

A large, stylized pink ribbon graphic is positioned on the left side of the cover. It is a light pink color with a darker pink shadow or outline, giving it a three-dimensional appearance. The ribbon is tied in a loop at the top left and then extends downwards and to the right, crossing itself.

2018

# Surgical oncology sheets

University of Jordan  
4th year medical students

# **Lecture 1: principles of cancer management**

**Written by: Lina Mansour**

**Corrected by: Abdullah Qaswal**

# Principles of cancer management

## IMPORTANT TERMINOLOGY:

### Single VS multi-modality approaches to treat cancer

- to treat cancer we can use :
  - **Surgery**
  - **Chemotherapy**
  - **Radiotherapy**
  - **Hormonal therapy**
- if we use one of these options this is single approach , but if we use a combination of these this is a multi-modality approach.
- **PRINCIPLES OF CANCER MANAGEMENT**
- Usually we use multi-modality approach to treat cancer.

### Surgical oncologist

- The surgical oncologist is a qualified general surgeon , has experience in management of cancer including the other modalities of the treatment (not only surgery) and he is capable to work in multi-disciplinary team manage patients with cancer.

## ROLE OF SURGERY IN MANAGEMENT OF MALIGNANCY

- The surgery can be used to manage cancer in diverse ways:
  - Prevention
  - Diagnosis
  - Treatment of primary tumor
  - Resection of metastasis
  - Management of oncological emergencies
  - Surgery for palliation
  - Surgery for residual disease
  - Surgery for reconstruction
  - Cytoreduction (reducing the bulk of the tumor)
  - Regional chemotherapy

## Cancer surgery for prevention

In certain group of people we can prevent cancer , these people have very high risk to develop cancer, typical examples :

•• Precancerous conditions like : Leukoplakia of the tongue, Thyroid gland in MENS II, Colon in FAP, Colon in HNPCC and Breast in BRCA mutations.

- Leukoplakia of the tongue if left untreated the pt will develop cancer in the oral cavity. Such a lesion must be closely observed and shaved.

there is also erythroplakia that make the pt more prone to malignancy.

these lesions come after some predisposing factors like alcoholism , smoking ... these factors must also be stopped.

- Familial adenomatous polyposis (FAP) the pt has hundreds of adenomatous polyps .pts will 100% develop colon cancer after 40 years old if they are not treated. These pts must remove the colon before the age of 40 (primary prevention).
- In MENS II (multiple endocrine neoplasm II) removal of the thyroid will protect against developing medullary carcinoma.
- Pts who are at high risk of developing breast cancer (BRCA mutation) must be observed carefully , early screening , hormonal treatment (reduce the risk by 50% ) and if the pt is in very high risk she can be offered to do skin-sparing-mastectomy and filling the space by implants.

Note : there is also now skin and nipple sparing mastectomy.



Figure1:  
Leukoplakia of the tongue  
(precancerous)



Figure2:  
FAP precancerous for colon  
cancer

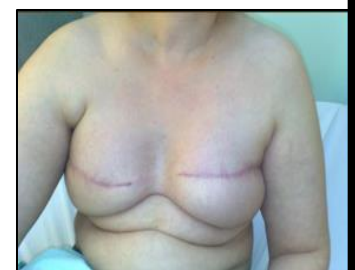


Figure3:  
Skin sparing mastectomy

## Clinical diagnosis of cancer

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The diagnosis starts by **history & physical examination**, by history you detect the complaints of the pt, usually the complaints are related to organ affected for example : pt with lung cancer will develop cough, hemoptysis, shortness of breath ... lately at the course of the disease the pt will develop loss of appetite, wt loss, reduce in immunity and recurrent infxns. So, early presentation is organ specific.

After that you start to do **investigations** to assess the stage of the disease and to assess the fitness of the pt to tolerate the management (surgery, chemo..). then we do **Histologic studies** this is the most important tool. It is what really proof the pt has cancer or not.

To have cytological/ Histological diagnosis we have multiple types of biopsies:

1. **Fine needle aspiration (FNA):** u will obtain just cells not tissues. After obtaining the specimen u send it to the histopathology lab.  
the malignant cell has some special characteristics like : variation in size, increase in affinity to the stain, number of nucleoli increase, the nuclear: cytoplasm ratio increase.  
they used to think that the needle will spread the tumor cells but in practice it does not. Nowadays, FNA is used only for thyroid tumors to differentiate bw benign and malignant conditions. U can diagnose papillary ca, lymphoma and anaplastic ca based on FNA but not follicular ca (needs histologic study not cytologic). But we can really do FNA in all organs.
2. **Trucut biopsy :** done in breast ca, prostatic ca or any accessible tumor. The accessibility of the tumor is assessed by imaging tech (ultrasound, CT..). the true cut biopsy provides TISSUES. We take from the organ several cores and send them to histopathology. but u have to give them enough tissues in order to have the diagnosis usually 5 or 6 cores are enough. this type of biopsies can differentiate bw infiltrative and in-situ ca (in FNA u cannot). Also, we can do hormonal studies (estrogen and progesterone receptors, HER2 for breast ca) these studies cannot be done in FNA.

The tru-cut biopsy is of 2 types : Incisional VS excisional.

- **Incisional biopsy** : we take part of the tumor as a biopsy . this is not the standard of care in breast ca but usually used in colon or gastric ca.
- **Excisional biopsy** : we take the whole mass as a biopsy. Like in a suspicious pigmented lesion on the skin.
- **Lumpectomy** : is removing the lump . it is not an oncological surgical principle. It is basically excisional biopsy + negative margins.



Figure 4:

SCC we need to take biopsy before doing the surgery.

Here the biopsy should be taken from the periphery of the lesion as the center contain necrotic dead cells. And should contain normal cells to look for the transition zone.

Note: the biopsy is always needed for diagnosis and management of cancer with some exceptions like deep lesions in the brain.

The biopsy MUST be adequate , the biopsy should be :

- ✓ Taken from the right site
- ✓ Taken enough tissue
- ✓ Put in proper material in order not to destroy or damage the cells.
- ✓ Made sure that it reach the lab
- ✓ Have access to the result and have contact of the pt.



Figure 5:

pre-op Marking of excisional biopsy over knee. U should think about the contracture of the biopsy wound post-op.

## Surgery to treat cancer

The surgery is part of **multimodality treatment** that is used nearly to all cancers (with some exceptions like BCC and small melanoma.) in this approach we aim to **cure** or **palliate** the pt. palliation is very important as we do care about the quality of life for every human being.

### **There is no absolute CURENESS in cancer !**

Cancer cells might metastasize to other organs at the time of diagnosis or earlier. In such cases and despite of very effective local treatment the pt will have recurrence. For this reason we add radio/chemo / hormonal therapy to surgery to prevent metastasis and recurrence.

also despite this systemic management recurrence also occur. Now they depend on period of time that the pt stay cancer-free after treatment to define cureness (!). so now we talk about 5-year survival rate or 10-year survival ..

but, why ?!!

at cellular level : in 1 mm breast cancer we have 1 million cells (these are not detectable by all means available nowadays) these non detectable cells can shoot metastasis very early. This make u questioning the clinical practice of considering < 5cm breast mass without LN involvement an early cancer (stage 1 and 2) ... so early tumors also carry the risk of metastasis!!!

### **ALSO**

A 1 g malignant mass contain 1 billion cells ,in every 1000 cells there is an inherited resistance to treatment in one cell.

so, there's no absolute cureness because of early metastasis and resistant cells.

u cannot say that the pt is cured from cancer with some exceptions like skin cancers and in-situ lesions treated properly.

What do we mean when we say that the 5-year-survival is 90%?

This means that 90% of pts after receiving proper treatment, did not demonstrate any evidence of cancer recurrence at the end of five years.

for different cancers we care about different year-survival periods to determine if this pt is cured(!) or not. For example in Wilms tumor we care about 2-year-survival >> the 2-year-survival rate is 90% this means that if the pt did not demonstrate recurrence within 2 years this pt is declared to be cure. The idea is that we wait for resistant cells to reveal themselves within this period before telling the pt that he is cured.

for breast cancer they used to use 5-year survival but now we use 10-year survival or even 15-year survival. This means tha u cannot tell the pt that she is cured before 15 years.

As said earlier there are some cancers with **high cure rate** :

- ✓ The wide excision of primary melanomas in the skin that can be cured locally by surgery alone in about 90% of cases.
- ✓ The resection of colon cancers with a 5-cm margin from the tumor results in anastomotic recurrences in less than 5% of cases.

How to determine the magnitude of surgical resection ?

- ✓ Radio/chemo-therapy are used as neoadjuvant therapy (before surgery) to decrease the size of tumor.

- ✓ **Local resection** :it is removal of the tumor with 1 mm around like in BCC.

