INTRDUCTION

Worldwide, breast cancer is the most common malignancy in women, comprising 15% of all female cancers, making it the second most common type of cancer after lung and the fifth most common cause of cancer death.[1]

In Egypt, breast cancer is the most common malignant tumor among women, representing 18.9% of total cancer cases (35.1% in women and 2.2% in men) among the Egypt National Cancer Institute (NCI) series of 10 556 patients during the year 2001.[2]

At ultrasonography (US), purely or predominantly echogenic breast masses are rare. These lesions were once assumed to be benign, but recent data suggest that approximately 0.5% of malignant breast lesions appear echogenic. An echogenic breast mass is defined as a lesion that is hyperechoic in comparison with subcutaneous adipose tissue at ultrasonography (US), in accordance with the US lexicon of the Breast Imaging Reporting and Data System (BI-RADS) of the American College of Radiology although the vast majority of echogenic breast masses are benign, hyperechogenicity at US alone does not allow exclusion of malignancy.[3]

Anatomy of the breasts

1. Anatomical description

The breasts have a conical shape and are located one on each side within the subcutaneous layer of the thoracic wall anterior to the pectoralis major muscle. They extend superiorly as far as the level of the second rib, inferiorly as far as the level of the sixth or seventh ribs, laterally as far as the anterior axillary line (sometimes as far as the middle axillary line) and medially they reach the lateral margin of the sternum. Posteriorly, they make contact with the fascia of the pectoralis major, serratus anterior and obliquus externus muscles and the most cranial portion of the rectus abdominis muscle.[4,5]

Its base is circular and measures around 10 to 12 cm, but its volume is very variable. The weight of a non-lactating breast ranges from 150 to 225g, while a lactating breast may exceed 500g in weight. The breasts of nulliparous women have a hemispherical shape, while those of multiparous women are broader and pendulant. With aging, the breast volume decreases and the breast becomes less firm, flatter and pendulant.[5]

Three portions are distinguished anatomically: the gland itself (glandula mammaria), the mammary papilla (papilla mammariae) and the areola (areola mammae). The mammary gland is formed by fifteen to twenty lobes (lobiglandulae mammariae) that are arranged radially and delimited by septa of conjunctive tissue and adipose tissue in the subcutaneous layer (Figure 1).

The mammary parenchyma is more abundant in the upper half of the gland especially in the superolateral quadrant. The mammary tissue frequently extends beyond the apparent outline of the breast, projecting towards the axilla as an axillary process (sometimes called tail of Spence). The principal duct of each lobe, the lactiferous duct (ductus lactiferi) opens separately into the mammary papilla. In turn, the lobe is formed by smaller functional units, the lobules (lobuli) from which ducts converge towards the main duct of the lobe.[6] The mammary papilla (nipple) represents the apex of the cone and contains the openings for all the lactiferous ducts from the lobes. Close to the apex of the papilla, each duct presents a distal saclike dilatation known as the lactiferous sinus (sinuslactiferi).[4,6]

The areola is a slightly raised disc-shaped area of variable size surrounding the papilla. Initially, it has a rosy hue but becomes irreversibly pigmented (chestnut brown) from the second month of gestation. On its surface, it presents granular and pointlike elevations known as areolar tubercles (tubercula areolares) or Montgomery's tubercles.[4,5]

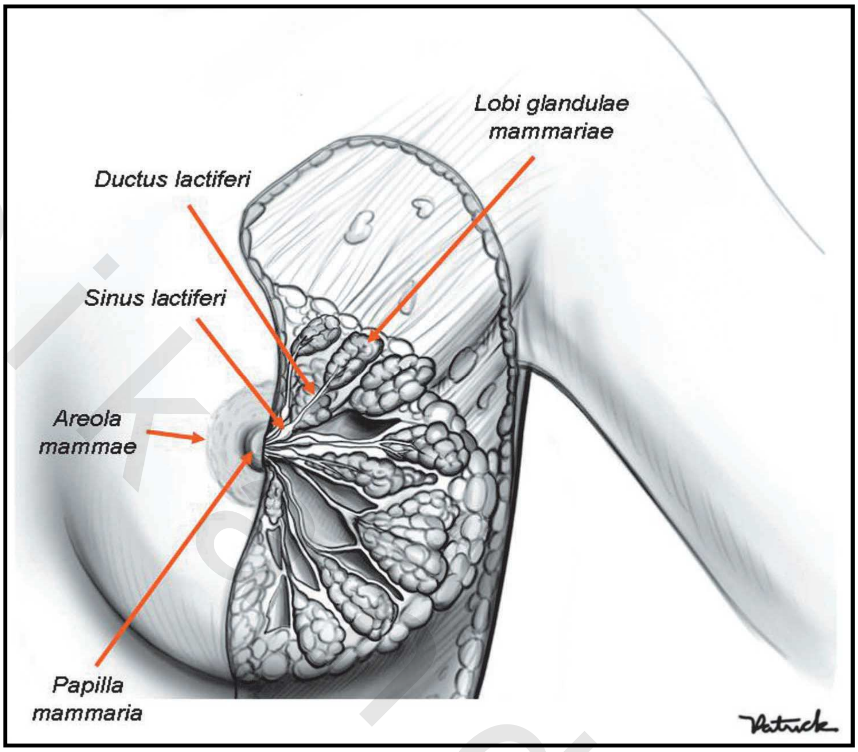


Figure (1): Right breast. The skin and subcutaneous layer have been extracted in order to view the lobi glandulae mammariae, ductus lactiferi and sinus lactiferi (anterior view).[7]

Zonal anatomy of the breast: Figure (2)

The breast is divided into three zones

(1) Premammary zone

- Most superficial.
- Defined anteriorly by skin, and posteriorly by the anterior mammary fascia (AMF).
- It contains fat, blood vessels and anterior suspensory ligaments (ASLs).

(2) Mammary zone

- Defined anteriorly by the (AMF), and posteriorly by the posterior mammary fascia (PMF).
- It contains majority of the ducts, terminal ductal lobular units (TDLUs), stromal fat and connective tissue.

(3) Retromammary zone

- Defined anteriorly by the (PMF) and posteriorly by the chest wall.
- It contains fat and posterior suspensory ligaments (PSL s).[8]

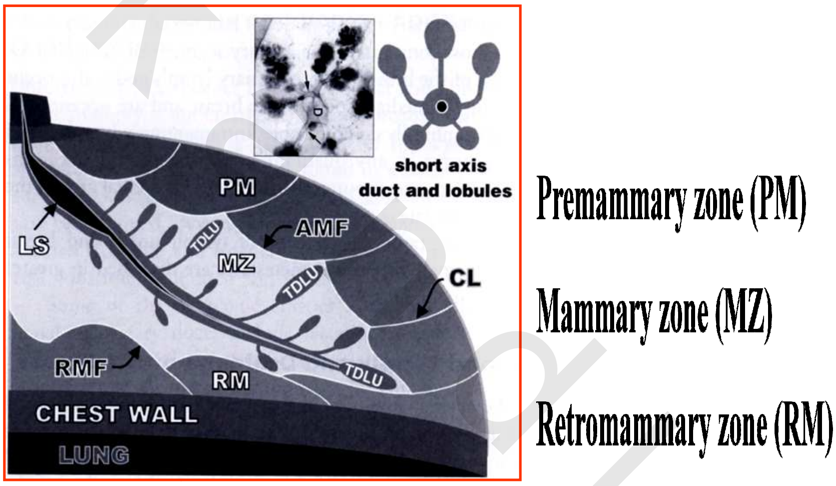


Figure (2): Zonal Anatomy of Breast.[9]

Blood supply of the breast

Arterial supply

1) Lateral mammary artery: which predominantly originate from lateral thoracic artery (a branch of the second portion of the axillary artery) formerly called the external mammary artery. It supplies 30 % of the breast, mainly the upper outer quadrant.
2) Medial mammary artery: originate from penetrating branches of the internal mammary (thoracic) artery (a branch of the subclavian artery), which emerges from the second, third and fourth intercostal spaces. It supplies 60 % of the breast medially and centrally.
3) Small perforating branches arise from the lateral cutaneous branches of the posterior intercostal arteries of the second, third and fourth spaces, also some blood coming from the subscapular and thoracodorsal arteries.
4) Pectoral branches of the thoracoacromialis artery (a branch of the second portion of the axillary artery); supply upper part of the breast.
5) Superior thoracic artery (a branch of the first portion of the axillary artery).[10,11]

Venous drainage

1) **Superficial system:** Usually doesn't accompany arteries. They are presented profusely anastomosed and easily visible during gestation. It forms an anastomotic venous plexus of circular shape around the nipple areolar complex, known as the venous circle, and drains to the periphery of the breast and joins the deep venous system.
2) **Deep system:** May provide direct pathway for metastasis to the lungs. Generally these veins accompany the arteries supplying the breast.
   These are 3 main routes:
   - Medially, the veins drain to the internal mammary (thoracic) vein (a tributary of the brachiocephalica vein),
   - Laterally to the axillary vein.
   - Drainage is also done by the posterior intercostal veins. Those of the second and third intercostal spaces drain into the superior intercostal vein, which on the right side is a tributary of the arch of the azygos vein and on the left side, of the left brachiocephalic vein. Those of the fourth space drain to the azygos vein (on the right side) and hemiazygos vein (on the left side).
3) **Vertebral plexus:** This is composed of valveless venous channels that surround the vertebral column. They are in contiguity with the posterior intercostal vessels. They form a route for metastasis to the spine, ribs and brain.[9,10]

Lymph drainage of the breast

For the purposes of simplicity, the whole of the breast can be divided into:

- Superficial: The skin, except the nipple and areola, and the immediate subcutaneous area.
- Deep: The parenchymatous, fatty and fibrous tissues. The deep area, in turn, can be subdivided into:-
  - An anterior two-thirds including the nipple and areola;
  - A posterior one-third adjacent to the deep fascia and pectoralis major.

The lymphatics of the superficial cutaneous area of the whole breast, except the nipple and areola, drain centrifugally, as follows:

1. The lateral side of the breast drains to the pectoral group.
2. The upper part drains to the supraclavicular group.
3. The medial side drains to the internal mammary glands Iying along the internal mammary vessels.
4. The lower medial area may drain into the para-umbilical Iymphatics and then along the ligamentum teres to the hepatic glands; or this area may drain to the subperitoneal plexus of lymphatics.

The lymphatics of the anterior two-thirds of the deep area as well as the lymph from the nipple and areola drain into the subareolar plexus (of Sappey). This plexus is drained by a medial and a lateral trunk which join to form a common trunk. The common trunk drains into the pectoral group of glands. The plexus also has numerous wide communications with the plexus of lymphatics situated on the anterior sheath (deep fascia) of the pectoralis major-often called the Lake of Stiles.

The lymph from the posterior one-third of the deep area is pooled into the Lake of Stiles plexus on the deep fascia, as the lymph drains centrifugally in a manner similar to the cutaneous lymphatics, most of the lymph again being carried to the pectoral group of glands.

In addition, the upper outer quadrant of this posterior area has a separate drainage into the apical glands. The axillary tail of Spence may be regarded as part of the posterior one-third of the breast. Consequently, both the cutaneous and deep areas drain to the pectoral group of glands which lie adjacent to the tip of the tail after it has passed through the deep fascia.(10,12)

In general the lymph nodes of the breast classified to:

1) Axillary lymph nodes

a) **The Pectoral Group** (anterior group): Situated along the lateral thoracic vessels adjoining the lateral and lower border of the pectoralis minor. It may drain into the subclavicular group directly. Also it identified by **external mammary group.**

b) **The Subscapular Group** It situated around the subscapular vessels on the posterior wall of the axilla. It drains into central and subclavicular groups.

c) **Axillary vein group** (lateral group) Situated along the axillary vessels and draining most of the upper limb.

d) **The Central Group**. It lies in the axillary fat deep to pectoralis minor muscle. It drains into the apical and infraclavicular group. It is the most superficial group**.**

e) **The Apical or Infraclavicular Group**. It situated just below the middle third of the clavicle, behind the clavipectoral fascia and related to the first part of the axillary artery anterior to and just below the first rib. This group receives the efferents of the central group and thus receives the lymph from the preceding four groups. The efferents from this group pass to the supraclavicular group.

f) **Interpectoral (rotter) group:** Between the pectoralis major and minor muscles. It drains into the central and the subclavicular groups.(8,9)

2) Internal mammary lymph nodes

They lie in the intercostal spaces in the parasternal region, from the 2nd intercostal space downward. The nodes lie close to the internal mammary vessels in the extra pleural fat and separated from the pleura by a thin layer of fascia. They predominantely drain the far medial and deep medial breast tissue.(13)

3) Intramammary lymph nodes

25-28% of normal women have intramammary lymph nodes. They can occur anywhere, but mainly in the far lateral, axillary and posteromedial aspects of the breast.(8,9)

Embryology and Development of the breast

During the fourth week of gestation, paired ectodermal thickenings termed mammary ridges or milk lines develop on the ventral surface of the embryo and extend in a curvilinear fashion convex towards the midline from the axilla to the medial thigh. This is the first morphologic evidence of mammary gland development. In normal human development, these ridges disappear except at the level of the fourth intercostal space on the anterior thorax, where the mammary gland subsequently develops.(14)

During the fifth week of gestation, the remnant of the mammary ridge ectoderm begins to proliferate and is termed the primary mammary bud. This primary bud subsequently begins growth downward as a solid diverticulum into the underlying dermis during the seventh week. By the 10th week, the primary bud begins to branch, yielding secondary buds by the 12th week, which eventually develop into the mammary lobules of the adult breast.(14)

- During the remainder of gestation, these buds continue lengthening and branching.
- During the 20th week, small lumina develop within the buds that coalesce and elongate to form the lactiferous ducts.

