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Imaging of the breast masses and the BIRADS classification

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Abstract:Background: Breast lumps are localized swellings that feel different from the surrounding breast tissue. It is a symptom/sign for a variety of conditions. As approximately 10% of breast lumps ultimately lead to a diagnosis of breast cancer. Mammography and sonography are the standard imaging techniques for detection and evaluation of breast disease. Mammography is the most established screening modality. Especially in young women and women with dense breasts, sonography appears superior to mammography, and differentiation between solid tumors and cysts is easier. Sensitivity and specificity of sonography or mammography are higher if sonography and mammography are combined. The latest edition of BI-RADS does not use percentages. Factors that can increase breast density include hormone replacement therapy, the effect is greater with combination hormone therapy than with oestrogen therapy alone, pregnancy, lactation, weight loss from reduction of breast fat, breast cancer especially inflammatory breast cancer, inflammation as mastitis. Factors that can decrease breast density include, age, post-menopausal state, medications: e.g. Danazol , vitamin D and calcium intake in pre-menopausal women, increasing age, weight gain, acromegaly

Keywords:*breast masses, BIRADS*

Introduction

Imaging of the breast masses and the BIRADS classification

Breast lumps are localized swellings that feel different from the surrounding breast tissue. It is a symptom/sign for a variety of conditions. As approximately 10% of breast lumps ultimately lead to a diagnosis of breast cancer **(1).**

Table (1): Findings in women seeking evaluation of apparent breast lump **(2)**

Finding	**Percentage of total**
Fibrocystic breast changes	40%
No disease	30%
Fibroadenoma	7%
Other benign mammary dysplasia and neoplasms	13%
Breast cancer	10%

Mammography and sonography are the standard imaging techniques for detection and evaluation of breast disease **(3)**.

Mammography is the most established screening modality**.** Especially in young women and women with dense breasts, sonography appears superior to mammography, and differentiation between solid tumors and cysts is easier. Sensitivity and specificity of sonography or mammography are higher if sonography and mammography are combined **(4).**

Table (2): Mammographic features of benign and malignant masses according to newest BIRADS lexicon. **(4).**

Mass type Mammographic feature	**Benign**	**Malignant**
Shape	• Rounded • Oval	• Irregular
Margin	• Circumscribed	• Obscured • Micro-lobulated • Indistinct • Spiculated
Mass density	• Fat • Low • Equal	• High
Calcification	• Macrocalcification: e.g Skin calcification • Vascular • Rounded • Egg Shell	• Amorphous • Coarse • Fine pleomorphic • Fine linear branching

Table (3): Ultra-sonographic features of benign and malignant breast mass according to the newest BIRADS lexicon. **((4).**

Mass **Ultra-sonographic Features**	**Benign**	**Malignant**
Shape	• Round • Oval	• Irregular
Margin	• Circumscribed	• Indistinct • Angular • Micro lobulated • Spiculated
Orientation	• Parallel	• Not parallel
Echo pattern	• Anechoic Hyper	• Hypoechoic
Posterior features	• Enhancement	• Shadowing

BIRADS lexicon and BIRADS assessment categories:

Breast composition:

Breast density on mammography can significantly vary between individuals. The density is a function of the relationship between radiolucent fat and radio dense glandular tissue.Breast density varies with age and generally younger women have denser breasts (i.e. more glandular tissue relative to fat) and post menopausal women have progressively less gland and more fat as involution of the breast takes place with increasing age.(**5)**

There are four BI-RADS categories for breast density:

- **A**: **fatty**; breast is almost entirely fat
- **B**: **scattered fibroglandular**; breast has scattered areas of fibroglandular density
- **C**: **heterogeneously dense**; breast tissue is heterogeneously dense which may obscure small lesions
- **D**: **dense**; breast tissue is extremely dense which lower sensitivity of mammography, the incidence of cancer is higher in this group than in other groups of breast density likely as a combination of the amount of gland present as well as possible observation error, it is in this group where screening ultrasound is potentially beneficial**. (6).**

The latest edition of BI-RADS does not use percentages.

Factors that can increase breast density include hormone replacement therapy, the effect is greater with combination hormone therapy than with oestrogen therapy alone, pregnancy, lactation, weight loss from reduction of breast fat, breast cancer especially inflammatory breast cancer, inflammation as mastitis .**(6)**

Factors that can decrease breast density include, age, post-menopausal state, medications: e.g. Danazol , vitamin D and calcium intake in pre-menopausal women, increasing age, weight gain, acromegaly. (**7)**

The use of density determination is now mandatory. Patients have to be informed of the fact that they have "dense" breasts with the implication that the dense breast has a potentially higher chance of developing a breast cancer. **(**7**).**

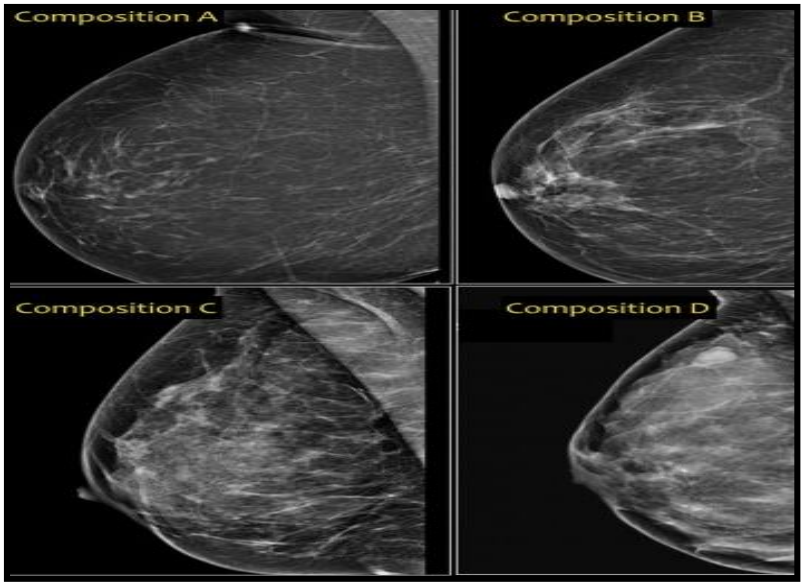


Fig. (1): breast composition A,B,C,D, **(8).**

Breast Mass:

A 'Mass' is a space occupying 3D lesion seen in two different projections. If a potential mass is seen in only a single projection it should be called a 'asymmetry' until its three-dimensionality is confirmed **(8).**

The density of a mass is related to the expected attenuation of an equal volume of fibroglandular tissue. High density is associated with malignancy. It is extremely rare for breast cancer to be low density**. (9)**

Architectural distortion:

It is distortion of normal architecture with no definite mass visible. It includes thin straight lines or spiculations radiating from a point, and focal retraction, distortion or straightening at the edges of the parenchyma. The differential diagnosis is scar tissue or carcinoma **(8).**

Asymmetry:

It is unilateral fibro-glandular deposits not conforming to the definition of a mass.

- **Asymmetry:** an area of fibroglandular tissue visible on only one mammographic projection.
- **Focal asymmetry:** isasymmetryyetvisible on two mammographic projections.
- **Global asymmetry:** Consisting of an asymmetry over at least one quarter of the breast.
- **Developing asymmetry:** is a new, larger and more conspicuous than on a previous examination **(8).**

Types of asymmetry in mammography lexicon and appropriate assessment category: (10):

- Single view asymmetry …. BIRADS I.
- Global asymmetry …. BIRADS II.
- Focal asymmetry…. BIRADS III.
- Developing asymmetry …. BIRADS IV.

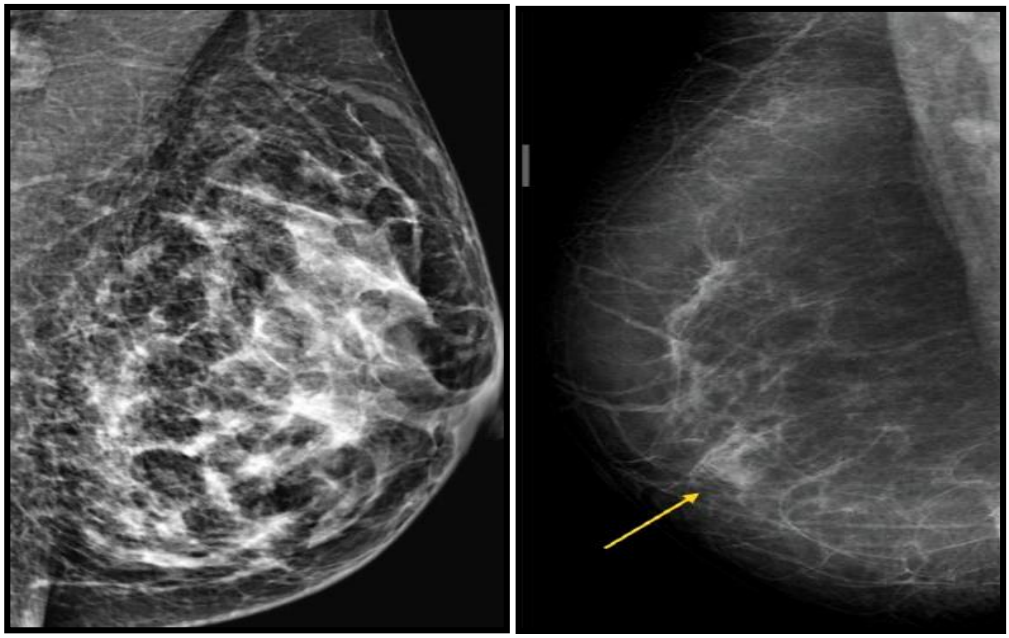


Fig. (2): Example of focal asymmetry (left image, arrowed) and UOQ global asymmetry (right image) according to updated BIRADS **(8).**

Calcifications:

Typical benign calcification:

Skin, vascular, coarse, large rod-like, round or punctate (< 1mm), rim, dystrophic, milk of calcium and suture calcifications.

