Skin thickening in the Breast - It's not always Cancer!

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Learning objectives

Recognize skin thickening in different imaging modalities, including US, mammography and MRI.

Describe the main differential diagnoses for this imaging finding, including benign and malignant causes, such as carcinoma, lymphoma, infection, post radiation therapy, post surgical changes, anasarca secondary to renal insufficiency and mixed connective tissue disorders, among others.
Background

Skin thickening in the breast is a not common finding in diagnostic imaging even though it is well known to be associated with infiltration by invasive breast cancer. It is important to review the principal differential diagnosis of skin thickening in the breast, so that radiologist can give another possible diagnosis beside invasive cancer.
Findings and procedure details

Normal anatomy of breast skin.

The skin of the breast consists of epidermal, dermal and hypodermic layers. The epidermis is the most superficial layer and is usually very thin, it is composed of five different cell layers that slough completely every 3 or 4 weeks; this layer is separated from the dermis by the basement membrane. The dermis attach the epidermal skin to the underlying tissue, and is composed mainly of collagen and elastin, as well as blood vessels, motor and sensory nerves, muscle fibers, hair follicles and sebaceous glands; on this layer of breast skin, the anterior mammary fascia helps providing a fixation site for the retinacula cutis, the continuation of the suspensory Cooper ligaments [1]. The hypodermis, as its name says, is located beneath the dermis and is composed mainly by fatty tissue, also contains the major vasculature supplying the skin.

The innervation of the skin is given by the lateral cutaneous branches of the second to sixth intercostal nerves. The irrigation of skin in the breast is given by branches of the anterior and posterior intercostal arteries and the lateral thoracic artery, complementary veins provide blood drainage. Dermal, periareolar, axillary and internal mammary lymphatics are responsible of lymphatic drainage.

Forming part of the skin of the breast, there is an intensely pigmented portion of breast skin known as the nipple-areolar complex. It contains additional sensory nerves and sebaceous glands, in the areola can also be found apocrine sweat glands, hair follicles and accessory areolar glands of Montgomery, as well as a prominent lymphatic system called the subareolar or Sappey plexus.

Breast skin and imaging modalities

Breast skin can be difficult to assess at mammography and ultrasound, for that reason breast MR imaging can be the imaging modality of choice in cases of skin breast pathology. On mammography and ultrasound the skin should be really thin in a regular fashion, with mean thickness of 0.5-2mm (Fig 1). On MR imaging, the skin presents mild thin enhancement; the nipple-areola complex typically enhances more prominently and the nipples usually shows a thin rim of enhancement and appear symmetric (Fig 2); this appearance usually persist even though is retracted or inverted [2].

Differential diagnosis of skin thickening in the breast

The differential diagnosis of skin thickening in the breast is wide, and includes benign and malignant diseases, the most common causes are being discussed.
Locally advanced cancer: In a few cases, there is ectopic terminal ductal lobular units superficially, near the dermal attachment to the Cooper ligaments, therefore breast cancer can arise or extend to superficial layers of the breast and involve the skin; approximately 64% of invasive ductal carcinoma and ductal carcinoma in situ occur at the periphery of the breast so skin involvement can be more frequent (Fig 3) [1]. It is important to be certain about skin involvement, superficial breast malignancies can obstruct lymphatic or venous drainage, causing edema or inflammation without skin invasion (Fig 4).

Inflammatory breast cancer: It is an extremely aggressive form of breast cancer and accounts for 1-2% of all breast cancer cases [3], 90% of patients with ipsilateral lymphadenopathy at presentation and 20% of cases being metastatic at the time of diagnosis [1]. The extension of disease can be underestimated with mammography, therefore MR imaging is the imaging method of choice. Usually presents with unilateral breast enlargement and skin thickening, on MR imaging presents with patchy asymmetric enhancement of breast parenchyma and Cooper ligaments, as well as diffuse and nodular enhancement of the skin. It is important to exclude mastitis as a possible diagnosis in this patients; inflammatory breast cancer most often involves a larger portion of the breast, whereas mastitis involves mainly the subareolar region.

Paget disease: Usually presents with ulcerated nipple skin and unilateral skin thickening, and is characterized by neoplastic cells in the epidermis, most of the times involves an occult breast cancer, usually ductal carcinoma in situ (CDIS) and rarely invasive ductal cancer; in 15% of the cases is occult at mammography and in 13% at mammography and ultrasound [2]. The radiologist must suspect this entity if the skin changes are unilateral and associated with a breast mass, breast calcifications or nipple discharge: when an invasive component is involved, physical manifestation may include skin retraction.

Lymphoma of the breast: Accounts for only 0.1-0.5% of malignant neoplasms of the breast [4,5], and the most common subtype is non-Hodgkin; in most of the cases is the result of secondary involvement in patients with disseminated lymphoma. There are not pathognomonic imaging features, but typical presentation consist of breast nodule or mass, usually solitary but can present as multiple lesions. Skin thickening in this patients occur in approximately 30%, it has been reported that in 7% of cases skin involvement can be the only imaging finding (Fig 5).

Post surgical changes: Skin thickening, focal or diffuse, can be evident after percutaneous biopsy or surgery, this imaging finding can be seen for a short time and usually resolves; even though mild skin thickening at the post surgical bed may persist indefinitely (Fig 6).