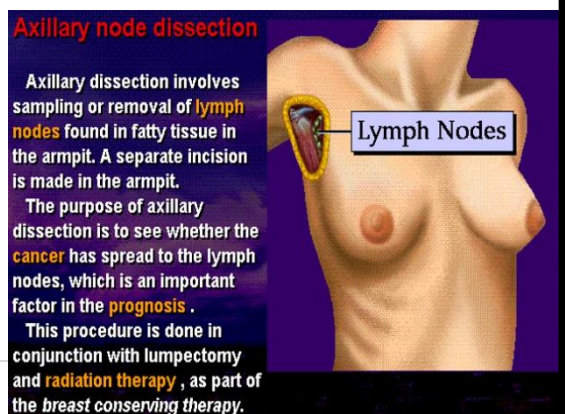
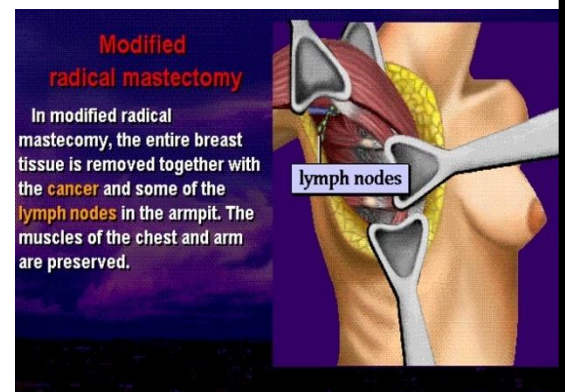
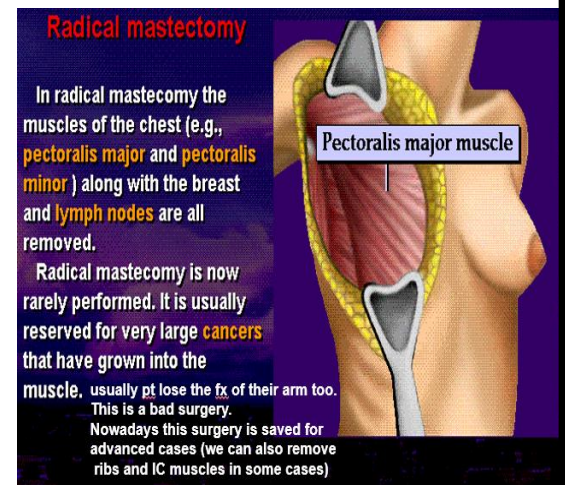
- ✓ **Wide local excision** :removing the tumor with safety margin (1 cm in breast and  $\geq$  2cm in melanoma )

Note we have gross and histological safety margin. Now the histological safety margin is reduced to .1 mm ( previously was 1cm )

- ✓ **Radical local excision** : this term is used for soft tissue sarcomas >> like if there is sarcoma at the ant aspect of the thigh we do radical local excision by removing the whole anterior compartment of the thigh. (actually in practice this is not a true compartment removal as we do not remove all the nerves and vessels) .

- ✓ **En-block excision**: u remove the tumor with regional LN together (rarely used now)

- ✓ **Adequate excision** :this is the standard of care , it can include any of the above mentioned teq.when we choose the surgery we must ask if it can or can not control the





disease locally, is it enough alone or should I add chemo/ radio ,is it adequate or not??

#### Principles of surgical resection of tumor

- ✓ Adequate margin of resection
- ✓ Prevention of tumor spillage ( do not squeeze the tumor) -that's why we do not see the tumor intra-op. u remove the tumor intact. As Spillage increase risk of ca metastasis.
- ✓ Minimal manipulation
- ✓ Reconstruction (by using flaps)

#### Surgery for palliation

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To improve the quality of life like doing colonostomy to pts who cannot defecate , or gastrostomy for pts who cannot eat or amputation of fungating oozy painful limb.

Every tumor has its own personality, so we cannot treat all the pts the same.

## **Lecture 2: Breast cancer-1**

**Written by: Aseel Hababeh**

**Corrected by: Abdullah Qaswal**

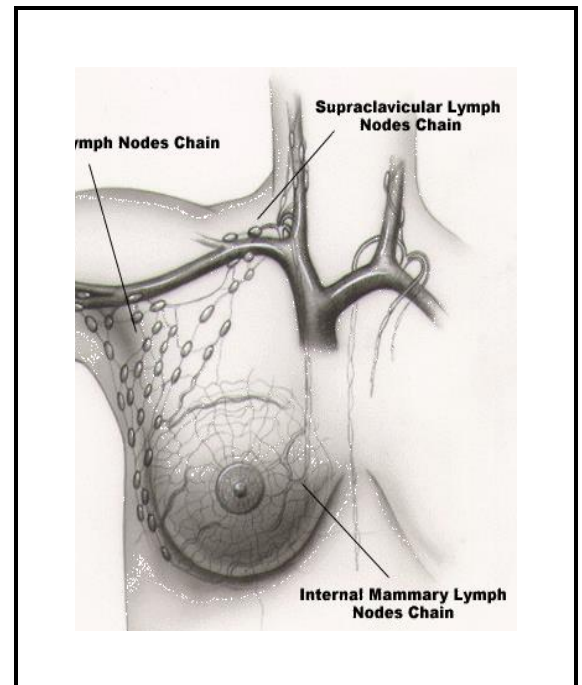
Note: the first three pages are basic information about the breast anatomy, they were NOT mentioned in the lecture, but they were mentioned in the notes in the slides.

## Anatomy:

- Site: The breasts are between the second and sixth ribs. Composed of breast tissue, skin, and subcutaneous tissue.
- The breast tissue is composed of parenchyma and stroma.
- The parenchyma is composed of 15-25 lobes, and each lobe contains 20-40 lobules. Each lobule consists of 10-100 alveoli. Fifteen to 25 lactiferous ducts provide separate drainage to the corresponding lobes. Before opening at the nipple, these ducts become dilated, forming the lactiferous sinuses.
- The breast tissue is enveloped superficially by the superficial pectoral fascia and deeply by the deep pectoral fascia, with the 2 layers connected by fibrous bands called Cooper suspensory ligaments.

## Lymphatics:

- The lymphatic drainage of the breast is unidirectional, from the superficial to the deep lymphatic plexus.
- The lymph then flows centrifugally to the regional lymph nodes after traveling through the lymphatic vessels of the lactiferous ducts.
- Ninety-seven percent of this flow is collected in the axillary lymph nodes, while only 3% goes to the internal mammary nodes.
- Axillary lymph nodes are divided into apical lymph nodes, interpectoral (Rotter) lymph nodes, axillary vein lymph nodes, central lymph nodes, scapular lymph nodes, and external mammary lymph nodes.



- An arbitrary method divides these lymph nodes into 3 levels relative to their relationship with the pectoralis minor muscle. Lateral to the lateral border of this muscle lie the level I lymph nodes, and medial to it lie the level III lymph nodes. Level II lymph nodes are located between and behind the muscle.
- Several structures, including vessels and muscles with their nerve supply, are related to the breasts and should be preserved during mastectomy or axillary node dissection.

### **Innervation:**

- The pectoralis minor muscle and the lateral portion of the pectoralis major muscle are innervated by the medial pectoral nerve.
- Preservation of this nerve is particularly important to prevent atrophy of the pectoral muscles if a submuscular implant reconstruction is planned.
- Additionally, the serratus anterior muscle is innervated by the long thoracic nerve of Bell, whose preservation is crucial to prevent winging of the scapula.
- Resection of the thoracodorsal nerve supplying the latissimus dorsi muscle should be avoided whenever possible, although resection does not result in any cosmetic or functional sequelae. Exposure of the axillary artery and brachial plexus should be avoided.
- Also, injury to certain sensory branches of the brachial plexus that occasionally pass superficially to the axillary vein may result in arm numbness extending to the wrist.
- Injury to the intercostobrachial nerve results in numbness over the triceps area. It can be identified by its large size (2 mm) and its location near the axillary vein. Occasionally, this nerve is composed of multiple, thin branches that cannot be preserved. In this case, the nerve should be sectioned with the knife to prevent postoperative causalgia (severe burning pain in a limb caused by injury to a peripheral nerve) related to the use of electrocautery.

- Invasive or non-invasive Breast Cancer?

The single most important factor in the personality of any breast cancer is whether it is non-invasive ("in situ") or invasive. This will determine your treatment path and, to some extent, your expectations for results.

- Note: Non-invasive (or "in situ") cancers confine themselves to the ducts or lobules and do not spread to the surrounding tissues in the breast or other parts of the body. They can, however, develop into or raise your risk for a more serious, invasive cancer.
- Invasive (or infiltrating) cancers have started to break through normal breast tissue barriers and invade surrounding areas. Much more serious than non-invasive cancers, invasive cancers can spread cancer to other parts of the body through the bloodstream and lymphatic system.

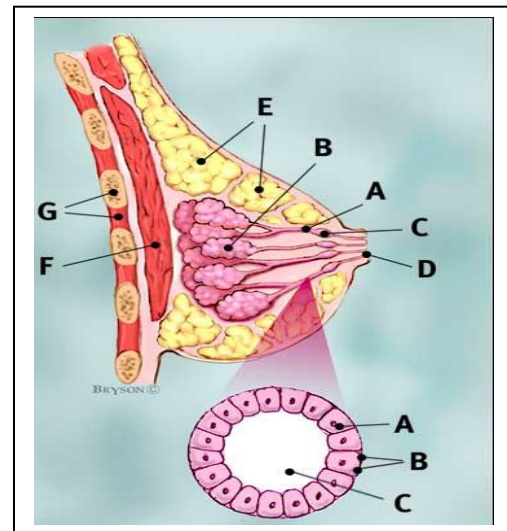
Normal Breast with an enlarged cross-section of normal duct

Breast profile:

- A Ducts
- B Lobules
- C Dilated section of duct to hold milk
- E Fat
- F Pectoralis major muscle
- G Chest wall/rib cage

Enlargement

- A Normal duct cells
- B Basement membrane
- C Lumen (center of duct)



Note: the lecture begins here.

