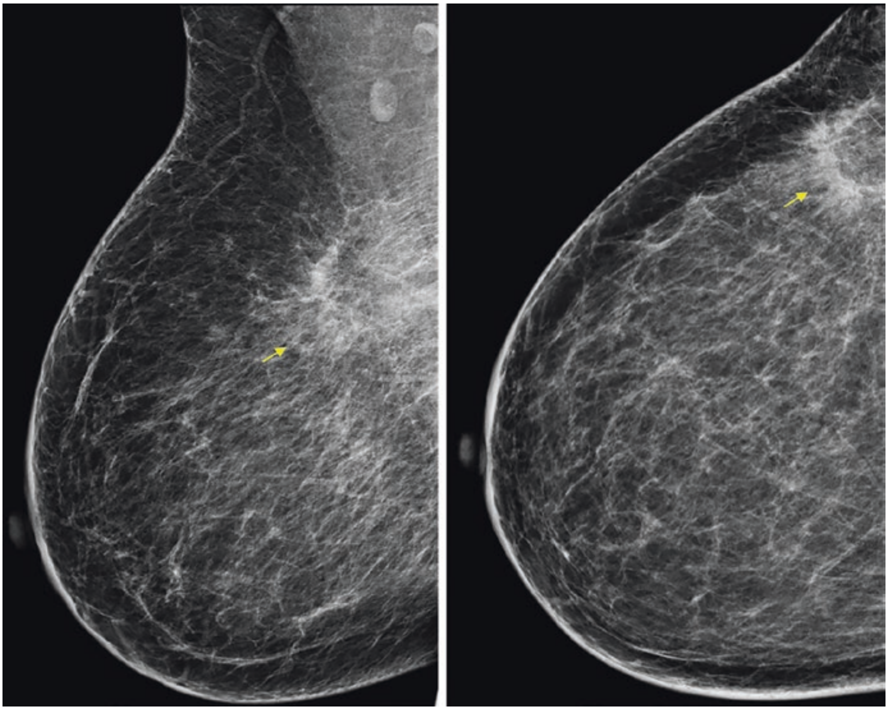

Fig. 18.10 Mediolateral oblique and craniocaudal mammogram of the right breast shows post-lumpectomy site as an area of architectural distortion in the upper outer quadrant (arrows). Note the presence of central lucency and thick, curvilinear spiculations suggestive of surgical scar

18.2.2.5 Benign Calcifications

Benign calcifications may develop at the postoperative site, with a reported incidence of 28% within the first 6–12 months after radiation therapy.

Dystrophic calcifications generally develop in areas of fat necrosis and are usually round and coarse and typically large and often have lucent centers (Fig. 18.11). Suture material left in the breast may also calcify, forming distinctive shapes such as knot like, rod-shaped, and curvilinear (Fig. 18.12).

On magnification views, these benign forms of calcifications can often be recognized and differentiated from pleomorphic or other suspicious calcifications associated with malignancy (Fig. 18.13).

At times, however, dystrophic calcifications may simulate malignancy. As previously described, early calcification of evolving fat necrosis may produce an appearance that is mammographically inconclusive. In such cases, careful inspection of the previous mammograms may help by showing regression of the calcifications over time or formation of the calcifications around a radiolucent center of fat, suggesting the benign nature (Fig. 18.14). If calcifications cannot be distinguished from a possible malignant process radiographically, biopsy should be considered.

