

## Breast DCE-MRI in long-term breast cancer survivors: What lies beneath dystrophic calcifications due to fat necrosis?

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### Abstract

Breast cancer becomes a chronic condition due to advances in diagnosis and treatment. This fact emphasizes the awareness of late post-treatment sequelae, such as dystrophic calcifications due to fat necrosis. In the case of extremely numerous, diffuse dystrophic calcifications, a coexistent carcinoma can be masked on the clinical, mammographic and ultrasound examination. Breast dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a problem solving tool, allowing visualization of soft tissues and detection of angiogenesis.

**Keywords:** Breast cancer; fat necrosis; dystrophic calcifications; mammography; ultrasound; magnetic resonance imaging.

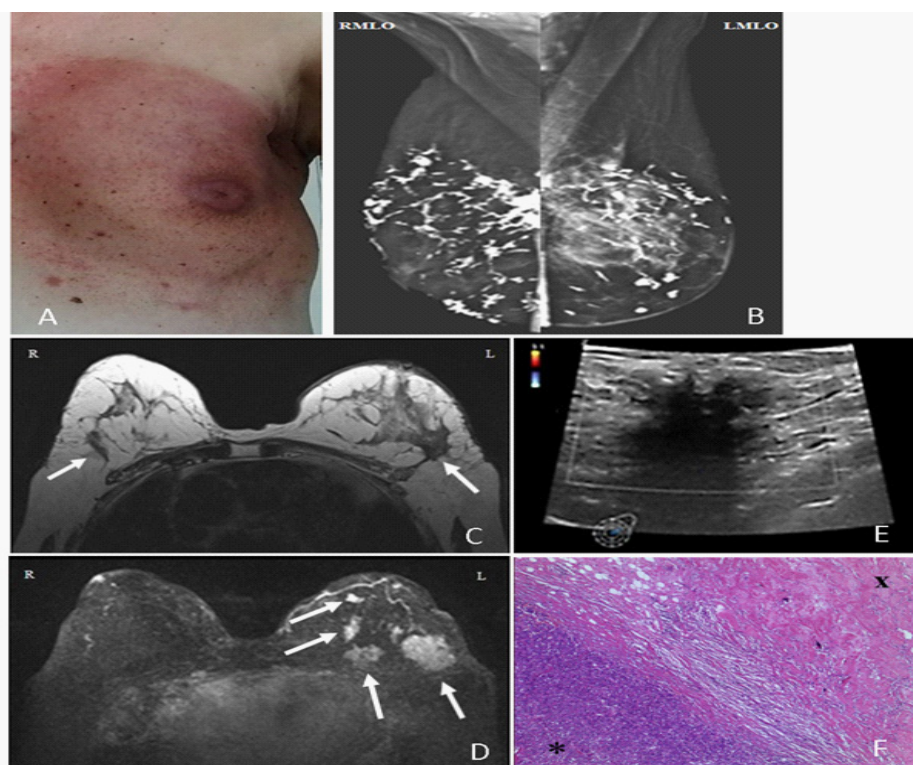
### Introduction

Fat necrosis of the breast is a benign non-suppurative inflammation of adipose tissue that is usually caused by trauma [1]. It can develop after different surgical procedures (biopsy, lumpectomy, breast-conserving surgery, reduction mammoplasty, implant removal, breast reconstruction with tissue transfer) and different modalities of radiation therapy for breast cancer, including some novel techniques, such as intraoperative electron beam radiotherapy or fractionated percutaneous boost after breast-conserving surgery [2, 3]. The damaged breast fat, mainly localized in the subcutaneous compartment, undergoes painless, sterile autolysis or heterolysis. Healing occurs by fibrosis that starts at the periphery of fat necrosis. Depending on the degree of fat necrosis, the lesion is either completely replaced by fibrous tissue, or remains as an encapsulated oil cyst. Dystrophic calcifications can develop in the preformed fibrous tissue about three to five years after tissue damage [4]. Although their morphology on mammography is undoubtedly benign, they have a masking effect and can obscure soft-tissue lesions or microcalcifications. On ultrasound, the posterior acoustic shadowing of calcifications can mimic cancer recurrence, or can mask deeply situated breast lesions [5]. Here we show the correlative findings of different medical imaging modalities (clinical findings, mammography, ultrasound, DCE-MRI and histological image) of concomitant dystrophic calcifications and local relapse of breast cancer.

