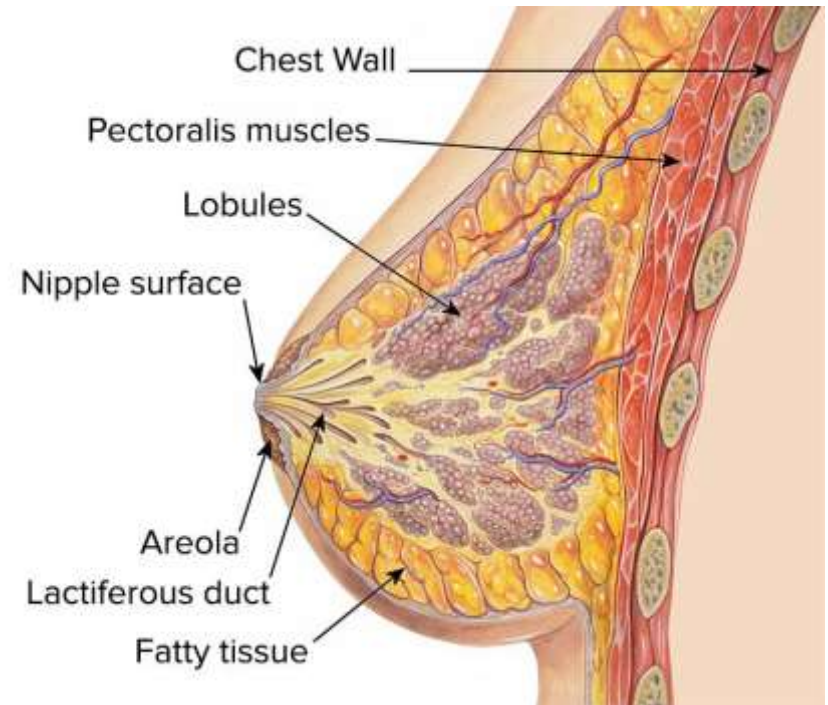


Carcinoma of Breast

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Introduction

- Most frequently diagnosed life-threatening cancer in women
- Many early breast carcinomas are asymptomatic
- Pain or discomfort is not usually a symptom of breast cancer



Pathophysiology

- Difficult to subtypes
- Luminal A
- But generally align with ER, PR & HER2 presence or absence
- Luminal B
- Basal-like
- The Cancer Genome Atlas Network (TCGA) confirms the following 4 main breast tumor subtypes
- HER2-positive

Intrinsic Subtypes of Breast Cancer

Luminal A (ER+ &/or PR+, HER2-)

- Most common subtype
- Less aggressive
- Lower histological grade
- Good prognosis
- Hormone responsive
- Associated with increasing age

Luminal B (ER+ &/or PR+, HER2+)

- Similar to Luminal A
- More frequently ER+/PR-
- Worse Outcome than Luminal A

HER2+ (ER-)

- Less common, highly aggressive subtype
- High grade histology
- Risk at young age (<40) greater than luminal subtypes
- African American ethnicity may be a risk factor
- Outcome improved with HER2

Basal-Like

(Triple Negative, cytokeratin 5/6+ &/or EGFR+)

- Aggressive Subtype
- High grade histology, and high mitotic rate
- Risk at younger age (<40)
- More likely premenopausal African American women

Types of Breast Cancers

- **1. Infiltrating ductal carcinoma**

- 75%
- Metastasis by lymphatics

- **2. LCIS**

- Incidence doubled
- Peak at age 40-50 Yrs.

- **3. Infiltrating lobular carcinoma**

- Fewer than 15% of invasive breast cancers

- **4. Medullary carcinoma**

- 5%
- Generally occurs in younger women

Types of Breast Cancers

- **5. Mucinous (colloid) carcinoma**
- Fewer than 5% of invasive breast cancer
- **6. Tubular carcinoma**
- 1-2%
- **7. Papillary carcinoma**
- 1-2%
- Over 60 Yrs.
- **8. Metaplastic breast cancer**
- 1% & Average age sixth decade
- **9. Mammary Paget disease**
- 1-4% & Peak incidence in sixth decade of life

Etiology

- Age & Gender
- F/H of breast cancer
- F/H of ovarian cancer
- Late pregnancy
- Early menarache
- Late menopause
- Oral contraception
- HRT

