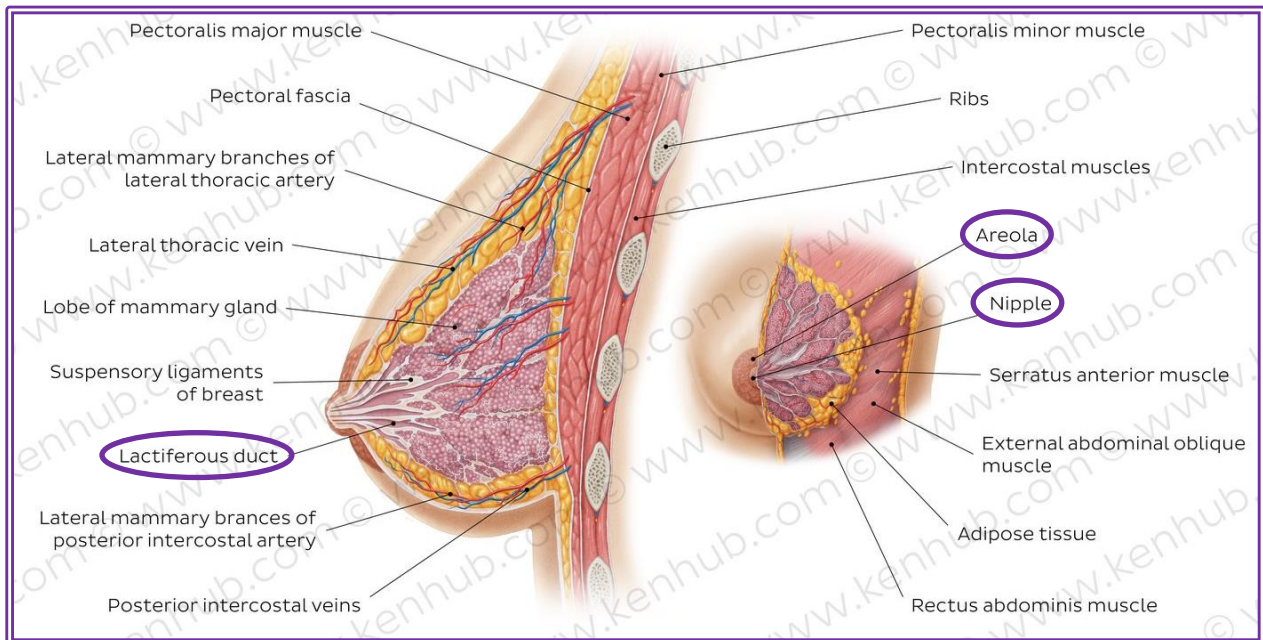


BREAST CANCER

Done by Ahmad Alrfou'

Anatomy :



The Breast is found in the midline of chest and extends to mid-axillary line and from the 2nd to 6th rib. It overlies pectoralis major, serratus anterior and external oblique. It consists of **15-20** Lobes, each lobe having multiple lobules. The most important structure in the breast is the **Mammary gland (Lactiferous gland)** which is found in each lobe, its function is to produce milk for the baby. Each gland "lobe" is separated from the other by **suspensory ligaments** and each gland is connected to a **Lactiferous duct** which drains to the **nipple**. The pigmented area of skin that surrounds the base of the nipple is called the **Areola**, it is rich in modified sebaceous gland particularly at the outer margin. These become enlarged during pregnancy and lactation to form **tubercles of Montgomery**. It is supplied medially by **internal thoracic + anterior intercostal arteries(2-6)** and laterally by **thoracoacromial** and **lateral thoracic arteries**.

Most (**75-90%**) of the lymphatic drainage of the breast is to the ipsilateral **axillary nodes**. The other 10-25% is drained by **parasternal nodes**. Axillary nodes are divided into 5 groups : Anterior, posterior , central , apical and lateral.

