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Fat Necrosis

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1. Introduction

Fat necrosis is a benign inflammatory process that arises from damage to breast adipose tissue. Knowledge about the pathophysiology of fat necrosis is fundamental to enable the correct diagnosis of this entity whose appearance on different imaging modalities ranges from typically benign findings to findings normally associated with malignant lesions.

In this chapter, we aim to provide a detailed description of the mechanisms involved in the development of fat necrosis as well as of the findings at mammography, sonography, magnetic resonance imaging, and other modalities. We also include a diagnostic algorithm that can be useful in the management of patients in whom fat necrosis is suspected.

2. Etiology

Breast fat necrosis is a benign inflammatory process. Although it is often considered idiopathic, breast fat necrosis is usually caused by trauma, and many idiopathic cases are probably due to microtrauma. Trauma leading to breast fat necrosis can result from accidents or clinical treatment. Among accidental agents, injury from safety belts in traffic accidents is common. Iatrogenic agents include breast surgery (including incisional biopsy; lumpectomy; breast reduction; breast augmentation by implants or injection of silicone, paraffin, or other exogenous substances; and flap breast construction techniques like TRAM, DIEP, etc.) and, less frequently, percutaneous procedures (including core biopsy, vacuum-assisted core biopsy, or fine-needle aspiration cytology), radiotherapy, and chemical irritation caused by anticoagulants or rupture of cysts or ductal ectasia. Some systemic diseases like panniculitis (Weber-Christian syndrome) have a pathogenesis and imaging manifestations similar to those of fat necrosis.

3. Clinical findings

Breast fat necrosis is often a clinically silent process. It most commonly debuts as a palpable mass, which may be accompanied by ecchymosis and erythema, or less frequently by skin thickening or retraction.

As Lee and Adair stated in the first report of breast fat necrosis (Lee&Adair, 1920), these clinical manifestations are so similar to those of breast cancer that we are obliged to use all the available means to differentiate between these two entities. Conventional imaging

techniques like mammography or sonography can help in this differentiation, but they can also lead to confusion due to myriad appearances of fat necrosis on these modalities.

To better understand the wide spectrum of possible manifestations (ranging from perfectly differentiated benign findings to findings characteristic of malignant lesions), it is essential to know the pathogenesis of breast fat necrosis.

4. Pathophysiology

Fat necrosis occurs more often in breasts predominantly composed of adipose tissue; likewise, in breasts in which adipose tissue does not predominate, fat necrosis tends to occur close to the skin, where adipose tissue is most abundant.

In breast trauma, damage occurs mainly to adipocytes and to the microvascularization, which is abundant in adipose tissue.

Vascular damage results in an immediate inflammatory reaction consisting of arteriolar contraction to check bleeding. This contraction leads to increased arteriolar and capillary pressure, which cause transudation of fluid to the interstitial space and increased pressure in the venules, which in turn increases the permeability of the venous walls, thus resulting in the loss of proteins and consequently of fluid. All these factors that contribute to the increase in the amount of fluid in the interstitial space lead to the **edema** that is characteristic of the hyperacute inflammatory phase.

On the other hand, the release of cytoplasmic triglycerides into the interstitial space after adipocyte rupture also leads to a series of chemical and inflammatory reactions.

Shortly afterward, the damaged vessels release fibrinogen into the interstitial space, where the enzyme thrombin will convert it to active fibrin. Fibrin, which is elastic and insoluble, combines with the platelets to form a mesh to control bleeding. Furthermore, the “free” fat from the adipocytes will be encompassed by a sort of defense conglomerate, **granulation tissue**, which is mainly composed of macrophages, leukocytes (mainly neutrophils), fibrin, fibroblasts, and angioblasts. This fat-containing granulation tissue is called an **oil cyst**.

With time, the oil cyst can either calcify or it can be reabsorbed and replaced with connective tissue. It is important to understand each of these processes.

The fatty acids that make up the triglycerides can react with the calcium ions in the interstitial space to form calcium stearate, which will accumulate around the granulation tissue, resulting in a sphere of varying size contained within a shell of calcium, referred to as a **calcified oil cyst**.

On the other hand, the nonencapsulated fatty acids or even the granulation tissue itself can be attacked by the immune system and reabsorbed, leaving a **fibrous scar** that can also calcify with time.

These are the stages that can take place after trauma to breast adipose tissue. Although these stages tend to occur in the same order, the duration of each phase can differ widely, even within the same area of adipose tissue, so that different phenomena can be present at the same time (Ganau et al, 2009).

The wide variability of phenomena associated with fat necrosis and the wide time window in which they can appear can make the diagnosis challenging. For this reason, one of the main aims of this chapter is to provide the tools to ensure an accurate imaging diagnosis. It is essential to obtain a thorough clinical history including possible trauma or surgery.

5. Imaging&pathological findings

5.1 Mammographic findings

5.1.1 Edema

In many cases, edema does not manifest on the mammogram. When it does, the findings are very subtle, usually consisting of focal skin thickening, which may or may not be associated with an increase in the density of subcutaneous fat and trabecular thickening (1). These findings have low specificity, being similar to those of mastitis (although the clinical presentation tends to be different). In inflammatory carcinoma, these same findings tend to be more evident and to involve the entire breast.