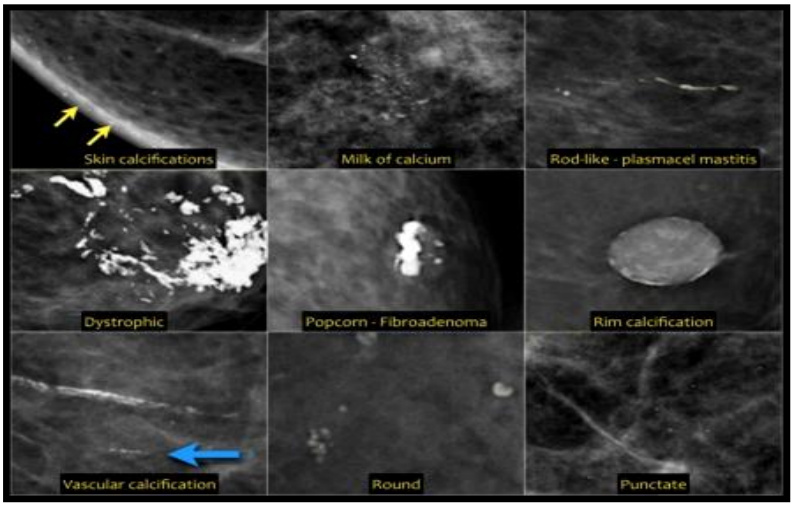


Fig. (3): Examples of benign calcifications according to updated BIRADS **(11).**

Suspicious calcifications:

- **Amorphous** (BI-RADS 4B), so small that a specific particle cannot be determined.
- **Coarseheterogeneous** (BI-RADS 4B), irregular and conspicuous, ranging 0.5-1 mm, tend to coalesce but are smaller than dystrophic calcifications.
- **Finepleomorphic** (BI-RADS 4C), more conspicuous than amorphous forms, usually < 0.5, without fine linear and linear branching.
- **Fine linear or fine-linear branching** (BI-RADS 4C), thin linear irregular calcifications with or without branching, usually < 0.5 mm **(11).**

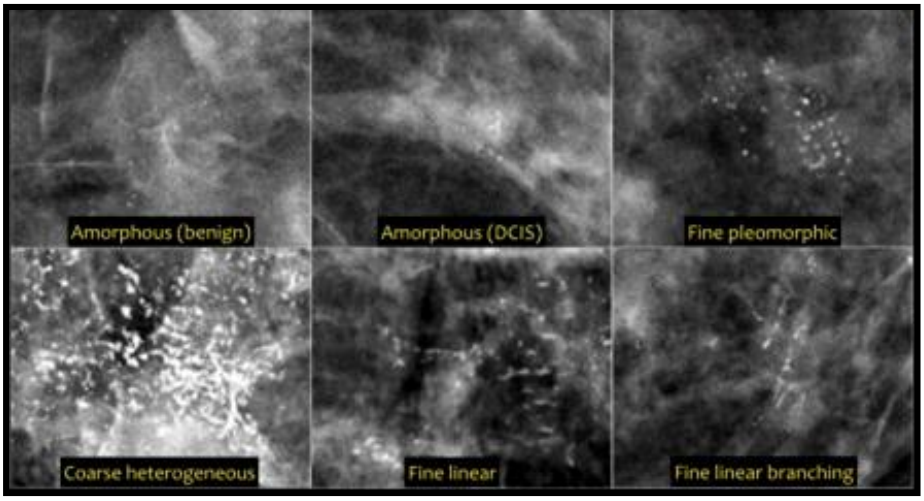


Fig. (4): Examples of malignant calcifications according to updated BIRADS **(11).**

Distribution of calcifications:

The morphology and distribution of calcifications determine their nature; the most important is the diagnosis of malignant micro-calcifications, which can be the early and only presenting sign of breast cancer. The arrangements of calcifications are as follows:

- Diffuse: distributed randomly throughout the breast.
- Regional: > 2 cm in greatest dimension
- Grouped (historically cluster): few calcifications occupying a small portion of breast tissue; ranging from 5 calcifications within 1 cm to >5 calcifications within 2 cm
- Linear: arranged in a line.
- Segmental: suggests deposits in ducts and their branches **(8).**

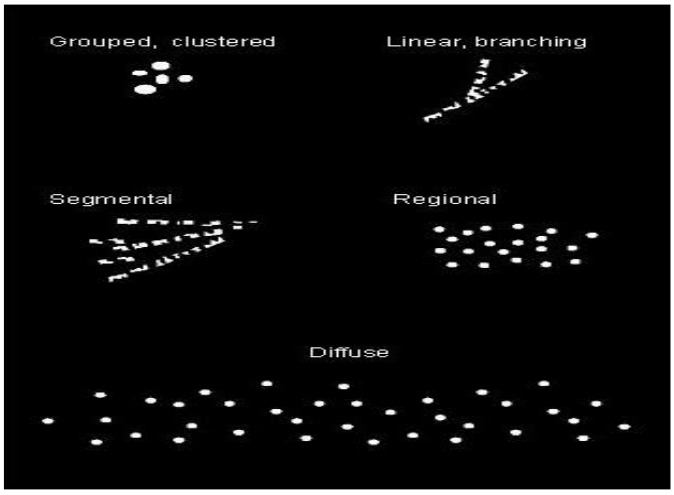


Fig. (5): Breast calcifications distribution according to updated BIRADS **(8).**

The 5th edition of the ACR BI-RADS Lexicon Atlas has been released in 2013 and last update was in November 2015

Table (4): The newest BIRADS lexicon for mammography and ultrasound **(12).**

Mammography Lexicon				Ultrasound Lexicon		
Breast composition	A. entirely fatty B. scattered areas of fibroglandular density C. heterogeneously dense, which may obscure masses D. extremely dense, which lowers sensitivity			**Breast composition**	a. homogeneous - fat b. homogeneous - fibroglandular c. heterogeneous	
Mass	**shape**	oval - round - irregular		**Mass**	**shape**	oval - round - irregular
	margin	circumscribed - obscured - microlobulated - indistinct - spiculated			**margin**	Circumscribed ***or*** Not-circumscribed: indistinct, angular, microlobulated, spiculated
	density	fat - low - equal - high			**orienta-tion**	parallel - not parallel
Asymmetry	asymmetry - global - focal - developing				**echo pattern**	anechoic - hyperechoic - complex cystic/solid hypoechoic - isoechoic - heterogeneous
Architectural distortion	distorted parenchyma with no visible mass				**posterior features**	no features - enhancement - shadowing - combined pattern
Calcifications	**morpho-logy**	typically benign		**Calcifications**	in mass - outside mass - intraductal	
		suspi-cious	1. amorphous 2. coarse heterogeneous 3. fine pleiomorphic 4. fine linear or fine linear branching	**Associated features**	architectural distortion - duct changes - skin thickening - skin retraction - edema - vascularity (absent, internal, rim) - elasticity	
	distribu-tion	diffuse - regional - grouped - linear - segmental		**Special cases** *(cases with a unique diagnosis)*	simple cyst - clustered microcysts - complicated cyst - mass in or on skin - foreign body (including implants) - intramammary lymph node - AVM - Mondor disease - postsurgical fluid collection - fat necrosis	
Associated features	skin retraction - nipple retraction - skin thickening - trabecular thickening - axillary adenopathy - architectural distortion - calcifications					

BI-RADS Assessment Categories:

BI-RADS assessment categories were designed to be concordant with specific management recommendations. We should include the text corresponding to each category **(12).**

The latest version classifies lesions into six categories: (**13)**.

BIRADS 0:

- Incomplete, further imaging or information is required, e.g. compression, magnification, special mammographic views and ultrasound.
- This is also used when requesting previous images not available at the time of reading.

BIRADS I:

- Negative, symmetrical and no masses, architectural disturbances or suspicious calcifications present.

BIRADS II:

- Category 2 is a definitive benign finding and a routine screening. That is, there is something abnormal on mammogram but it is not breast cancer or malignant in any way.

BI-RADS category 2 findings often include:

- Round opacities with macro-calcifications (typical calcified fibroadenoma or cyst)
- Round opacities corresponding to a typical cyst at ultrasonography.
- Oval opacities with a radiolucent center.
- Fatty densities or partially fatty images: lipoma **,** galactocele, oil cyst, hamartoma.
- Fatty densities or partially fatty images: lipoma **,** galactocele, oil cyst, hamartoma.

BIRADS III:

- Probably benign, short interval follow-up suggested Findings typical of this category include:
- Clusters of tiny calcifications – round or oval

- Non-calcified solid nodules(no size limitation but non-palpable on physical examination), round, ovoid and well-defined.
- Selected focal asymmetrical areas of fibro glandular densities (not palpable): This might include concave-outward defined margins, interspersed with fat and without central increased fibular density on two projections.
- Miscellaneous focal findings, such as a dilated duct or post biopsy architectural distortion without central density.
- Generalized distribution in both breasts. For example, multiple similar lesions with tiny calcifications or nodules distributed randomly.

BIRADS IV:

- Suspicious abnormality
- There is a mammographic appearance which is suspicious for malignancy.
- Biopsy should be considered for such a lesion.
- these can be further divided as
    - **BIRADS IVa**: low level of suspicion for malignancy (Partially circumscribed mass, suggestive of (atypical) fibroadenoma. Palpable, solitary, complex cystic and solid cyst Probable abscess)
    - **BIRADS IVb**: intermediate suspicion for malignancy (Group amorphous or fine pleomorphic calcifications. Nondescript solid mass with indistinct margins
    - **BIRADS IVc**: moderate suspicion for malignancy. (New group of fine linear calcifications. New indistinct, irregular solitary mass).
- **BI-RADS V**: highly suggestive of malignancy
    - >95% probability of malignancy
    - appropriate action should be taken

Classifications of breast lesions:

The most majority of the lesions that occur in the breast arebenign. Much concern is given to malignant lesions of the breastbecause breast cancer is the most common malignancy in womenin Western countries; however, benign lesions of the breastare far more frequent than malignant ones(**14)**

Benign lesions are classified as follows:-

I. Developmental abnormalities:
- Ectopic breast (mammary heterotopia).
- Underdevelopment of the breast (hypoplasia).

II. Inflammatory lesions:-
- Lactational mastitis.
- Abscess.
- Nonspecific inflammation.

III. Fibrocystic changes

IV. Proliferative stromal lesions:
- Diabetic Fibrous Mastopathy
- Pseudoangiomatous Stromal Hyperplasia of the Breast

V. Traumatic:-
- Fat necrosis.
- Radial scar.
- Foreign body granulomata.

VI. Neoplasm:
- Fibroadenoma
- Lipoma

- Hamartoma
- Nipple adenoma
- Lactating adenoma**. (15)**.

Malignant breast lesions:

"WHO" Histologic Classification of Breast Carcinoma:

Precancerous lesions:

- New WHO lists both Intraductal carcinoma in situ (DCIS) and Lobular carcinoma in situ (LCIS) as precursor lesion of the breast.
- Intraductal proliferative lesions: (e.g Usual ductal hyperplasia…)
- Papillary lesions: (e.g Intraductal papilloma…)

Invasive (infiltrating) Carcinoma:

- Invasive duct carcinoma, not otherwise specified (NOS) now known as invasive carcinoma of no special type (NST).
- Invasive lobular carcinoma.
- Tubularcarcinoma.
- Invasive cribriform carcinoma.
- Mucinous carcinoma (Colloid carcinoma).
- Carcinoma with medullary feature.
- Carcinoma with apocrine differentiation.
- Invasivepapillary carcinoma.
- Carcinoma with signet ring differentiation (e.g Invasive micropapillary carcinoma...)
- Metaplastic carcinoma
- Epithelial-myoepithelialtumors (e.gadenoidcystic carcinoma).
- Other rare types (e.gcarinoma with neuroendocrine differentiation). **(16)**

Breast lesions:

Inflammatory breast lesions

1) Fat necrosis:

Fat necrosis can present as a painless palpable mass, mammographic density, or mammographic calcifications. The majority of women will give a history of trauma or prior surgery. The major clinical significance of the condition is its possible confusion with breast carcinoma as palpable mass or mammographic calcifications. Lipid cysts on mammography are diagnostic of fat necrosis. Fat necrosis may be seen as a hypoechoic mass with well-defined margins andmural nodules on ultrasound. **(17)**