Physiology :

The breast tissue is hormone sensitive, affected by :

- 1- **Estrogens** : Major effect on ducts. Breast size increase in puberty, menstrual cycle and pregnancy.
- 2- **Progesterone** : Major effect on lobules. Growth in lobules in preparation for pregnancy and delivery.
- 3- **Prolactin** : Increases breast size. ↑ Levels in pregnancy.

Lactation

The process of milk production requires removal of milk and nipple stimulation, if there's absence of milk removal breast tissue involution will occur! So after removal of milk and nipple stimulation **Prolactin** and **Oxytocin** are released from pituitary gland to maintain milk production from breast tissue.

Some Abnormalities

- Galactorrhea : production of milk outside lactation. Most causes related to Prolactin.
- Gynecomastia : Abnormal breast development in males. Common in newborn male babies, puberty in males and older men >50 years. Pathological causes are Cirrhosis and Klinefilter syndrome.

Breast Cancer :

- **Epidemiology** : Breast cancer is the second most common malignant disease in women and second leading cause of cancer death in women in the US. Peak incidence at postmenopausal, increases with age and 50% of breast cancers are diagnosed in women ≥ 65 years of age.
- **Predisposing factors** :
 - Sex: female
 - Age: ≥ 65
 - Low-fiber and high-fat diet
 - Smoking
 - Alcohol consumption

- History of breast cancer in the contralateral breast + Breast conditions with cellular atypia (e.g., fibrocystic change, fibroadenoma) + Endometrial cancer, ovarian, or colorectal cancer + Radiation therapy during childhood.
- Positive family history (e.g., in first-degree relatives).
- BRCA1 and BRCA2 mutations : BRCA are tumor suppressor genes that code for a DNA repair protein.
- Oncogenes (e.g., RAS)
- Increased exposure to endogenous estrogen : First viable pregnancy after 35 years of age, Nulliparity and/or absence of breastfeeding, Early menarche and/or late menopause. Hormone replacement therapy after menopause.

- **Types :**

***Almost all 95% are Adenocarcinomas.**

- 1- **Ductal carcinoma in situ (DCIS)** : No penetration of the basement membrane, appears as a pattern of grouped microcalcifications on mammography. Higher risk of subsequent ipsilateral invasive carcinoma.
- 2- **Lobar carcinoma in situ (LCIS)** : No penetration of the basement membrane, doesn't lead to microcalcifications, usually incidental finding. Risk of invasive carcinoma in both breasts.
- 3- **Invasive ductal carcinoma (IDC)** : Most common type of invasive breast cancer ~ 80%, Aggressive formation of metastases. Unilateral and unifocal. Important subtypes are medullary breast cancer and inflammatory BC.
- 4- **Invasive lobular carcinoma (ILC)** : ~ 10% of all invasive breast carcinomas. Less aggressive than ductal carcinoma, Bilateral in ~ 20% of cases and frequently multifocal.