Family History

- Two or more relatives with breast or ovarian cancer
- Breast cancer occurring in an affected relative younger than 50 years
- Relatives with both breast cancer and ovarian cancer
- One or more relatives with two cancers (breast and ovarian cancer or 2 independent breast cancers)
- Male relatives with breast cancer
- *BRCA1* and *BRCA2* mutations
- Ataxia telangiectasia heterozygotes (quadrupled risk)
- Ashkenazi Jewish descent (doubled risk)

Prior Breast Health History

- H/O breast cancer 3-4 folds risk contralateral cancer of breast
- DCIS or LCIS means 8-10 times risk
- Hyperplasia, fibroadenoma with complex features, sclerosing adenosis, and solitary papilloma 1.5 -2 times of risk
- Atypical hyperplasia that is ductal or lobular in nature, especially in a woman under the age of 45 years, carries a 4- to 5-fold increased risk of breast cancer, with the increase rising to 8- to 10-fold among women with multiple foci of atypia or calcifications in the breast

Lifestyle Risk Factors

- Diets rich in grains, fruits, and vegetables; low in saturated fats; low in energy (calories); and low in alcohol - are thought to be protective against breast cancer



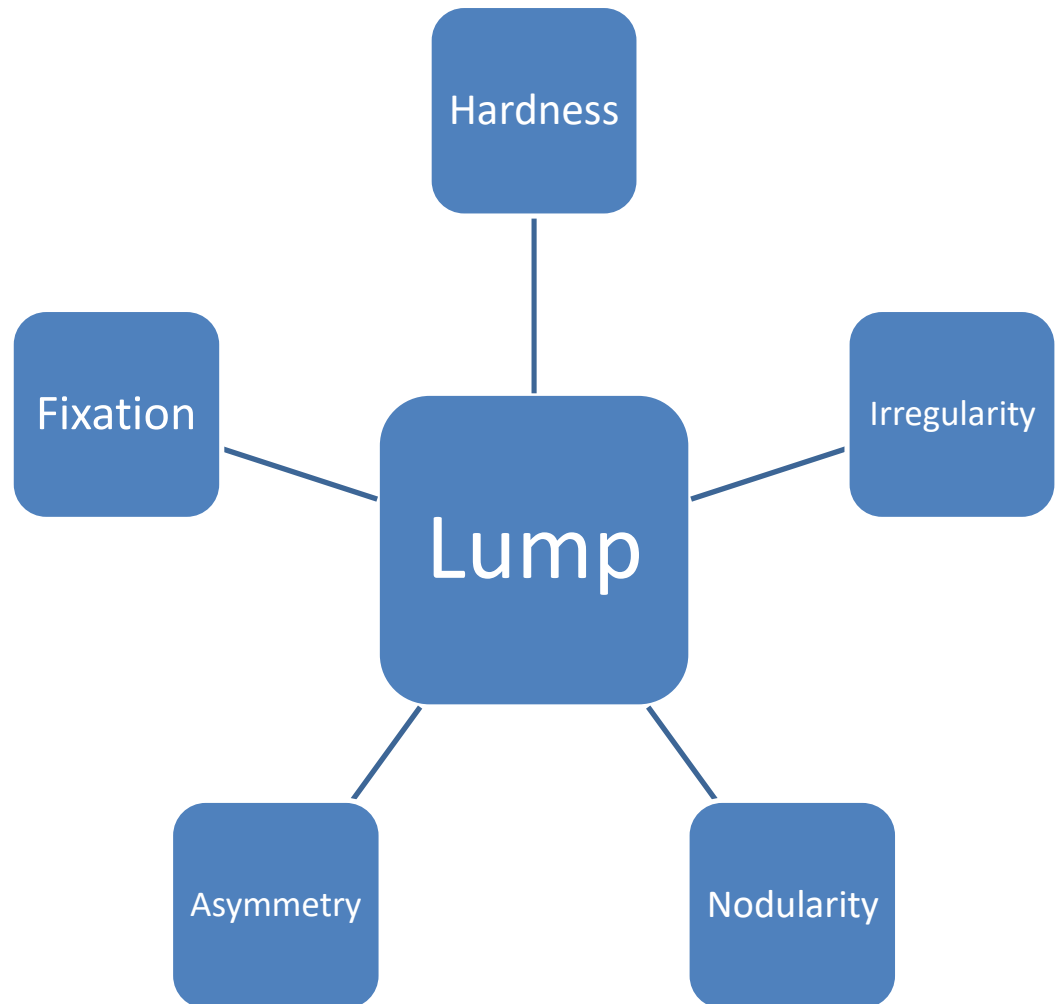
- Other risk factors
- Obesity
- Alcohol
- Chest radiation
- Environmental carcinogens

Clinical Features

- Many Asymptomatic
- Painless mass
- Only 5% have pain
- Change in breast size or shape
- Skin dimpling or skin changes (e.g., thickening, swelling, or redness)
- Recent nipple inversion or skin change or other nipple abnormalities (e.g., ulceration, retraction, or spontaneous bloody discharge)
- Nipple discharge, particularly if bloodstained
- Axillary lump

Examination Must Include patient upright with arms raised.