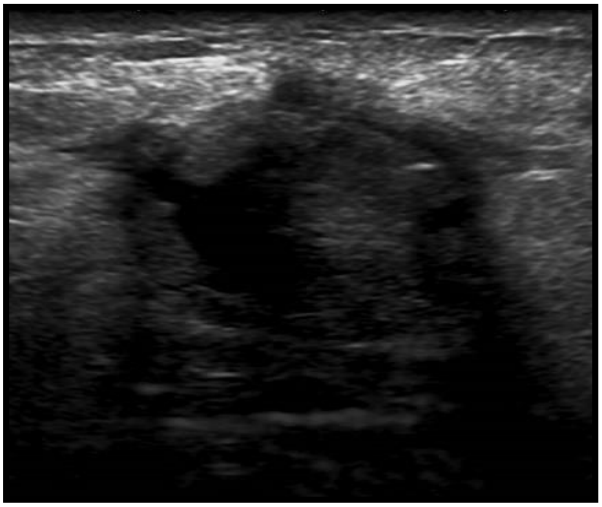


Fig (6): Sonographic appearance of fat necrosis **(18).**

Fat necrosis appear as a well defined lucent area , the calcification is typically peripheral with a stippled curvilinear appearance creating the appearance of lucent "bubbles" in the breast parenchyma on mammography with time it giving rise to oil cyst. **(19).**

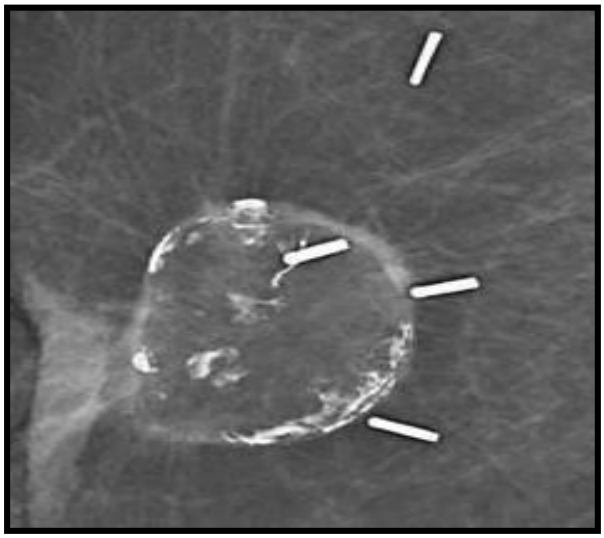
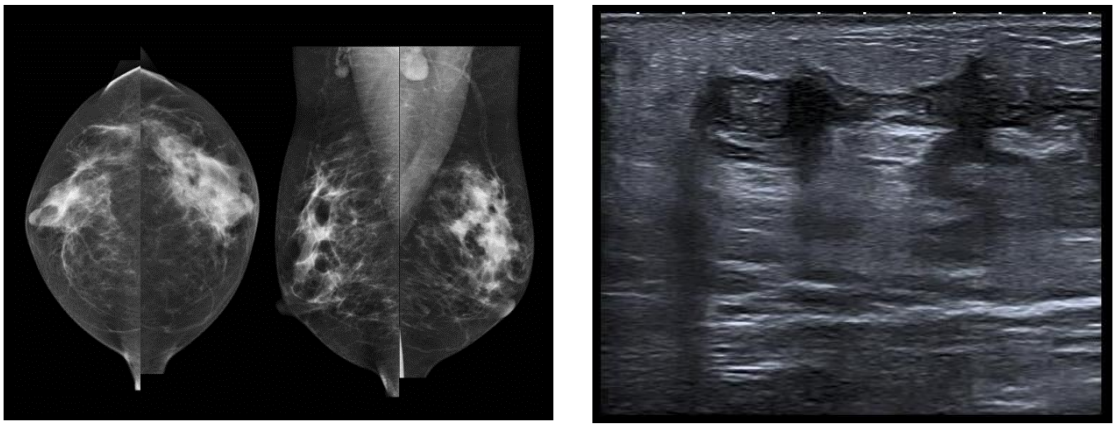


Fig (7): mammographic appearance of fat necrosis **(20)**.

Grossly, it is opaque bright yellow. Microscopically, the lesion is characterized by infiltration of foamy histiocytes, lymphocytes, plasma cells and giant cells around fat cells **(20)**.

2) Granulomatous mastitis:

Granulomas present less than 1% of all breast biopsies. Systemic granulomatous (e.g. sarcoidosis) and infections (mycobacterial, fungal), most commonly in immunocompromised patients. It is caused by many etiologies, including infectious agents, reaction to systemic disease, antigen-antibody reaction and idiopathic. Microscopically, the granulomatous reaction consisting of epithelioid histiocytes, giant cells and inflammatory cells surrounds the breast lobules, in chronic cases non-caseating granuloma exist **(21).**



(A) (B)

Fig. (8): Mammographic images shows left UOQ focal asymmetry with abnormal axillary lymph node (A). By Ultrasound shows irregular-shaped with not-circumscribed margins and hypoechoic echo pattern mass with tubular extension. (B) **(22).**

3) Periductal mastitis/ Duct ectasia:

It tends to occur in the fifth or sixth decade of life, in multiparous women. Its clinical significance is it can be mistaken for carcinoma as it may appear as irregular intra-ductal mass in mammography. Clinically usually

associated with nipple discharge and characterized by dilatation of major ducts in sub areolar region grossly and microscopically the ducts contain eosinophilic granular secretions within the duct lumen with or without mass. **(23).**

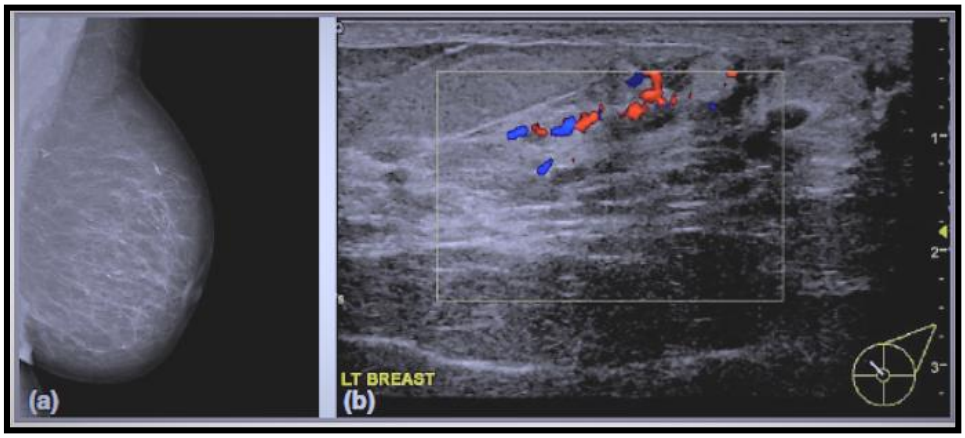


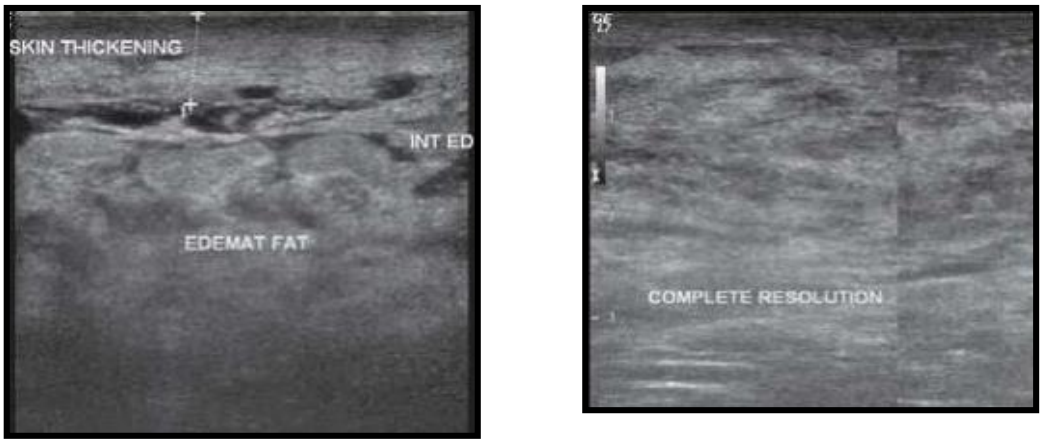
Fig (9): Duct ectasia. (a) Screening mammogram showing ductal distribution of needle shaped calcification in the left breast characteristic of duct ectasia. (b)Ultrasound shows multiple dilated ducts and intervening echogenic parenchyma with increased vascularity in the area of the mass. (**24)**

Simple Mastitis Mammography

Mammography is not a first line investigation in lactating women, it is often difficult to interpret, given the edema and insufficient compression. It may reveal non- specific signs, such as subcutaneous edema, density asymmetry **(24).**

Ultrasound examination reveals non-specific signs such as thickening of the skin (more than 3 mm), hyper - echogenicity of the fatty lobules related to the edema, or dilatation of ducts (more than 3 mm). At a more advanced stage, intra- mammary collections may be seen as round or oval masses with thick walls and a vascularized hyper- echoic corona. They are anechoic or heterogeneous, possibly with posterior strengthening of the echoes. **(24).**

Adenopathy is frequently to be found in the axillae **(24).**



(A) (B)

Fig. (10): Acute lactational mastitis. A 22-year-old lactating female presenting with acute inflammatory signs of the right breast. Ultrasound examination (a) showed edematous fat lobules delineated by interstitial edema lines with marked overlying skin thickening. The patient was asked to come for a follow-up ultrasound examination on a 2 weeks basis (under antibiotic coverage) until complete resolution of the inflammatory process was assured (b). **(25).**

Superficial abscesses usually had associated skin thickening .Patients with severe mastitis should be periodically assessed with US until clinical symptoms have resolved. Periodic assessment can help to detect the development of an abscess at an early stage **(25).**

Benign Epithelial lesions

A wide variety of benign epithelial lesions are observed in breast. These changes have been divided into three groups, according to the risk of developing breast cancer: (I) non proliferative breast changes, (II) proliferative breast disease, and (III) atypical hyperplasia. Non proliferative changes do not increase the risk of cancer. Proliferative disease is associated with a mild increase in risk. Proliferative disease with atypia (ADH and ALH) confers a moderate increase in risk **(26).**

1) Non proliferative breast changes (Fibrocystic changes):

This group includes changes grouped under the term "fibrocystic changes" (FCCs). It constitutes the most frequent benign disorder of the breast, it generally affects premenopausal women between 20 and 50 years of age.

Grossly, they show variable size visible cysts, contains clear or yellow fluid. Microscopically, they are lined by double layer of flat/cuboidal cells or no lining, with Variable apocrine metaplasia.