****Less common subtypes :**

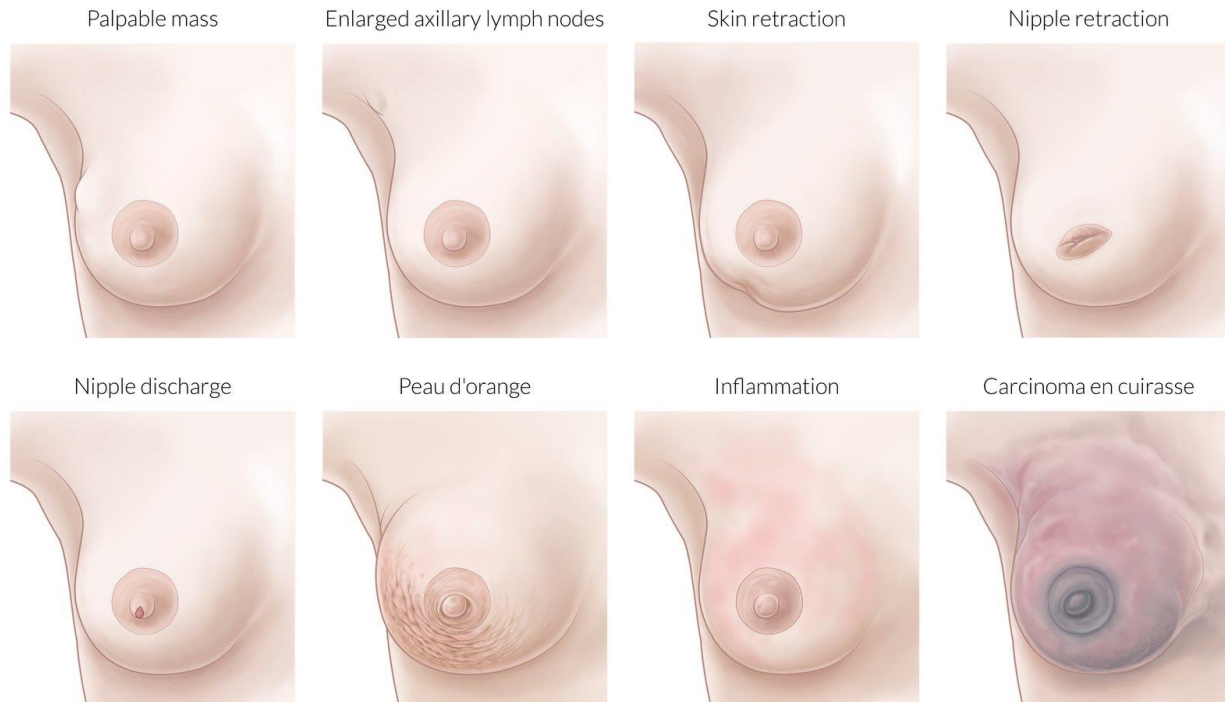
- Mucinous carcinoma (< 5%; more common in older women)
- Mixed carcinoma (ductal/lobular)
- Tubular carcinoma
- Papillary carcinoma
- Micropapillary carcinoma

- **Clinical Features :**

- **Early stages** = Typically single, nontender, firm, poorly defined margins. Most commonly located in the upper outer quadrant (~ 55%).
- **Locally advanced** = changes in size and/or shape → asymmetric breasts. Skin retractions or dimpling (due to fixation to the pectoral muscles, deep fascia, Cooper ligaments, and/or overlying skin) + Peau d'orange. Nipple Inversion or Blood-tinged discharge.
- **Progressive** = Ulcerations, Edema of the arm, Paget disease of the nipple.

➤ **Metastasis = Lymphatic spread or Hematogenous spread :**

- Lymphadenopathy
- Bone metastasis
- Liver metastasis
- Lung metastasis
- Brain metastasis



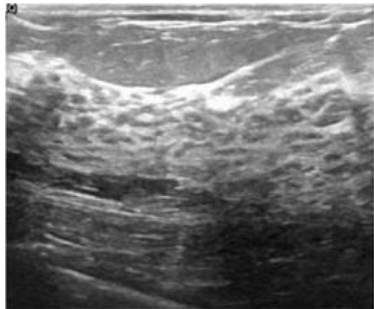
• **Diagnosis :**

Most patients are referred for assessment after abnormalities are detected on routine mammography screening. Alternatively, young women, who are not routinely screened, may present with a mass they have found during self-examination. Women < 40 years of age should undergo breast **ultrasound**; higher breast tissue density makes detection of breast abnormalities with mammography more difficult. Women \geq 40 years of age (35 if there's risk factors) should undergo **mammography**.

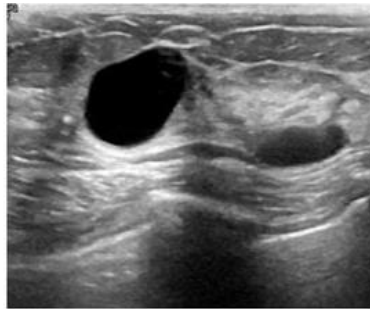
- **Ultrasound** : Allows solid lesions to be differentiated from benign cysts. Includes the evaluation of axillary, supraclavicular, and infraclavicular lymph nodes.