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- Why are we concerned about the breast?

The Breast is an important organ, because:

1. Most of our hormones work on this organ
  2. Gives woman positive psychological support/ balance, plus body image and well being
  3. Milk production for nutrition of children
- Epidemiology: Commonest cancer in females. Major cause of mortality in middle age groups.
  - Definition: Breast is an enlarged sweat gland that occurs along the mammary line (which extends from the axilla to the groin). In humans, only the pectoral portion of the mammary line is well developed.

**Note : This leads us to the cause of some abnormalities that occur across this mammary line , such as , accessory breast tissue , accessory nipple , or accessory areola .**

- Breast is composed of a glandular structure that is imbedded with fat.
- Boundaries: 2nd to 6th rib / edge of the sternum to the mid axillary line.
- Breasts are fixed in their place by a fibrous tissue called , cooper's ligament .but with , time , movement , repeated pregnancies, obesity, and without the support of an external bra , ptosis of the breasts can occur, in which the breast tissue migrates from its original area to occupy a narrow area lower down on the chest wall

- Lymphatic drainage :
  1. mainly through the axilla
  2. Plus some few mammary lymph nodes.
- In cases of malignancy, breast cancer can extend to involve the lymph nodes, especially infra and supra clavicular lymph nodes, so make sure to examine those too.
- Triple assessment :
  1. Clinical evaluation: Hx and PE
  2. Imaging studies: U/S, Mammogram, CT scan, MRI.
  3. Cytological / Histological studies

#### Hx:

- Most common chief complaints of breast cancer are :
  1. Mass
  2. Nipple discharge
  3. Deformity in breast shape

#### **First: A Mass:**

- Could be single / multiple, unilateral/ bilateral, in the breast tissue or in the axilla.
- Axillary masses could be accessory breast tissue or lymph node enlargement due to inflammatory or malignant process happening in the breast.
- Masses are usually discovered accidentally or during self exam at home.

#### **Second: Nipple discharges:**

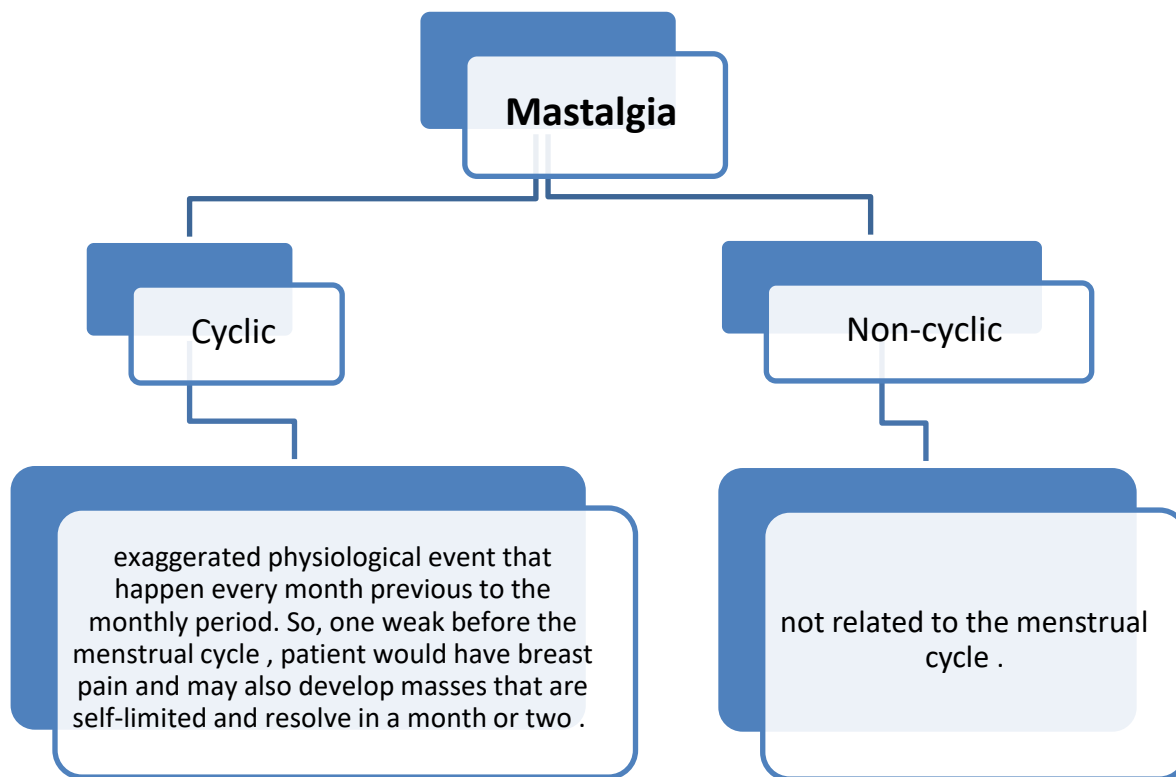
- Happens in 2-3% in patients with breast cancer.
- Most important discharge is bloody discharge.
- Most common cause for bloody discharge is duct papilloma, 2nd most common in carcinoma.
- Most significant discharge comes from a single duct and it's a bloody discharge.

- We have other types of nipple discharge, like milk discharge. If it happens during pregnancy or lactation then it's a normal physiological discharge, otherwise, the patient should be further investigated.
- One of the possible causes for milky discharge is pituitary adenoma, pituitary hyperplasia, and drugs.
- History taking for nipple discharge :
  1. Unilateral/ bilateral
  2. Single duct / multiple
  3. Nature of discharge (milky / bloody / frothy)
  4. Consistency (sticky / thick / watery)
  5. Presence of masses
  6. Presence of an infection Patient with nipple discharge should be fully evaluated.
- You can see the discharge on the patient's bra, and the discharge is usually detected by the patient while showering or while changing.

### **Third: Deformity in the breast shape / size:**

- If it's accompanied with inflammatory process it may indicate inflammatory carcinoma (worst type of breast cancer).
- Other symptoms ( chief complaints ) :
  1. Nipple retraction
  2. Crusting and scaling of the nipple (Paget's disease of the nipple)
  3. Mastalgia (breast pain): it's a very common symptom and is divided into cyclic and non-cyclic mastalgia.





- Non-cyclic mastalgia have many causes :
  1. Cervical disc prolapse with radiculopathy / myelopathy: causes pain bilaterally/ ipsilaterally in the dermatome of the effected nerve root.
  2. Mastitis: inflammatory condition could be lactational or non-lactational mastitis.
  3. Tietze syndrome: a rare inflammatory disorder causes swelling in the cartilage of the costochondreal junction of the upper 6th ribs which causes breast pain.
  4. Mondor's disease: superficial thrombophlebitis of the breast.
    - May be related to a trauma of the breast like seat belt injury in car accidents. Trauma also includes breast surgeries/ taking biopsy/ or during management of breast cancer.

- Mondor's disease could happen in the axilla and other parts of the body, so it's a disease that is related to the skin of the breast and not the glandular structure of the breast.
- Mondor's disease could be present with breast cancer or with the treatment of breast cancer.
- Patients with Mondor's disease present with cord like tender masses early in the course of the disease, you may see an inflammatory process happening after inserting a canula.
- Later if we are late the mass will get sclerosed and will appear like a ribbon or retraction of the skin, which could be misjudged as dimpling in the skin that appears in breast cancer.

<b>Risk factors:</b>
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1. **Age:** usually it's a benign condition in younger age group, and malignant in older age group. But there are exceptions.
2. **Obesity:** fat can be turned into estrogen by peripheral aromatization, which may predispose for breast cancer.
3. **Use of hormones :** ocp/ hrt
  - In both HRT and OCP, estrogen is the carcinogenic agent which may cause malignancy in the breast.
  - HRT: used by women after menopause to treat their hot flushes. It's mainly estrogen, and using estrogen for long periods of time leads to high risk of developing breast cancer.
  - OCP: do not significantly increase the risk for breast cancer. OCPs are mainly made of estrogen with a little of progesterone. But OCPs are usually used for a short periods of time (1-2years) so the caused damage is little. But if the usage extends to longer periods of time it could increase the risk for breast cancer
4. **Hx of breast surgery:** you should never neglect any histological examination of any tissue removed from the breast.

5. **Previous Hx of breast cancer:** patient would have a higher risk for breast cancer in the other breast or in the same breast if not all the malignant cells been removed previously. That's why you should keep a follow up with your patient for the rest of her life.

6. **Family Hx of breast cancer:** members in the family from the paternal/ maternal side.

7. **Known Genetic mutations :** BRCA1 / BRCA2

8. **Other factors:** like alcohol / smoking / exposure to radiation/ early menarche/ late menopause.

- Unfortunately, 70% of breast cancer patients don't have risk factors.