A wide range of lesions are associated, including epithelial metaplasia, hyperplasia, adenosis, cyst formation, inflammatory changes, apocrine metaplasia, fibrosis, as well as calcification. The three principal patterns of morphologic change, cyst formation, fibrosis and adenosis. **(27).**

They are seen as well-defined, round or oval masses .Sometimes a characteristic halo is visible on mammography. **(27).**

Ultrasound demonstrates well-defined margins, with an oval or round shape. There is an absence of internal echoes indicating the presence of fluid. The area of breast tissue behind a cyst appears bright on ultrasound (posterior enhancement). **(27).**

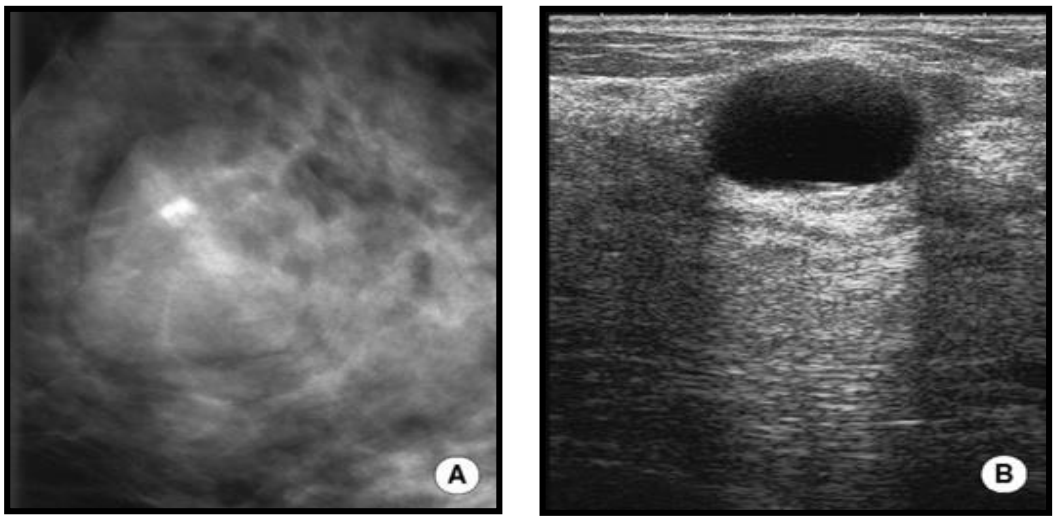


Fig (11): Mammography shows: well defined rounded mass with typical halo sign (A), Ultrasounds shows rounded anechoic cyst (the absence of internal echoes and posterior enhancement is diagnostic of the cyst) (B). **(28)**

2) Proliferative breast disease without atypia:

These changes rarely form palpable masses. More commonly, they are detected as mammographic densities or calcifications or as incidental findings in biopsies performed for other reasons.

This group of disorders is characterized by proliferation of ductal epithelium and/or stroma without cellular abnormalities, including:

1) Moderate or florid epithelial hyperplasia
2) Sclerosing adenosis

3) Complex sclerosing lesions
4) Papillomas
5) Fibroadenoma with complex features **(15)**.

I. Epithelial hyperplasia:

Hyperplasia is moderate when there are more than four epithelial layers. The proliferating epithelium, often including both luminal and myoepithelial cells, fills and distends the ducts and lobules. **(29).**

II. Sclerosing adenosis:

Grossly, it is hyperplastic proliferation of breast glandular component. Microscopically, formed of elongated and compressed glands of atrophied epithelial cells, surrounded by sclerosed stroma. It mimic cancer and hard to differentiate in mammography **(30).**

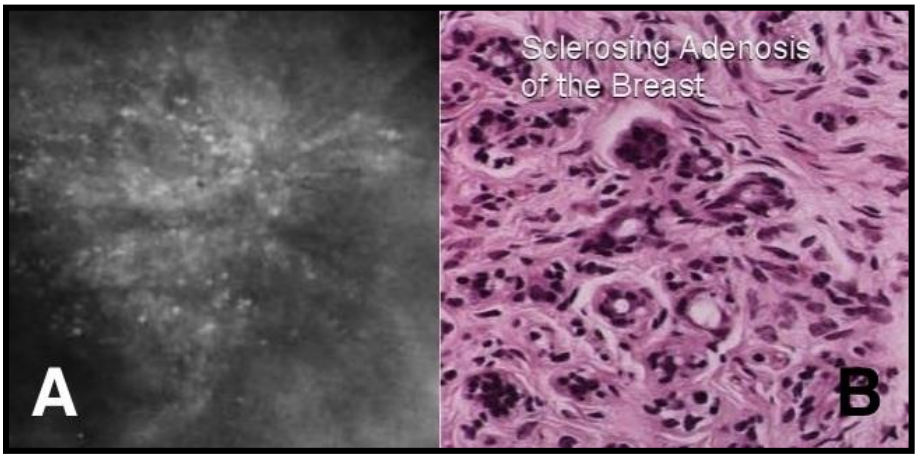
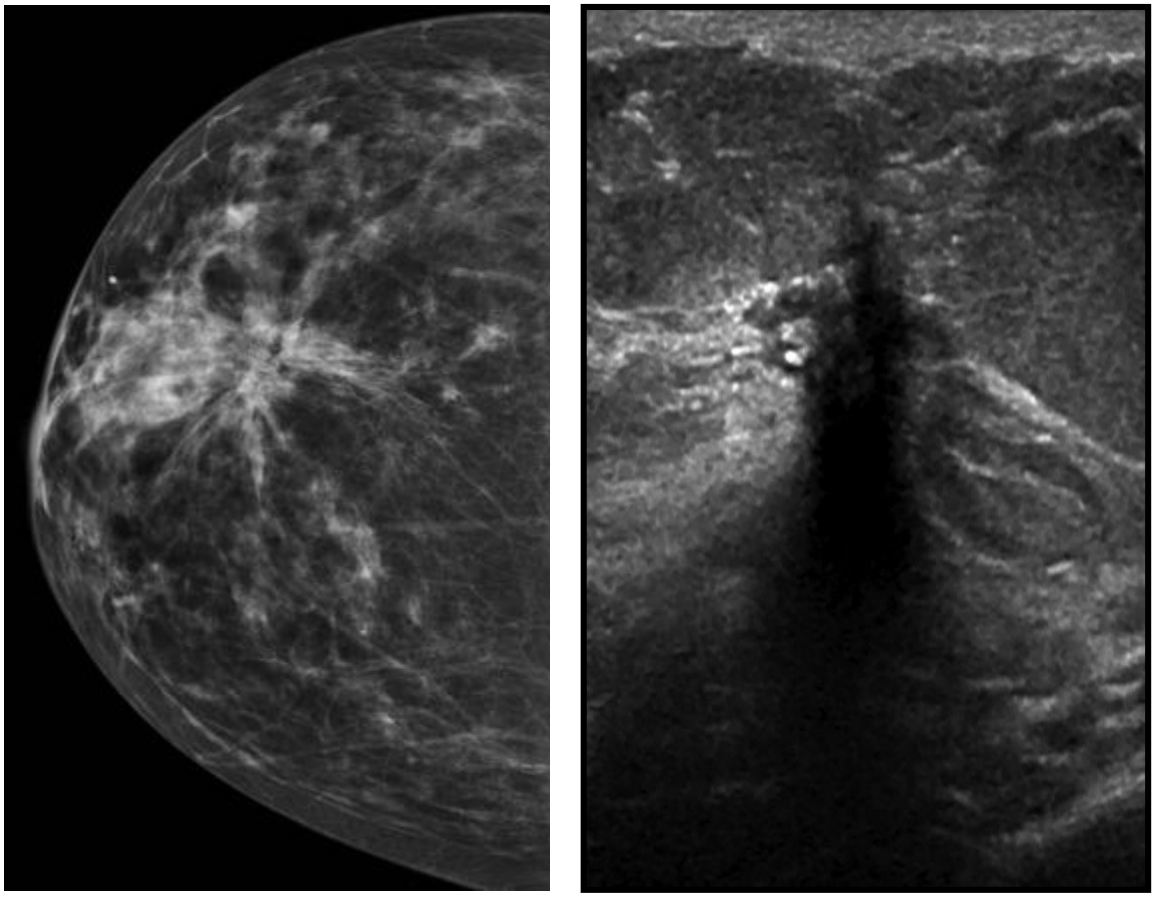


Fig. (12): Sclerosing adenosis, (A) at mammography (B) microscopically **(30).**

III. Complex sclerosing adenosis (Radial Scar):

Radial scars are stellate lesions characterized by a central nidus of entrapped glands in hyalinized stroma. They can resemble irregular invasive carcinomas mammographically or on gross examination. The term "scar" refers to the morphologic appearance, as they are not associated with prior trauma or surgery**.** A radial scar has a spiculated appearance similar to carcinoma, but the center tends to be a translucent, low-density area rather than a mass. The breast tissue behind the lesion is almost visible through the lesion. The relatively low density of the centre is a relevant and visible difference between carcinoma and a radial scar. **(31).**



(A) **(B)**

Fig. (13): breast mammograghy in CC view shows spiculated mass (arrow) with lucent center and prominent thin spicules radiating outward (A), ultrasound image shows correlative irregular hypoechoic mass with posterior acoustic shadowing. Although mammographic features suggest possibility of radial scar, neither mammography nor ultrasound excluded possibility of breast cancer, and biopsy is mandatory. **(32)**

IV. Papillomas:

It can be divided into solitary or multiple. Solitary papilloma is usually located beneath the nipple, whereas multiple papillomas are more peripherally located.

Microscopically, papillomas are characterized by growth of a dilated duct wall, they have a fibrovascular cores and lined by epithelial cells, together with an intervening layer of myoepithelial cells. papillomas are benign, but apocrine or squamous metaplasia may be seen. Frequently, it obliterates the ductal lumen **(33).**

Mammograms are frequently normal (particularly with small intraductal papillomas). When imaging findings are present, they include solitary or multiple dilated ducts, a circumscribed benign-appearing mass (often subareolar in location), or a cluster of calcification. **(6).**

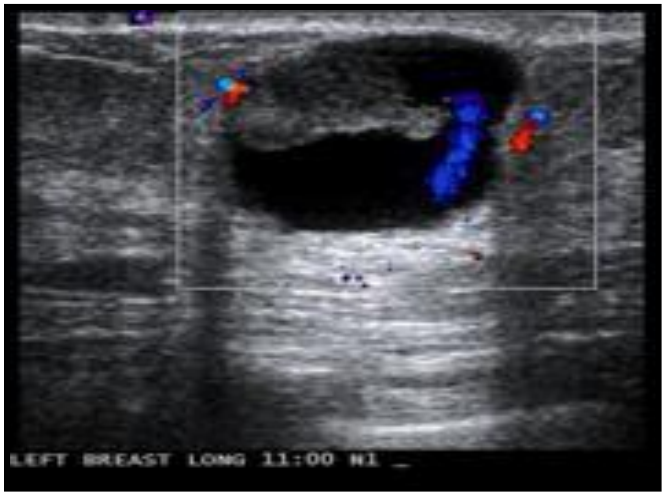


Fig. (14): Ultrasound shows intracystic papillary breast carcinoma**. (34).**

On the whole, papillomas are benign but are associated with slightly increased risk for cancer (2-6 %), more for the multiple papillomas (papillomatosis) than for the solitary papilloma **(34).**

V. Complex fibroadenoma:

Complex fibroadenomas show cysts larger than 3 mm, sclerosing adenosis, epithelial calcifications, or papillary apocrine changes, and this group of fibroadenomas shows higher by 1.6 times cancer risk compared to the usual fibroadenomas. **(35).**

Benign stromal lesions

The two types of stroma in the breast, (1) intralobular and (2) interlobular. The breast-specific biphasic tumors **(I) fibroadenoma** and **(II)phyllodes tumor** arise in the interlobular stroma. Another unknown origin tumor can be added in this group **(III) Hamartoma** (fibroadeno-lipoma).