- **Mammography** : Two low-dose x-rays of the breast are obtained (mediolateral oblique and craniocaudal) to screen for breast abnormalities. Used for early detection of breast abnormalities, detects the majority of cancers and can detect lesions ~ 2 years before they are clinically evident.

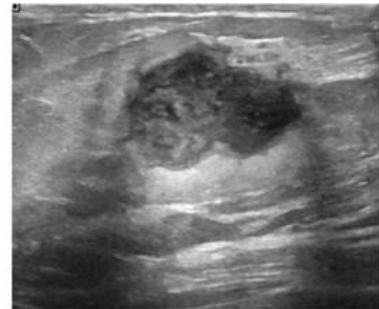
Ultrasound :



Normal

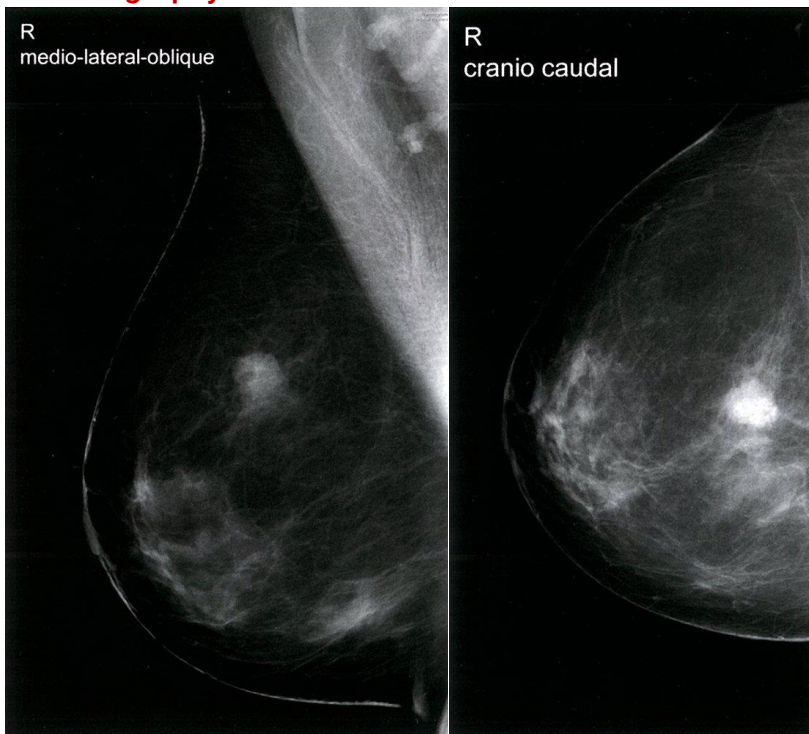


Benign



Malignant

Mammography :



- Biopsy :

- **Fine-needle aspiration (FNA)** : Preferred tool for assessing a breast mass with a low probability of being malignant, may also be used for follow-up and assessment of response to treatment. Especially suited for lesions close to the skin.
- **Core needle biopsy (CNB)** : preferred tool for assessing a suspicious breast mass on ultrasound or mammography. Can be used to confirm the diagnosis (preferred test), used to distinguish between noninvasive and

invasive carcinoma based on histology unlike FNA, allows testing for receptor status.

- **Surgical biopsy** : Should only be used if CNB is not feasible or results of CNB are inconclusive. Full-thickness skin biopsy (punch biopsy) should be performed if inflammatory breast cancer or Paget disease of the breast is suspected. This method provides a larger tissue sample for a more accurate diagnosis and immediate resection of the tumor is possible.

- Receptor testing

Receptor status is crucial in the development of treatment strategies because tumors with overexpression can be targeted directly with hormone therapy or biologics.