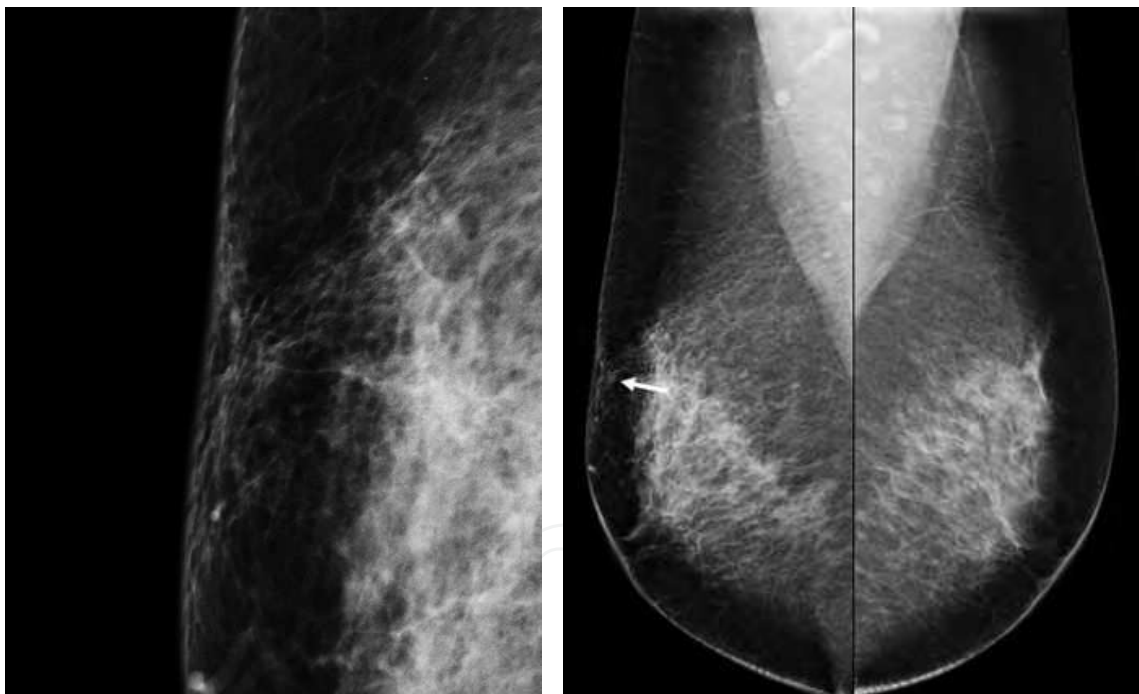


Fig. 1. Increased density and trabeculation of subcutaneous fat associated with slight skin retraction (arrow).

5.1.2 Granulation tissue

The density of granulation tissue is indistinguishable from fibroglandular breast tissue from a mass or from an asymmetry (2). However, granulation tissue is easy to recognize if other findings of fat necrosis are present.

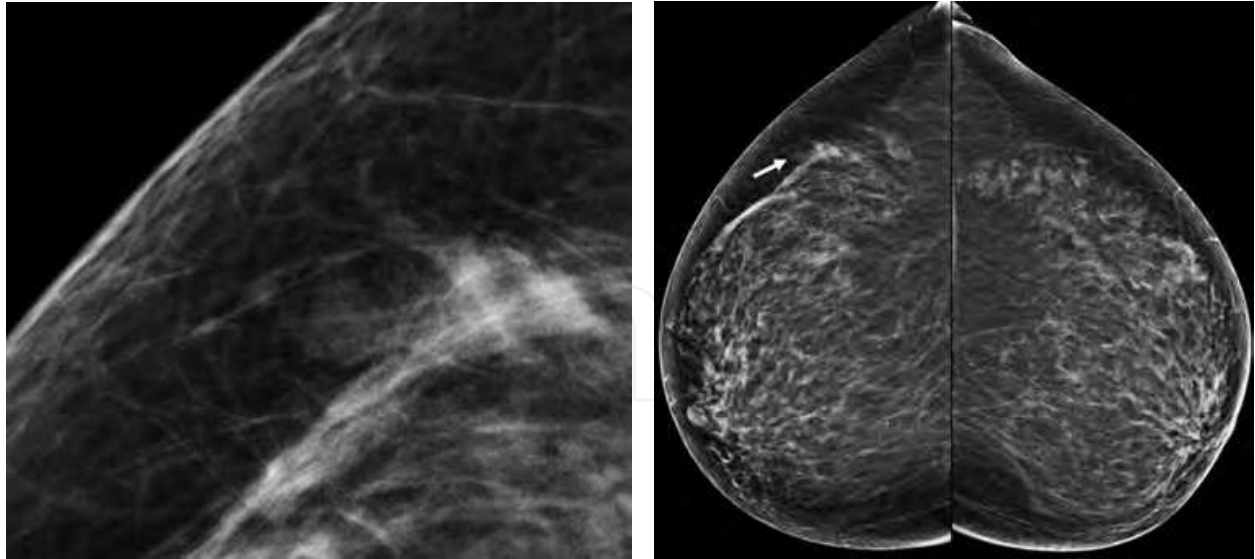


Fig. 2. Nodular image not present on previous mammograms (arrow), with a slightly lower density than the fibroglandular tissue in the same area, corresponding to a focus of fat necrosis.

5.1.3 Oil cyst

Oil cysts are easy to recognize. They are round or oval, with well-defined margins that may be partially or completely calcified or not at all, and their fatty content makes them radiolucent (3). The calcifications tend to be smooth and curvilinear and distributed from the periphery to the center (like an eggshell), although they may also adopt a more irregular shape (4). Oil cysts have been classified in function of their size as *liponecrosis microcystica calcificans* (< 3 mm in diameter) and *liponecrosis macrocystica calcificans* (> 3 mm in diameter) (Lanyi, 1986).