The canalization of the mammary buds with formation of the lactiferous ducts is induced by placental hormones entering the fetal circulation. These hormones include progesterone, growth hormone, insulin like growth factor, estrogen, prolactin, adrenal corticoids.(14)

- At term, approximately 15-20 lobes of glandular tissue have formed, each containing a lactiferous duct. The supporting fibrous connective tissue, Cooper ligaments, and fat of the mammary gland develop from the surrounding mesoderm.
- The lactiferous ducts drain into retroareolar ampullae that converge into a depressed pit in the overlying skin.

Each of the 15-20 lobes of the mammary gland has an ampulla with an orifice opening into this mammary pit. Stimulated by the inward growth of the ectoderm, the mesoderm surrounding this area proliferates, creating the nipple with circular and longitudinally oriented smooth muscle fibers.(14)

- The surrounding areola is formed by the ectoderm during the fifth month of gestation.
- At birth, the breast is composed of radially arranged mammary lobes draining via lactiferous ducts into ampullae that empty onto the nipple.
- These rudimentary mammary glands are identical in males and females.
- The nipple appears as a small pit in the center of a thickened areola.
- Shortly after birth, the nipples become everted from proliferation of the surrounding mesoderm, and the areolae develop a slight increase in pigmentation. The development of erectile tissue in the nipple areolar complex causes the nipple to protrude even further upon stimulation.

Development of the mammary glands is initiated during embryologic life but is only complete in the postpartum lactation of the adult female. After the transient secretion stimulated by prolactin production in the neonate, the mammary glands, with their relatively simple architecture, remain quiescent until puberty. During this period, the supporting stromal structures and ducts enlarge in proportion to the increase in body size of the individual, but no lobular development occurs.(14)

- If pregnancy occurs, the glands complete their differentiation and reach functional maturity with the intralobular-branched ducts forming buds that become secretory alveoli.

This occurs under the influence of sustained increases in the levels of circulating progesterone, estrogens, prolactin, and placental lactogen.(14)

Physiology of breast

The connective tissue and glandular structure of the breast are in fact essentially hormonal receptors. It should be understood that the breast is an organ which is subjected, to changes, both clinically and mammographicIly, under hormonal influence. Many studies have been conducted in order to categorize the specific actions of various hormones on the breast.(15,16)

a) **Effect of oestrogen**: The influence of oestrogens is specifically directed to mammary tissue where they produce two effects:
   1. On the epithelium: Estrogens increase the number, the length and the caliber of the lactiferous ducts and promote epithelial proliferation.

2. On the connective tissue: Estrogens promote water retention, leading to saturation of the mammary connective tissue which becomes transformed into a muco-edematous substance. Also it becomes more believed that prostaglandins have an eventual role. These substances could increase capillary permeability and oppose the vasoconstrictive effect of adrenalin.[15,16]

b) Effect of progesterone

1) On the mammary epithelium: It promotes the development of acini, increasing their number and preparing the gland for lactation. It inhibits galactophore epithelial proliferation.
2) On the connective tissue: It opposes the action of estrogens by its diuretic effect.

In summary, estrogens and progesterone have a complementary effect on the development of the glandular part of the breast, and have opposing actions on capillary permeability in the connective tissue.[15,16]

Four factors are brought into play in the study of anatomico-physiological and radiological correlations of the mammary gland.

1. A vascular factor induced by capillary exudation and oedema of the gland substance.
2. A connective tissue factor which is the cellular reaction to the exudation leading to sclerosis of the connective tissue.
3. An epithelial factor represented by hyperplasia of the neighboring galactophore cells.
4. A neural element which transmits and interprets the pain. It can in its turn interfere with hormonal control and induce a self-maintaining cycle.

The action of these hormones on the breast will produce a permanent restructuring which varies from one patient to another according to tissue sensitivity, which is under control of mammary receptors.[16]

Normal menstrual changes

Schedule of Normal Menstrual Effects

Week 1

- Onset of menses.
- Regression of epithelial secretory activity and tissue edema.
- Minimum breast volume on days 5-7 (This is the best time for visualization of the breast on a mammogram).

Week 2

- Estrogen rise.
- Epithelial tissue proliferation.
- Follicular development

Weeks 3 & 4

- Progesterone rise.
- Postovulatory luteal phase.
- Duct dilatation.
- Intraluminal secretions.
- Maximal breast blood flow 3-4 days before menses.
- Breasts swollen and tender.

Mammograms, clinical breast exam, and self-breast examination are best performed during days 5-7 of the cycle (just after menstruation). The tissue will be least tender and least lumpy at this time.(17)

Breast changes during pregnancy

Lobular formation predominates. Alveoli contain Marked ductal, lobular, and alveolar growths occur due to the influence of luteal and placental sex steroids, placental lactogen, prolactin, and chorionic gonadotropin. Prolactin increases slowly during the first half of pregnancy. The two-cell layer of the alveoli sheds to a single layer (this contributes to the high protein content of colostrum).(17)

The First 3-4 Weeks

Ductal elongation occurs, with some branching, and lobular formation. Breast pain is frequently the first symptom of pregnancy, often occurring before a woman notices that.(17)

Weeks 5-8 of Gestation

Significant breast enlargement occurs, along with dilation of superficial veins, heaviness, and increased pigmentation of the nipple-areolar complex.(17)

Second Trimester

Colostrum, but no fat. Lactation may be adequate from the 16th week of pregnancy.(17)

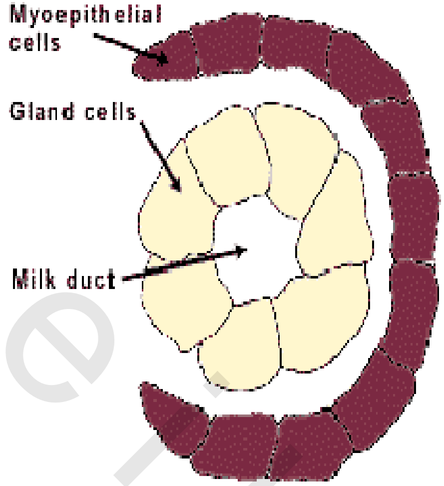
Third Trimester

Breast size continues to increase due to increasing colostrum volume and hypertrophy of myoepithelial cells, connective tissue, and fat.

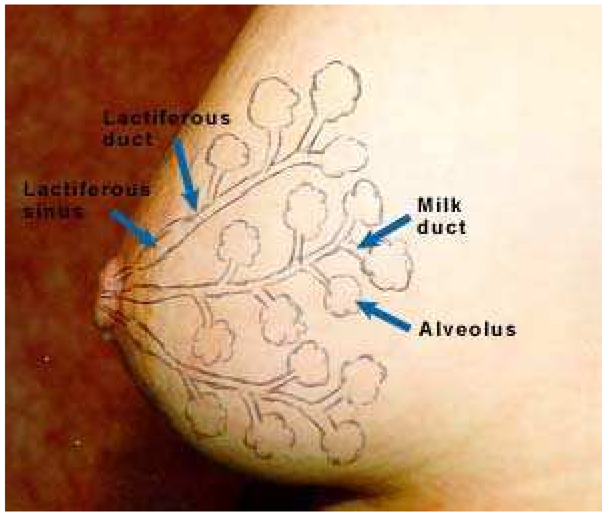
Lactation

At parturition, prolactin increases, which when combined with growth hormone, insulin, and cortisol effects, converts mammary cells from a presecretory to a secretory state. Tactile stimulation of the nipple results in release of oxytocin from the pituitary gland, which causes myoepithelial cells surrounding the lobules and small ducts to contract, thus expressing milk. Galactoceoles, or milk cysts, can occur during pregnancy or lactation. These present as palpable lumps, often tender. If imaging is performed, a fat-fluid level may be seen due to separation of these milk components.(17)

Physiology of Breast feeding



(A)



(B)

Figure (3): (A) A cross-section view of the alveolus. (B): Lateral view with anatomical overlay.

Milk is produced in the alveolus. The alveolus is made up of gland cells around a central duct. The milk is produced by the gland cells. Surrounding the gland cells are the myoepithelial cells which contract to cause milk ejection into the milk duct. The milk then travels down into the lactiferous ducts and into the lactiferous sinuses. Milk is stored in these ducts and sinuses in the period between breast feeding. Mothers continue to make milk between feedings and they make more milk during feedings.(18)

Menopause

Declining ovarian function results in regression of the breast epithelium. Lobules are resorbed. Ducts also are resurged, but to a much lesser extent. Over decades of menopause, nipples may flatten or retract. This normal change should occur gradually over 1-2 years and bilaterally, as opposed to unilaterally, which would raise a concern.

Pathological entities of echogenic lesions of the breast

An echogenic mass on US corresponding to a developing asymmetry at mammography in a patient with no history of recent trauma would warrant biopsy in most circumstances.(19)

Echogenic breast masses with other mammographically worrisome features such as a spiculated margin, interval enlargement, or association with suspicious microcalcifications or lymphadenopathy would also require biopsy, regardless of a benign clinical history.(20-22) Similarly, lesions with internal vascularity at doppler US warrant close attention.(23)

Table (I): Differential diagnostic considerations for echogenic breast masses include both benign and malignant entities

Benign lesions
Lipoma
Angiolipoma
Hematoma
Seroma
Fat necrosis
Silicone granuloma
Sebaceous or epidermal inclusion cyst
Abscess
PASH (pseudoangiomatous stromal hyperplasia).
Galactocele or lactating adenoma
Duct ectasia
Apocrine metaplasia within fibrocystic disease
Malignant lesions
Invasive ductal carcinoma
Invasive lobular carcinoma
Metastasis
Lymphoma
Angiosarcoma

Benign Lesions

Lipoma: Lipomas are common benign tumors that are composed of mature adipocytes and are most often unilateral and solitary. Typically manifesting as a palpable soft mass at clinical breast examination, a lipoma can be homogeneously hypoechoic, isoechoic, or hyperechoic with no associated internal or peripheral vascularity at US. Mammography shows a uniformly radiolucent and smoothly marginated mass without intrinsic density. Lipomas can enlarge in response to hormonal stimulation. In cases of enlarging or symptomatic lipomas, surgical excision could be performed.[23]

Angiolipoma: Breast angiolipomas are unusual fat-containing tumors with mature adipocytes intermixed with vascular proliferations. More commonly encountered in men and typically involving the back, neck, or shoulder, an angiolipoma is an unusual benign tumor that rarely involves the breast. It represents a variant of lipoma, accounting for 5%–17% of all benign fatty tumors. Histologic analysis shows a vascular lesion with cellular atypia and mitotic activity. The hallmark of angiolipoma at pathologic analysis is scattered microthrombi in small blood vessels.

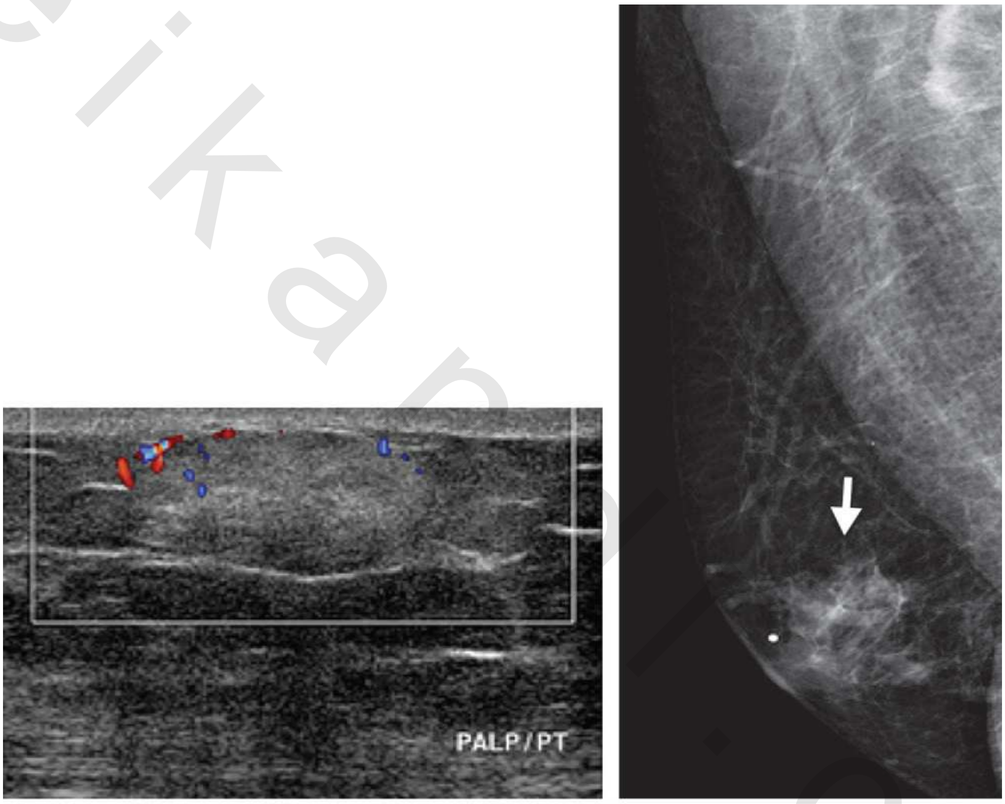
There are two types of angiolipoma-the infiltrative type and the non infiltrative type-neither of which has malignant potential.

Angiolipomas in the breast have been reported to be the non infiltrative type, and physical examination may reveal faint skin discoloration.

There is no characteristic imaging finding of an angiolipoma of the breast.

Its variable appearance overlaps with those of other benign and malignant lesions.

Most commonly, US demonstrates a circumscribed iso- to hyperechoic mass (Fig.4a) with internal vascularity (Fig.4a). Correlation with mammography often shows a solid mass or an asymmetry with mixed densities (ie, soft-tissue density interspersed with fat density) (Fig 4b). Since these imaging features are nonspecific, biopsy is required for definitive diagnosis.[24,25]



a. b.

Figure (4): Angiolipoma in a 64-year-old man with a palpable mass at the 1-O'clock position in the right breast. (a) US image shows a predominantly echogenic lesion with associated vascularity. (b) On an MLO mammogram, the lesion has mixed density (arrow). Biopsy demonstrated angiolipoma.