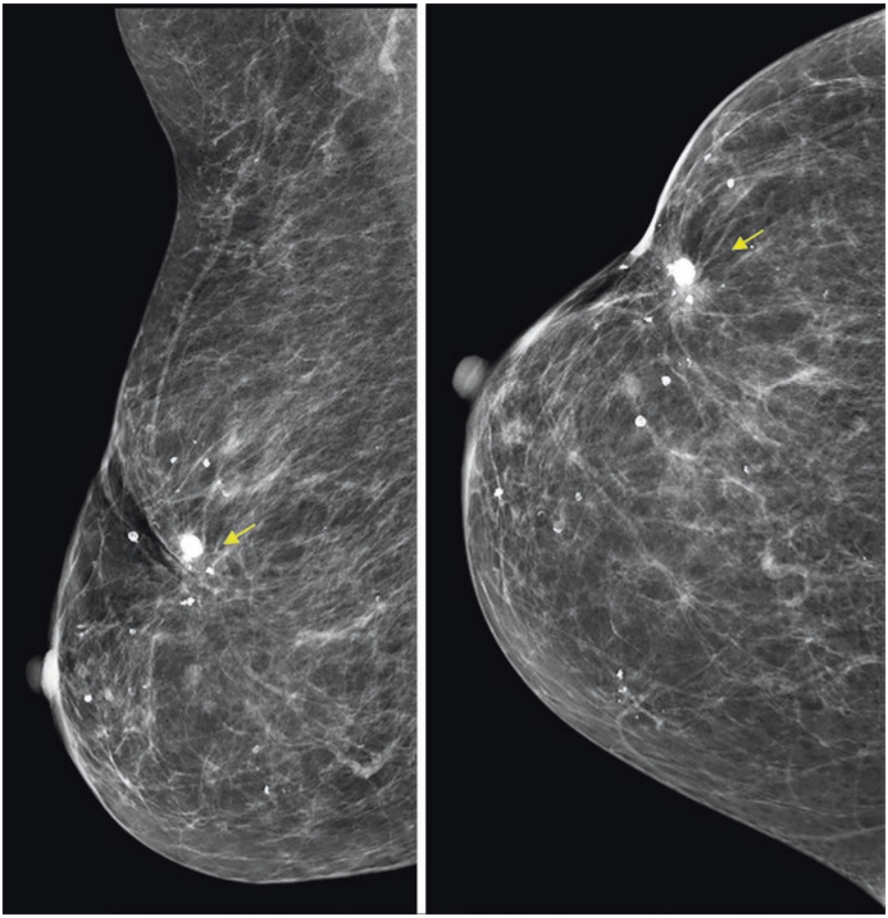

Fig. 18.11 Dystrophic calcifications in 72-year-old woman with history of right breast carcinoma. Mediolateral oblique and craniocaudal mammograms of right breast obtained 12 years after lumpectomy and radiation therapy. Large coarse calcifications (arrows), representing dystrophic calcifications, are seen within tumor excision site

18.3 Imaging Methods

18.3.1 Mammography

There is currently no universal guideline for posttreatment imaging surveillance. There are multiple proposed guidelines, and they recommend mammography as part of routine follow-up after BCT [10].