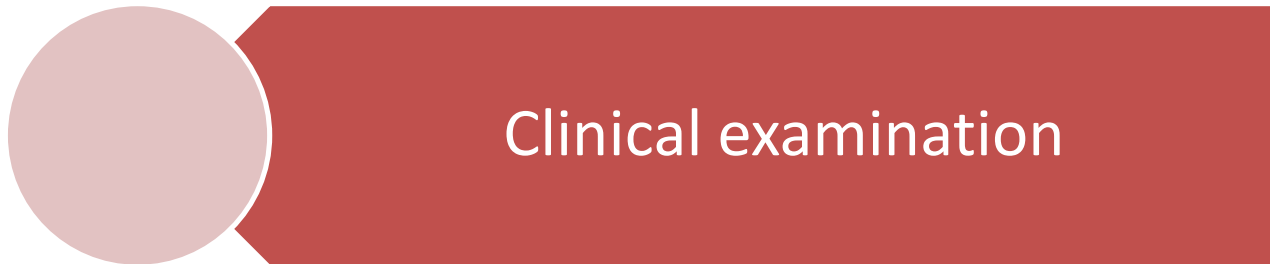
- Lump or contour change
- Skin tethering
- Nipple inversion
- Dilated veins
- Ulceration
- [Mammary Paget disease](#)
- Edema or peau d'orange



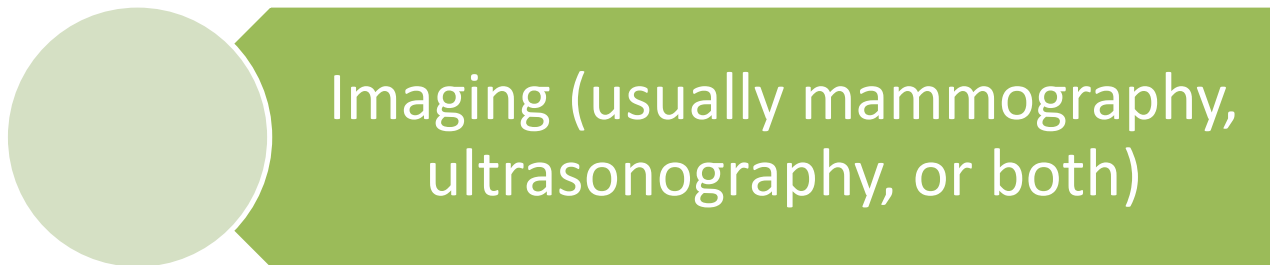
Examination Must Include

- Axillae
 - Supraclavicular fossae
 - Chest
 - Abdomen
 - Skeleton
- **Be alert of**
 - Breathing difficulties
 - Bone pain
 - Symptoms of hypercalcemia
 - Abdominal distention
 - Jaundice
 - Localizing neurologic signs
 - Altered cognitive function
 - Headache

Approach Considerations



Clinical examination



Imaging (usually mammography, ultrasonography, or both)