Hematoma: A hematoma represents an area of localized hemorrhage that is most often related to recent trauma or surgery.

The sonographic appearance of a hematoma varies depending on the age of the blood products. An evolving hematoma typically decreases in size and becomes hypoechoic or, less commonly, more echogenic before complete resolution (Figure 5). At mammography, hematomas can mimic malignancy.[26] Correlation with the patient's clinical history is key to making the diagnosis.

A clear history of trauma makes immediate biopsy unnecessary. Short-term follow-up imaging to ensure resolution of the finding represents a reasonable approach to management. If short-term follow-up does not show improvement or complete resolution of the abnormal finding, biopsy may be indicated to exclude malignancy.

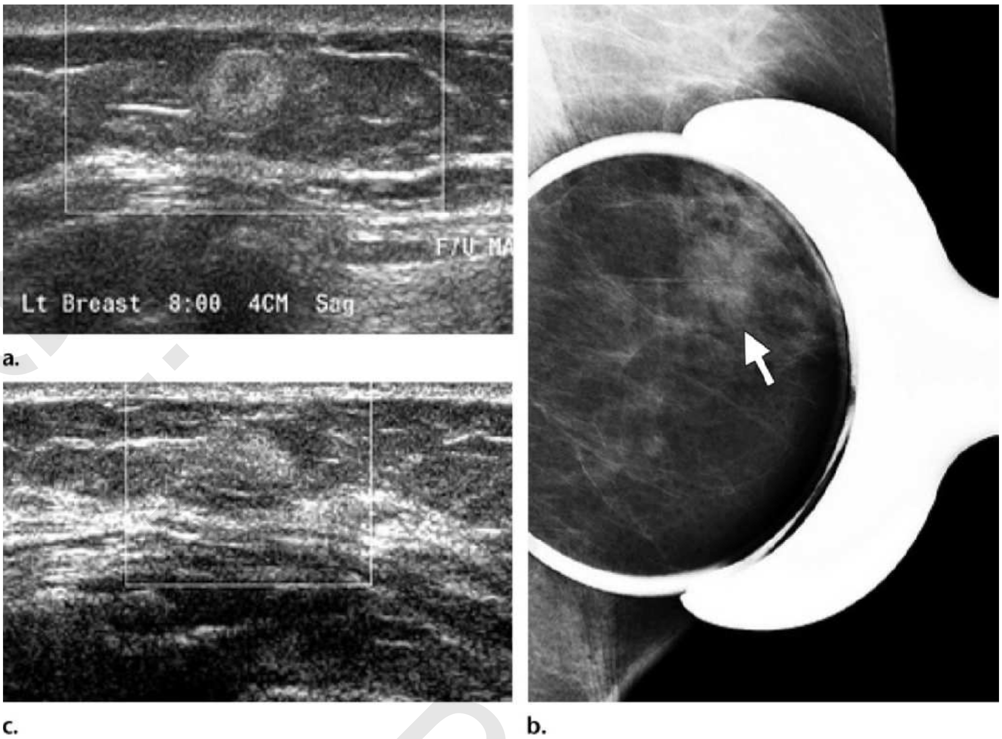


Figure (5): Evolving hematoma in a 68-year-old woman with a history of trauma. (a) Initial US image shows a lesion that is peripherally echogenic and centrally hypoechoic. (b) Mammogram shows an obscured asymmetry (arrow) in the left breast, which corresponds to the lesion seen at US. (c) US image obtained 4 weeks later shows that the lesion has become smaller and homogeneously echogenic. After 6 months, the lesion had completely resolved.

Seroma

Seromas are postoperative fluid collections that usually develop early in the postsurgical period and are well-known sequelae of mastectomy and breast reconstruction.[27] Seromas can occasionally reaccumulate or persist, but most decrease in size over time and eventually resolve. Typically complex at imaging, a seroma can contain solid echogenic components, which likely represent resolving postoperative hematomas (Figure 6). Correlation with the appropriate clinical history avoids the need for intervention. Follow-up to confirm resolution or stability is usually the appropriate management.

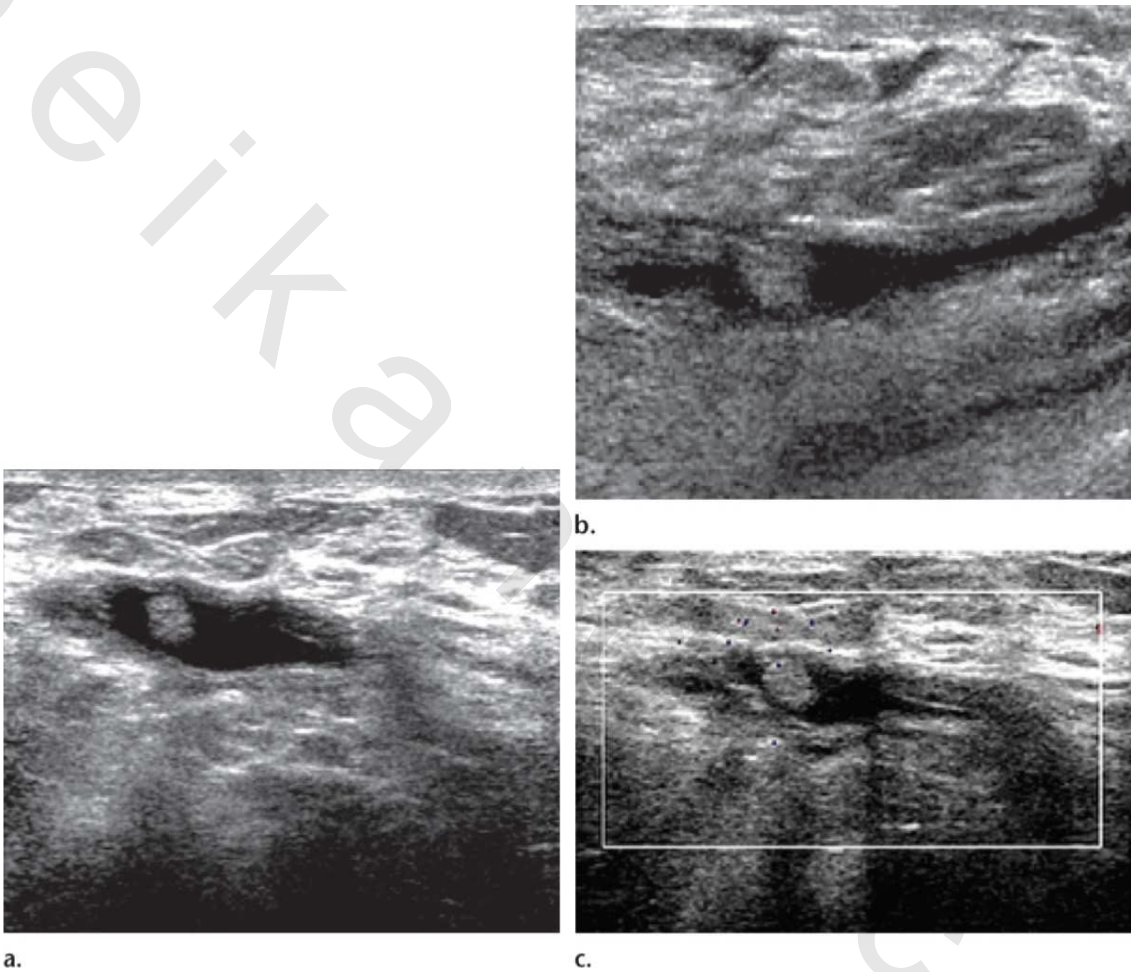
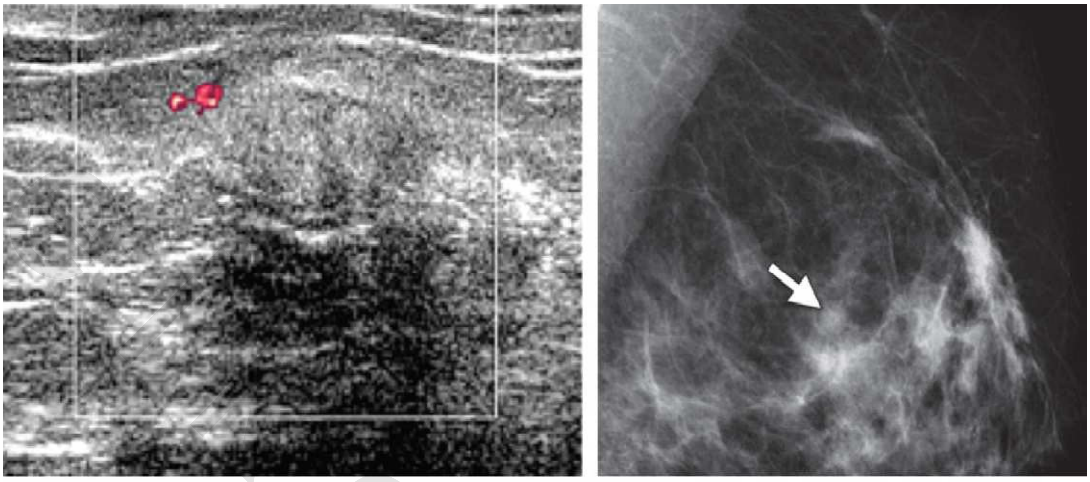


Figure (6): Postoperative seroma in a 66-year-old woman with a history of ductal carcinoma in situ (DCIS) and right breast lumpectomy. Radial (a) and antiradial (b) US images and color Doppler image (c) show an anechoic collection with an intracystic echogenic nodule that is nonvascular.

Fat Necrosis: Fat necrosis represents nonsuppurative fatty inflammation related to injury. It has been described in the setting of direct trauma, infection, cyst aspiration, biopsy, reduction mammoplasty, implant removal, silicone or paraffin injections, lumpectomy, reconstructive surgery, and radiation therapy. Correlation with the clinical history is key to suggesting the correct diagnosis. An echogenic lesion in a patient with a clear history of trauma (eg, reduction mammoplasty) may be safely followed up with imaging (Fig 7). Histopathologically, it shows adipose tissue with aggregates of foamy macrophages admixed with lymphoplasmacytic infiltrates.[28]

The sonographic appearance of fat necrosis is variable; at times, it can appear echogenic (Figure 7a).[29] The mammographic appearance ranges from radiolucent cystic areas that may have associated dystrophic coarse calcifications to an irregular or spiculated mass or distortion.



a. b.

Figure (7): Fat necrosis in a 55-year-old woman with a history of cancer in the right breast who underwent breast reconstruction, along with reduction mammoplasty of the left breast. (a) US image shows a predominantly echogenic lesion with posterior shadowing in the upper left breast. (b) Spot MLO mammogram shows a round mass (arrow). Because the patient had recently undergone breast reduction, follow-up imaging in 6 months was recommended. However, the patient opted for biopsy, which demonstrated fat necrosis and a foreign-body giant cell reaction.[29]

Silicone Granuloma: Typically seen at the edge of a breast implant or in the axilla, silicone granulomas represent inflammatory masses enveloping free silicone gel droplets (foreign bodies) in the breast. They are commonly associated with extracapsular rupture of an implant[20] or injection of free silicone.[21]

At US, a silicone granuloma appears as a hyperechoic mass with fine internal echoes, which extend deep to the posterior wall of the mass and obscure distal structures. This classic "snowstorm" appearance at US is due to acoustic scattering by silicone (Figure 8a). The presence of the snowstorm appearance at US, along with corresponding mammographic masses isodense to an adjacent silicone implant (Figure 8b), is diagnostic for silicone granulomas.[30]

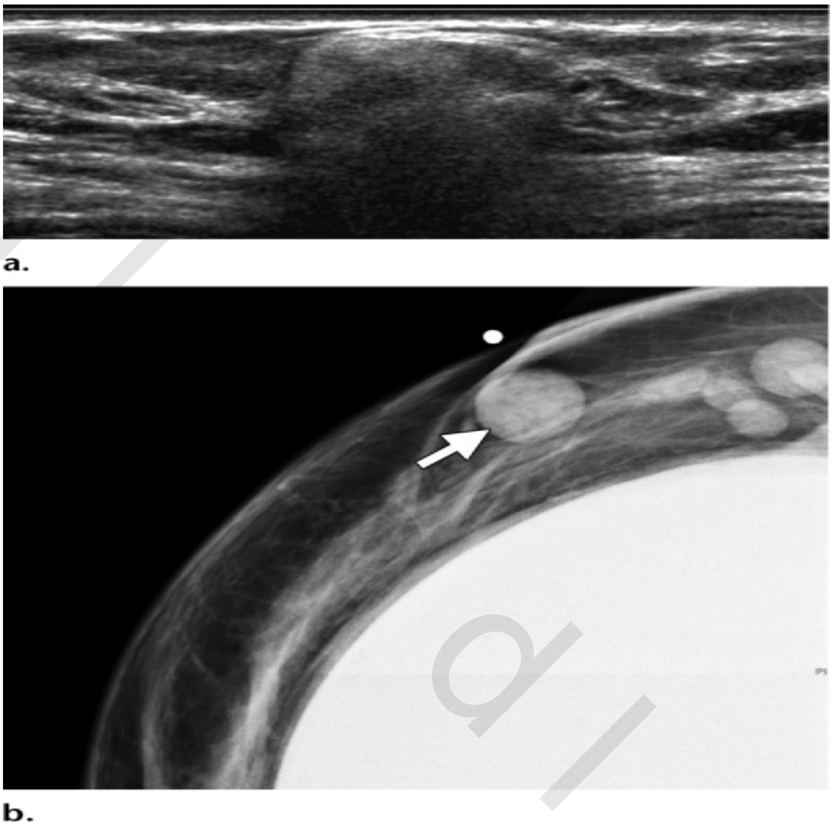


Figure (8): Silicone granulomas in a 35-year-old woman with palpable breast masses. (a) US image of one of the masses shows the classic snowstorm appearance of a silicone granuloma. (b) CC mammogram shows circumscribed round masses (arrow) adjacent to a silicone breast implant. Because the patient had a strong family history of breast cancer, she opted for biopsy, which demonstrated that the masses were silicone granulomas.[29]

Abscess: a breast abscess is a localized collection of pus in the breast[24]. Mammography typically shows a circumscribed or obscured mass (Figure 9b). Although an abscess may be echogenic at US, it more often has mixed echotexture (Figure 9a).