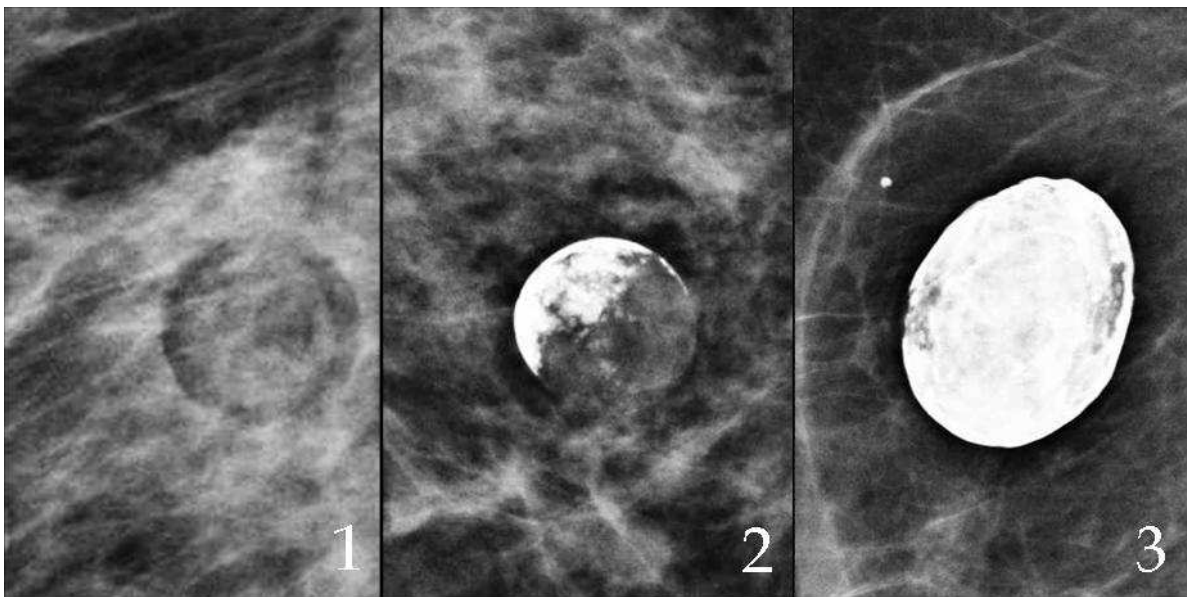


Fig. 3. Well-defined oil cysts: 1. Without calcified walls; 2. With partially calcified walls; 3. With nearly entirely calcified walls.



Fig. 4. Irregular oil cysts: 1. After breast reduction surgery; 2. After transverse rectus abdominus myocutaneous (TRAM) flap oncoplastic surgery.

If the salts have not precipitated completely in the peripheral granulation tissue they may remain “floating” on the cyst’s fatty fluid, causing a level (5).

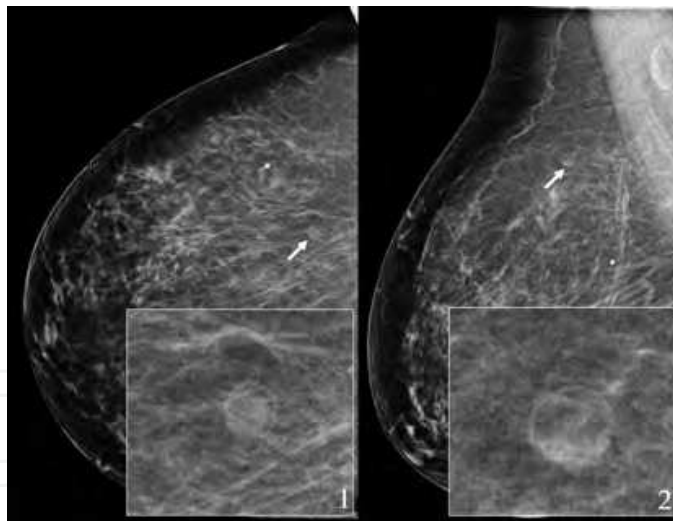


Fig. 5. Oil cyst with precipitated calcium salts (arrow) that separate from the oil in the mediolateral oblique projection to form a level (1. craniocaudal projection; 2. oblique mediolateral projection).

These findings are sometimes difficult to differentiate from a galactocele or from a bleeding oil cyst, although neither of these results are a reason for suspicion.

In some cases, the immune system can react when the cyst is still radiolucent due to its fatty content, and the walls of the cyst can thicken and adopt an irregular or ill-defined shape, simulating a malignant lesion (6).

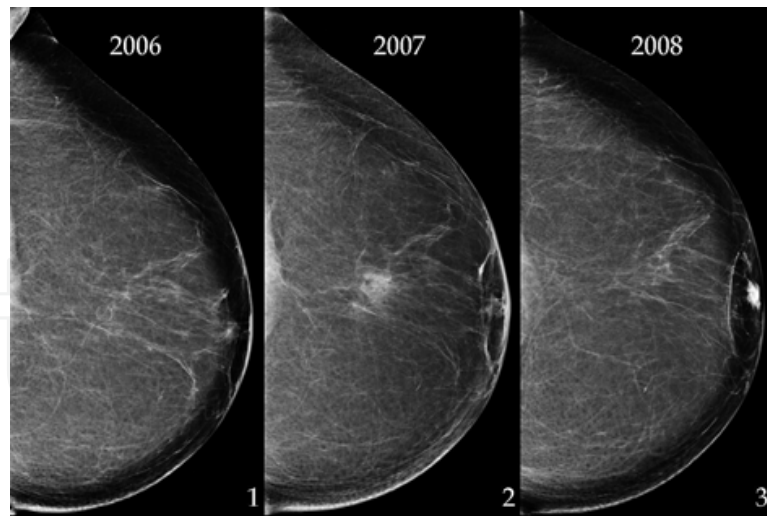


Fig. 6. Oil cyst (1). One year later, the patient had a reaction to a foreign body that simulated a malignant lesion (2). Core biopsy: fat necrosis. The disappearance of the lesion during follow-up (3) confirmed that this was a benign process.

Again, the clinical context and associated mammographic findings are important in distinguishing complicated oil cysts from other, less innocuous entities.

5.1.4 Fibrous scar

The fibrous scar that replaces the oil cyst can take on different shapes, and accordingly the mammographic findings can vary, ranging from asymmetry to an ill-defined or well-defined mass. These are the findings that make it most difficult to differentiate fat necrosis from a malignant mass, especially when the retraction of the scar tissue gives the mass a spiculated or irregular shape. When the scar also calcifies, the findings are completely different from those of a calcified oil cyst; the numerous amorphous and even pleomorphic calcifications that often occur with the scar (7) make histological study and the differential diagnosis with a neoplasm process essential.

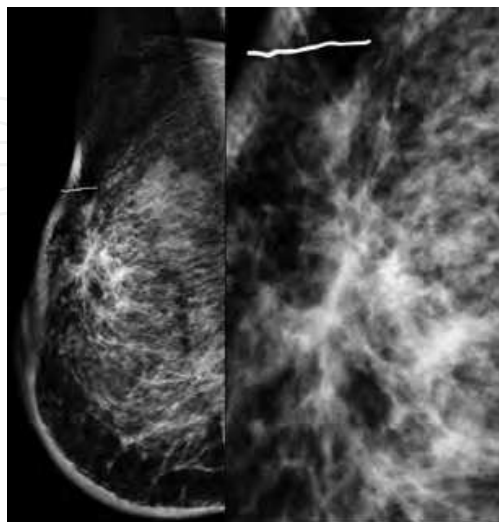


Fig. 7. Parenchymal distortion together with pleomorphic calcifications adjacent to the surgical scar. Vacuum-assisted biopsy: fat necrosis.