Interlobular stroma is the source of the same types of tumors found in connective tissue in other sites of the body (e.g., lipomas and angiosarcomas) as well as tumors arising more commonly in the breast (e.g.**(IV) pseudoangiomatous stromal hyperplasia** and **(V) fibrous tumors) (35).**

(I) Fibroadenoma:

This is the most common benign tumor of female breast. Occurring at any age within the reproductive period of life, more common before age 30. They are frequently multiple and bilateral. Young women usually present with a palpable mass and older women with a mammographic density or mammographic popcorn calcifications for the involuted type **(36).**

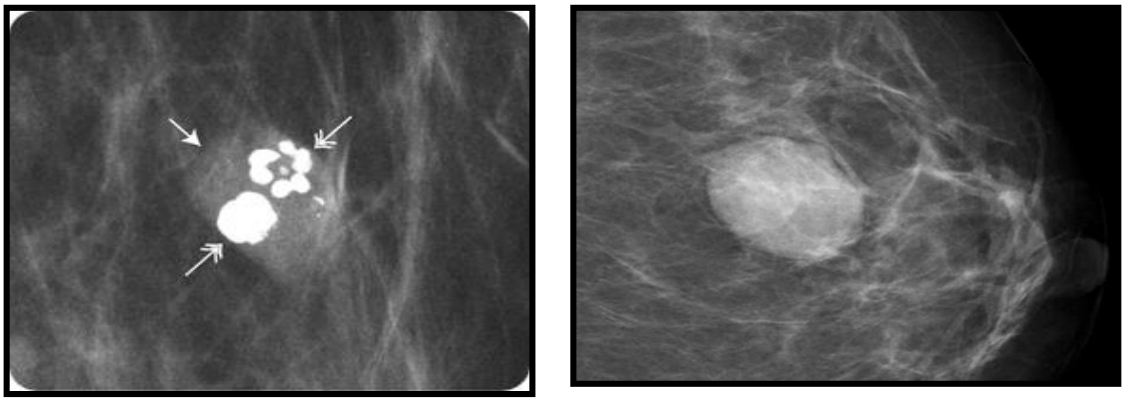


Fig. (15): Fibroadenomas in mammography, pop corn calcification (left image) and Fibroadenoma mass (right image) **(36).**

By ultrasoundFibroadenoma Typically seen as a well-circumscribed, round to ovoid , or macrolobulated mass with generally uniform hypoechogenicity on ultrasound. **(31).**

SWE was conducted with the aid of a movable intelligent unit displaying tissue stiffness on a color scale; progression from blue to red indicates increasing shear modulus (stiffness). Tissue data were also displayed in kilopascals (kPa), guiding delineation of regions of interest (ROIs). Inbuilt SWE software allowed the operator to delineate circular ROIs of various diameters within the elastographic window, and automatically displayed shear modulus data (in kPa) for each ROI; these included maximum, minimum, and mean values with standard deviations. As each ROI was moved around the image with a cursor, the elastographic values were immediately displayed in a data box, allowing the ROI to be placed in the area of greatest stiffness. We used ROIs 2 mm in diameter. Minimum, mean, and maximum elasticity values were calculated in ROIs placed over the stiffest areas on the color maps, and mass/fat ratios were also determined **(37)**

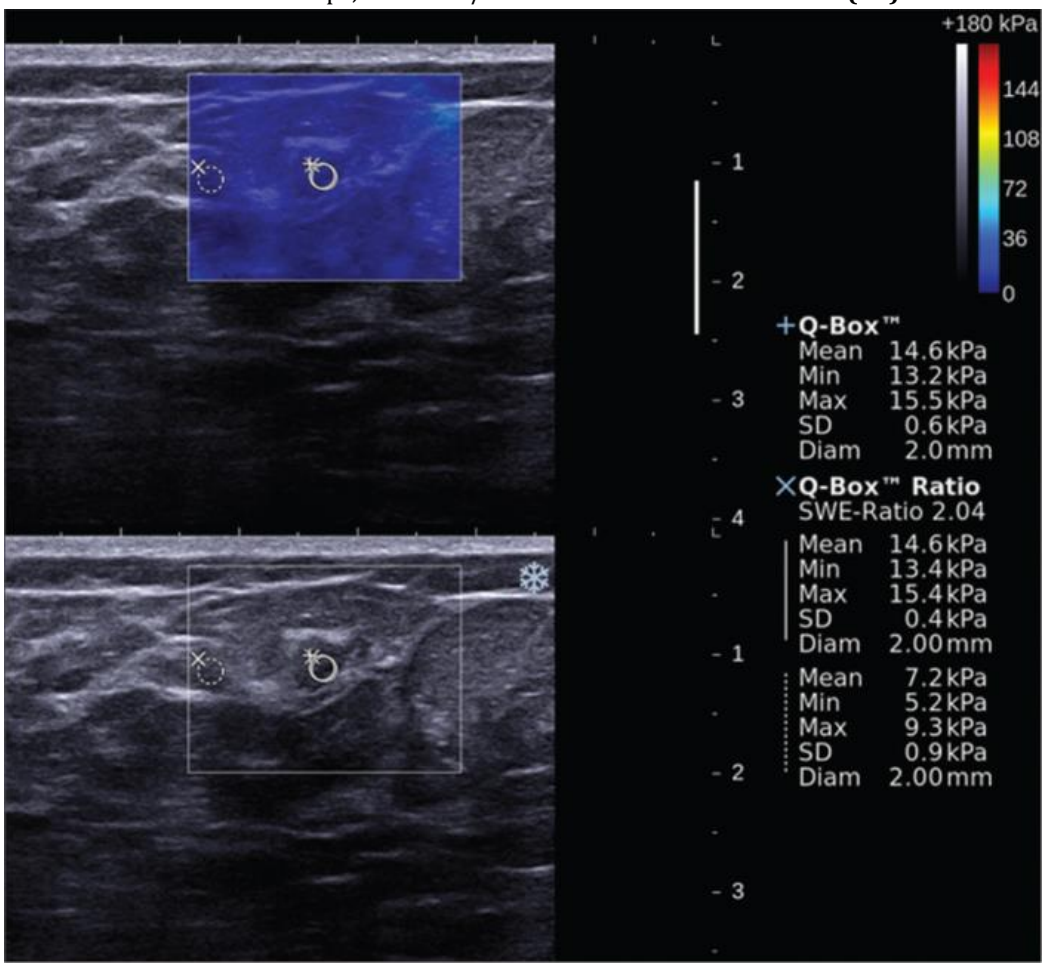


Fig .(16) Shear wave elastographic evaluation of a BI-RADS III biopsy-proven fibroadenoma. The B-mode image is shown below the color-coded elasticity map. ROIs were delineated around the stiffest areas on the color maps. All lesions were coded blue during shear wave elastographic ultrasound examination. The ROI of breast fat tissue was of the same size and depth as that of the corresponding lesion. Mean lesion elasticity, 14.6 kPa; mean fat tissue elasticity, 7.2 kPa; mass/fat ratio, 2.04; ROI diameter, 2 mm **(38**)

(II) Phyllodes tumor:

Grossly the tumor is firm, round and well circumscribed. Some cleft- like spaces may be evident on cut sections. Microscopically, the tumor is composed of epithelial and stromal components. Epithelial part is made of slit-like double layered ducts, surrounded by hypercellular stroma. This hyper cellularity

distinguishes the phyllodes tumor from fibroadenoma. Phyllodes tumor has been divided into three grades: benign, borderline and malignant**.** Phyllodes tumors typically seen as non-specific large rounded oval or lobulated, generally well circumscribed, lesions with smooth margins. A radiolucent halo may be present. Calcification (typically coarse and plaque like) may be seen in a very small proportion on mammography. **(39).**

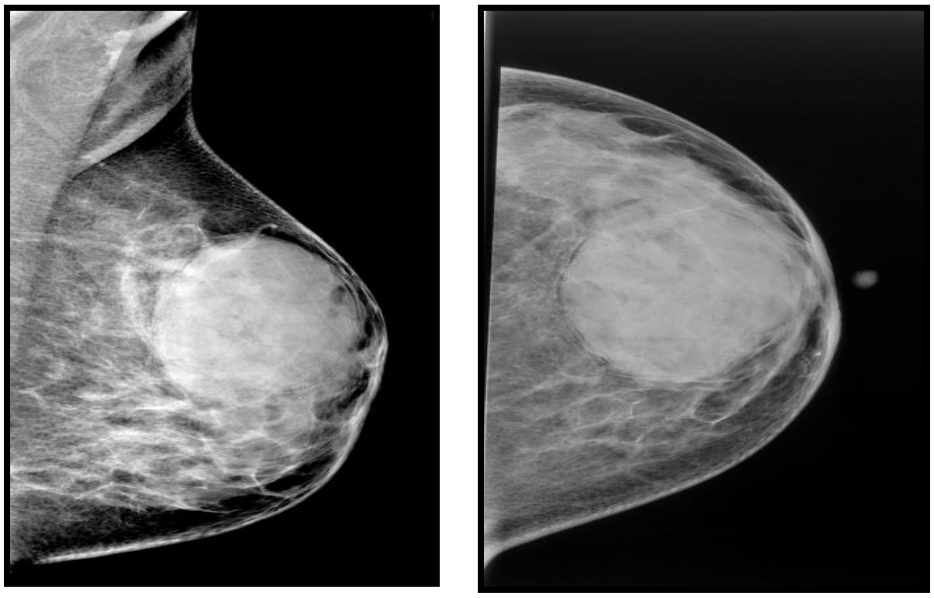


Fig. (17): Craniocaudal and Medio lateral oblique views showing large well circumscribed dense lesion with halo sign**. (39).**

General sonographic features are non-specific and can mimic that of a fibroadenoma. On ultrasound, an inhomogeneous, solid-appearing mass is the most common manifestation. A solid mass containing single or multiple, round or cleft like cystic spaces and demonstrating posterior acoustic enhancement strongly suggests the diagnosis of phyllodes tumour. Vascularization is usually present in the solid components. **(39).**

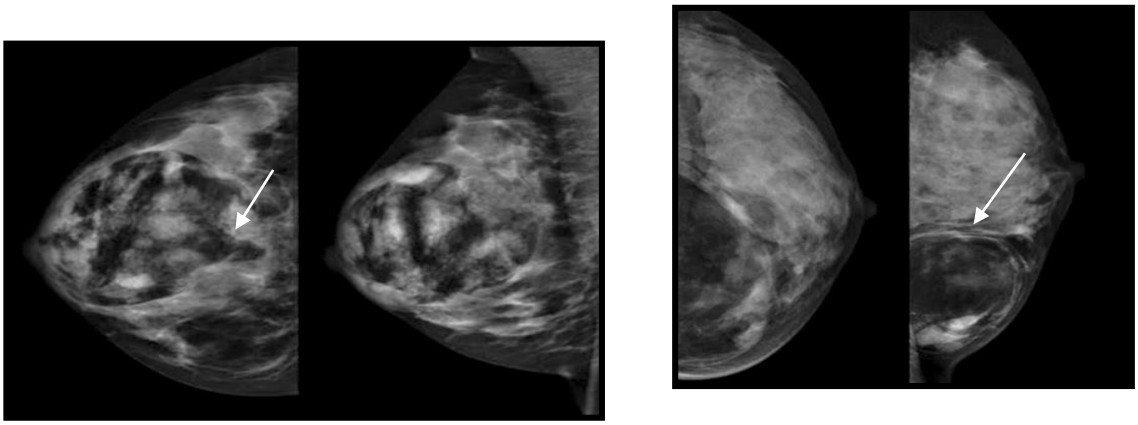
Fig. (18): ultrasound shows inhomogeneous solid mass with multiple cleft like cystic space. **(39).**

(I) Hamartoma:

This is a benign tumor and rarely recurs, usually round to oval and lobulated grossly. Under microscope, it shows ducts, lobules, interlobular fibrosis, smooth muscle, and adipose tissue in varying proportions **(40).**

Hamartomas are typically seen on mammography as oval or round formations, which are inhomogeneous with radio-opaque and radiotransparent areas reflecting the presence of tissues that differ in density. They are well defined by a thin radio-opaque pseudocapsule. Owing to the presence of scattered nodular opacities

within the radiotransparent fat tissue contained in the pseudocapsule, the mass typically resembles a slice of salami (**13)**.