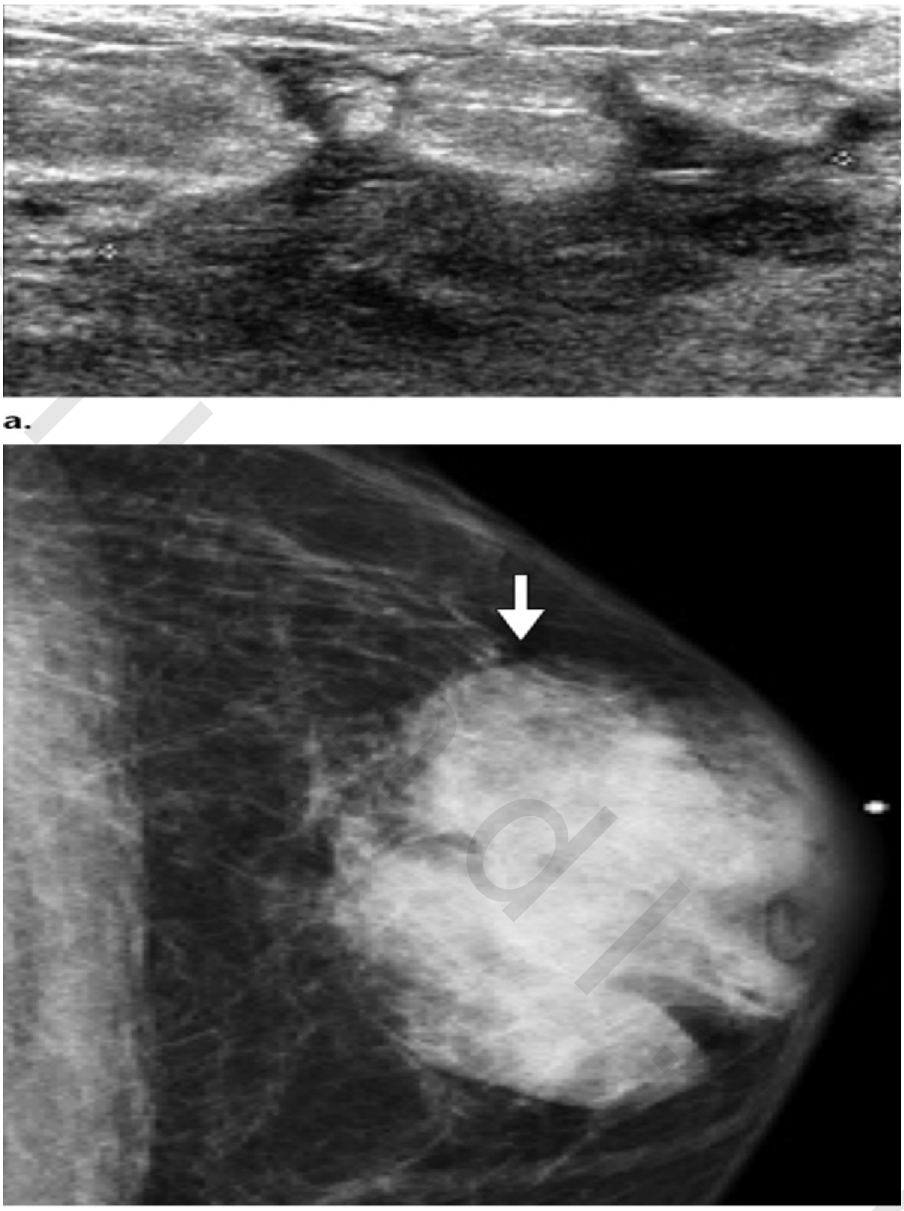


Figure (9): Breast abscess in a 64-year-old man with a palpable lump in the retroareolar left breast and a 4-week history of pain and redness. (a) US image shows an evolving phlegmon or abscess of mixed echogenicity. (b) CC mammogram shows a retroareolar mass (arrow), which is indicated by a BB marker over the area of concern. Percutaneous drainage was performed, and the patient received antibiotic therapy.[29]

Lactational Change or Galactocele

The appearances at US and mammography vary depending on the amount of fat and proteinaceous material within the galactocele, but a galactocele can appear echogenic (Figure 10). In a young lactating patient, an echogenic mass is more likely to represent lactational change or a galactocele. Clinical follow-up and aspiration or biopsy represent reasonable management options.[31] Lactational changes and galactoceles represent benign cystic spaces lined by true cuboidal epithelium that contain milk products. The patient typically presents with a palpable mass during lactation or shortly after cessation of lactation. The pathogenesis is thought to be mammary duct obstruction in the lactating breast, most commonly due to inflammation.

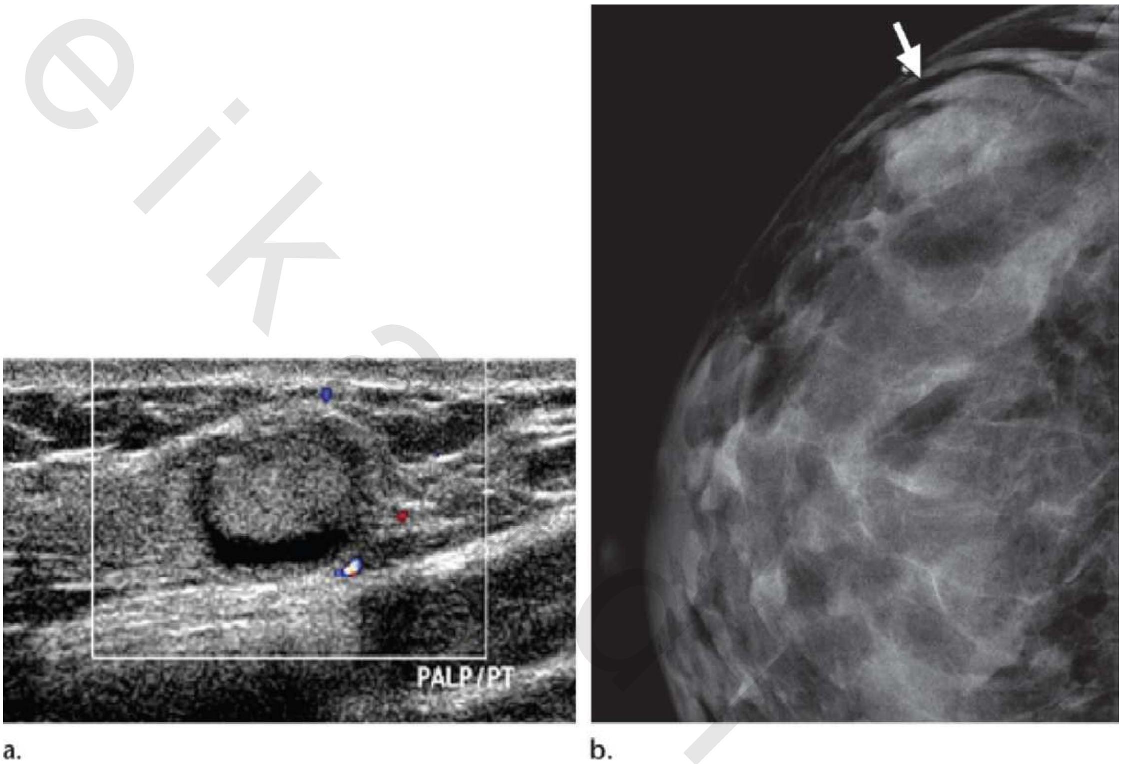


Figure (10): Lactational change in a 31-year-old lactating woman with a palpable lump in the right breast. (a) US image shows a circumscribed echogenic mass in the area of concern. (b) CC mammogram shows a partially obscured mass (arrow) in the outer breast. Aspiration yielded milky fluid.[29]

Duct Ectasia

At imaging, they are noted to have dilated ducts that may be associated with an intraductal mass or debris. However, a wide array of benign and malignant entities can manifest as dilated lactiferous ducts with or without an intraductal mass. These include fibrocystic change, intraductal papilloma, ductal hyperplasia, DCIS, and invasive ductal carcinoma.[31]

Therefore, an echogenic intraductal mass within an ectatic duct warrants biopsy to exclude malignancy. The findings of multiplicity, lack of internal vascularity, and a mass without distortion of ductal contour favor a benign origin.[32]

Apocrine Metaplasia

Recognized as a variant of fibrocystic change, apocrine metaplasia typically appears as a small cluster of microcysts with intervening septa.[18] On occasion it can mimic an enlarging intracystic mass.

Malignant Lesions

Primary Breast Carcinoma

Rarely, breast carcinomas can be purely echogenic (Figure 11). Despite the echotexture, sonographic features such as a spiculated or noncircumscribed margin, irregular shape, nonparallel orientation, posterior shadowing, and alteration of surrounding tissue remain highly predictive of malignancy.[19,24,33] certain polymorphous histologic patterns, such as cribriform, tubular, solid nests, and scirrhous patterns, may present as hyperechoic breast tumors. Densely packed tumor cells in invasive and in situ ductal carcinoma can appear hyperechoic on ultrasound.[28]

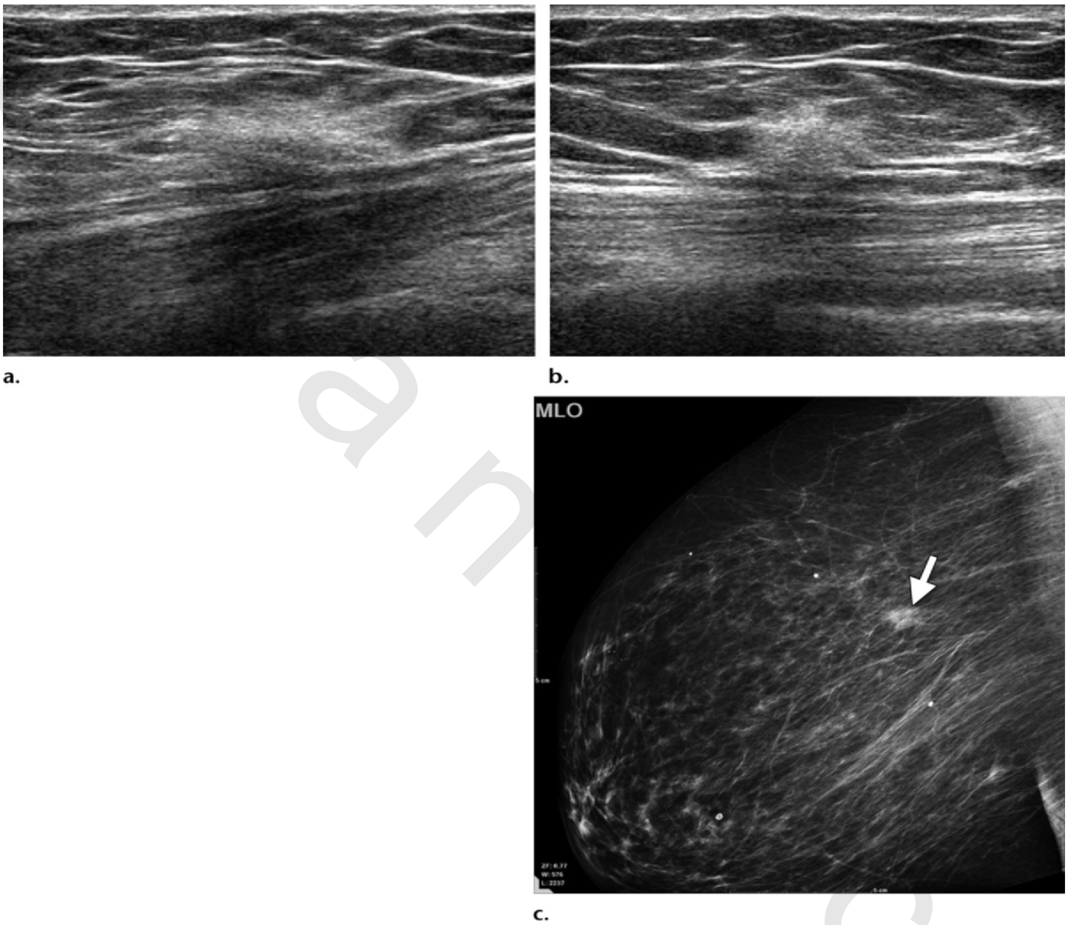


Figure (11): Invasive ductal carcinoma in a 75-year-old woman in whom a mass developed in the right breast since the preceding screening examination. (a, b) Transverse (a) and sagittal (b) US images show a spiculated echogenic mass with shadowing. (c) MLO mammogram shows a spiculated mass (arrow). Biopsy demonstrated grade 1 invasive ductal carcinoma.[29]

Metastasis

Metastasis to the breast can manifest as a sonographically echogenic mass. Although any malignancy can metastasize to the breast, the more common primary lesions include lung cancer, melanoma, ovarian cancer, and lymphoma. Internal vascularity in a predominantly echogenic breast mass warrants biopsy, since up to 64% of primary or secondary breast lymphomas are hypervascular(34) and melanoma metastases are almost always hypervascular.(35)

Angiosarcoma

Angiosarcoma is a rare and highly aggressive malignant stromal breast neoplasm. At US, angiosarcoma appears as a hypervascular circumscribed or ill-defined mass with heterogeneous echogenicity but occasionally is predominantly hyperechoic (Figure 12a, 12b).(36) This hyperechogenicity likely reflects the presence of irregular anastomotic vessels in conjunction with solid nests of spindle cells seen on histopathologic analysis.(28) At mammography, the lesion appears as an irregular or circumscribed mass (Figure 12c).