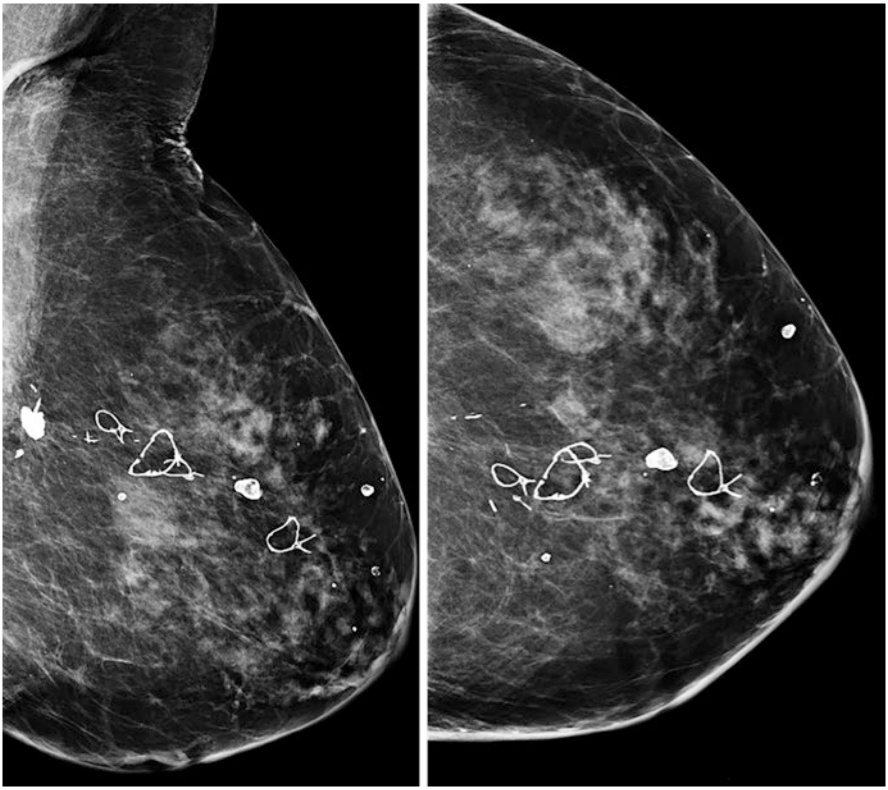

Fig. 18.12 Sutural calcifications in a 91-year-old woman with a history of left breast cancer that was treated with lumpectomy and radiation therapy. Mediolateral oblique and craniocaudal mammograms of post-lumpectomy and radiation of the left breast show curvilinear and knot-shaped calcifications. These findings are characteristic of sutural calcifications, which are most commonly seen in the irradiated breast and are rarely observed after benign breast surgery

Postsurgical mammograms can be obtained before the initiation of radiation therapy on selected cases to determine the completeness of tumor excision by identifying residual calcifications within the breast.

In most cases, however, mammograms of both breasts are obtained 6 months after the completion of radiation therapy. Images obtained at that time include craniocaudal and mediolateral oblique views. Magnification views of the lumpectomy bed are also routinely obtained even though there is no evidence to support improved outcome. Subsequently, annual mammography is normally performed [3, 5].

Mammographic imaging in patients after breast conservation surgery is challenging because surgery alters the normal breast architecture. The distinction of normal postoperative changes from true findings of recurrence becomes demanding making it essential to know what are the expected posttreatment findings.

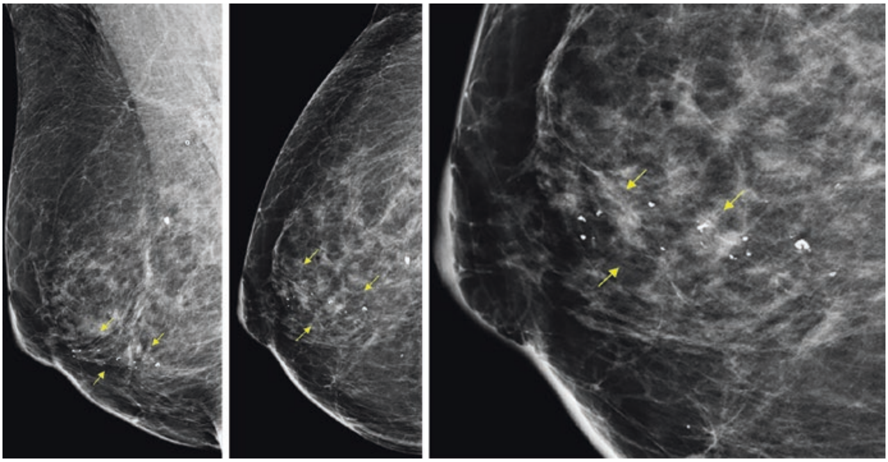

Fig. 18.13 Dystrophic calcifications in a 65-year-old woman with history of right breast carcinoma. Mediolateral oblique and craniocaudal mammograms of right breast obtained 5 years after lumpectomy and radiation therapy. Coarse calcifications (arrows), representing dystrophic calcifications, are seen within tumor excision site