5.1.5 Summary of the most common findings over time



Fig. 8. Phases of fat necrosis: 1. Normal mammogram, with no history of trauma. 2. Retroareolar trauma in the left breast. Oil cyst and increased density around the cyst, together with calcifications, compatible with granulation tissue. 3. The oil cyst and granulation tissue are progressive replaced with coarse calcifications. 4. The calcifications replace the granulation tissue completely.

5.1.6 Other classic (and not so classic) examples

Mammograms in women with seat belt injuries of the breast show typical fat necrosis findings in a bandlike distribution corresponding to the path of the safety belt (DiPiro et al, 1995).

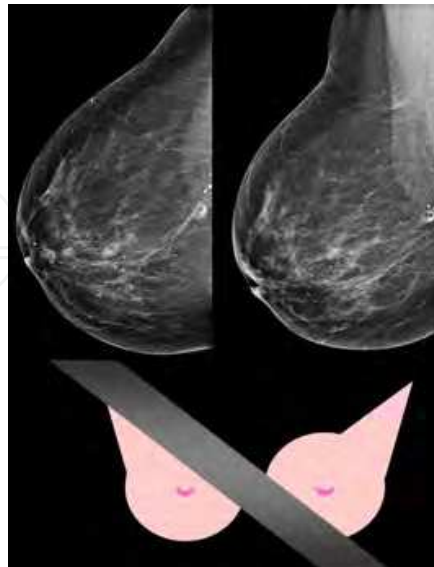


Fig. 9. Mammogram obtained a few months after a traffic accident shows calcifications compatible with fat necrosis; the calcifications are distributed throughout the anatomic region that comes in contact with the safety belt.



Fig. 10. Oil cysts in different phases. In this case, the lesions resulted from the injection of autologous fat for reconstructive-esthetic purposes (lipofilling).

5.2 Histologic findings.

Although fine-needle aspiration cytology can be sensitive and specific for the diagnosis of fat necrosis, core biopsy or vacuum-assisted biopsy are even more sensitive and specific. Nevertheless, in some cases diagnostic uncertainty may persist, requiring excisional surgical biopsy.

The histologic findings vary in function of the phase of the process of fat necrosis. Hemorrhagic changes in the adipocytes will give rise to a cavity filled with necrotized fat. The walls of this cavity will consist of a mesh of histiocytes, inflammatory cells, and giant multinucleated cells; with time, collagen-secreting fibroblasts responsible for scar formation will be progressively added. The calcifications mentioned in previous sections may also be identified.

5.3 Sonographic findings

5.3.1 Edema

Skin thickening (easily appreciable by comparison with the contralateral breast) and increased echogenicity of adipose tissue are characteristic of, although not specific to, fat necrosis (11). Other processes, most of them benign (e.g., lipomas) can cause the same findings. The clinical history is key. Malignant processes that can present as hyperechogenic areas must also be taken into account. Linda et al. found 0.4% of hyperechogenic lesions in a series of nearly two thousand malignant lesions (Linda et al., 2011).

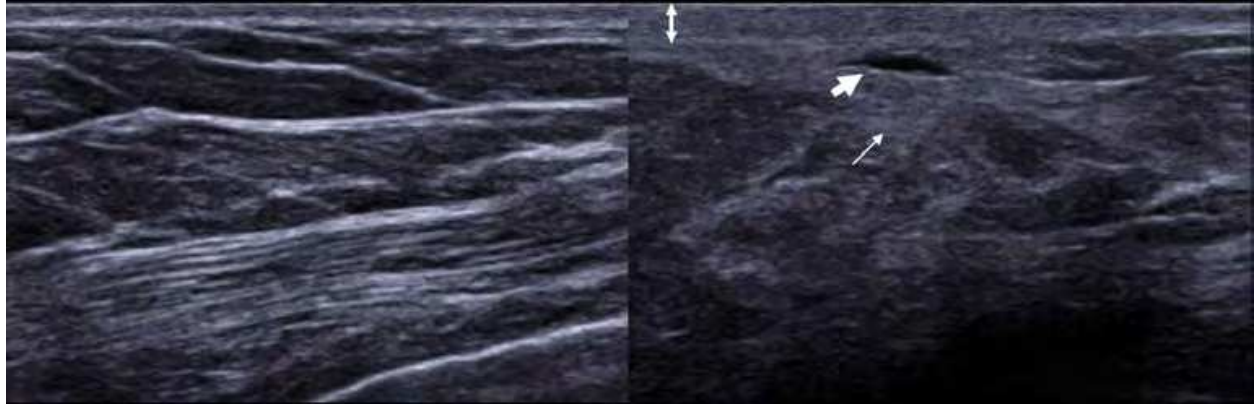


Fig. 11. 1. Normal breast adipose tissue. 2. Findings after trauma to the same breast: skin thickening (double-headed arrow), minimal free fluid (thick arrow), and increased echogenicity of the subcutaneous fat (thin arrow).

Sonoelastographic techniques can also be useful for evaluating the hardening of subcutaneous adipose tissue that occurs in these cases (12).