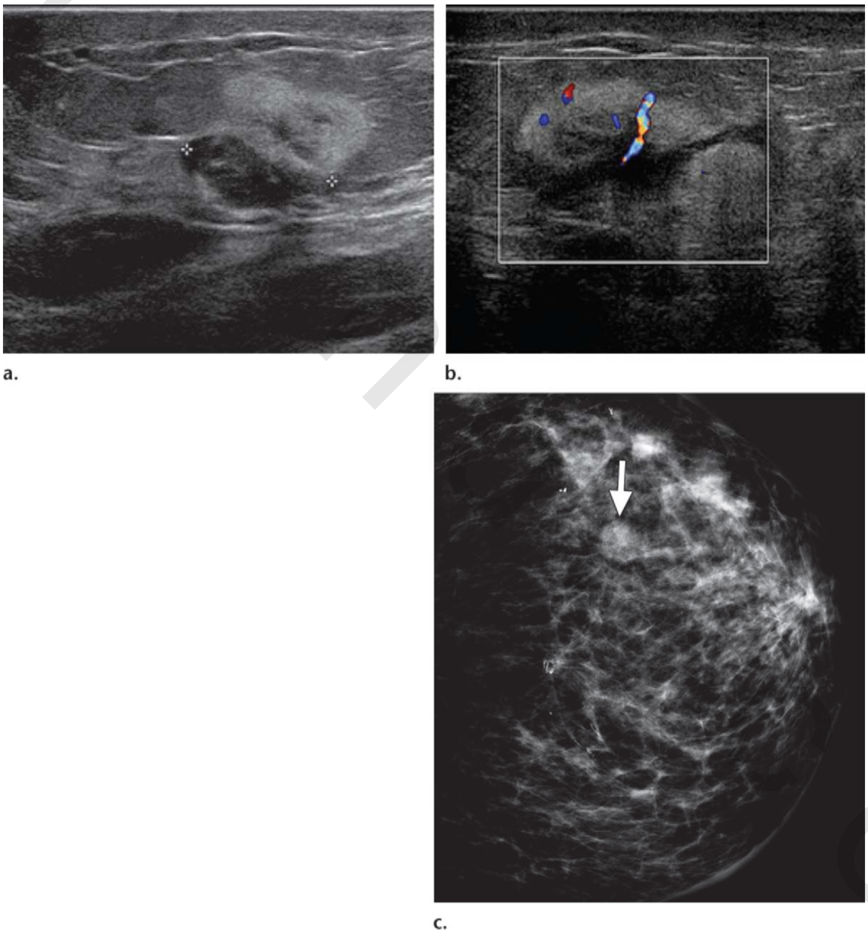


Figure (12): Angiosarcoma in a 64-year-old woman with a history of cancer in the left breast, lumpectomy, and radiation therapy who presented with an expanding "hematoma" in the left breast. (a, b) Gray-scale US (a) and color Doppler (b) images show a lobulated mass with mixed echogenicity (but predominantly echogenic) and internal vascularity. (c) CC mammogram shows a circumscribed, partially obscured mass (arrow). Biopsy demonstrated a high-grade sarcoma.(29)

Methods of breast imaging

I) Mammogram

Mammography is currently the most sensitive method for detecting early breast cancer, and it is also the most practical for screening. Mammography screening reduces breast cancer mortality rates in women as breast cancers detected on screening mammography are smaller and less likely to have spread to regional lymph nodes when compared with breast cancers detected at physical examination. There is a false-negative rate for mammography which is estimated to be approximately 5 to 15 percent, and this could be attributed to many causes such as inability to detect lesions in women with dense breasts, failure to image the region of interest, obscuration of the mass by overlying breast tissue, poor image quality, errors of perception, and cancer indistinguishable from normal tissues.[9,37,38]

Mammographic Anatomy

The mammographic appearance of the breast depends on the relative amounts of fat and glandular tissue which are present and this in turn varies greatly according to the female's age and stage of development and physiologic variations during the female's life, such as puberty, pregnancy, lactation and menopause.[8,39]

The young woman's breast contains a larger proportion of glandular tissue which appears as soft tissue density on the mammogram; in older women, when involution of the glandular tissue has occurred, most of the breast tissue appears of fatty density. During involution, there is a mixture of soft tissue and fat density present. The junction between the subcutaneous and retro-mammary fat layers and the glandular tissue should consist of a series of curved margins. Normally the glandular tissue is relatively symmetrical in both breasts, but asymmetry does occur, sometimes requiring further examination.[40,41]

During pregnancy, the overall density of the breast is increased and the trabeculae are somewhat broadened, fluffy and irregular in contour. In the lactational breast, the mammographic film shows that the ducts are more crowded.[40]

The lobules

The lobules measure 0.5 to l or 2 mm and are visualized as small nodules as long as they are separated from each other in the encompassing adipose tissue. Superimposition makes them appear confluent; resulting in densities of various sizes and forms. The single lobules are visible only along the border of involuted glandular tissue. In the center, they look bigger or even may form a homogenous density due to Superimposition.[40]

The lactiferous ducts

The lactiferous ducts appear as linear or slightly nodular densities, radiating from the nipple into the breast. The ducts have a diameter of l-2mm. The lactiferous sinuses (ampullae) are local dilatations up to 4mm of these ducts, just behind the nipple.[40]

Stromal tissue and Cooper's Ligaments

Stromal fibers are recognized in the subcutaneous fatty tissue as hair-like septa extending from the parenchyma to the skin, these are very difficult to be seen in the dense breasts. Cooper's ligaments are easily recognized as curvilinear densities and follow a scalloped course and extending from the parenchyma to the posterior aspect of the overlying epidermis. Under normal conditions the Cooper's ligaments are not thickened and exhibit a regular pattern. The reticular stromal tissue dominate in the mammographic pattern at menopausal and postmenopausal women due to replacement of glandular tissue by fat giving fatty atrophic breast.(41)

Fatty tissue

The subcutaneous fat is observed as a lucent zone between the skin and the breast parenchyma, while the retromammary fatty layer separates the breast parenchyma from the soft tissue of the thorax.(40)

The skin and nipple

The skin (epidermis and corium dermis) is 0.5-2mm thick, and increases inferiorly. The dermal papillae consist of relatively central radiolucent, vascularized connective tissue and epidermal ridges of more reticular radio densities around the papillae. May be seen in profile as it projects from the areola, but it may be flat or retracted, and can't be detected. The thickness of the areola in mammogram is 2-4 mm.(39,41)

Vessels

The arteries: The large arteries can be seen as linear densities that do not converge toward the nipple. Calcified vascular walls occur exclusively in arteries, which may be recognized as parallel, circular or interrupted streaks of calcium usually in old women.

The veins: cross the breast as curvilinear densities measuring 2-4 mm in diameter following a long sweeping course in the subcutaneous tissue as well as within the parenchyma. The venous pattern and caliber are best visualized in predominately fatty breast and generally symmetrical in both breasts.(6,41)

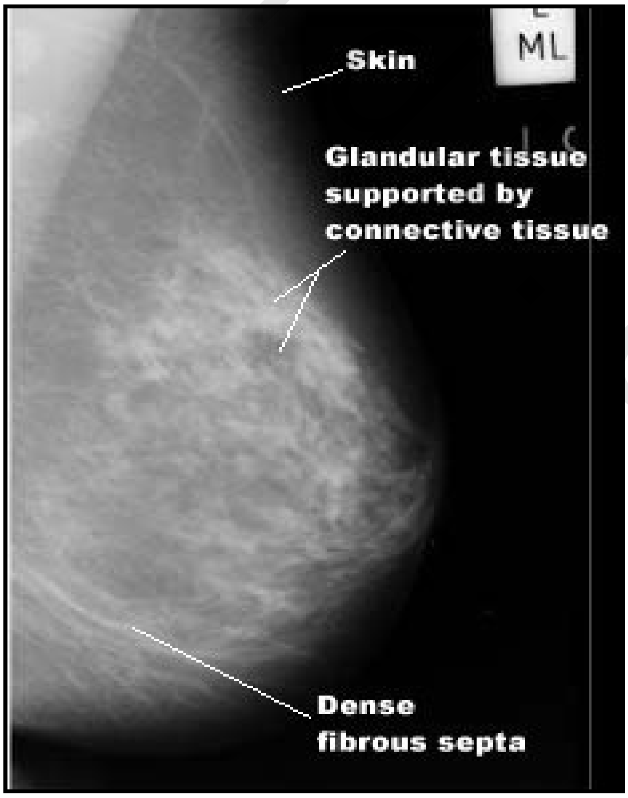


Figure (13): Mammographicanatomy of the breast.(42)

The axillary lymph nodes

The low axillary lymph nodes are seen in the mediolateral oblique (MLO) view, which differ in number and size. The variable positions of the lymph nodes account for the various appearance in different projections, varying from typical bean-shaped to spherical. The diameter ranges from 5 to 20mm. The number and size of mamographically visible lymph nodes are subject to individual variations.[43]

Mammographic density is classified into (New birads classification of breast composition)[44]

1. Almost entirely fatty (figure 14)(<25% breast parenchyma).
2. Scattered fibroglandular tissue (figure 15)(25-50% breast parenchyma).
3. Heterogeneously dense (figure 16)(breast parenchyma 50-75%).
4. Extremely dense (figure 17)(breast parenchyma >75%).

Figure (14): Almost entirely fatty.[14]

Figure(15): Scattered fibro glandular tissue.[14]

Figure (16): Heterogeneously Dense.[14]

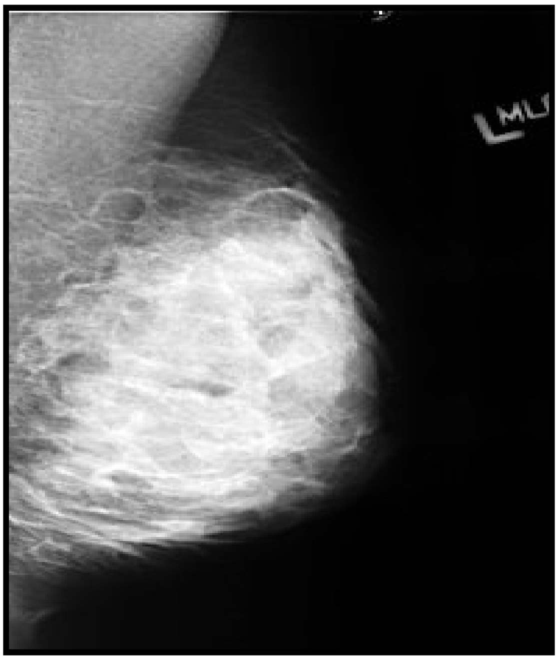


Figure (17): Extremely Dense.[14]

II) Breast ultrasound

The first line of imaging techniques for assessment of clinically or mammographically detected breast nodules is ultrasound.[45]

The valid roles of breast ultrasound include differentiation between cysts and solid masses, evaluation of palpable masses not visible in a radiologically dense breast, evaluation of young patient with palpable mass to limit radiation exposure, evaluation of infected breast for an abscess, evaluation of a mass that can't be completely evaluated with mammography because of location, evaluation of node status and guidance of interventional procedures.[46]

Ultrasound assessment of a breast mass includes evaluation of the shape, orientation, margins, boundaries, internal echo texture, posterior acoustic features, calcification, vascularity and surrounding tissue. The internal echo texture of a breast lesion can be anechoic, hypoechoic, hyperechoic, isoechoic or complex. Hyperechoic and hypoechoic breast lesions are those with increased or decreased echogenecity more than the subcutaneous fat respectively.[43]

Normal sonographic anatomy of the breast (Figure 18)

In contrast to other surface organs examined by high-resolution sonography, the breast tissue is not sharply delineated. It is embedded in the fatty tissue of the chest wall and exhibits large variations in its proportion of fatty and glandular tissue. Both components alter with age, nutritional status, and mastopathic changes in the glandular tissue. The appearance and pattern of the glandular elements of the breast vary remarkably from woman to woman and vary within the same woman depending on her stage in life. As the woman ages, the breast tissue becomes progressively replaced with fat, resulting in less echogenic sonographic pattern.[43]

The breast is divided into three layers located between the skin and the chest wall. These layers include the subcutaneous layer, the mammary layer, and the retro-mammary layer. The subcutaneous and retro-mammary layers are usually quite thin and are composed of fat surrounded by connective tissue septae. Although fat is often quite echogenic in other parts of the body, it is the least echogenic tissue within the breast. The multiple tissue interfaces between ducts, glands, and supporting ligaments cause these tissues to be very echogenic.(47)

The volume and echogenicity of the mammary layer depends heavily on the patient's general inherited breast tissue pattern, as well as the functional state of the breast (i. e., pubertal, lactating, postmenopausal).(48)

The skin

The sonographic pattern is a more or less homogeneous band that is more echogenic than the underlying fat tissue and appears as two, echogenic lines demarcating a narrow hypo-echoic band, the dermis. The skin is slightly thicker in young women than in elderly but is normally less than 3 mm (0.5-2 mm), and is usually maximum in the lower quadrants, towards the inframammary fold.(43)

The subcutaneous fat

The subcutaneous region displays fine, weakly echogenic reflections from fat lobules, interspersed with strong echoes from the suspensory ligaments of cooper; which run oblique to skin surface. It measures up to 2-3 cm and may be very thin or absent in patients with very dense breasts. Subcutaneous fat lobules and those within the breast are usually larger than fat lobules located in the pre-pectoral area (retro mammary fat).(49-51)

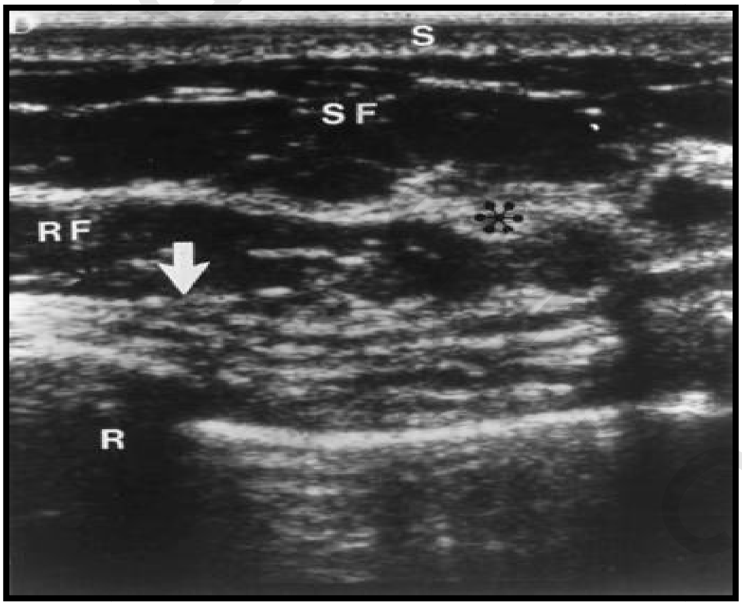


Figure (18): Normal sonographic anatomy of the breast.(11)

S: Skin.
SF: Subcutaneous Fat Lobule.
RF: Retroglandular Fat.
R: Rib
*: Fibroglandular tissue.
Arrow: Pectoralis major m.