- So what can we benefit from defining these risk factors?  
They could increase/ decrease your suspicion of malignancy when the patient is presented to you.
- Note: in young age group we can't rely on mammography for screening because the breast is dense, but we can screen using MRI.

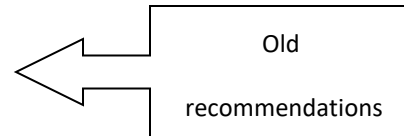
### **Prevention:**

- For young age groups that have accumulated many risk factors and have high risk for breast cancer in the upcoming years, they could be given anti-estrogen drugs like aromatase inhibitors or Tamoxifen (Tamoxifen-estrogen receptor antagonist) to lower their risk and prevent breast cancer.
- Studies proved that, patients with breast cancer and have received hormonal therapy like tamoxifen, have a reduction in the risk of developing breast cancer in the other breast by 50%.
- Other type of primary prevention for this particular age group is early mastectomy with skin sparing. More than 95% of breast tissue is removed and then the cavity is filled with biological tissue from the patient herself, like TRAM flap, SIEA flap, DIEP flap, or by silicone.

## Screening:

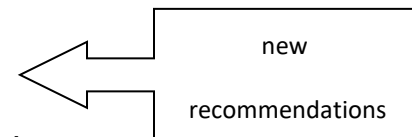
- Mainly by mammogram.
- Recommendations for mammogram screening :

1. (20-39 y/o) : every 3 years
2. (>40 y/o) : every year



This point in particular raised the concern about increasing the risk for breast cancer if the lady were to be exposed to screening every year. So the new recommendations were made .

1. (20-39 y/o) : every 3 years
2. (40-44 y/o) : screening is optional in this period
3. (45-54 y/o) : every year ( found to be the most common age to develop malignancy)
4. (>55 y/o) : every one or two years (profoundly that the patient would tolerate treatment for breast cancer if a malignancy is found .)
  - Meaning , a 70 y/o female patient , MF , no HTN ,no DM , no Hx of stroke , and is healthy , then we continue screening every one or two years having in mind that if a malignancy was found then the patient is healthy enough to tolerate the treatment.
  - But if the patient is 70 y/o and have HTN , DM , Hx of stroke , then there is no importance in continuing screening, as the patient is less likely to die from breast cancer than her existing comorbidities .



### New recommendations on breast cancer screening

The American Cancer Society has updated its guidelines for healthy women with an average risk of getting breast cancer.

Age range	Mammogram		Clinical breast exam	
	Old	New	Old	New
20-39	No	No	Every 3 years	No
40-44	Annual	Optional*	Annual	No
45-54	Annual	Annual	Annual	No
55+	Annual	Every one or two years*	Annual	No

\*Based on discussion with doctor about benefits and risks of mammography.

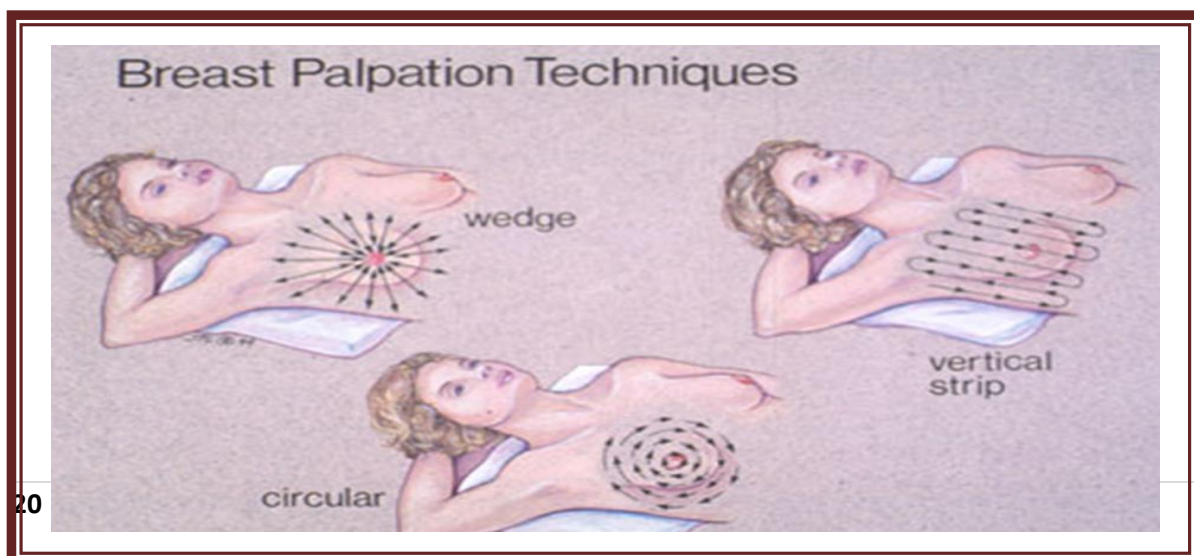
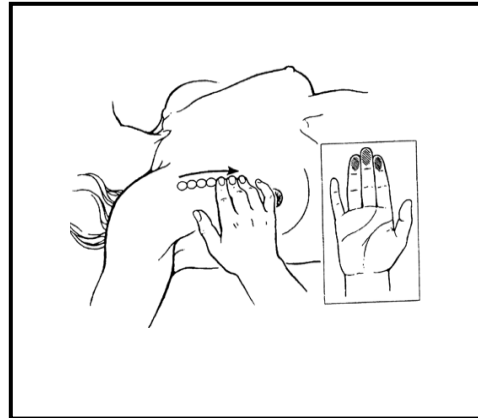
NOTE: Screenings should continue as long as a woman has a life expectancy of 10 years and is a good candidate for breast cancer treatment.

Source: American Cancer Society

@latimesgraphics

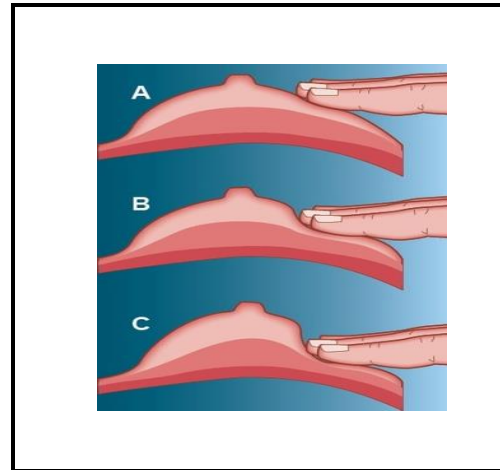
## Physical examination :

- detailed in OSCE dossier .
- It's very important to examine the regional lymph nodes and the axilla.
- Don't forget to have a chaperone , provide adequate privacy , and warmth so the patient can be comfortable.
- Patient should be supine ( other sources say 45 degree angle).
- To Examine the breast area the patients hands should be behind her head , and palpate by gentle rolling and dipping using the palmer aspect of your 3 middle fingers .
- Take your time while palpating, you need at least 2-3 min to examine the whole breast .
- Three methods for examination :
  1. Wedges : using rolling and dipping motion in a circular manner around the breast .
  2. Vertical strips : using rolling and dipping motion in vertical lines . ( this is a better method , as it covers the whole breast more efficiently. Plus it has a higher rate for finding masses than other methods ).
  3. Circular



- degree of palpation : we have three degrees :

1. Mild
2. Moderate
3. Deep



- **malignant masses are** hard in consistency, painless ( malignant masses are painful in only 10-15% of patients) , has little mobility, has irregular borders, fixed to the chest wall or to the skin , associated with skin dimpling , nipple retraction, bloody or watery nipple discharge .

- it's very important to document the topography of the glandular structure in the medical report of the patient , the glandular structure differs from one lady to another , but it's important to document it to see if there are any changes .
- malignancy can be accompanied with skin ulceration , these ulcers don't heal , even when they are resected with surgery they remain as unhealed wound .

Note : the next three pages are notes mentioned in the slides but not mentioned in the lecture .

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- The Breast Parenchyma: The breast is the specialized human tissue located on the chest between the pectoralis muscle, i.e. the superficial fascia and the subcutaneous tissue, i.e. right beneath the skin.
- The Retromammary Space: The breast rests on a rich vascular and lymphatic network within the pectoralis fascia. This represents the retromammary space which is positioned between the deep pectoralis fascia and the superficial pectoralis fascia.
- The Nipple-Areolar Complex: The Nipple-Areolar complex is the center of the breast. It is the end portion of the largest lactiferous duct.
- The Microscopic Anatomy: The microscopic anatomy is best visualized by analyzing the lactiferous complex. The breast is a milk producing organ and its microscopic anatomy is based on this function.
- The Lobules: The lobules, also called the lobular units, are responsible for the production of milk.
- The Ductal System: The milk is collected by distal lactiferous ducts or acini which merge into minor and then major lactiferous ducts. In most instances, these empty into the major duct or sinus which ends in the nipple.
- The ductal system has a ductal epithelium surrounded by a myo-epithelium. This ductal epithelium is responsible for the propulsion of milk through the ductal system as it has contractile capabilities. This ductal system is sealed and surrounded by an uninterrupted basement membrane.
- The Stroma: This interlobular tissue, also referred to as connective tissue, contains capillaries and other specialized cells.
- Cooper's Ligaments: These are dense strands of fascia found throughout the entire breast which end on the skin itself.
- The Basement Membrane of the Ductal System: It is essential to visualize the basement membrane in the microscopic analysis of a malignant breast tumor. This will assist in the assessment as to whether a tumor is "in situ"

(has not grown through the basement membrane) or "invasive" (has grown through the basement membrane).