### Case Report

A 69-year-old woman was referred to the Oncology institute due to tightness in her left breast. Twenty-four years earlier she was treated for bilateral, synchronous breast cancer with lumpectomy and radiotherapy (dose of 65 Gy, cobalt-60 teletherapy and electron boost), followed by ovarian ablation and tamoxifen. Meanwhile, she developed multiple comorbidities (deep vein thrombosis, hepatitis C, acquired antithrombin III deficiency, pulmonary embolism after hip replacement surgery). At the time of referral, clinical examination was inconclusive because of abundant breast radiation-induced fibrosis (**Figure 1 A**). Full-field digital mammography (FFDM) showed global asymmetry of the left breast and bilateral, multiple, coarse dystrophic calcifications, that caused posterior acoustic shadowing on ultrasound (**Figure 1 B, E**). Breast DCE-MRI revealed scarring in both upper outer quadrants. On the post-contrast images, several lesions suspicious for recurrence were found in the left breast (**Figure 1 C, D**). Core-needle biopsy was ineffective due to impenetrable breast tissue. After excisional biopsy of the dominant lesion, a grade 2, hormone receptor-positive, HER2-negative invasive lobular carcinoma with high Ki-67 values was confirmed (**Figure 1 F**). The patient refused any further cancer treatment, except anastrozole.

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**Figure 1:** (A-F). Late radiation morbidity (A) includes marked skin hyperpigmentation and atrophy, gross telangiectasia, severe induration, loss of subcutaneous tissue and breast contracture. Medio-lateral oblique FFDM (B) demonstrates extensive dystrophic calcifications within both breasts, and global asymmetry in the left breast. Axial, T2-weighted non-fat-suppressed MRI (C) shows architectural distortions (scarring) in both upper outer quadrants (arrows). Contrast-enhanced 3D-FLASH MRI, axial MIP image (D) shows multiple regions of heterogeneous non-mass enhancement in the left breast (arrows), measuring up to 3.5 cm, suspicious for recurrence. Ultrasound image (E) demonstrates an ill-defined hypoechoic area with posterior shadowing. Histopathology of surgical specimen (F) shows invasive lobular carcinoma (asterix) and fibrosis (X) (hematoxylin and eosin, original magnification  $\times 100$ ).

## Discussion and Conclusion

The pathogenesis of dystrophic calcifications following breast-conserving surgery and radiation therapy is multifactorial. Extravasation of blood after surgery induces swelling of connective tissue, ischemic and pressure cell necrosis, with subsequent disruption and fragmentation of fat cells. Radiation therapy induces occlusion of small vessels with ischemic injury of the parenchyma and leakage of tissue lipases into the parenchyma. The final biochemical process is an aseptic saponification of fat caused by blood and tissue lipases [4, 6]. Fat necrosis is a gradual pathological process that depends on the intensity and extensity of the primary breast injury. On this spectrum, extensive dystrophic calcifications represent an endpoint of initial severe fat necrosis.

Since extensive dystrophic calcifications on mammography or ultrasound raise concern that cancer recurrence could be missed, a supplemental breast DCE-MRI is recommended. Problem solving is based on the high negative predictive value (NPV) of breast DCE-MRI for cases that are not certainly benign, but where biopsy guided by conventional imaging guidance is not feasible. Generally, an absence of post-contrast en-

hancement at the site of calcifications is associated with a NPV of 93% [7]. The maturation of surgical scar and consecutive post-contrast enhancement on DCE-MRI usually last for approximately 12 months after the completion of radiotherapy. Fat necrosis is an exception to this rule, because enhancement can be found several years after surgery and radiotherapy. Finally, a hypovascular scar develops in place of fat necrosis, with little or no enhancement. Post-traumatic oil cysts can be seen as round, well-circumscribed hyperintense areas on pre-contrast images, sometimes with a typically benign, faint rim of post-contrast enhancement [4, 8]. Any post-contrast enhancement different from rim enhancement of the oil cysts is suspicious for breast cancer recurrence and requires biopsy.

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