The Cooper's ligaments

The Cooper's ligaments appear as echogenic stripes arise from the glandular tissue coursing through the subcutaneous fat to insert in the skin. These ligaments, especially behind their crossing points, cast acoustic shadows due to abrapt attenuation differences, which disappear when moving the transducer. The ligaments are well visualized both in subcutaneous fat as well as in fatty breasts, with a regular orientation and in contrast with hypoechoic fat. They disappear inside the hyperechoic structure of breasts with a fibroglandular pattern.(47)

The fascial envelope (superficial and deep layers)

These fascial layers may be identified as thin lines, although they are not usually visible. The superficial layer is sometimes seen below the dermis, and the deep layer lies over the retromammary fat and pectoralis muscle. The two layers are straddled by Cooper's ligaments.(50)

The breast parenchyma

The true breast tissue forms a conical disk of ducts and lobuli, intralobular connective tissue, and fat. The sonographic pattern varies with age and individually, and depends on the amount and type of contents, i.e. fat, fibrous and glandular tissues. The fibrous and glandular components are variably echogenic, while fat is hypoechoic, so breast parenchyma is not homogeneous.

- Fat may be represented as rounded or oval hypoechoic lobules, inside echogenic fibroglandular tissue, or may be the main breast constituent in fatty involution, a wholly hypoechoic breast crossed by the echogenic ligaments.
- A breast with a predominant glandular structure is homogeneously echogenic and not infrequently, is interlaced with small hypoechoic mammary ducts.
- A breast with a fibro glandular structure is non homogeneous because of hypoechoic bands, coursing in a radial array around and towards the nipple, representing the ductal pattern. But in general, fibroglandular tissue appears echogenic, whereas most masses appear as hypoechoic or anechoic structures. In younger women, with a rich glandular component, the hypoechoic bands contain echogenic lines, better demonstrated when the longitudinal scan is along the ducts' main axis. Going towards the nipple these lines progressively separate and delineate the peripheral ducts.(49,50)

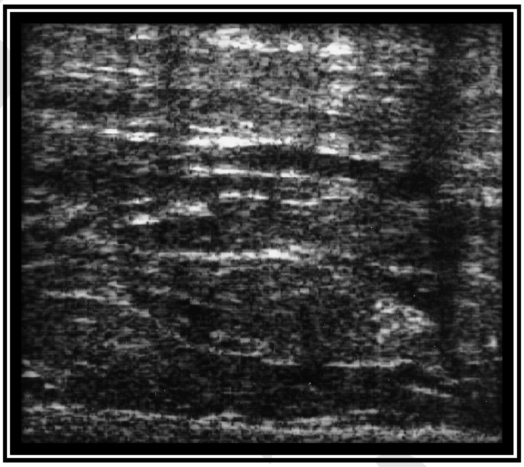
Physiological Sonographic Patterns of the Breast:

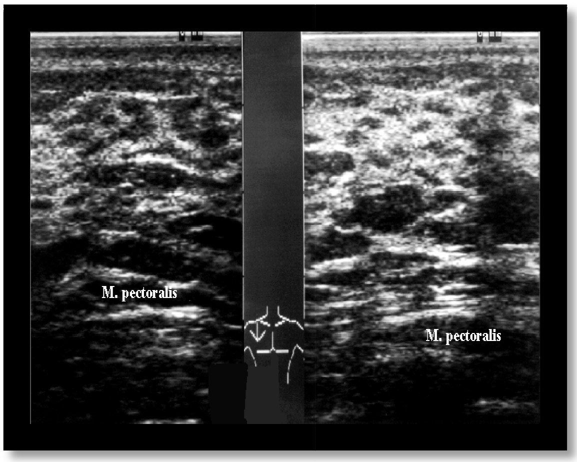
1. Prepubertal mammary gland is widely hypoechoic with no glandular echoes.
2. At puberty appears hyperechoic structure surrounded by little fat.
3. In adult women, the echogenicity varies according to age, menstrual cycle and hormonal condition.

During the menstrual cycle: An increase in size, density, nodularity and tenderness of the breast in the second half of the cycle do not produce a significant effect on the sonographic pattern; an increased echogenicity is sometimes appreciated, and improves the visualization of solid or cystic masses.(49-51)

In menopausal age, breast partly involuted in which the parenchyma has been partially replaced by fat and there are increased amounts of subcutaneous and retro-mammary fat.

4. The postmenopausal breast appears diffusely hypoechoic due to fatty involution.
5. Pregnancy and lactational pattern: in which increase in glandular tissue leads to a finally granular appearance with extreme compression of the subcutaneous and retromammary fat and appears widely hyperechoic.[48-51]





The nipple

The nipple is of medium-level echogenicity and produces a posterior acoustic shadow. Called "nipple shadow". One cause of this shadowing is nipple protrusion. In addition, the abundant connective tissue and muscle fibers within the nipple also cause US beam attenuation and thus produce posterior shadowing. When the nipple examined carefully, it is seen as a homogenous round or oval structure with slightly or markedly lowered echogenicity than the skin layer, and may sometimes appear resembling a superficial adenoma if imaged from an oblique angle. Scanning obliquely behind the nipple or using an offset pad will allow the area posterior to the nipple to be visualized.[50,52]

Transducer held at an angle. The ultrasound beam is perpendicular to the long axis of the duct. Properly contact and pressure. No acoustic shadow from the nipple.

The subareolar tissues

Are usually echogenic, because subcutaneous fat is interrupted at this level.[49,51]

The duct system

Main ducts coming to the nipple may be visualized as anechoic bands, with a progressively increasing diameter.[49,51]

The lactiferous ducts

The lactiferous sinus (Figure 19) is the widest portion of normal ducts, up to 3 mm. wide, and is located just behind the nipple can often be identified if they are slightly distended.[49,51]

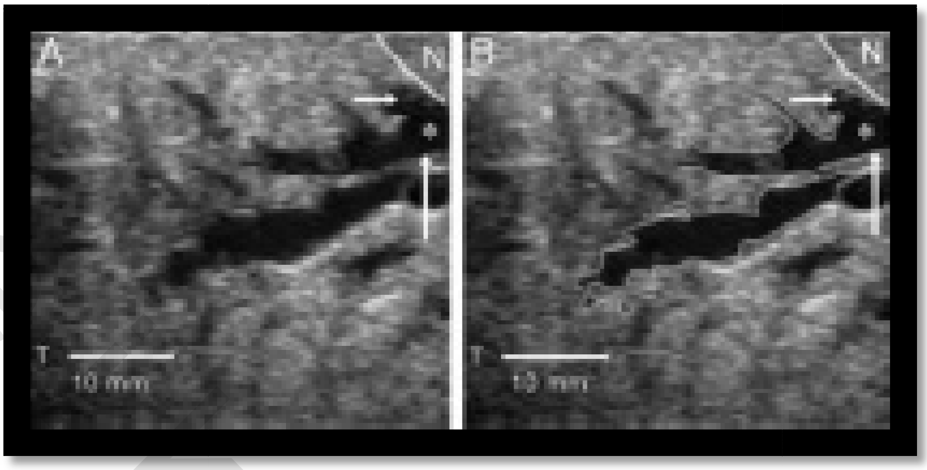


Figure (19): Mammary ducts.[52]

The terminal ductal lobular units (TDLUs)

The TDLUs may enlarge or involute, reflecting age and physiologic differences and proliferating in pregnancy Hyperplastic TDLUs are hypoechoic areas that can be recognized on a US image. A small normal TDLU may not be identified as a discrete anatomic structure.[53]

The retro-mammary space: On ultrasound, the retro-mammary space is seen as an echo-poor fatty layer present between the posterior surface of the gland and the fascia overlying the pectoralis muscle. The layer of retromammary fat is thinner than the subcutaneous region and the fat lobules are smaller.[51]

Pectoralis muscle

The pectoral fascia appears as an echogenic line bordering the chest wall and bound the breast parenchyma posteriorly. Muscle fibres are visible between the anterior and posterior fascial planes. The pectoralis muscle appears highly reflective especially in obese elderly women, and has a fibrillary pattern. The identification of this muscle is a guarantee that we are examining the gland in its whole depth.[51]

The ribs

The ribs are oval hypoechoic, periodic structures behind the pectoralis muscles. They produce a posterior acoustic shadow.[51]

Intercostal muscles

The intercostal muscles are identified in the spaces among the ribs and show a muscular pattern. The echogenic reflection of the pleural line that shifts during respiration is the deepest structure we can identify.[49,50]

The axilla

The axillary vessels present as tubular structures. Most lymph nodes in the axilla are isoechoic to the axillary fat, although some nodes feature an echogenic hilum.[51]

Intramammary lymph nodes

Can be demonstrated with sonography, and they are more often located in the upper outer quadrants of the breast. Normal lymph nodes have an elongated shape, with a hypoechoic rim surrounding an echogenic center, the node's hilum. The longest diameter is usually less than 1 cm. Morphology changes according to the scanning plane. Although pathology remains the gold standard to rule out malignancy, sonography can give some information on the size, shape and structure of lymph nodes. Color Doppler imaging can add information by showing blood flow at the hilum. Lymphatic drainage is to the axillary, subclavicular and internal mammary chain nodes, through penetrating lymphatics. All these nodes can be easily demonstrated when enlarged.[49,51]

Table (II): Echogenicity of the various breast tissues

Anatomic structure	Echogenicity
Skin	Hyper-echoic
Subcutaneous fat	Hypo-echoic
Cooper's ligaments	Hyper-echoic
Parenchyma	Hyper-echoic
Connective tissue	Hyper-echoic
Fatty infiltration	Hypo-echoic
Nipple	Hypo-echoic
Lactiferous ducts	Anechoic
Retro-mammary fat	Hypo-echoic
Pectoralis muscle	Hypo-echoic
Ribs	Hypo-echoic
Pleura	Hyper-echoic
Lung	Diffuse shadow
Axillary artery and vein	Anechoic
Humeral head	Bright entry echo with acoustic shadow

III) Magnetic Resonance Mammography (MRM)

For more than 15 years MR mammography has been clinically tested.[54]

Advantages of MRM

(1) Multiplanar and multiparameteric capabilities.
(2) Its high sensitivity to inherent differences among normal and pathological tissues (tissue characterization).
(3) Its capacity to acquire good spatial resolution.
(4) The absence of ionizing radiation or any known adverse biologic effect.
(5) Useful in characterization of small lesions.
(6) Can be useful in dense breasts.
(7) Can detect cutaneous anomalies as neurofibromatosis.[55]

The general requirements of an MR imaging system for breast imaging

- The ability to survey, in a single acquisition an entire breast (19 or more slices), with 3 mm or thinner sections with an in-plane resolution of under 1 mm. It must also have the capability of obtaining two or more echoes simultaneously, MR images of the breasts are obtained using a dedicated breast coil which ensures a high signal-to-noise ratio and allows reduced slice thickness and optimum spatial resolution. [56]
- A T1-weighted 3D FLASH sequence is used and the breasts are imaged before, and at one minute intervals following IV gadolinium-DTPA for four minutes post injection. Detection of enhancing lesions is made easier if subtraction images are obtained using appropriate software. The images are evaluated visually and the enhancement characteristics of individual lesions may be studied quantitatively.[57]

Indications of MRM

(1) The definite proof of malignant tumor and the exclusion of malignant tumor.
(2) The status after radiation or operation after more than 6 months, the differentiation between scars and recurrent cancer.
- Detect response to therapy
- Pre-operative surgical planning.

(3) The detection of multifocality/multicentricity.
(4) The delineation of implants and possibly the search for the primary tumor when lymph node metastases have been detected.[56]

The disadvantages of MRM

The unclear specificity, the high price, the inability to detect microcalcifications and, the need of contrast medium and the artifacts.[57]

Morphological sequences

Historically, breast MRI non-injected sequences were considered as being of little use because of the low diagnostic value of T2 and T1-weighted signals. Since then, several authors have demonstrated the usefulness of T2-weighted sequences for detecting the presence of cysts or microcysts, the presence of which suggests the benign character of enhancement (whether annular enhancement in the case of an inflammatory cyst or stippled non-masslike enhancement in fibrocystic mastopathy). The European recommendations (EUSOBI) advocate undertaking a T2-weighted sequence.