- The microscopic anatomy of the breast demonstrates why most breast cancers are ductal or lobular in origin.

- Age Dependant Anatomical Changes of the Breast:

With age, the breast tissue will change. In a young woman, the breast tissue is dense and parenchyma rich. As the woman ages, the fat content of the breast tissue will increase. This explains the overall aspect of the breast, as it will begin to droop. **The increased fat content of the breast in older patients accounts for the higher quality of their mammograms (increased fat content equals increased image quality).**

- Pathology Dependant Anatomical Changes:

**Peau d'Orange:** From the French term, orange skin, this identifies a malignant obstruction of the superficial lymphatic channels.

**Skin Retraction:** Skin or Cooper's ligament pulled in by a malignant lesion.

**Nipple Inversion:** Inward retraction of the nipple by a malignant ductal lesion.

**Breast Abscess:** Fluctuant, purulent collection within the breast parenchyma

**Mondor's Disease:** Thrombophlebitis of a superficial vein, usually by a nonmalignant lesion

**Inflammatory Breast Carcinoma:** Malignant invasion of the superficial skin lymphatic channels seen in advanced breast cancer.

**Gynecomastia:** This is an activation and hypertrophy of the breast tissue in men. It can occur frequently in young men (pubertal hypertrophy) and in older men. It can also be caused by numerous medications and hormones.



- Changes Secondary to Breast Augmentation Surgery

All surgeons should be familiar with the pathology generated by the placement of breast implants during augmentation mammoplasty. Earlier augmentation mammoplasty techniques placed the implants behind the skin or breast parenchyma. Newer techniques are placing it behind the pectoralis major muscle.

- The Axilla :

- The anatomy of the axilla or the axillary basin is important to all oncologic surgeons as it represents the principal lymphatic drainage region of the breast.
- Lymphatic metastasis from a malignant breast lesion will most often occur in this region.
- For inner quadrant lesions, it can occur in the internal mammary chain.
- Lymphatic metastasis can also be present in the supraclavicular nodes.

The surgeon should have an extensive knowledge of the anatomy of the axilla and its contents in order to perform a safe, precise and appropriate axillary dissection.

- The lymph node bearing area has been divided into three axillary regions:

- **Level I:** Lymph nodes lateral and inferior to the pectoralis minor muscle.
- **Level II:** Lymph nodes under the pectoralis minor muscle.
- **Level III:** Lymph nodes under and deep to the pectoralis minor muscle.

- Most axillary dissections include lymph nodes from Level I and II.

- In order to remove these lymph nodes with minimal morbidity, several structures will have to be identified unequivocally. They are as follow:
  1. The lateral border of the Pectoralis Minor and Major muscle.
  2. The Latissimus Dorsi Muscle.
  3. The Axillary Vein .
  4. The Long Thoracic Nerve which innervates the Serratus Anterior Muscle .
  5. The Thoraco-Dorsal Nerve which innervates the Latissimus Dorsi Muscle .
  6. The Intercostal Brachial Nerve which is a sensory nerve for the inferior aspect of the arm and the posterior aspect of the axilla.
  7. The Lateral Pectoral Nerve which innervates portions of the pectoralis muscle.

## **Lecture 3: Breast cancer-2**

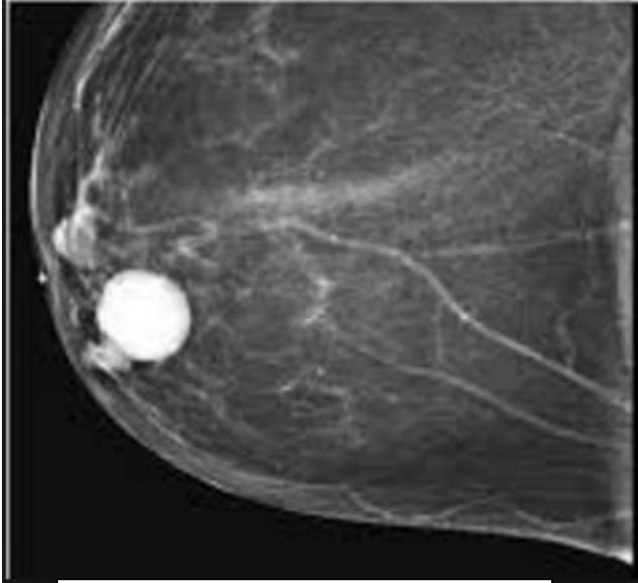
**Written by: Fareed Halteh**

## **Breast Imaging**

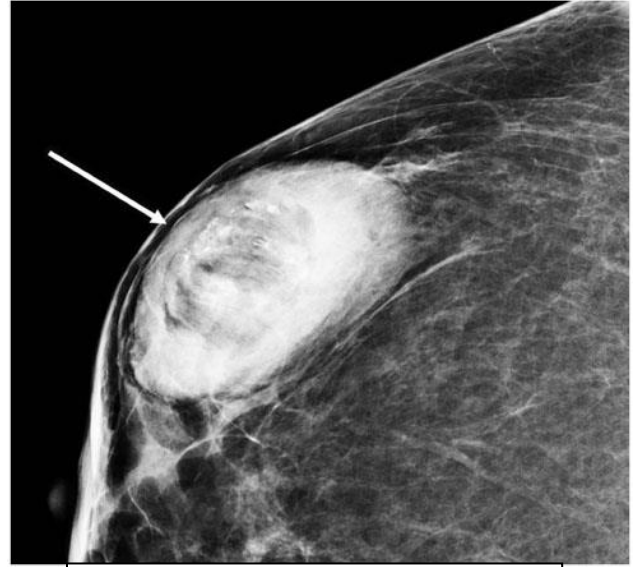
- A mammogram is a breast X-ray used for screening and diagnosis of breast cancer. It is used as a screening tool in women who do not complain of any symptoms, and perform it as part of their regular follow up. It is used as a diagnostic tool for patients who complain of symptoms and need a radiographic confirmation of the diagnosis.
- Risk factors of breast CA:
  - Family history
  - Personal history of breast cancer
  - Presence of breast changes on biopsy
  - Genetic mutations (BRCA1 and BRCA2 mutations)
  - Reproductive and menstrual history
- When to screen?
  - 20-34 without risk factors: no need for screening
  - 20-34 with risk factors: based on the clinician's decision
  - >40: a mammogram is advised every 2 years.
- Before the age of 35, we use ultrasound as a screening tool. Before the age of 35, the breast is more dense (more fibroglandular tissue; therefore, mammograms will not show the pathology clearly). If a breast is very dense after this age, this is called a dysplastic breast, and it carries a higher risk for malignancy.
- How to prepare for a mammogram?
  - It is usually done during the first few days of the menstrual cycle (days 2-10). During this period, the breast is the least tender. If it is done during a different time, the breast will be tender and non-compressible making the image less accurate.
  - We advise the patients not to put any perfume or deodorant, as the aerosole particles might look like calcifications on a mammogram.
- Views of a mammogram:
  - Craniocaudal (CC): the breast appears as a semi circle; the pectoralis muscle cannot be seen; extend line perpendicular to the nipple (divides breast into inner and outer quadrants). The X-ray beam is directed upward → downward
  - Medio-lateral oblique (MLO): the breast appears as a teardrop; the pectoralis muscle can be seen; extend a line perpendicular to the nipple (divided the breast into upper and lower quadrants). The x-ray beam is directed medial → lateral
- How to read a mammogram?
  - State the study: mammogram
  - State the view: CC or MLO
  - Mention the side: right or left breast
  - Look for primary signs of malignancy
  - Look for secondary signs of malignancy

- A mammogram can increase the risk of cancer development; however, its benefits outweigh its risks. Since we started using mammography, deaths due to breast cancer have decreased significantly.
- Sensitivity of a mammogram:
  - The sensitivity of an image is measured based on the amount of fibroglandular tissue present in the breast. The more the fibroglandular tissue, the less sensitive the image. This is called the ACR system.
  - ACR system:
    - ACR 1: fatty breast; usually in older females; <25% glandular tissue.  
Highly sensitive
    - ACR2: low amounts of fibroglandular tissue; 25-50% fibroglandular tissue
    - ACR3: heterogeneous breast; 50-75% fibroglandular tissue
    - ACR4: dense breast; >75% glandular tissue; sensitivity decreases to 60%.
- Primary signs of malignancy:
  - Masses
  - Calcifications
- Masses: We need to comment on the shape, margin and density:
  - Shape:
    - Round: coin shaped lesion
    - Oval: egg shaped
    - Lobulated: up to 3 lobes; if more than 3 lobes are present, it is considered irregular
    - Irregular: the presence of more than 3 lobes, an irregularly shaped mass, or a mass that looks different when viewed on CC and MLO views (ex looks round on CC and oval on MLO)
    - Architectural distortion: architectural distortion can be considered a primary or a secondary sign of malignancy. If another mass is present, architectural distortion is considered a secondary sign of malignancy. Architectural distortion indicates tethering of the parenchyma.
  - Margins:
    - Well circumscribed (well defined)
    - Obscured: part of the margin is covered due to an overlap between the mass and the breast parenchyma.
    - Microlobulated
    - Ill-defined: the edges of the mass cannot be defined
    - Speculated: sun-ray appearance; it is one of the most important signs of malignancy. The presence of a single speculation is highly suggestive of a malignant mass.
  - Density: the density of a mass is described in reference to the most hyperdense area in the breast.