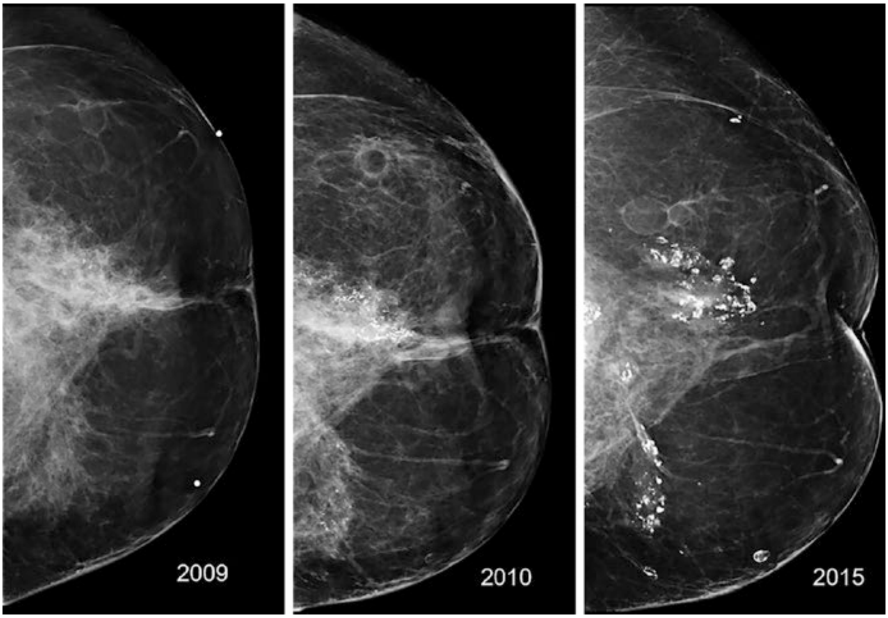

Fig. 18.14 Follow-up mammograms help showing the formation of the calcifications around the area of fat necrosis, suggesting the benign nature

18.3.2 Tomosynthesis

Digital breast tomosynthesis (DBT) is a mammographic technique that entails imaging of the breast tissue in multiple sections at varied angles. The overlap of parenchymal tissues is largely resolved, reducing the false positives as well as adequately identifying true lesions, increasing the sensitivity of a mammogram [7, 11].

DBT not only helps in triangulation of a lesion but also reduces the requirement for additional views and lowers the patient call-back rate.

Similar to screening mammography, DBT also helps resolve post conservation changes such as a scar or other asymmetries due to parenchymal edema from a true recurrence. The fat density within the scar and that associated with benign calcification may also be better appreciated on DBT whereas a true recurrence would demonstrate a mass.

A study by Sia et al. [11] also reported that DBT decreases the rate of indeterminate findings in surveillance imaging of conservatively treated breasts.

18.3.3 Ultrasound

Breast ultrasound is a widely used method adjuvant to mammography for the further characterization of lesions identified on mammography. It provides additional information on lesions' margin, shape, internal echotexture, vascularity, and elasticity [7, 12].

Ultrasonography is also useful in demonstrating the origin of a palpable mass either within the breast parenchyma or the implant, in cases of breast reconstruction.

If a lesion has suspicious morphology on any breast imaging method and is visible on ultrasound, ultrasound-guided biopsy is the procedure of choice. When performed correctly, this procedure is safe and minimally invasive and has a high diagnostic accuracy, comparable to surgical biopsy.

18.3.4 Magnetic Resonance

An important component in evaluating the role of MRI following BCS is to compare to the current standard of mammography. Whereas data support the concept that MRI is more sensitive than mammography as part of high-risk screening, less data are available in the post-BCT setting. Robertson et al. [10] performed a systematic review of nine studies and found that for ipsilateral breast tumor recurrences, the sensitivity/specificity of MRI was 86–100%/93% as compared with 64–67%/85–97% for mammography with MRI also having higher sensitivity for nonroutine ipsilateral breast recurrences.