According to Kuhl et al., T2-weighted sequences can be performed without fat saturation because a T2 signal greater than that of non-saturated fat has very good predictive value for a cyst being benign [54]. T2-weighted sequences with fat saturation are useful for creating indirect MRI ductography images where there is a discharge and seem to optimise the detection of small cancers. T1-weighted sequences are useful for detecting the presence of a fatty component within a lesion, which is also a major aspect predicting its benign nature. T1 sequences are therefore performed without fat saturation. They also allow metal markers to be detected which may have been positioned at the end of biopsy. When the biopsy was guided by MRI, T1 sequences can confirm the correct position of the marker in the biopsy site at the end of the procedure[56]. When the biopsy took place using stereotactic mammography or ultrasound, the marker provides confirmation that the position of the biopsied lesion and of contrast uptake in the MRI is the same. This detection of the biopsy marker is based on detecting the magnetic susceptibility artefact on T1 gradient-echo sequences, created by the metallic nature of the marker.

Advanced sequences of MRI include

1-Contrast enhanced MRI

It is a study that requires the administration of a gadolinium-containing contrast agent during the study.[58,59] Early studies have shown that breast MRI without contrast agent is not of diagnostic value.[60,61] The uptake of contrast medium in breast tissue in premenopausal women is also dependent on the phase of the menstrual cycle. It is essential to perform breast MRI in the correct phase of the cycle as enhancing normal breast tissue may otherwise complicate the interpretation of the study. The optimal time in pre-menopausal women to perform a breast MRI is between the 5th and 12th day after the start of the menstrual cycle.[62-64] The most commonly used sequence in breast MRI is a T1-weighted, dynamic contrast enhanced acquisition. The sequence is called ‘dynamic’ because it is first performed before contrast administration and is repeated multiple times after contrast administration. A T1-weighted 3D or 2D (multi-slice) spoiled gradient echo pulse sequence is obtained before contrast injection and then repeated as rapidly as possible for 5 to 7 min after a rapid intravenous bolus of a Gd-containing contrast agent. A 3D pulse sequence offers a stronger T1 contrast and enables thinner slices than 2D; in turn, a 2D sequence suffers less from motion and pulsation artifacts. Both sequences can be performed with and without fat-suppresion.[56,57]

A dedicated bilateral breast coil is mandatory for this investigation, and the patient should be placed in the prone position with both breasts hanging in the coil loops. The breasts may be supported to further reduce motion artifacts, but should not be compressed. An increasing field strength (1.5 T, 3 T) allows a higher spatial resolution at a similar temporal resolution and consequently may increase diagnostic confidence.[65]

A dynamic sequence demands at least six time points to be measured, that is, one before the administration of contrast medium, and five after administration of contrast material to evaluate whether a lesion continues to enhance, shows a plateau or shows early wash-out of the contrast agent (decrease of signal intensity).[66] It is thus recommended to perform at least two measurements after the contrast medium has been given, but the optimal number of repetitions is unknown. However, the temporal resolution should not compromise the spatial resolution. It was shown that an increase in spatial resolution results in higher diagnostic confidence even when the temporal resolution is slightly sacrificed.[67]

Types of time-intensity curves[65]

1. **Type I a curve** (“persistent enhancement”). Enhancement continues over the entire dynamic series; the emerging curve is a (more or less) straight line.
2. **Type I b curve** (“persistent with bowing”), enhancement continues over almost the entire dynamic period, but the rate is slowed down during the late post contrast phase, resulting in a flattening (bowing) of the curve.
3. **Type II curve** (“plateau curve”), enhancement reaches a steady state after the initial phase.
4. **Type III curve** (“washout curve”), enhancement decreases again directly after the strong signal increase in the early phase.

Kinetic Curve Assessment

The most suspicious curve pattern derivedfrom the fastest-enhancing part of a lesion was chosen to describe the enhancement curve. Theinitial enhancement phase (enhancementwithin the first 2 minutes after contrast injectionor until the curve started to change) was describedas slow, medium, or rapid. The delayed phase was described as persistent, plateau, or washout. Lesions with rapid or mediuminitial enhancement followed by a delayedphase plateau or washout have a positivepredictive value of 77% for malignancy.(66)

2-Diffusion weighted imaging

Diffusion-weighted imaging provides a novel contrast mechanism in magnetic resonance (MR) imaging and has a high sensitivity in the detection of changes in the local biologic environment. A significant advantage of diffusion-weighted MR imaging over conventional contrast material-enhanced MR imaging is its high sensitivity to change in the microscopic cellular environment without the need for intravenous contrast material injection. Approaches to the assessment of diffusion-weighted breast imaging findings include assessment of these data alone and interpretation of the data in conjunction with T2-weighted imaging findings. In addition, the analysis of apparent diffusion coefficient (ADC) value can be undertaken either in isolation or in combination with diffusion-weighted and T2-weighted imaging. Most previous studies have evaluated ADC value alone; however, overlap in the ADC values of malignant and benign disease has been observed. This overlap may be partly due to selection of b value, which can influence the concomitant effect of perfusion and emphasize the contribution of multicomponent model influences. The simultaneous assessment of diffusion-weighted and T2-weighted imaging data and ADC value has the potential to improve specificity. In addition, the use of diffusion-weighted imaging in a standard breast MR imaging protocol may heighten sensitivity and thereby improve diagnostic accuracy. Standardization of diffusion-weighted imaging parameters is needed to allow comparison of multicenter studies and assessment of the clinical utility of diffusion-weighted imaging and ADC values in breast evaluation.(68)

3-MRI spectroscopy

Magnetic resonance spectroscopy (MRS) is an application of MRI that provides biochemical information about tissue metabolism. Unlike MRI, which detects the resonance spectra of water in tissues, MRS detects the resonance spectra of a variety of chemical compounds, thereby allowing for a description of in situ chemistry. Historically MRS has been used in the detection and evaluation of brain cancer, but more recently has also been used to diagnose cancer in other regions of the body. Proton 1H (hydrogen one) MRS is increasingly being studied as a potential adjunct to MRI in the classification of suspicious lesions of the breast. The diagnostic value of proton 1H MRS is based on the detection of choline-containing compounds, which are markers of cancerous tissue. Studies have found that malignant lesions (and not benign lesions) contain choline-containing compounds, particularly phosphocholine, that resonate at a chemical shift of 3.2ppm.(68)

Recent evidence suggests that MRS, if incorporated into a standard MRI examination, may be effective in increasing the specificity and positive predictive value of lesion evaluation. For benign lesions where MRI is inconclusive, MRS may eliminate the need for biopsy by demonstrating the lack of a choline resonance at a chemical shift of 3.2ppm. The incorporation of MRS into a breast MRI examination takes less than 10 minutes, and therefore should be readily accepted by patients and radiologists if shown to be effective.

IV) Positron Emission tomography

Breast positron emission tomography (PET) is an organ-specific high-resolution technology that is used to visualize the metabolism of the breast. PET scanning is a nuclear medicine technique that images the flow of molecules in the body. This is made possible by attaching a radionuclide to a molecule that enters into metabolic pathways; the photons emitted when the radionuclide decays are then imaged. While anatomic imaging allows visualization of body structures, PET molecular imaging allows visualization of molecular flow and metabolic processes within the body.[(69)]

The primary benefit of PET imaging is that diseases such as cancer often first manifest as disordered metabolism before anatomic changes can be seen. In addition, dense breast tissue or scarring may cause anatomic techniques (mammography, MRI, ultrasonography) to be indeterminate. In such cases, knowing whether an anatomic structure is glucose hypermetabolic can be critical in the determination of proper medical management.[(69)]

Breast PET typically utilizes the radiotracer F-18 fluorodeoxyglucose (F-18 FDG) to image glucose metabolism; however, other radiotracers are under development.[(69)]

Radiological Manifestation of Suspicious Breast Masses

1. Mammographic picture of suspicious breast masses

Mammography remains the most accurate imaging method for early diagnosis of breast lesions. It is capable of detecting clinically occult lesions early in large percentage of cases, especially in fatty breast.[(70)]

It was found that, 50% of all malignant tumors are discovered by mammography because of the presence of suspicious calcification. Once detected, calcifications should be categorized as definitely benign, malignant, or suspicious as biopsy is necessary.

In asymptomatic women 75% of small clustered calcifications are benign and 25% are associated with cancer.[(71)]

A. Calcifications: (Figure 20)

Malignant calcifications measure less than 1mm, more than 5 per cm, being clustered in distribution, have wild unordered and fine linear branching shape, and varying in size and shape (pleomorphic).[(72)]

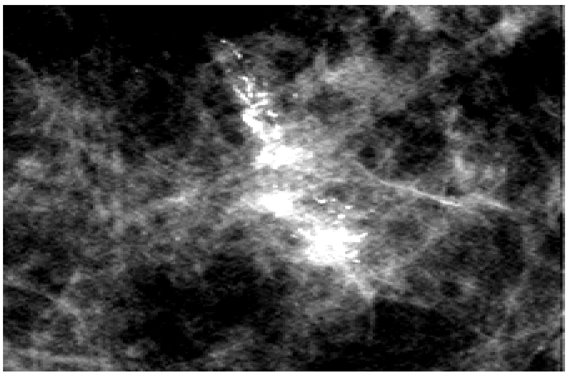


Figure (20): Magnified CC image: Calcifications are pleomorphic, linearly arranged, and have jagged irregular margins, all of which are suspicious features for malignancy.[(70)]

B. Masses: (Figure 21)

The irregular mass (stellate lesion) suggests malignancy. The most common mammographic appearance of invasive carcinoma is a spiculated mass.[70]

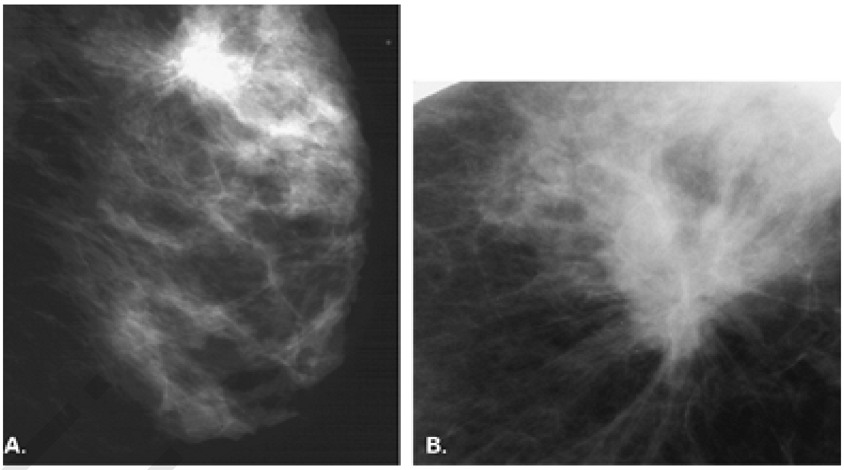


Figure (21): Left MLO (A) views show a high-density, irregular mass superiorly. On spot compression (B), the mass is noted to have markedly speculated margins.[70]

C. Architectural distortion and developing asymmetry

For accurate interpretation, the right and left oblique lateral views as well as the two craniocaudal views should be placed side by side. Although normal breasts are often not completely symmetrical, any significant departure from symmetry should be evaluated for the presence of speculations or underlying mass. Although it is difficult to detect architectural distortion in its early stage, it is defined as tethering of glandular tissue (the presence of abnormal trabecular markings) with the production of radiating fine spicules unassociated with a central dense mass. It is very often associated with malignancy and may be the only evidence of carcinoma as in inflammatory carcinoma.[73]

D. Prominent ductal pattern: (Figure 22)

Dilated ducts are an uncommon presentation of carcinoma but occasionally may be the only sign of this disease. A unilateral dilated duct or ducts, especially those with associated microcalcifications, are suspicious for the possibility of malignancy.[70]

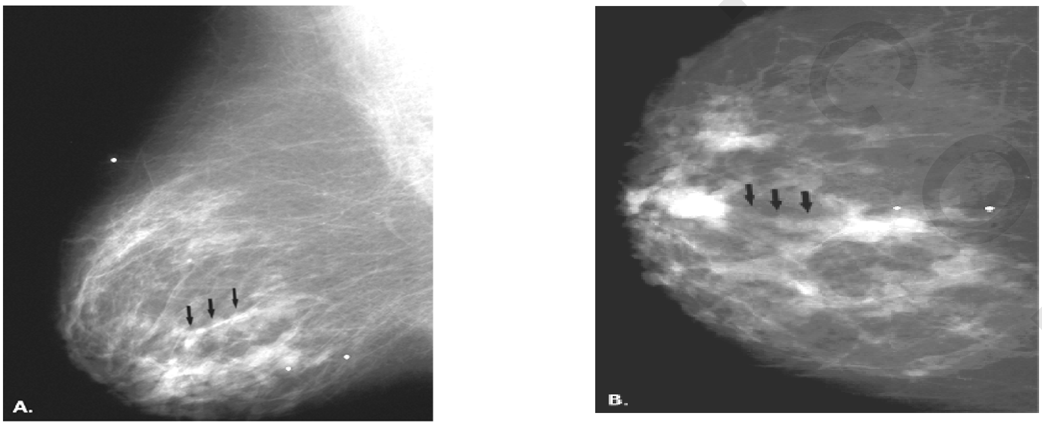


Figure (22): MLO (A) and CC (B) views show a-segment of dilated ducts. Tubular-nodular densities extend from the nipple posteriorly into the breast (arrows).[70]

E. Skin thickening

The normal skin thickness of the breast has been described as generally less than 1.5 mm. Unilateral edema is caused by impairment of lymph drainage, axillary lymphatic obstruction by metastasis, and inflammatory carcinoma. However, a bilateral edema pattern suggests a systemic etiology, such as congestive heart failure or renal failure. Other image modalities, such as ultrasound and MRI, are particularly helpful in the patient with unilateral edema of unknown etiology. These may identify a suspicious mass in the patient with inflammatory carcinoma when the edema obscures the mass on mammography.(70)

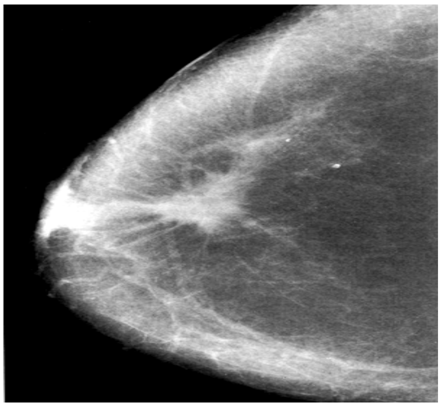


Figure (23): Right CC view shows a high-density speculated mass is present in the subareolar area. Long spicules surround the mass and extend anteriorly to the periareolar area, where they tether the skin. Focal prominent skin thickening is seen.(70)

BI-RADs Classification

The assessment and description of the mammographic findings are defined in a standardized lexicon known as the Breast Imaging Reporting and Data System (BI-RADS).