Needle biopsy

Mammography

- Screening mammography
- Diagnostic Mammography
- Digital mammography

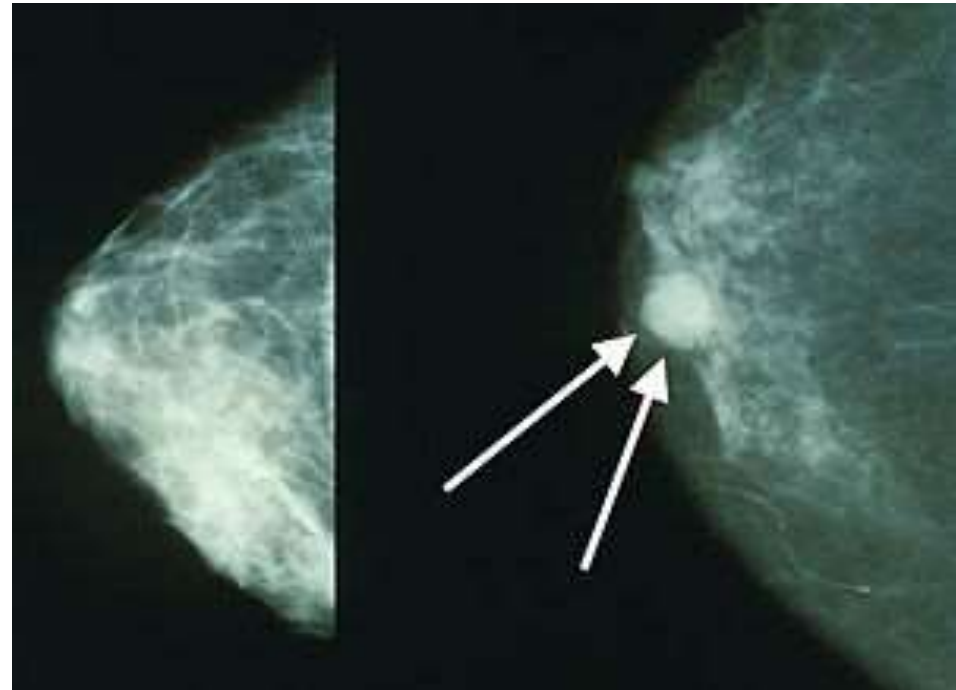
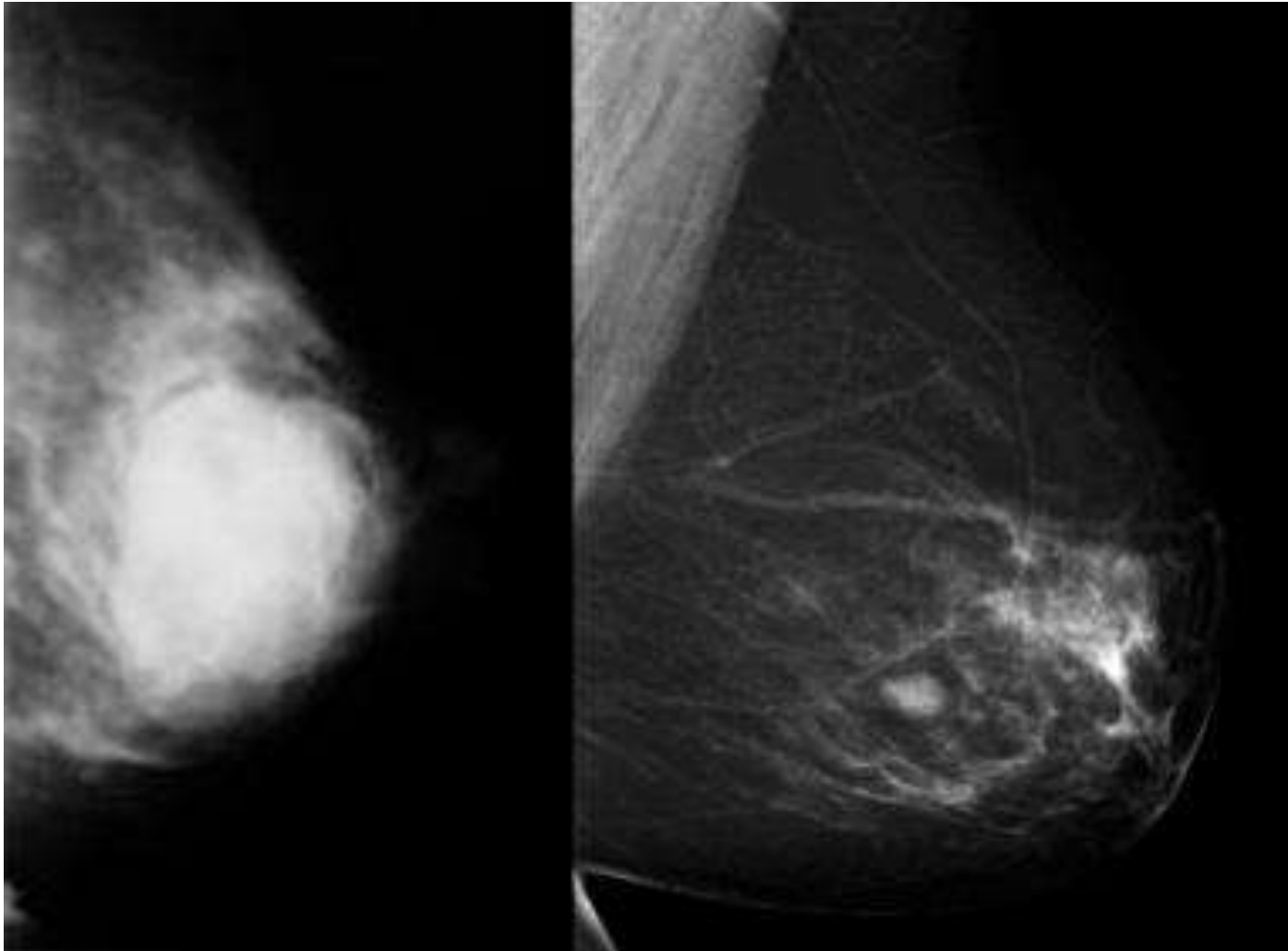
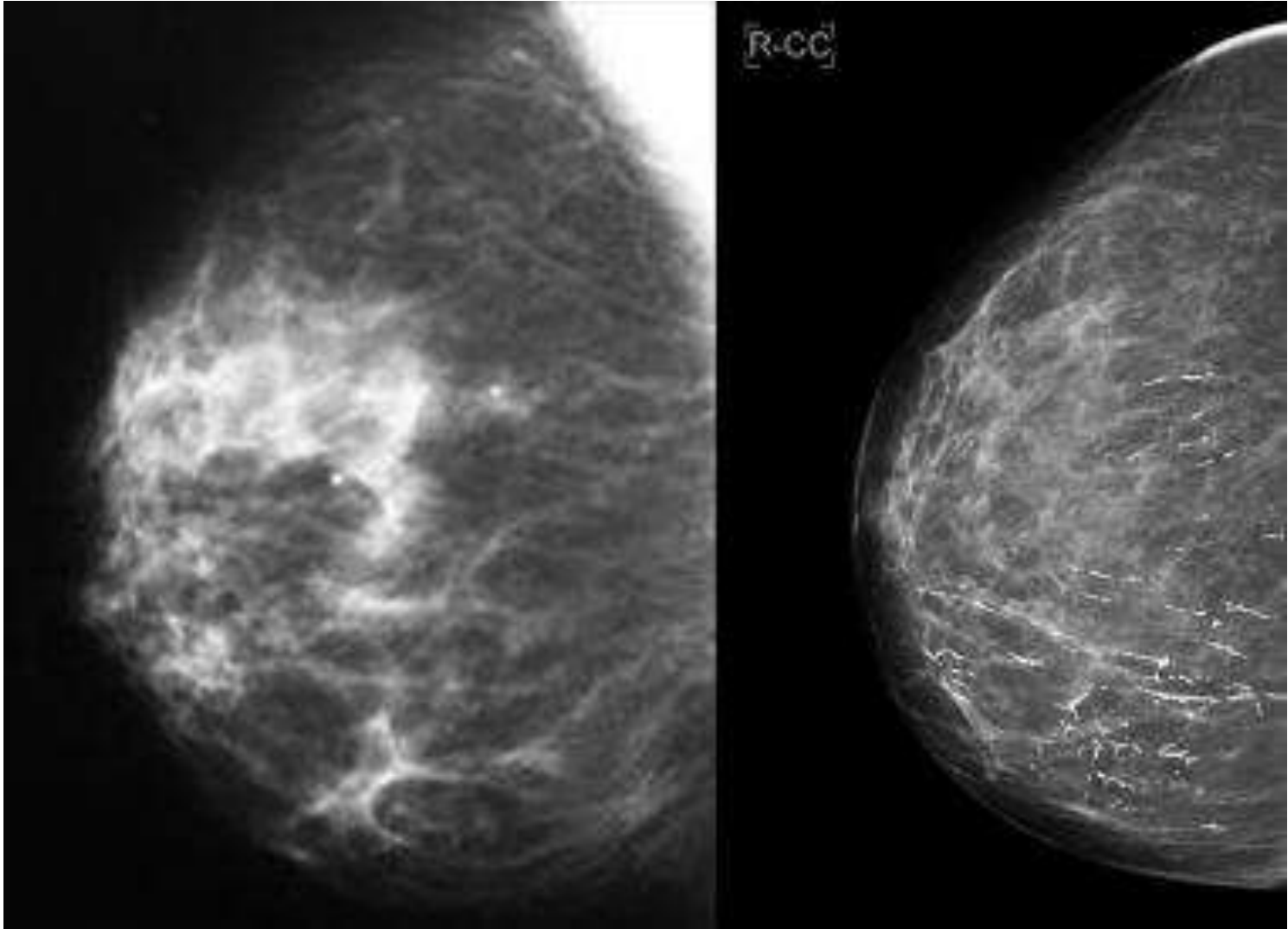