Another potential role for MRI in patients following BCS is to evaluate findings identified on surveillance mammography. Differentiating benign and malignant lesions on MRI were summarized by Drukteinis et al. [13] who concluded that MRI is useful in evaluating posttreatment changes. Breast MR imaging is especially useful in differentiating scar tissue from tumor recurrence, as non-enhancing areas have a high negative predictive value for malignancy (88–96%).

Another challenging finding is fat necrosis, which can mimic tumor recurrence on mammography and ultrasonography and lead to increased numbers of biopsies/interventions. As described above, MRI can help identify fat signals within lesions and characterize these areas as benign.

Skin thickening, architectural distortion, resolving edema, and signal voids from surgical or biopsy clips or from prior bleeding (hemosiderin) are frequent findings in the post-BCT breast [4, 12–14].

The majority of these findings progressively decrease over time. Stability or less prominent findings are expected and typically occur within 3 years. Edema in the post-BCS breast may never resolve entirely, but increasing edema may be a sign of recurrent cancer.

The normal appearance of a post-lumpectomy breast often includes a fluid cavity filled with blood or serum (seroma) at the surgical site. Smooth, thin (≤5 mm) rim enhancement around a seroma should be considered benign (Fig. 18.15). Most seromas slowly diminish in size and evolve into scars (architectural distortion) by 1 year after surgery.

A minimal or small focal area of enhancement or thin linear non-mass-like enhancement (NME) without an associated mass can be seen for up to 18 months at the lumpectomy site. This enhancement likely represents the healing process after surgery and radiation therapy and can be considered appropriate for 6-month follow-up (BI-RADS 3 category) if no previous study is available for comparison, and no clinical or worrisome mammographic findings are present.

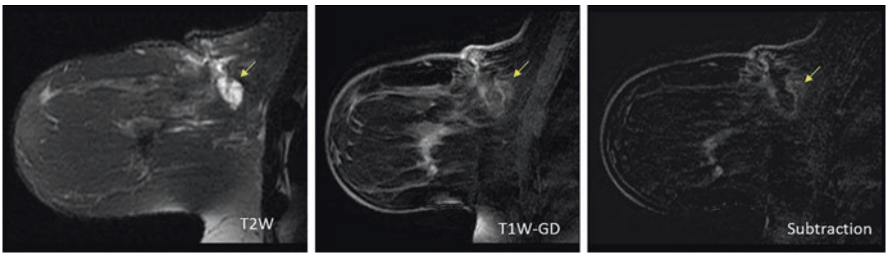

Fig. 18.15 MRI of post-lumpectomy and radiation therapy of the right breast shows fluid cavity at the surgical site with smooth, thin rim enhancement (arrows)

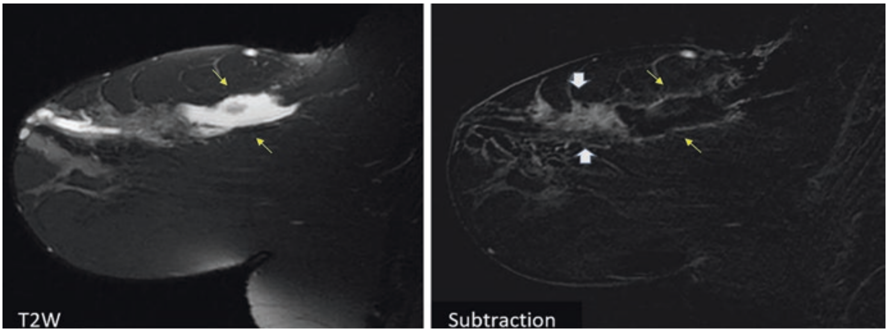

Fig. 18.16 Post-lumpectomy with positive margins MRI was performed before the radiation therapy of the right breast. Fluid cavity at the surgical site with smooth, thin rim enhancement (thin arrows). Anterior to the seroma, it is possible to identify a suspicious non-mass-like segmental enhancement (large arrows)