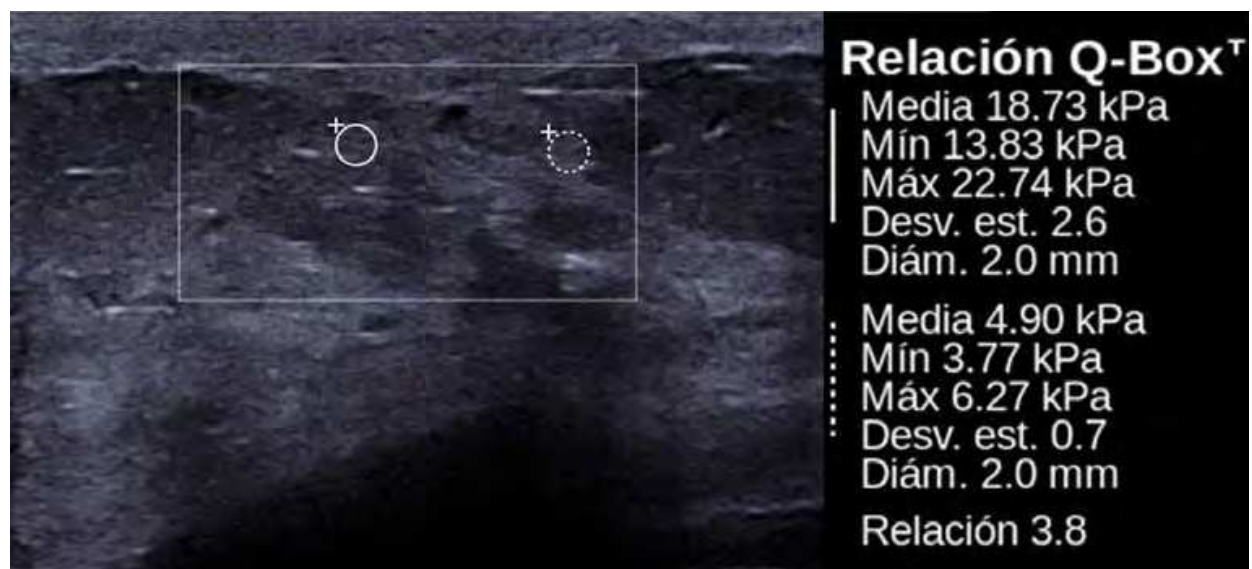


Fig. 12. Shear-wave quantitative sonoelastography. Variability in the maximum, mean, and minimum elasticity of the subcutaneous fat between two ROIs in the same area (continuous line: edematous fat; broken line: normal fat).

5.3.2 Granulation tissue

The only way to differentiate granulation tissue on sonography is by taking the absence of echogenicity of the oil cyst as a reference. The degree of calcification of the margins of these cystic cavities reflects their phase of development.

Color Doppler can also be useful for demonstrating the increased vascularization in the periphery of the cyst that occurs with the formation of the granulation tissue (13).

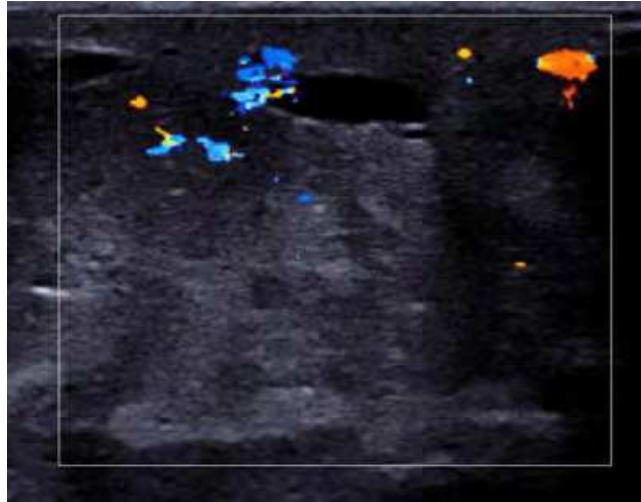


Fig. 13. Increased color Doppler signal reflects the increase in vascularization after trauma.

5.3.3 Oil cyst

Oil cysts are round or oval anechoic lesions with smooth, well-defined, generally hyperechoic margins. Therefore, they are very easy to recognize and practically impossible to differentiate from simple cysts, except for the adjacent structures (generally, areas of echogenic adipose tissue) or if we decide to puncture and drain them, thus obtaining an oily fluid.

Nevertheless, calcium stearate is often seen floating in oil cysts and accumulating in the base, forming a level that moves with patient's movement, simulating a galactocele.

Depending on the degree of calcification of the wall, we can identify a single or double echogenic ring as well as a posterior acoustic shadow which, if considerable, can cause an artifact that hinders the visualization of the cyst (14).

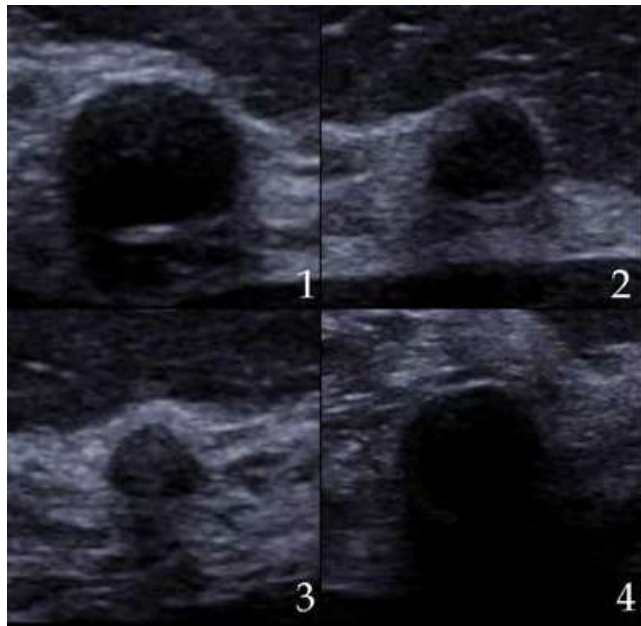


Fig. 14. Oil cysts with different degrees of calcification, In case 4, the posterior acoustic shadow hinders the visualization of the cyst.

5.3.4 Fibrous scar

As mentioned above, sonography can be very useful in the diagnosis during the initial phases of fat necrosis. However, in more advanced phases, the scars adopt the form of spiculated or irregular-shaped masses that can make it difficult to differentiate fat necrosis from malignant disease (15).

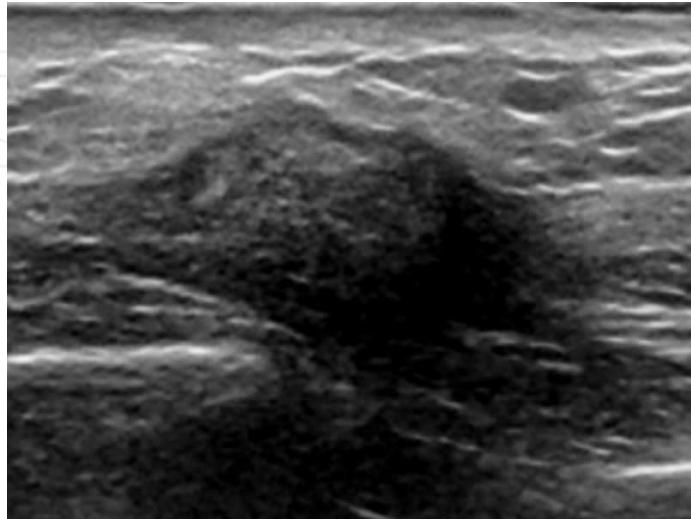


Fig. 15. A slightly heterogeneous mass with irregular margins. Core biopsy: fat necrosis.