Table (III): BI-RADS classification for mammographic findings.(70)

Category	Diagnosis	Number of Criteria
0	Incomplete	Your mammogram or ultrasound didn't give the radiologist enough information to make a clear diagnosis; follow-up imaging is necessary
1	Negative	There is nothing to comment on; routine screening recommended
2	Benign	A definite benign finding; routine screening recommended
3	Probably Benign	Findings that have a high probability of being benign (>98%); six-month short interval follow-up
4	Suspicious Abnormality	Not characteristic of breast cancer, but reasonable probability of being malignant (3 to 94%); biopsy should be considered
5	Highly Suspicious of Malignancy	Lesion that has a high probability of being malignant (>= 95%); take appropriate action
6	Known Biopsy Proven Malignancy	Lesions known to be malignant that are being imaged prior to definitive treatment; assure that treatment is completed

2. Ultrsonographic signs and features of suspicious breast masses

Stavros et al proposed an US scheme for prospectively classifying breast nodules into 1 of 3 categories:[74,75]

- Benign.
- Indeterminate.
- Malignant.

To be classified as benign, a nodule had to have no malignant characteristics. In addition, 1 of the following 3 combinations of benign characteristics had to be demonstrated:

- Intense uniform hyperechogenicity.
- Ellipsoid or wider-than-tall (parallel) orientation, along with a thin, echogenic capsule.
- 2 or 3 gentle lobulations and a thin, echogenic capsule.

A nodule was classified as indeterminate by default if it had no malignant characteristics and none of the 3 benign characteristic combinations listed above.

To be classified as malignant, a mass needed to have any of the following characteristics:

- Spiculated contour.
- Taller-than-wide (not parallel) orientation.
- Angular margins.
- Marked hypoechogenicity.
- Posterior acoustic shadowing.
- Punctate calcifications.
- Duct extension.
- Branch pattern.
- Microlobulation.

A-shape: (Figure 24)

Masses tend to have a characteristic lie within the breast tissue with their long axis laying either parallel or at right angles to the skin. The nature of the mass can be suggested according to the ratio of anteroposterior (depth) to transverse (width) diameter (D:W), in the malignancies, the D:W ratio may be 1.0 or even greater because of their incompressibility and invasive growth pattern. So the malignant mass has taller than wider configuration with branching pattern and may be associated with ductal extension.[75]

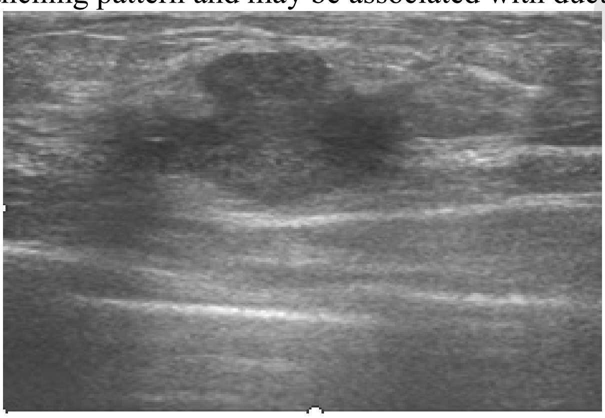


Figure (24): Depth: Width ratio is about 1 or more by the malignant breast mass.[76]

B-Margin

- Irregular contour.
- Angular or microlobulated margins.
- Speculated margin.

C-Echogenicity

Hypoechoic mass may be associated with thick hyperechoic halo.

D- Calcifications: (Figure 25)

The calcifications associated with malignancy typically form numerous small foci less than 1 mm in diameter. These foci may lie within the tumor or in the surrounding parenchyma.[52]

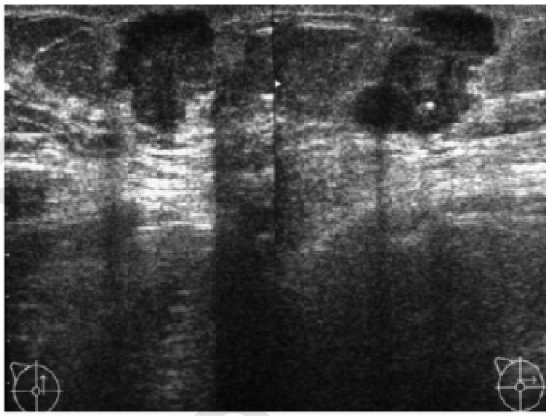


Figure (25): Irregular shape malignant breast mass with internal echoes.[76]

E-Others features

Posterior acoustic shadowing and increased vascularity.[76]

Percutaneous breast biopsy

Percutaneous image–guided needle biopsy has increasingly become an alternative to surgical biopsy for the histological assessment of breast lesions, with the advantages of being faster and more feasible, less invasive, less expensive than surgical biopsy with less normal breast tissue removal resulting in no deformity of the breast with minimal scarring and cosmetic impairment and so low risk of complications and high patient satisfaction are achieved.[77]

Many methods of percutaneous breast biopsy are currently being used as; fine needle aspiration biopsy (FNAB), core needle biopsy (CNB) and recently, vacuum assisted biopsy (VAB). These methods are used as a diagnostic tool under different guided image modalities.[78]

Interventional procedures of the breast comprise different radiological and imaging modalities guidance of various techniques of tissue sampling including (stereotactic x-ray, high frequency ultrasound and MRI) that aim to obtain a representative sample of cells or tissues through accurate pinpointing and mapping the area to be biopsied, to obtain final diagnosis of the suspicious lesion and so replacing a high number of open surgical biopsies.[77]

Types of Percutaneous needle biopsies

- Fine needle aspiration biopsy (FNA).
- Core needle biopsy (CNB).

(A) Fine Needle Aspiration Cytology

There are critical components which are necessary to achieve reliable results by using FNAB, these include the following:

1- Lesions selected for biopsy should undergo a complete tailored imaging evaluation before the needle biopsy is scheduled.
2- Accuracy in needle placement.
3- Skill in performance of FNAB.
4- Expert cytopathologist analysis.(76)

For FNA, needles are usually available, inexpensive and disposable needles with transparent plastic hubs can be used for these procedures.

The needles length required depends on the depth of the lesion; in the breast usually 3.8cm long needles are adequate. For lesions deeply situated in large non compressible breast, longer needles (7 and 9cm) may be needed.(79)

The needle is moved to and fro within the lesion under imaging guidance with simultaneous rotation and with negative pressure applied. Aspiration is continued until material is seen within the hub of the needle. The aspirate is then delivered onto slides. Alcohol- fixed smears were prepared for routine diagnosis. The rest of the cytopuncture material used for preparing cell blocks and fixed in 10% formalin.(76)

- Ultrasonogaphy guided FNAB.
- A- Horizontal (Parallel approach).
- B- Vertical (direct approach).

(B) Core Needle Biopsy

Automated gun-needle combination

The idea

These are designed to move a cutting needle rapidly through the breast. These needles consist of an inner needle that captures tissue in a tissue acquisition chamber and an outer cutting needle that separates this tissue from the breast. Long-throw needles travel more than 2 cm after being fired, obtain better specimens, and are able to move more effectively through dense tissue. Short-throw needles may be necessary when compressed breast thickness is 2 cm or less.(77) (Fig. 26).

Figure (26): Automated core biopsy gun.(78)

US- guided methods

US-guided core biopsy

Ultrasound-guided core biopsy is preferred to stereotactic core biopsy for all masses that can be seen at ultrasound. As well, it is less time consuming and does not require expensive stereotactic equipment or additional floor space or use ionizing radiation. Ultrasound guided large-core needle biopsy is acknowledged as provides a histological diagnosis with a comparable high degree to surgical biopsy. As well, US-CNB has been proved to reduce the number of unnecessary surgeries for benign disease.(80)

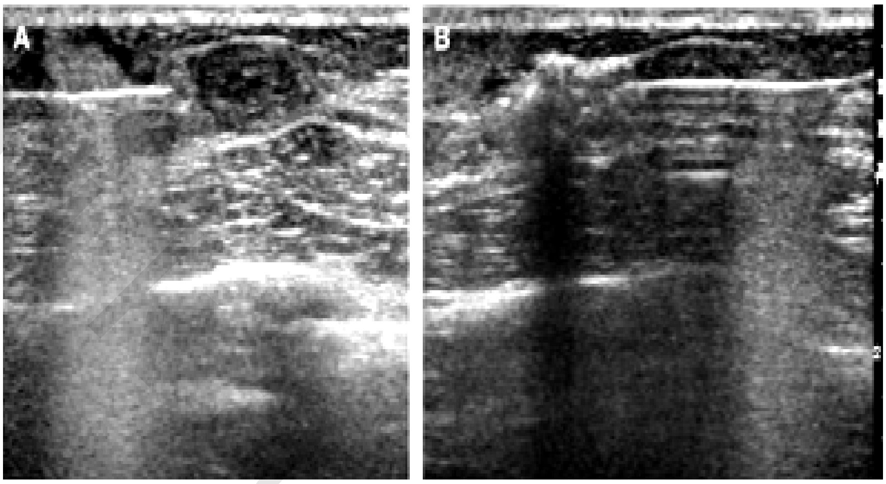


Figure (27): Ultrasound-guided CNB performed with an automated large core device.
(A) Prefire image with the needle tip at the proximal edge of a solid mass.
(B) Postfire image demonstrates the needle traversing the mass.(70)

Ultrasound guidedance

US-guided needle biopsy of breast lesions (Figure 27) should always be performed after mammography to avoid false negative interpretations of post-biopsy hematomas.(81)

For best results in breast sonography, it is critical to use a high frequency (7.5-10 MHz), hand-held flat linear array transducer whose non-diverting beam guarantees an excellent near-field resolution, rather than a sector scanner. A 5-MHz linear-array transducer should also be available for examining lesions located in large breasts beyond the field of view of the 7.5-10 MHz probe.(81)

Different techniques of US-guidance

The optimal approach according to needle placement is chosen based on the location and appearance of the lesion with two different techniques available:

- Horizontal needle insertion. (Parallel approach).
- Vertical needle insertion. (Direct approach).

Vertical needle insertion

For vertical needle insertion, the target lesion is identified and the transducer placed so that the lesion lies approximately on the midline of the scan then, the needle is inserted lateral to the transducer midpoint (Figure 28).

The needle degree of obliquity must be adjusted, depending on the depth of the lesion. With this technique, the needle is not seen until it has reached the scan plane at the level of the lesion, where its tip appears as a bright echo.[82]

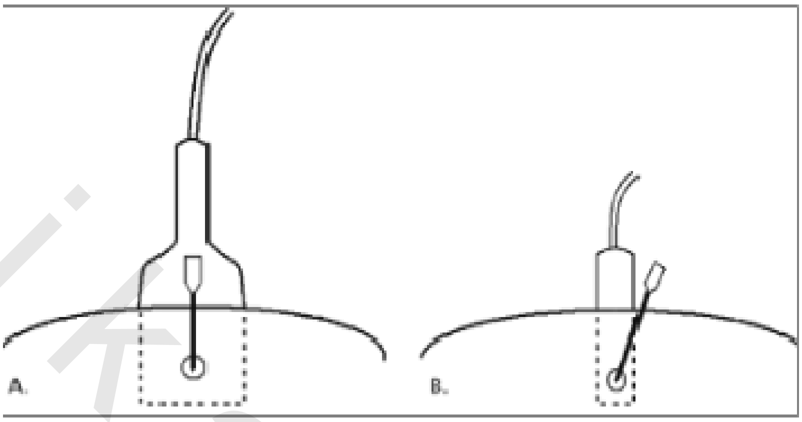


Figure (28): Schematic for ultrasound-guided cyst aspiration shows that the needle is placed vertically, directly toward the mass. The needle tip is visible when it bisects the scan plane at the level of the lesion.[76]

Horizontal needle insertion

For horizontal needle insertion (Figure 29), the transducer is placed so that the lesion is displaced close to the lateral margin of the scan. The needle is then placed close to the corresponding end of the transducer and inserted along the scan plane with a variable obliquity depending on the depth of the target. With this technique, not just the tip but the entire distal portion of the needle is seen as soon as the needle enters the scan plane. Only a few millimeters of the needle's course in the subcutaneous tissues are not visualized. As a guiding principle, the needle should be advanced only if it is seen clearly. This technique is virtually 100% accurate and it should be used for the biopsy of minute lesions that lie close to the chest wall or near breast implants.[82]

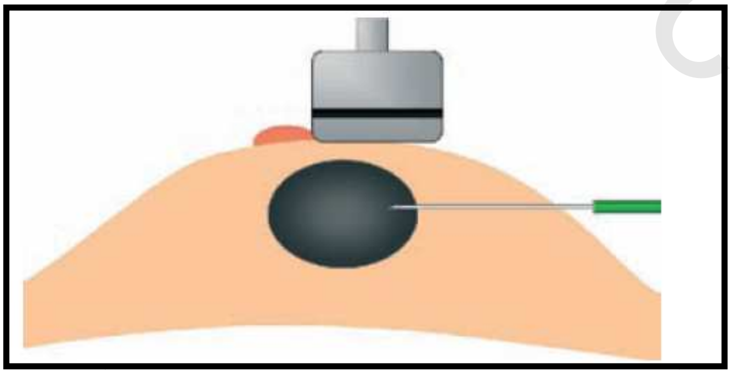


Figure (29): Illustrative image showing the Technique of horizontal needle insertion.[76]