In contrast, mass-like enhancement or NME of ductal or segmental distribution can indicate recurrence (Fig. 18.16). Therefore, at MR imaging of the post-BCS breast, it is important to identify lesions that are benign or appropriate for short-interval imaging surveillance to minimize unnecessary intervention, as well as to discern suspicious lesions and optimize the diagnosis of recurrence.

Although there is no randomized evidence supporting the routine use of MRI in surveillance post-BCS, a review of the literature by Fisher et al. [2] demonstrates that MRI has increased sensitivity compared to mammography to detect recurrences and can help evaluate inconclusive mammographic abnormalities before biopsy (Fig. 18.17).

In patients with higher risk of local recurrence, surveillance with MRI may represent an effective surveillance strategy although no subgroups have been identified that could benefit from its use and neither has the impact on cost and quality of life been evaluated.

18.4 Conclusion

After breast-conserving surgery and radiation therapy, several alterations of the breast occur and evolve over time.

As surgery and radiotherapy alter the appearance of the breasts, distinguishing between recurrence and benign postsurgical changes can be challenging due to overlapping features. Despite this, differentiation between these two entities is usually possible by recognizing characteristic features of posttreatment sequelae and the evolution of the appearance of the conservatively treated breast by comparing interval findings on serial studies. However, certain features of these benign changes may simulate patterns of tumor recurrence and biopsy may be warranted.

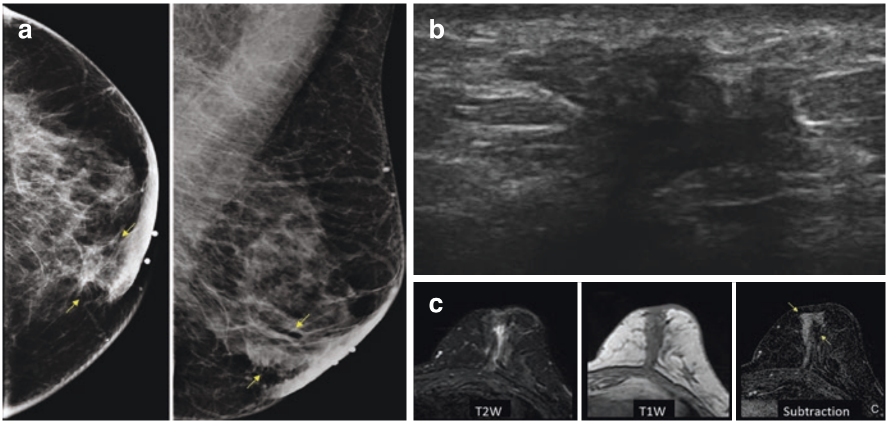

Fig. 18.17 Mediolateral oblique and craniocaudal mammogram (**a**) of the left breast after lumpectomy and radiation therapy shows area of architectural distortion at the lumpectomy site in the retroareolar region, with associated increased density (arrows). Target ultrasound (**b**) shows irregular mass with angulated margins. MRI (**c**) was performed to better access this finding and demonstrated segmentar enhancement of the area and biopsy was recommended. Histologic result was steatonecrosis associated with chronic granulomatous inflammatory process with multinucleated giant foreign body cells

18.5 Summary

The posttreatment alterations include fluid collections, breast edema, skin thickening, fat necrosis, architectural distortion, and calcifications. There is an expected chronological appearance for these findings on the conservatively treated breast, and this is important to know for the correct diagnosis and conduct.

Mammograms and other imaging modalities should be evaluated and compared with earlier studies to maximize detection of recurrent breast carcinoma while minimizing unnecessary recalls and biopsies.

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