1. **Hormone Receptors** : Estrogen and progesterone receptors are present on all breast tissue cells. But in cancerous breast tissue, overexpression of such receptors may be detected, in which case the breast cancer is referred to as receptor-positive. 80% of breast cancers are positive for overexpression of at least one hormone receptor (ER+ / PR+).
2. **Human epidermal growth factor receptor 2 (HER2)** : ~ 20% of breast cancers are HER2-positive. HER2-positive breast cancer can be treated with therapeutic receptor inhibition, which can help to slow cancerous growth and decrease cancer mass. Treatment is Trastuzumab.
3. **Triple-negative breast cancer** : ~ 10–15% of breast cancers are hormone receptor-negative and HER2-negative. Typically more aggressive, high-grade tumors treated with chemotherapy.

- Hormone-negative breast cancer has a poorer prognosis than hormone-positive breast cancer. HER2-positive tumors show aggressive growth and metastasize quickly compared to HER2-negative tumors. Triple-negative disease is associated with a poor prognosis.

* So, for the diagnosis we do the **TRIPLE ASSESSMENT** which is : history and examination, diagnostic imaging by mammography and/or ultrasound scanning and cytology or histology by biopsy.

- TNM Staging :

1. Tumor

- Tis : Carcinoma in situ
- T1 : Tumor size < 2 cm
- T2 : Tumor size >2 cm and <5 cm
- T3 : Tumor size > 5 cm
- T4 : Tumor of any size with infiltration of the skin or chest wall

2. Lymph node

- **N1** : Involvement of mobile level I and II axillary lymph nodes.
- **N2** : Metastases in fixed level I and II axillary lymph nodes or isolated metastases to ipsilateral internal mammary lymph nodes.
- **N3** : Metastases in supraclavicular or infraclavicular lymph nodes (level III) or simultaneous metastases in axillary and internal mammary lymph nodes.

3. Metastasis

- **M0** : no metastasis
- **M1** : distant metastasis

Stage	Primary Tumor	Nodes	Metastases
Stage 1A	≤ 20 mm T1	None	None
Stage 1B	≤ 20 mm T1	Nodal Micrometastases (>0.2 mm <2.0 mm)	None
Stage IIA	≤ 20 mm T1 > 20 mm ≤ 50 mm T2	N1 None	None None
Stage IIB	> 20 mm ≤ 50 mm T2 > 50 mm T3	N1 None	None
Stage IIIA	≤ 50 mm T1,T2 > 50 mm T3	N2 N1 or N2	None
Stage IIIB	Extension to chest wall and/or skin T4	N0 - N2	None
Stage IIIC	Any size	N3	None
Stage IV	Any size	Any involvement	Detectable

- **Treatment :**

Depends on the histopathologic classification and cancer stage. Involves a combination of surgical management and systemic therapy (chemotherapy, hormone therapy, targeted therapy).

5 main lines of treatment :

1. **Surgical tumor removal**

Breast-conserving surgery (BCT), Mastectomy and Intraoperative lymph node evaluation.

2. **Radiation**

follows surgery, Indicated for patients with a high risk of local recurrence.

3. **Chemotherapy**

Can be given as neoadjuvant or adjuvant chemotherapy, indicated in Tumor size > 2 cm, Triple-negative breast cancer and tumor size \geq 0.5 cm, HER-2 positive breast cancer and tumor size > 1 cm, Positive lymph nodes.

4. **Hormone therapy**

Indicated in all ER/PR-positive tumors.

Premenopausal: Tamoxifen

Postmenopausal: Aromatase inhibitors

Preventive: Raloxifene

5. **Targeted therapy**

Indicated in all HER2-positive tumors, Trastuzumab is used which is a humanized monoclonal antibody against the HER2 tyrosine kinase receptor.

- **Prognosis :**

The most important prognostic factor is the breast cancer stage at time of diagnosis. Earlier stages have a significantly better prognosis than late stages.