Nevertheless, sonography is very useful for guiding interventional procedures that may be necessary when suspicious findings are present.

The role of color Doppler in these cases is uncertain, because like the formation of granulation tissue, which can persist for at least two years, some low grade tumors with a significant desmoplastic reaction can have scant vascularization.

Sonoelastography is also not useful for differentiating between a fibrous scar and a malignant lesion, because both are very stiff (16).

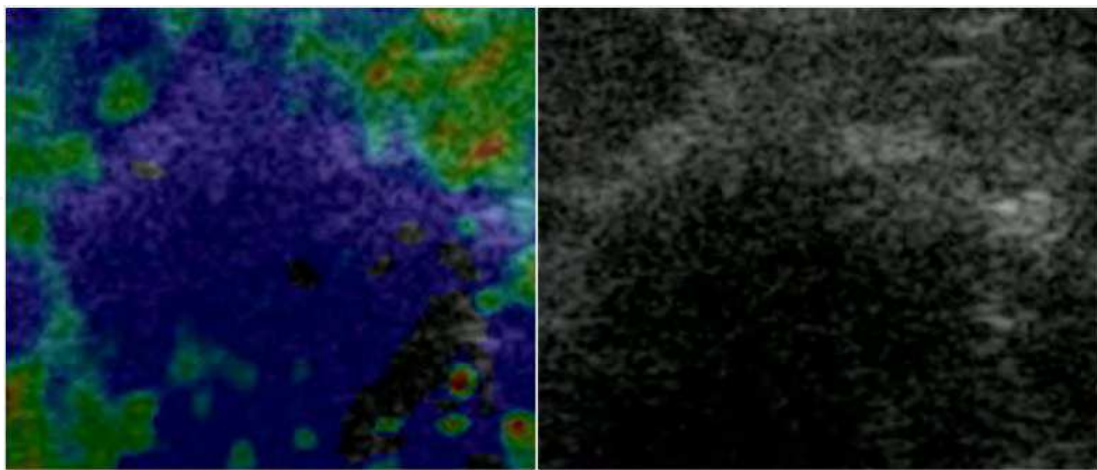


Fig. 16. A hypoechoic mass with an echogenic halo and irregular margins that has high stiffness on sonoelastography (score 5 in Ueno's classification) and is thus suggestive of malignancy. Core biopsy: fat necrosis.

5.4 MRI findings

5.4.1 Edema

Edema is hyperintense on T2-weighted sequences and hypointense on T1-weighted sequences (17). Edema does not enhance after the administration of intravenous contrast material.

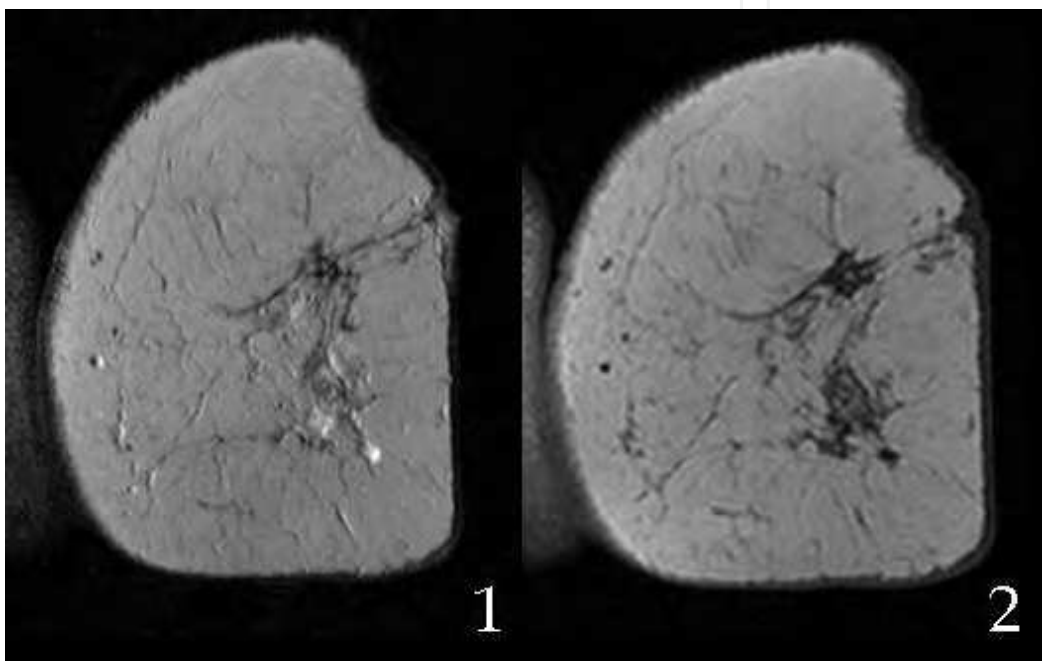


Fig. 17. Postsurgical changes in a breast treated for carcinoma. Some areas are hyperintense in T2-weighted sequences (1) and hypointense on T1-weighted sequences (2), corresponding to edema (fluid signal).

5.4.2 Granulation tissue

Granulation tissue is the main cause of contrast agent uptake in fat necrosis. Owing to the peripheral distribution of the granulation tissue around the oil cyst, ring enhancement, also characteristic of malignant lesions, is common. However, the nearly unequivocal MRI findings for oil cysts (see below) mean that the benign nature of this ring enhancement is rarely in doubt.

In some cases, however, the arrangement of the granulation tissue is less well defined, so it is important to consider the signal intensity in T1-weighted sequences. The presence of fat, which is typically hyperintense in T1-weighted sequences, together with the patient's clinical history, can help to rule out a neoplasm and diagnose fat necrosis (18). (Ganau et al., 2009; Taboada et al., 2009; Tan et al., 2005).