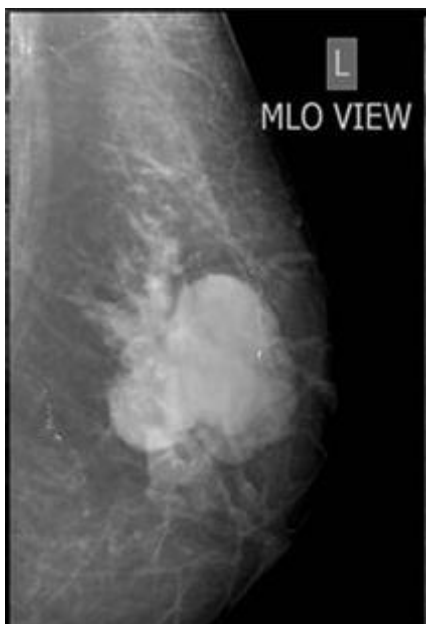
- Hypodense
- Isodense
- Hyperdense
- Fat containing: heterogenous with a rim of calcification called eggshell calcification. Image: round, hyperdense, well circumscribed mass. Another type of fat containing mass is a lymph node a lymph nodes appears kidney shaped with a hyperdense cortex and hypodense medulla (Fat).



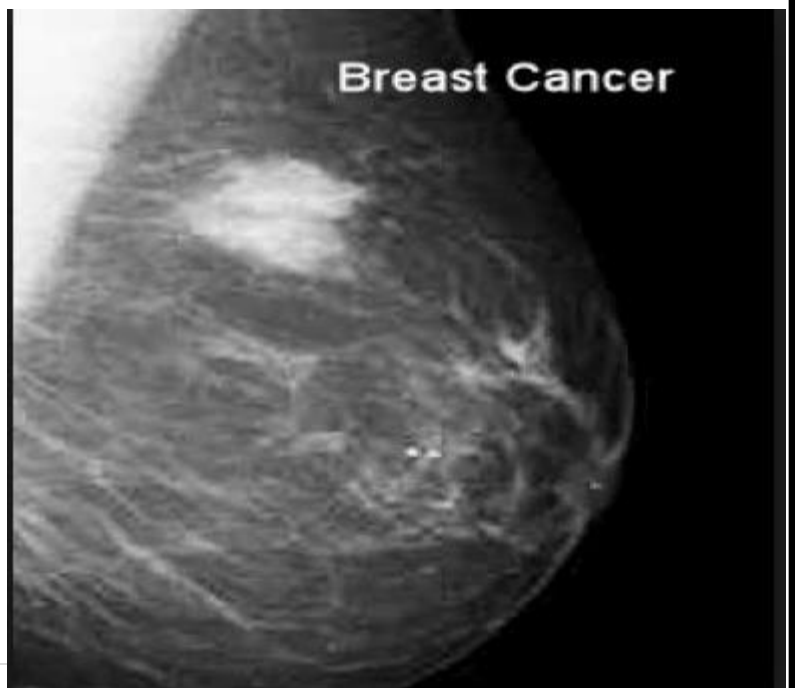
Mammogram showing a round breast mass; well circumscribed margin



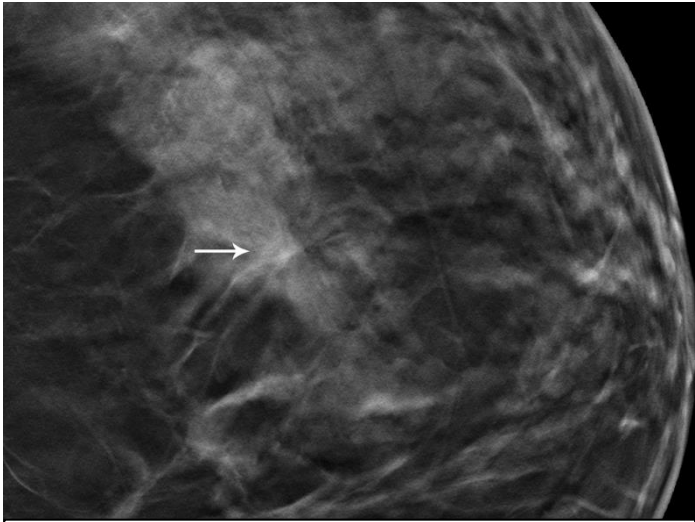
Mammogram showing an oval breast mass



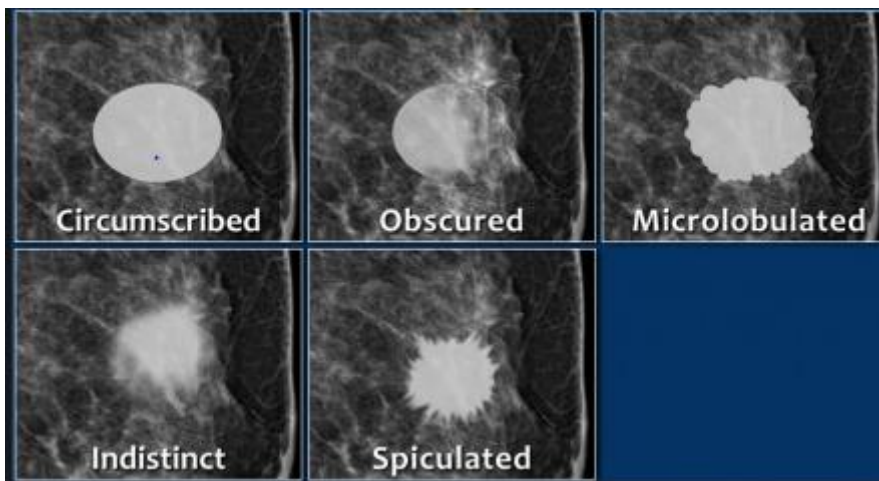
Mammogram showing a trilobed breast mass



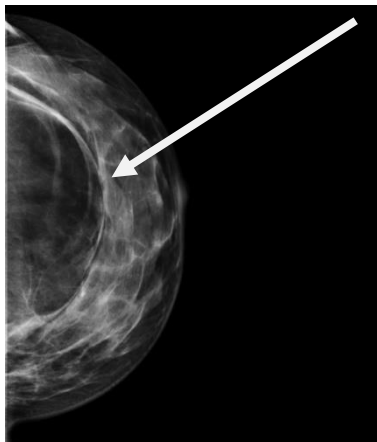
Mammogram showing an irregular breast mass



Mammogram showing architectural distortion

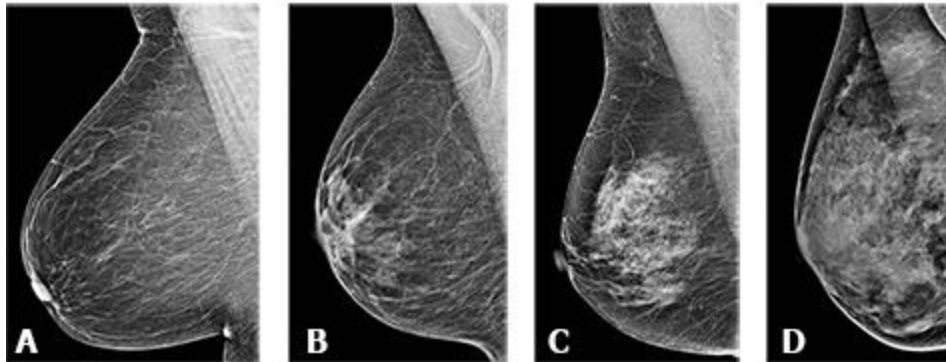


A diagram showing types of margins



Mammogram showing a well circumscribed fatty lesion with eggshell calcification; suggestive of lipoma

According to BI-RADS®, breast density ranges among (A) an almost entirely fatty breast, (B) a breast with scattered areas of fibroglandular density, (C) a heterogeneously dense breast, and (D) an extremely dense breast.