(A) (B)

Fig. (19): CC and MLO views showing typical appearance of a hamartoma on mammography: a well-defined mass containing a substantial amount of fat (radiotransparent) and fibroepithelial components (radio-opaque). The "slice of salami" appearance is shown in (A), while (B) provides better visualization of the pseudocapsule. (**41)**

Breast carcinoma

Etiology of Breast cancer:

The most common risk factors for the development of breast cancer, identified by many epidemiologic studies, the most important are as follows;

1) **Age:** Breast cancer is rarely before 25 years except in certain familial cases. The incidence rises throughout a woman's lifetime. 77% of cases occur in women over 50 years.
2) **Late menopause:** also increases risk.
3) **First live birth:** Women with a first full-term pregnancy at younger than 20 years of age have half the risk of nulliparous women or women over the age of 35 at their first birth.
4) **First-degree relatives with breast cancer:** The risk of breast cancer increases with the number of affected first-degree relatives, due to BRCA1 or BRCA2 gene mutation.
5) **Estrogen exposure:** Postmenopausal hormone replacement increases the risk of breast cancer; estrogen and progesterone together increase the risk more than does estrogen alone.
6) **Carcinoma of the contralateral breast or endometrium**: owing to the share hormonal risk factors for these tumors.
7) **Obesity:** There is decreased risk in obese women younger than 40 years owing to the association with anovulatory cycles and lower progesterone levels and increased risk in postmenopausal obese women, which is attributed to synthesis of estrogens in fat depots.
8) **Breast-feeding:**The longer breast-feeding, reduces breast cancer risk. (**14)**

Breast carcinoma subtypes:

Breast cancer classified in many subtypes, by morphology (e.g., ductal and lobular carcinomas), by protein expression (e.g. ER-positive and HER2/neu-positive carcinomas), and by germ-line mutations (e.g. BRCA1 and BRCA2 carcinomas), by new subtypes that were not previously well defined have been identified (e.g., the basal-like carcinomas) **(42).**

Classification of breast carcinoma:

Almost all breast malignancies are adenocarcinomas, all other types (i.e., squamous cell carcinomas, phyllodes tumors, sarcomas, and lymphomas) making up fewer than 5% of the total. Carcinomas are divided into (I) **in situ carcinomas;** limited to ducts and lobules basement membrane without crossing it and (II)

invasive carcinomas; have invaded beyond the basement membrane into stroma. Invasive ductal and lobular carcinomas were named by their association with the characteristic in situ component.

Other rare types of adenocarcinoma (e.g., apocrine carcinomas, carcinomas with neuroendocrine differentiation, and clear cell carcinomas) are similar to carcinomas of no special type in behavior and prognosis **(43).**

Table (5): Showing distribution of breast invasive carcinoma histological subtypes **(44).**

Total cancers	**Percentage**
Carcinoma in situ	**15-30**
• Ductal carcinoma in situ (DCIS)	• 80
• Lobular carcinoma in situ (LCIS)	• 20
Invasive carcinoma	**70-85**
• No special type carcinoma	• 79
• Lobular carcinoma	• 10
• Tubular carcinoma	• 6
• Mucinous carcinoma	• 2
• Medullary carcinoma	• 2
• Papillary carcinoma	• 1
• Metaplastic carcinoma	• <1

(I) In situ lesions:

(1) Ductal Carcinoma In-Situ:

It represents 15% to 30% of carcinomas in the mammography of well-screened populations, in mammographically detected cancers, almost half are DCIS, frequently presents as mammographic calcifications.

DCIS is divided into 5 different morphology subtypes: comedo, cribiform, micropapillary, papillary, and solid and divided into three grades, comedo carcinoma has been placed in grade 3, solid, cribriform and micropapillary carcinomas were designated according to their cytomorphology, grade 1 if low and grade 2 if intermediate, in pathology it can be subdivided as **(I) comedo** and **(II) Non comedo (30).**

(I) Comedo: is characterized by solid sheets of pleomorphic cells with high-grade nuclei and central necrosis. The necrotic cell membranes commonly calcify and are detected on mammography as clusters or linear and branching microcalcifications **(45).**

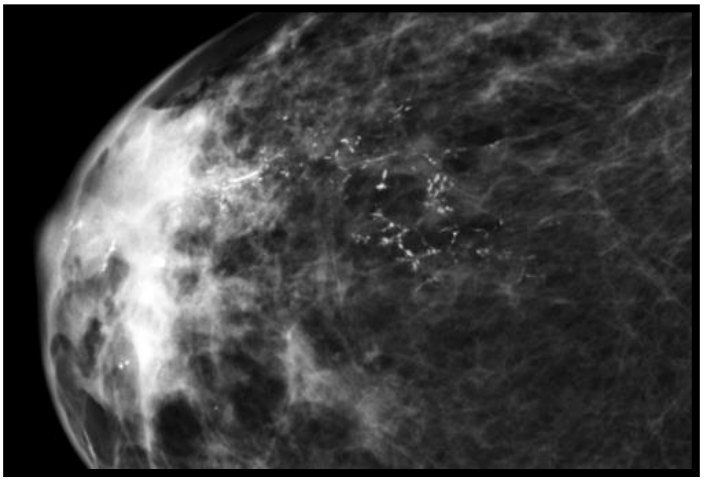


Fig. (20): DCIS as classically seen in mammography **(45).**

By ultrasound DCIS presented as an irregular hypoechoic mass with an indistinct margin, microcalcifications, ductal changes, and structural distortion, but few reports focused on systematic analysis

of ultrasonographic features and ducts abnormalities of DCIS .The ultrasonographic features of DCIS are not specific, and there is variability in interpretation, understanding the classification of the features can improve the diagnostic accuracy. The evaluation of ducts abnormalities will provide valuable clues to predict the benign or malignant of breast lesions. The evaluation of the ability of ultrasonography in predicting DCIS can provide useful message for clinical decision. **(45)**

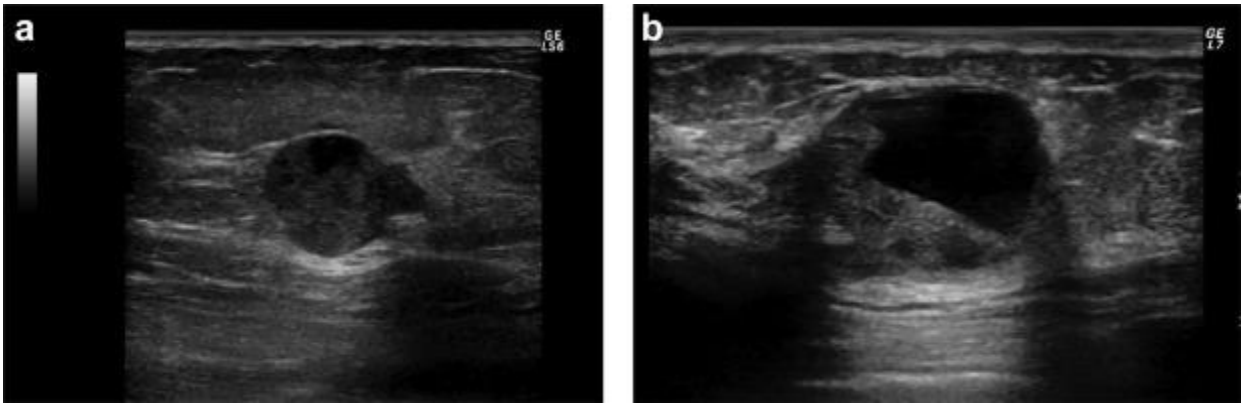


Fig.21. Typical solid mass and mixed mass images. (a) Solid mass. (b) Mixed mass. Both lesions are ductal carcinoma *in situ*. (**46**)

SWE was applied , which was equipped with a 4- to 15-MHz linear-array transducer, to investigate mass stiffness of the lesion quantitatively. The maximum elasticity value of the mass, measured in a 2 mm diameter region of interest, was 106.1 kPa in the lateral portion (far from the nipple) and 21.8 kPa in the medial portion (close to the nipple)

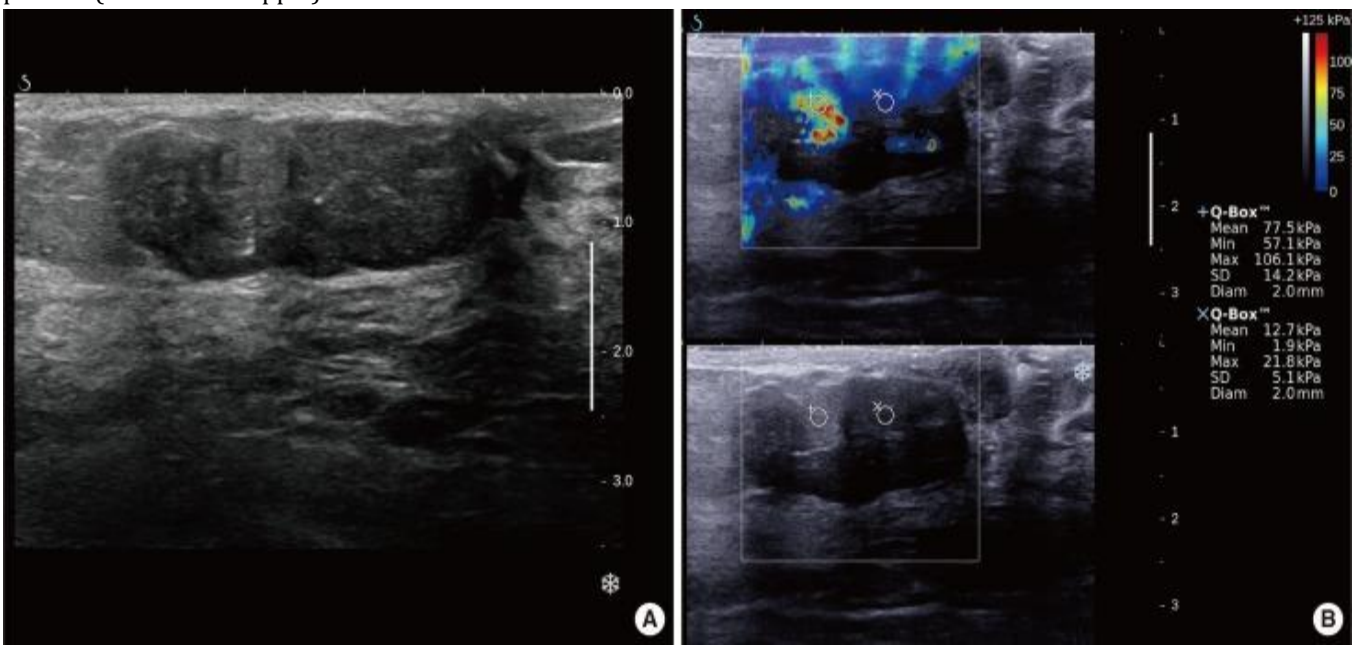


Fig. (22 B) In the elastography image, 2 mm diameter region of interest calculates maximum elasticity value of lateral portion of mass as 106.1 kPa, on the other hand it was measured 21.8 kPa on medial portion. Note that display was saturated no shear wave elastography artefact was present. **Kilic F et .al (47).**

(II) **Non-comedo:** DCIS consists of a monomorphic population of cells with nuclear grades ranging from low to high. In **cribriform** DCIS, intraepithelial spaces are evenly distributed and regular in shape. **Solid** DCIS completely fills the involved spaces. **Papillary** DCIS grows into spaces and

lines fibrovascular cores typically lacking the normal myoepithelial cell layer. **Micropapillary** DCIS is recognized by bulbous protrusions without a fibrovascular core **(6).**

Paget's disease:

Paget disease of the nipple is a rare manifestation of breast cancer (1% to 2% of cases). Malignant cells, referred to as Paget cells, extend from ductal carcinoma insitu within the ductal system into nipple skin without crossing the basement membrane and extracellular fluid seep out onto the nipple surface. The Paget cells are easily detected by nipple biopsy or cytologic preparations of the exudate. It ispresents as nipple redness, excoriation, usually unilateral, may be confused with eczema. Microscopically; large cells with clear cytoplasm and atypical nuclei are seen in epidermis **(48)**.