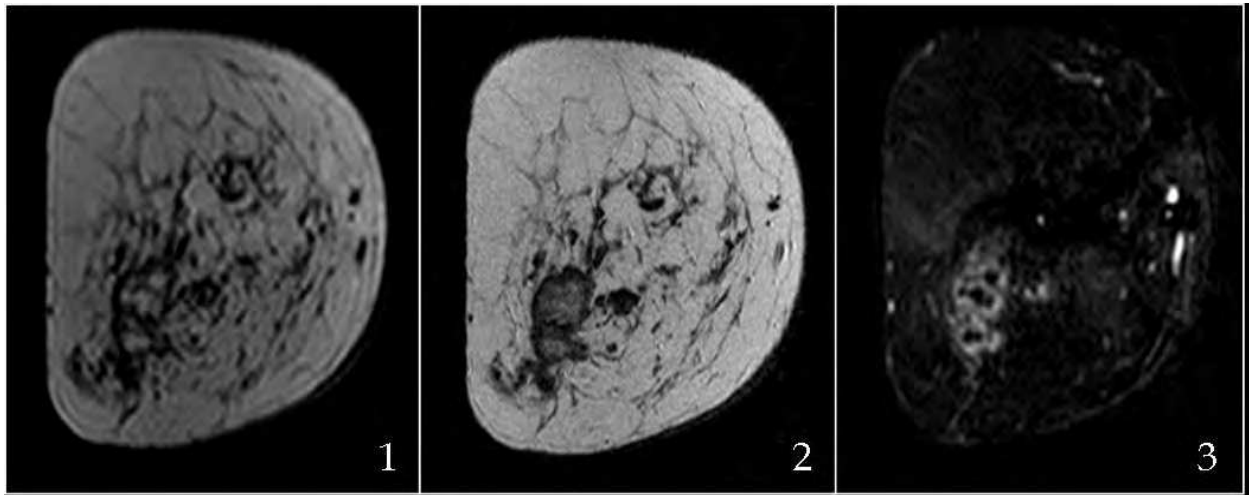


Fig. 18. Right breast three years after surgery for infiltrating ductal carcinoma. MRI shows an irregular mass with hyperintense foci in T1-weighted sequences (1) that are slightly hypointense in T2-weighted sequences (2); the mass has irregular peripheral enhancement after intravenous contrast administration (3). In this clinical context, it is imperative to rule out relapse of the tumor. Vacuum-assisted biopsy: fat necrosis.

5.4.3 Oil cyst

Oil cysts are shown as rounded or oval masses with well-defined margins; they are hyperintense in T1-weighted sequences and can be either hypo- or hyper-intense on T2-weighted sequences. Depending on whether granulation tissue surrounds the cyst, the typical ring enhancement may or may not be observed. Depending on the degree of calcification of the cyst, a signal void may be present in T1-weighted sequences.

The contents of oil cysts never enhance (19).

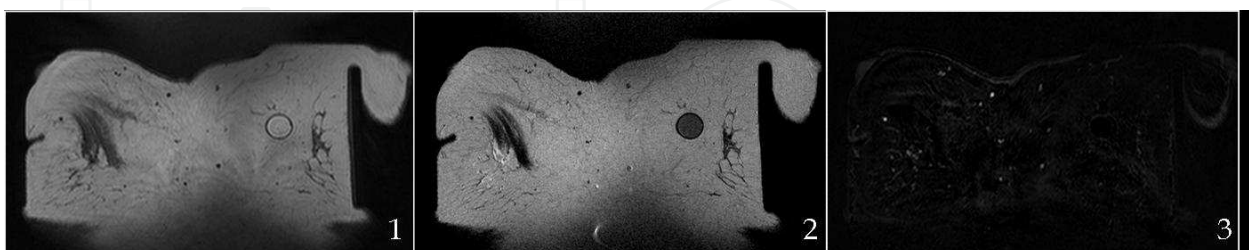


Fig. 19. Typical findings for an oil cyst: A nodular cystic lesion with well-defined margins; it is hyperintense on T1-weighted images (1), slightly hypointense on T2-weighted images (2), and does not enhance (3).

5.4.4 Fibrous scar

MRI is essential for imaging fibrous scars. The greater the fibrotic content of the scar, the less likely the scar can take up contrast material. However, the persistence of granulation tissue

can cause enhancement of the scar. Hyperintense foci may also be seen within the scar in T1-weighted sequences due to the persistence of fat (20).

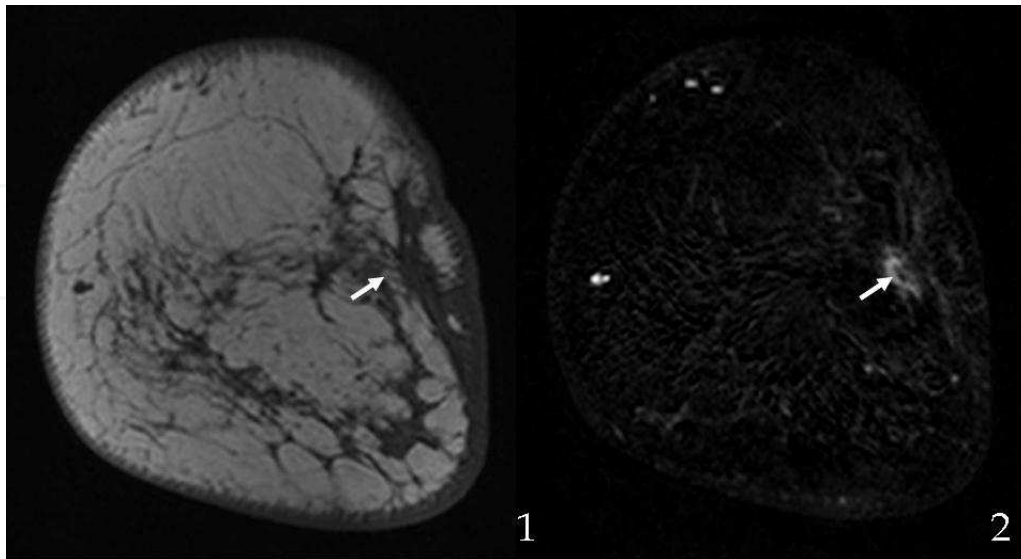


Fig. 20. A woman with a personal history of infiltrating ductal carcinoma of the left breast treated with surgery and radiotherapy. One and a half years later, hyperintense areas are seen adjacent to the surgical scar on T1-weighted images (1), with peripheral enhancement (2) (arrows). It is essential to rule out relapse. Vacuum-assisted biopsy: Fat necrosis.