Post radiation therapy: After radiation therapy, focal or diffuse skin breast thickening can be evident (Fig 7), this finding usually has a linear border with a nonanatomic distribution secondary to the radiation portal used. Posterior to treatment, there is enhancement of the parenchyma and skin near the site of radiation field, this enhancement is considered
a normal finding during the first 18 months after treatment. In cases of increase in skin thickening or enhancement after 18 months following radiation therapy, the radiologist should suspect for tumor recurrence.

**Infectious and inflammatory process:** Infectious and inflammatory mastitis presents clinically with skin thickening, breast enlargement, pain, and hyperemia and hyperthermia of the skin (Fig 8). It is not uncommon for abscesses to develop (Fig 9). It can occur most often in lactating women with *Staphylococcus* being the most common pathogen, but it happens also on non-puerperal patients, especially in women with known ductal ectasia or those who smoke, in this patients *Streptococcus* and *Escherichia coli* are commonly isolated. It can be difficult to distinguish infectious mastitis from inflammatory breast carcinoma, usually breast MR imaging helps to elucidate this diagnostic doubt. Inflammatory noninfectious mastitis usually presents in a background of autoimmune or connective tissue disorders.

**Edema:** Generally manifested at mammography as bilateral smooth skin thickening, breast enlargement, increased parenchymal density and trabecular thickening. Principal causes are congestive heart failure, renal failure, hypoalbuminemia and lymphedema secondary to lymph node dissection or axillary obstruction from lymphadenopathy, among others. Congestive heart disease commonly affects both breasts, nevertheless findings can be unilateral without a clear explanation for this presentation, some suggest this happens when the patient maintains the same position for a considerable amount of time and the findings lateralize to the dependent breast [3,6].

**Connective tissue disease:** The most important example in this group of diseases is scleroderma. Manifestations can be localized or systemic, the former causing sclerosis of both the skin and other organs. It manifests as an indurated, erythematous painful lesion on the skin. On mammography there is skin thickening and increase in breast density. It is mandatory skin biopsy for definitive diagnosis [6].
Fig. 1. Normal appearance of breast skin on ultrasound and mammography.
A. Ultrasound of the breast shows heterogeneous background echotexture of breast parenchyma, as well as normal thickness of breast skin, it barely measures 1.5mm.
B. Cranio-caudal projection of the left breast shows normal skin breast, which is almost imperceptible but regular in thickness.

Fig. 1: Figure 1.

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Fig 2. Normal appearance of breast skin and nipple-areola complex on MR imaging. Dynamic post-gadolinium sequence, shows normal thickness and enhancement of the skin of the left breast. The nipple-areola complex usually presents a more intense and homogeneous enhancement, as a normal expected finding.

**Fig. 2:** Figure 2.

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Fig 3. 53 year-old patient with right invasive ductal breast cancer. Presents with multiple breast masses, the biggest mass is ulcerated, as well as increased skin thickness and increased density of breast tissue, due to invasion of the skin and lymphatic drainage. Lung metastasis can also be seen, more evident in the right lung.

Fig. 3: Figure 3.

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Fig. 4: Bilateral invasive ductal carcinoma diagnosed by percutaneous biopsy.
a. Ultrasound of medial inferior quadrant of the left breast shows increase in skin thickness, as well as posterior shadowing.
b. Enhanced chest CT where bilateral skin thickening is evident, due to lymphatic invasion and secondary edema.

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Fig. 5: CC and MLO bilateral mammography projections (a) in a patient with disseminated lymphoma, with bilateral and asymmetric breast skin thickening. Enhanced chest CT in the same patient (b), shows bilateral and asymmetric breast skin thickening, as well as a soft tissue mass surrounding the sternum which extends superficially to the subcutaneous tissue and deeply to the mediastinum; there is pericardial effusion and bilateral pleural effusion, conditioned by pleural metastases.

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Fig 6: 44 year-old patient with DISC treated with conservative surgery of the left breast for a cluster of microcalcifications. Screening mammography 5 years post-surgery (a) shows architectural distortion of the lateral quadrants with a radiopaque marker at the surgical scar, is evident also focal skin thickening. MR breast imaging of the same patient, shows marked background parenchymal enhancement at dynamic sequences (b), additionally focal skin thickening in topography of the surgical bed.
Fig 7. Right CC and MLO mammography projections (a, b) and MR breast imaging in a patient with history of radiotherapy for invasive ductal carcinoma show skin breast regular thickening, more evident at internal quadrants. There is arquitectual distortion at the lateral superior quadrant and a metallic marker at the biopsy bed; vascular calcifications are also present as a benign finding. STIR (c) and dynamic sequences (d) demonstrates decrease in left breast size, as well as skin diffuse thickening and homogeneous enhancement.

Fig. 7: Figure 7.

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Fig. 8. Infectious mastitis in a puerperal patient display increase in the echogenicity of breast parenchyma and increase in skin thickness; there is anechoic material in the subcutaneous tissue, secondary to edema.

**Fig. 8:** Figure 8.

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Fig 9. 23 year-old lactating patient who presents with breast enlargement, pain and hyperthermia of breast skin. Ultrasound findings demonstrate a well-defined inhomogeneous mass, associated with increased echogenicity of breast tissue and skin thickening, this findings secondary to infectious mastitis with abscess formation.

Fig. 9: Figure 9.

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Conclusion

Skin thickening is a common feature on breast imaging and invasive breast cancer is usually considered the only possible diagnosis. Nevertheless, this imaging finding has a wide range of diagnostic possibilities, including benign and malignant entities, for this reason general radiologist need to be aware of the patient’s clinical history in order to give a more certain diagnosis.
References