Mammary Paget disease can be undetectable on mammography in about 50% of cases. Features that may be evident on mammography include skin thickening, nipple retraction, subareolar or more diffuse malignant microcalcifications, and discrete subareolar masses. **(48)**.

Fig. (23): Craniocaudal mammogram shows areolar skin thickening, nipple retraction, and diffuse, scattered, fine pleomorphic and linear microcalcifications in the entire breast including the subareolar region. **(49)**

Ultrasound is used not only to confirm the mammography findings in a case of Paget's disease, but also when the mammogram is negative. The findings on ultrasound include heterogeneous hypoechoic areas in breast parenchyma, presence of a discrete mass or dilated ducts. Microcalcifications are not appreciated on ultrasound. Sometimes, there may be an area of DCIS with pleomorphic calcification on mammogram with an underlying mass, which is better appreciated on ultrasound .In some cases, however, even when there is pleomorphic calcification with nipple areolar thickening on mammogram, ultrasound findings can be non-specific and may show only skin thickening in the nipple areolar region. **(50)**

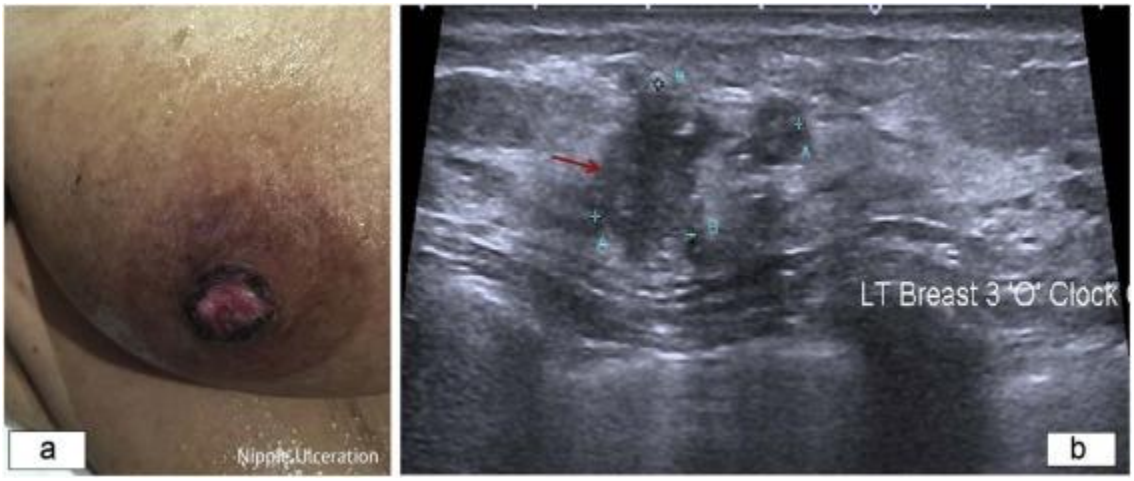


Fig. 24 (A) Clinical image of the right breast showing nipple ulceration. (B) Ultrasound image showing an irregular, ill-defined hypoechoic lesion measuring approximately 2.0 × 1.1 cm at the 3-o' clock position, circle 1, zones B and C of the left breast (arrow). **Lim**, **etal**(**49**).

(2) Lobular carcinoma in situ:

It is always an incidental finding in a biopsy performed for another reason, as it is not associated with calcifications or density, presents 1% to 6% of all carcinomas in mammography. LCIS is bilateral in 20% to 40% of women when both breasts are biopsied, compared to 10% to 20% of cases of DCIS. LCIS is more common in young women, 80% to 90% of cases occurring prior to menopause. Microscopically, the lobules are enlarged, filled with uniform, round, small to medium sized cells usually obliterating the lumen. The cells lost their cohesion **(50).**

(II) Invasive carcinoma:

Invasive carcinomas are classified based on their histological features, and their clinical behavior, the most common is invasive ductal carcinoma, not otherwise specified (IDC, NOS) **(43).**

(1) Invasive ductal carcinoa:

In young women or not screening older women, it presents as palpable mass. By the time it becomes palpable, over half the patients will have axillary lymph nodes. In older screening women, invasive carcinomas most commonly present as a density **(50).**

(I) Invasive ductal carcinoma, not otherwise specified:

Invasive carcinomas of no special type include the majority of carcinomas (70% to 80%). Grossly, the lesions are firm with ill-defined border and ''chalky streaks'' appearance on cut sections. Microscopically, the tumor cells may grow in sheets, nests, cords or single cell. Glandular formation varies between cases (**43).**

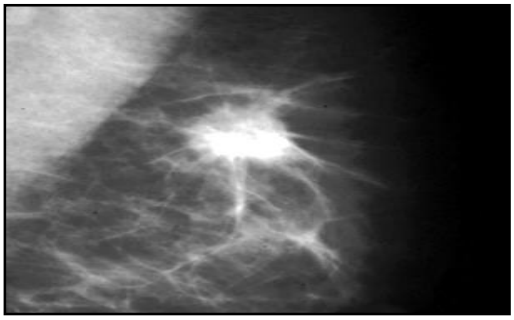


Fig. (25): IDC, NOS at mammography **(50).**

Radiographic features of ultrasound : (37)

- ill-defined
- hypoechoic mass
- hyperechoic angular margins
- posterior acoustic shadowing: 71% in grade 1
- posterior enhancement: 45% in grade 3
- ductal extension may be seen: represents extension of the mass into the surrounding parenchyma
- branched or spiculated pattern
- microcalcifications

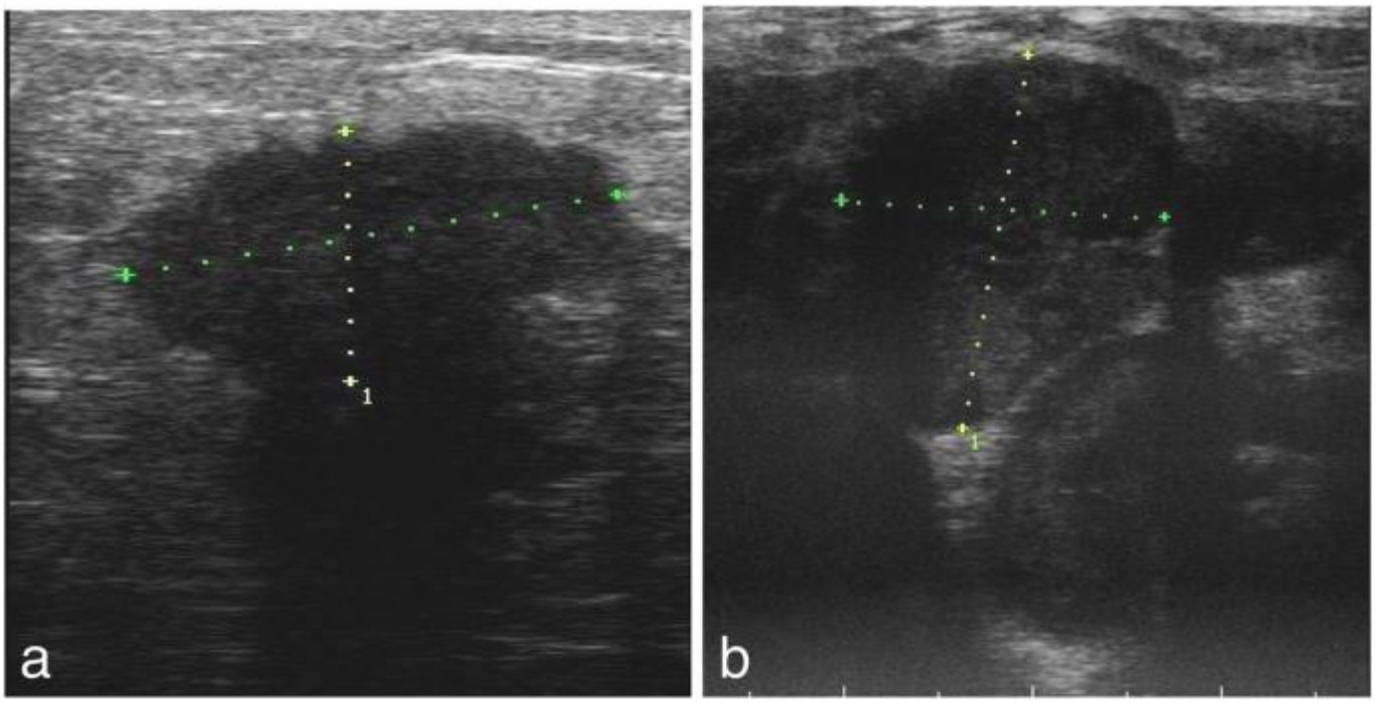


Fig .26a Ultrasound of the right breast and **b** right axilla in 40 years old women shows **a** a unifocal mass with irregular shape, spiculated margin, echogenic halo with non-parallel orientation, and posterior shadowing; it measures 15 × 9 mm. **b** Multiple malignant featuring right axillary lymph nodes. The mass proved pathologically to be low grade invasive ductal carcinoma with malignant infiltration of the LN and luminal B subtype. **(52**)

Shear wave Elastography depicts increased stiffness of the mass and the surrounding tissue. This feature correlates with the tumor grade (**53**)

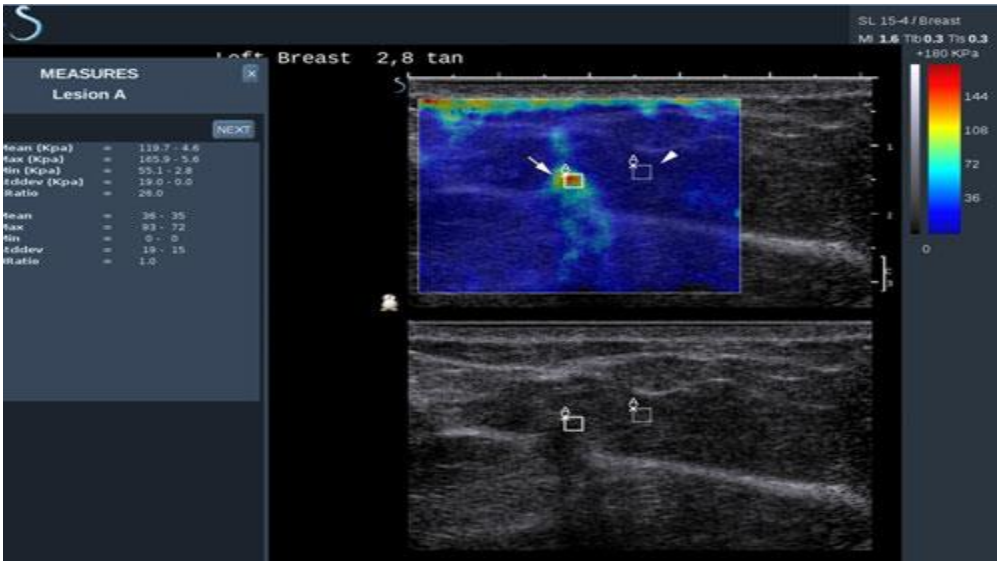


fig.27 A 52-year-old woman with invasive ductal carcinoma. Shear wave elastography shows high stiffness values around the lesion (red tints in the upper frame). One ROI is in the stiffest part of the lesion (arrow) and another is in the adjacent subcutaneous fat (arrowhead). The quantitative values for the two ROIs are shown in kPa in the panel on the left: the lesion value is given first (here, mean 6.3 m/s), followed by the value in fat (here 1.2 m/s).(**54**)

(II) Invasive lobular carcinoma:

Usually presents as a palpable mass or mammographic density. However, about one-fourth of cases might produce only subtle architectural changes on mammography. Its incidence is increasing among postmenopausal women. It represents 5–10 % of the invasive breast tumors.