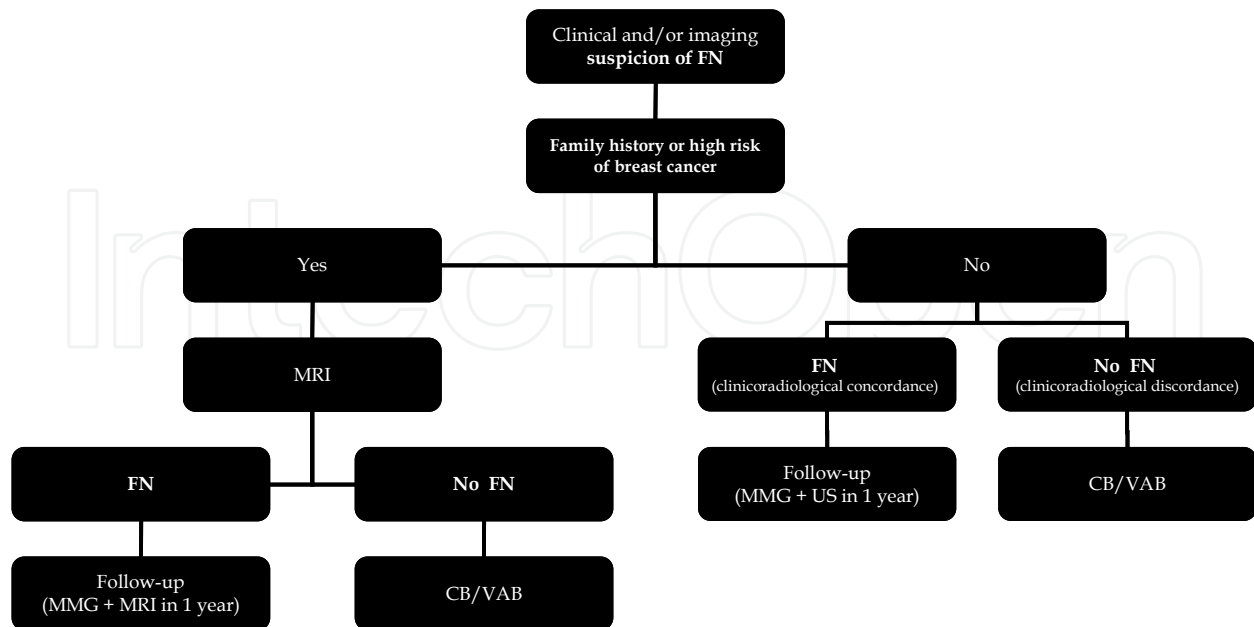
The negative predictive value of screening with MRI approaches 100% in patients with a history of surgery for breast cancer. In these cases, it is important to evaluate the morphokinetic behavior of the contrast agent in scars. The absence of enhancement suggests the absence of malignancy. Nevertheless, uptake in the area of the scar requires relapse to be ruled out.

Echo-planar MRI techniques can be useful in these cases. Thus, for example, high apparent diffusion coefficients in diffusion-weighted sequences of these cicatricial lesions suggest the absence of tumor recurrence. On the other hand, on MR spectroscopy, choline peaks in a fibrous scar suggest tumor recurrence.

If any uncertainty persists about whether a lesion represents fat necrosis or a malignant process, histologic study is necessary.

In summary, fat necrosis is complex from both the clinical and diagnostic points of view. On the one hand, it can be extremely easy to diagnose in patients with a clear history of trauma and characteristic clinical and imaging findings. On the other hand, it can be very difficult to diagnose in patients with or without a known history of trauma in whom the imaging findings are identical to those of malignant breast disease.

For this reason, with the aim of preventing underdiagnosis (considering a malignant process to be an episode of fat necrosis) and avoiding unnecessary diagnostic procedures (considering an episode of fat necrosis to be a malignant process), we present an algorithm for the management of these patients that takes into account three fundamental factors: the clinical presentation, the personal risk of breast cancer, and the findings on different diagnostic imaging techniques.



CB = core biopsy; FN = fat necrosis; MMG = mammography; MRI = magnetic resonance imaging; US = ultrasound; VAB = vacuum-assisted biopsy.

Table 1. Diagnostic algorithm for the management of patients with suspected fat necrosis.

6. Conclusions

Knowledge about the pathogenesis of fat necrosis is fundamental for recognizing the many different findings that can be seen on different imaging modalities. A multimodal approach, assessing the findings in the context of the patient’s risk profile, can improve the accuracy of the diagnosis of fat necrosis.

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8. References

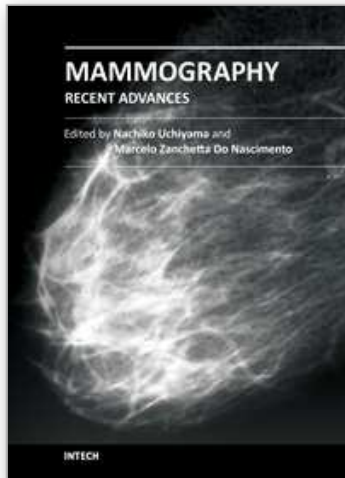
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Mammography - Recent Advances

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In this volume, the topics are constructed from a variety of contents: the bases of mammography systems, optimization of screening mammography with reference to evidence-based research, new technologies of image acquisition and its surrounding systems, and case reports with reference to up-to-date multimodality images of breast cancer. Mammography has been lagged in the transition to digital imaging systems because of the necessity of high resolution for diagnosis. However, in the past ten years, technical improvement has resolved the difficulties and boosted new diagnostic systems. We hope that the reader will learn the essentials of mammography and will be forward-looking for the new technologies. We want to express our sincere gratitude and appreciation to all the co-authors who have contributed their work to this volume.

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