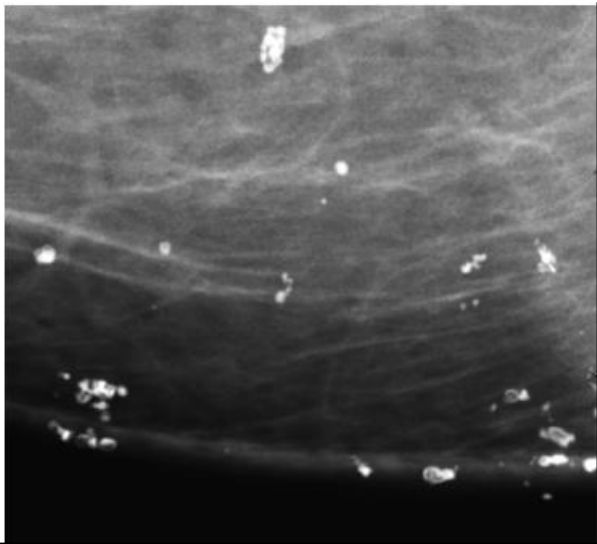


#### ACR 1-4 breasts

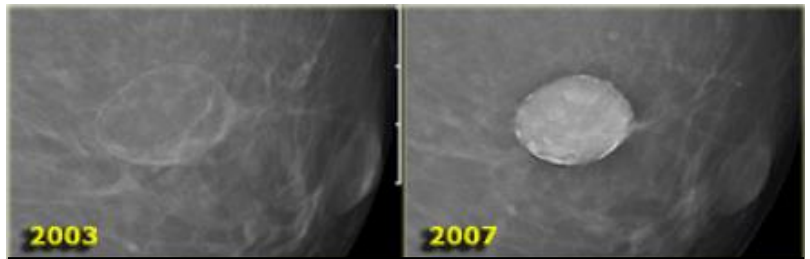
- Signs of malignancy in a lymph node:
  - Thickening of the cortex (>1cm)
  - Loss of fatty meddulla (hilum)
  - Increased in size (least important criterion)
- Classification of masses:
  - Benign: Round or oval mass, well circumscribed, fat containing mass
  - Malignant: Speculated, irregular, ill defined margins
  - Other masses are equivocal
- Calcifications: We comment on the morphology and distribution of calcifications
  - Morphology:
    - Benign:
      - Skin calcifications: round or oval calcifications within 1 cm of the skin
      - Round calcification away from the skin
      - Eggshell calcifications away from skin: indicate fat necrosis
      - Vascular calcifications: railroad appearance; they appear as either continuous or fragmented masses; increase with age
      - Popcorn calcifications: also called coarse calcifications; the presence of a popcorn calcification inside an isodense/hypodense well circumscribed mass is diagnostic of an involutingfibroadenoma which is a benign lesion.
      - Plasma cell mastitis: large rod calcifications
      - Dystrophic: ill defined calcifications usually following a surgery or a biopsy
      - Suture calcifications: calcifications at a suture site. Now rarely seen due to the use of absorbable sutures.



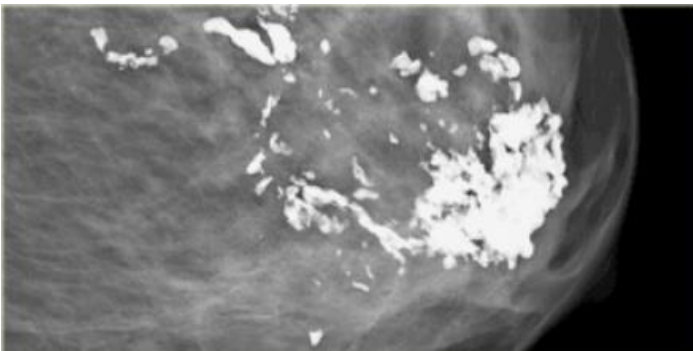
- Intermediate risk:
  - Amorphous calcifications: powder like calcifications; can indicate sclerosing adenosis (benign) or low grade DCIS (malignant). They need to be biopsied.
- Malignant calcifications:
  - Pleomorphic: multiple calcifications that are irregular; crushed stone appearance. Indicate high grade DCIS
  - Fine linear branching calcifications; indicate high grade DCIS. 5 microcalcifications per  $\text{cm}^2$  is significant



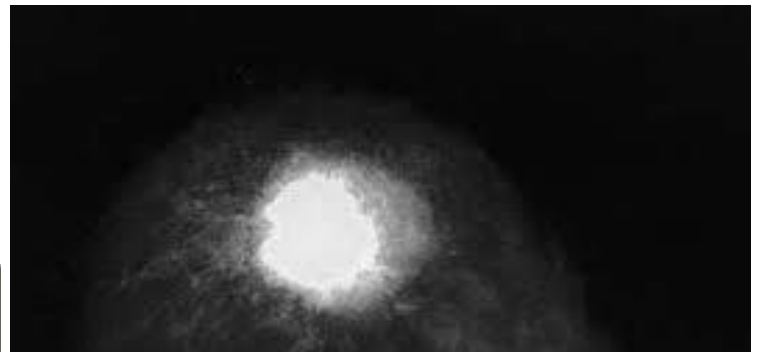
Multiple skin calcifications



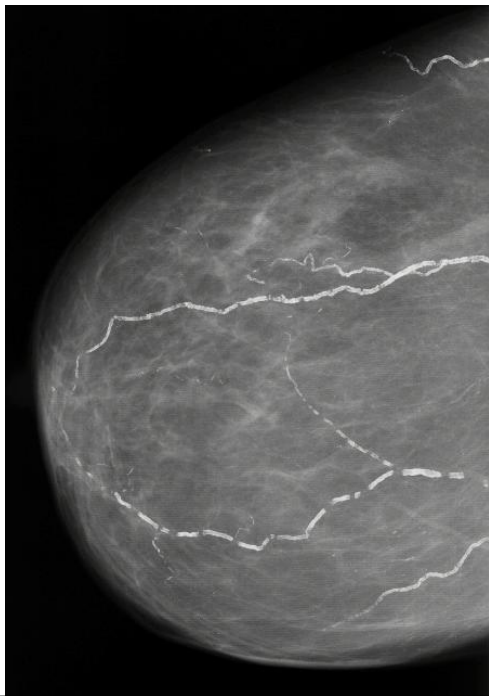
Eggshell calcifications



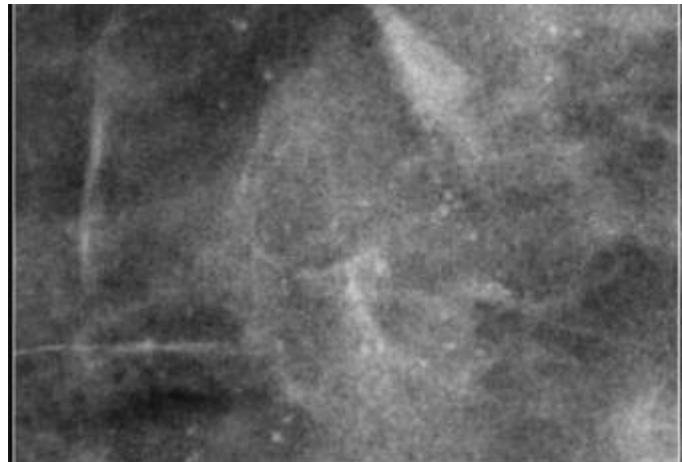
Dystrophic calcifications



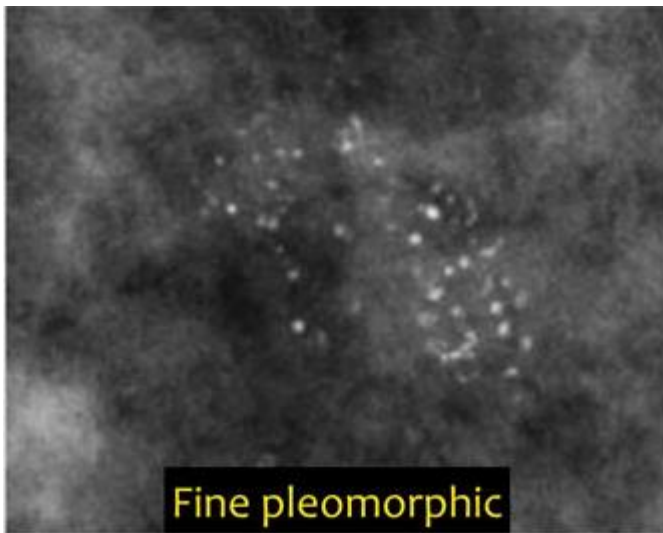
Popcorn calcification in a well circumscribed mass; involuting fibroadenoma