Grossly, the tumor can be relatively small and possesses poorly defined edges. Microscopically, tumor cells are small and subtle, containing small amounts of cytoplasm with the formation of cords or single file pattern. Contralateral invasive carcinoma is frequent **(55).**

(III) Mucinous carcinoma:

Presents 1% to 6% of all breast carcinomas, commonly presents as a circumscribed mass grow slowly during many years and tends to occur in older women. Its incidence is slightly higher in women with BRCA1 mutations.

Grossly, a large gelatinous appearance is appreciated. Microscopically, the tumor cells are usually in tubules, clusters, and small sheets floating in pools of mucin **(56).**

(IV) Medullary carcinoma:

Presents as a well-circumscribed mass and may be mistaken radiologically for fibroadenoma. Grossly the tumor is a sharply circumscribed mass, having a gray and solid cut surface. Microscopically, the sheets of poorly differentiated large pleomorphic cells with prominent nucleoli are seen with mitosis **(56).**

(V) Tubular carcinoma:

Represents up to 10% of carcinomas less than 1 cm, typically detected as irregular mammographic densities. Women usually present in their late forties. Tumors are multifocal within one breast in 10% to 56% of cases and bilateral in 9% to 38%. Grossly, the lesion is firm with ill-defined border. Microscopically, the tumor composed of small glands or tubules with irregular contours, lacking myoepithelial layer. **(56).**

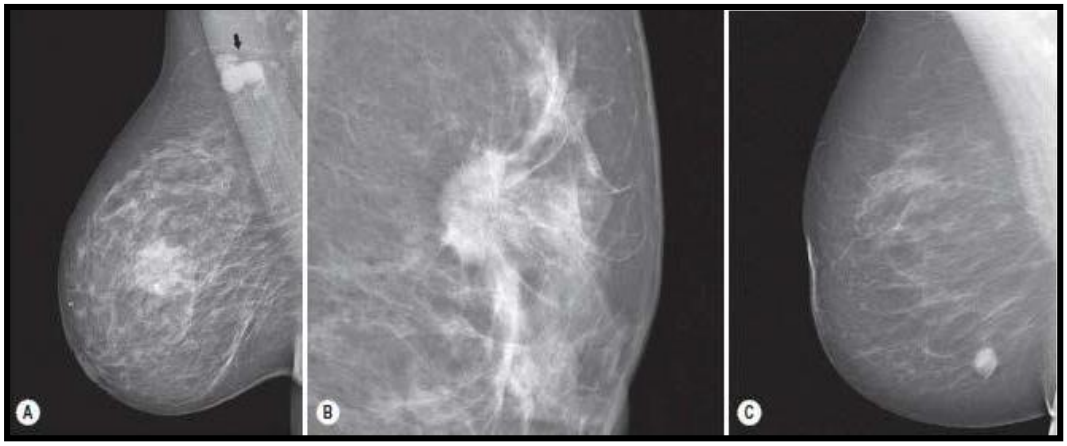


Fig. (28): Mammographic appearances of invasive carcinoma. Ill-defined and spiculated masses are typical of malignancy.(A) There is an ill-defined mass lying centrally in the right breast, containing some microcalcifications. Calcifications, representing DCIS, may be found in association with invasive carcinoma. There are also several enlarged lymph nodes in the axilla (arrow) which were proven to contain tumour on ultrasound-guided biopsy. (B) A speculated mass that proved to be a ductal NST tumor of intermediate histological grade on ultrasound-guided biopsy. (C) Sometimes high grade tumors that exhibit rapid growth may appear well defined. **(57)**

(VI) Invasive Papillary Carcinoma

They are rare represent 1% or fewer of all invasive cancers. Papillary architecture is more commonly seen in DCIS. The overall prognosis is better **(58)**

(VII) Metaplastic Carcinoma

It includes a wide variety of rare types of breast cancer (<1% of all cases), including conventional adenocarcinomas with a chondroid stroma, squamous cell carcinomas, and carcinomas with a prominent spindle cell component. Some of these carcinomas arise from myoepithelial cell type **(43).**

Other malignant breast lesions:

Inflammatory breast carcinoma (IBC):

Inflammatory carcinoma is clinically present with edema and redness of the breast skin, resembling mastitis. Microscopically, it is a type of ordinary breast cancer in which dermal lymphatic invasions by tumor is evident **(59).**

On mammography it appears as Skin thickening, predominantly seen in the inferior areolar region on initial stages, stromal coarsening or trabecular thickening and diffuse increase of parenchymal density/diffuse asymmetry comprise the main mammographic findings of IBC. Intramammary mass, architectural distortion, focal asymmetric density and micro calcification are less commonly seen in the mammography, with a percentage varying among studies, ranging between 10 and 80% **(59).**

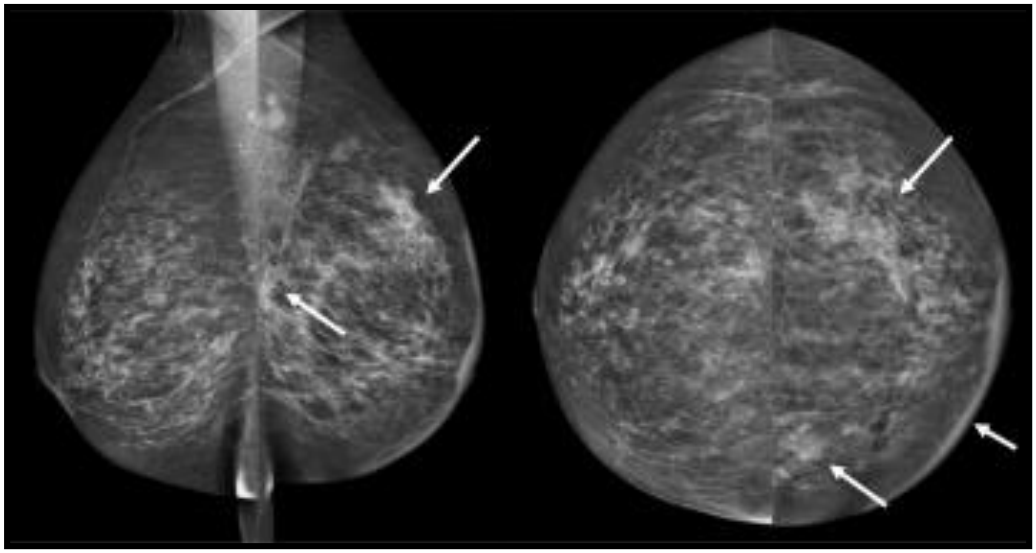


Fig. (29): Mammogram: Left breast - coarsening of parenchymal pattern with marked skin thickening. There is asymmetry with ill defined density in upper outer aspect with a further irregular mass in the medial aspect posteriorly. Abnormal dense rounded lymph nodes in axilla. Right breast – normal. (**60).**

Abnormal findings on US include: marked skin thickening seen in most cases (up to 95%), diffuse hyperechoic changes of the breast parenchyma, consisted with oedema, coarsening of the Cooper's ligaments and intraparenchymal mass/lesions with or without stromal distortion. The mammary lesion most commonly appears as ill-defined irregular focal hypoechoic lesion with/ without spicules, disturbing or interrupting the normal architecture, often with posterior shadowing. On colour doppler imaging there is often increased vascularity. In some cases, involvement of the overlying skin or the pectoral muscle can be identified (**60).**

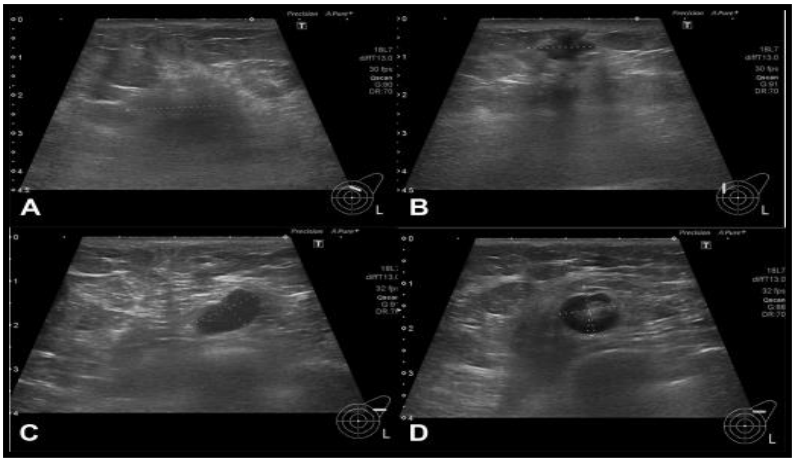


Fig. (30): Ultrasound Left Breast – A. Skin thickening with ill defined hypo echoic irregular mass (blue dotted line) in upper outer breast. B. irregular hypo echoic mass in upper medial breast. C. well defined hypo echoic mass with loss of hilum – abnormal lymph node. D. lymph node with thickened cortex. **(60).**

Othermalignant tumors may arise from the skin of the breast, sweat glands, sebaceous glands, and hair shafts; these tumors are identical to their counterparts found in other sites of the body. Lymphomas may arise primarily in the breast, or the breasts may be secondarily involved by a systemic lymphoma, most are of large cell type of B-cell origin. Metastases to the breast are rare and most commonly arise from a contralateral breast carcinoma. The most frequent non mammary metastases are from melanomas and lung cancers **(60).**

Clinical stages of breast carcinoma:

- **Stage 0**: DCIS or LCIS (5-year survival rate: 92%).

- **Stage I**: **Invasive** carcinoma 2 cm or less without nodal involvement (or only metastases < 0.02 cm diameter) (5-year survival rate: 87%)
- **Stage II**:
  - Invasive carcinoma 5 cm or less with up to three involved axillary nodes
  - Invasive carcinoma greater than 5 cm without nodal involvement
  - (5-year survival rate: 75%)
- **Stage III**:
  - Invasive carcinoma 5 cm or less with four or more involved axillary nodes
  - Invasive carcinoma greater than 5 cm with nodal involvement
  - Invasive carcinoma with 10 or more involved axillary nodes
  - Invasive carcinoma with involvement of the ipsilateral internal mammary lymph nodes
  - Invasive carcinoma with skin involvement (edema, ulceration, or satellite skin nodules), chest wall fixation, or clinical inflammatory carcinoma
  - (5-year survival rate: 46%).
- **Stage IV:** Any breast cancer with distant metastases (5-year survival rate: 13%) **(61)**.

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