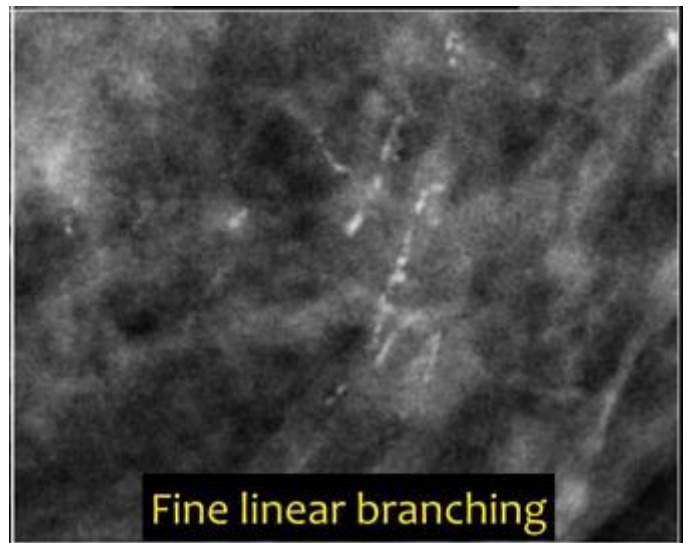
Vascular calcifications breast



Amorphous calcifications



Fine pleomorphic

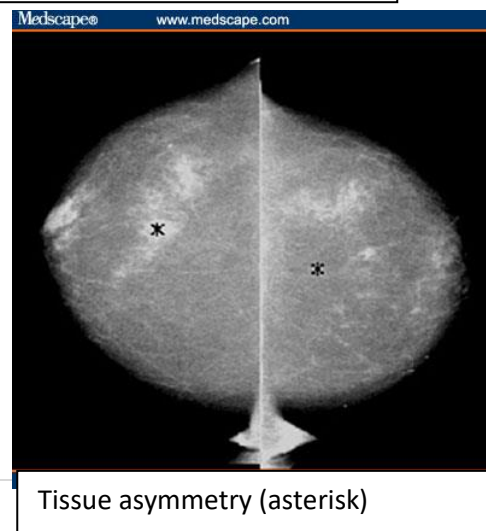
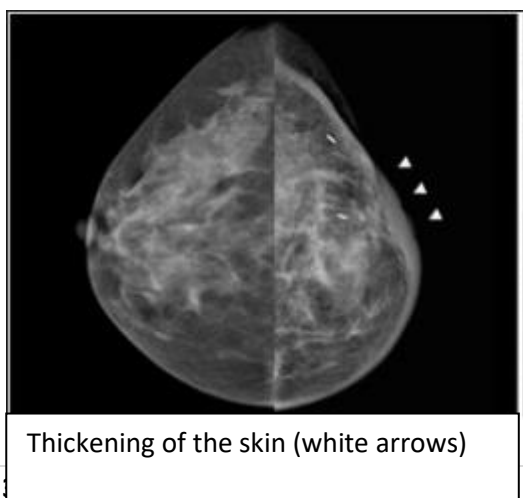
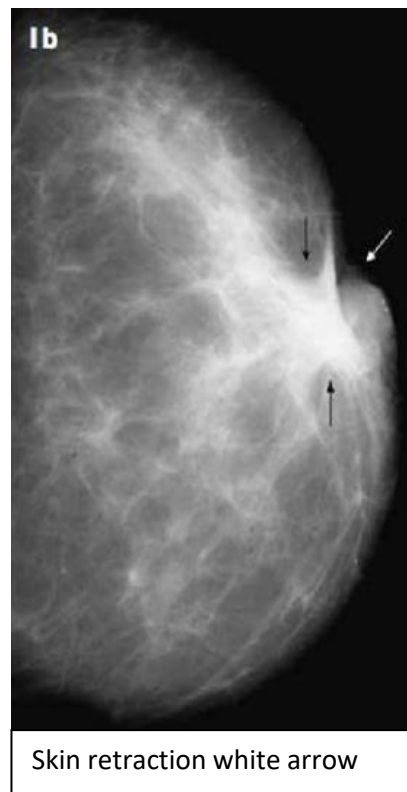


Fine linear branching

○ Distribution of calcifications:

- Clustered: the calcifications are close to each other (1-2 cm apart)
- Linear calcifications: can be localized within two imaginary lines.
- Segmental: triangular distribution; the base of the triangle is towards the chest wall and the apex is at the nipple
- Regional: calcifications occupying 2-3 quadrants of the breast
- Diffuse: calcifications distributed throughout the breast; mostly seen post-radiation due to fat necrosis.

- Classification of calcifications based on distribution:
  - Regional, loosely grouped or diffuse calcifications are usually benign
  - Segmental and cluster calcifications are usually malignant.
- Secondary signs of cancer:
  - Nipple inversion (nipple going inside)
  - Architectural distortion
  - Thickened skin
  - Axillary lymphadenopathy
  - Skin retraction
  - Tissue asymmetry: differences in fibroglandular tissue distribution between the two breasts.



- The most common site of a mass is at the upper outer quadrant
- BI-RADS classification (breast mammogram report):
  - BI-RADS: 0 needs additional imaging and further evaluation; cannot assess the image.
  - BI-RADS 1: negative findings: there is nothing to comment on (no positive findings)
  - BI-RADS 2: benign finding; no need for short interval follow up; ex. Involuting fibroadenoma
  - BI-RADS 3: probably benign finding; <2% malignancy; follow up at 6,12,24 months (Initial short-interval follow up) ex. Fibroadenoma without a calcification
  - BI-RADS 4: suspicious finding (amorphous calcification); needs biopsy; 2-95% malignancy
  - BI-RADS 5: highly suggestive of malignancy >95% chance of malignancy; appropriate action needs to be taken
  - BI-RADS 6: a case of a proven malignancy by a biopsy; here the image is taken as follow up for treatment or to look for a different focus of metastasis. After chemotherapy or radiotherapy; the patient remains a BI-RADS 6. However, after surgical removal of a lesion, the patient returns to BI-RADS 1.
- Other imaging modalities:
  - Ultrasound:
    - Breast ultrasound is mainly used in younger females due to the density of their breast tissue
    - US can be used to distinguish between solid and cystic masses
    - It can be used to aspirate cysts; the fluid aspirate is sent for cytology
  - MRI:
    - Breast MRI is a fairly accurate device for diagnosis of breast CA; however, it is not used as a standard of care
    - Breast MRI is typically used for patients who are less than 35 years old of age and have a significant risk for breast CA due to family history.
    - Although it is accurate, false positives and false negatives still exist.
  - PET scans:
    - PET scans are rarely used for detection of breast masses.
    - It is an expensive tool; however, it is sensitive for masses. Any mass with an increased metabolic demand will have an increased uptake visible on PET scan.
- Extra notes:
  - 50% of breast masses are localized; 25% of masses are multifocal.

- Compression view of mammography: a special view where the radiologist focuses on a certain suspicious area and zooms in on that area. Sometimes, a suspicious lesion might be formed of a compilation of shadows of benign structures (vessels and lymphatics). Using the normal view, such structures might appear as masses. When you zoom in on the structure, the mass formation disappears and the shadows are separated into their original components.
- 25-30% of significant microcalcifications are malignant; therefore a biopsy is needed
- Increased levels of PTH or PTH like hormone can cause calcium mobilization. The mobilized calcium can be deposited in any tissue including the breast.
- Fine needle aspiration can be used for cytological testing; however, it doesn't give information about the histology of the tumor (invasive Vs. in situ). Therefore, a true cut biopsy or core biopsy can be used for this purpose.
- Suspicious calcifications biopsy:
  - If there are no visible masses on a mammogram, but suspicious calcifications are present, you need to biopsy these calcifications.
  - To biopsy these calcifications, an advanced technique called stereotactic biopsy is used.
  - A stereotactic biopsy is a biopsy using the mammography machine.
  - If this suspicious mass proved to malignant, it needs to be excised. However, because this mass is not visible, the surgeon cannot excise it easily.
  - To make the surgeon's job easier, a radiologist inserts a guide-wire and extends it to the mass. During the surgery, the surgeon removes the mass with the guide-wire.
  - This mass is sent for specimen mammography to make sure that the calcifications have been excised.
  - The specimen is then sent for histopathological evaluation
- When you image a breast, make sure to image the other breast. There is a higher chance for malignancy in the other breast. If there are masses detected bilaterally, we call this case a synchronous metastasis.
- How to deal with a malignant mass?
  - Once you confirm the presence of a malignant mass, the tumor must be staged.
  - Staging is based on the size of the mass, involvement of lymph nodes, and the presence of distant metastases.
  - To evaluate for distant metastases:
    - Brain CT
    - Chest CT
    - Abdominal CT
    - Bone scan (Technetium scan):

- If a bone lesion is present, the bone lesion is dealt with first because morbidity of bone lesions is higher than the lesion in the breast.
  - The most feared complications of bony metastases are pathological fractures and spinal cord metastases.
- Staging the tumor directs the treatment and carries a prognostic value.
- To stage breast cancer we use the TNM classification. (review it)
- Important blood tests: these tests are done to assess the patient's fitness for surgery and assess for certain tumor markers:
  - CBC: blood counts are important for chemotherapeutic purposes
  - KFT
  - LFT: sometimes, the only sign of liver metastases is an abnormal LFT.
  - Tumor markers: the breast tumor marker is CA 15.3 (ovarian cancer tumor is CA125).
    - These markers are used for follow up of treatment and not for diagnosis
- Basic principles of breast surgery:
  - Halsted theory:
    - Halsted was an American surgeon and a pioneer in breast surgery.
    - He theorized that the development of breast cancer is as follows:
      - A single cell becomes oncogenic
      - It multiplies
      - After reaching an adequate size, the cells travel through the lymphatics to lymph nodes
      - After spreading the lymph nodes, they spread to the distant organs.
    - He devised the procedure of radical mastectomy.
    - His theory was proven wrong by Bernard Fisher a pioneering American biologist who suggested that breast cancer can metastasize during very early stages.
  - In its beginnings, breast surgery was very aggressive. With further advances and further understanding of the pathogenesis of breast CA, the surgeries became less aggressive. Now, we advocate the concept of adequate surgery; which means removing an adequate amount of tissue while to preserve the breast as much as possible.
  - If the mass is not multicentric or multifocal, we can generally remove the mass only with excellent results. A safety margin of 1cm is left around the mass.
    - In the recent years, the concept of onco-plastic surgery is becoming more popular. Many surgeons try to remove the breast tissue while keeping the aesthetics of the breast. This is done either through prosthetic implants or special surgical techniques using the leftover fatty tissue in the breast area.