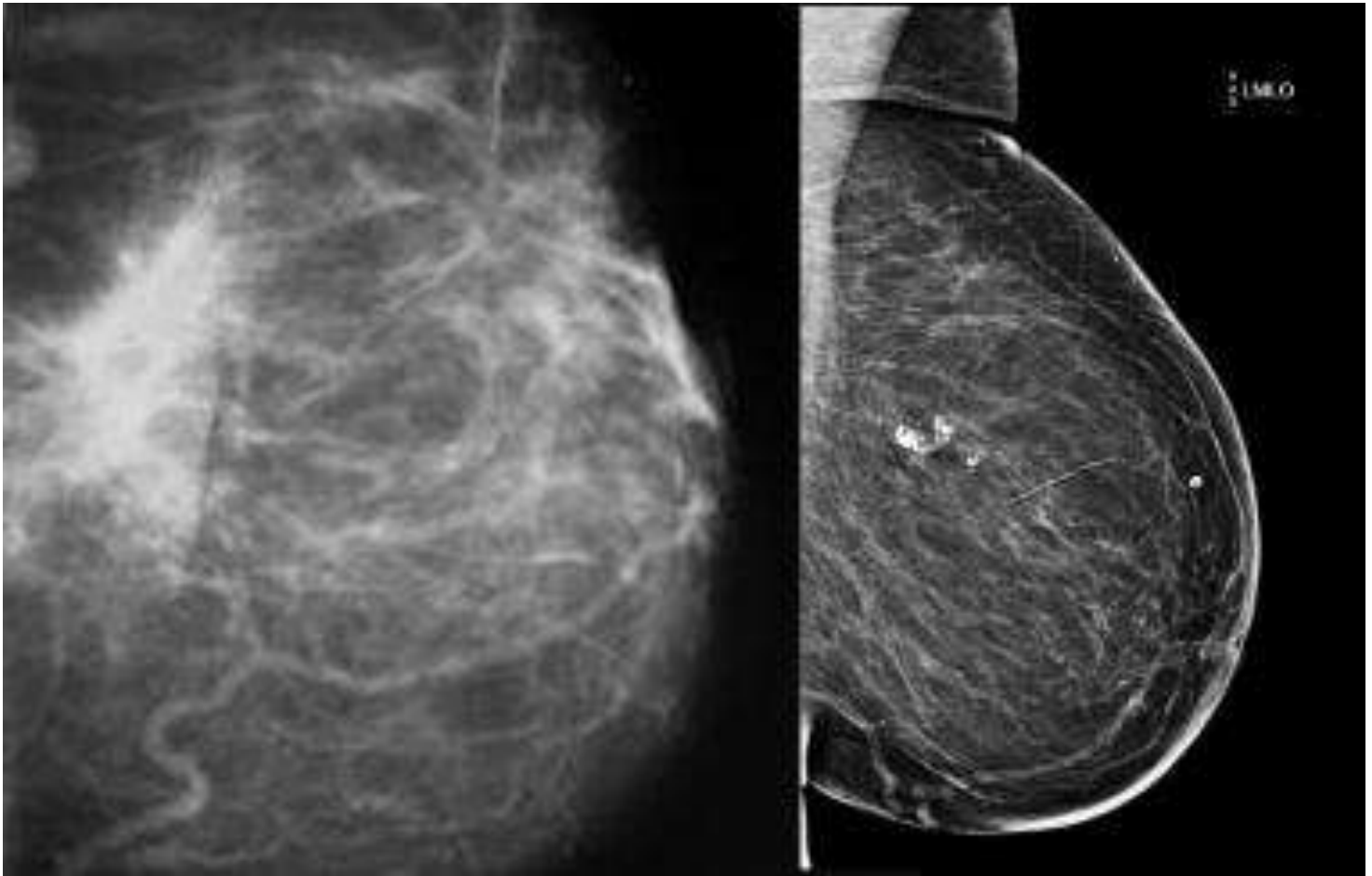
Image from a mammogram shows a benign mass: a fibroadenoma with well-defined edges and a halo sign.



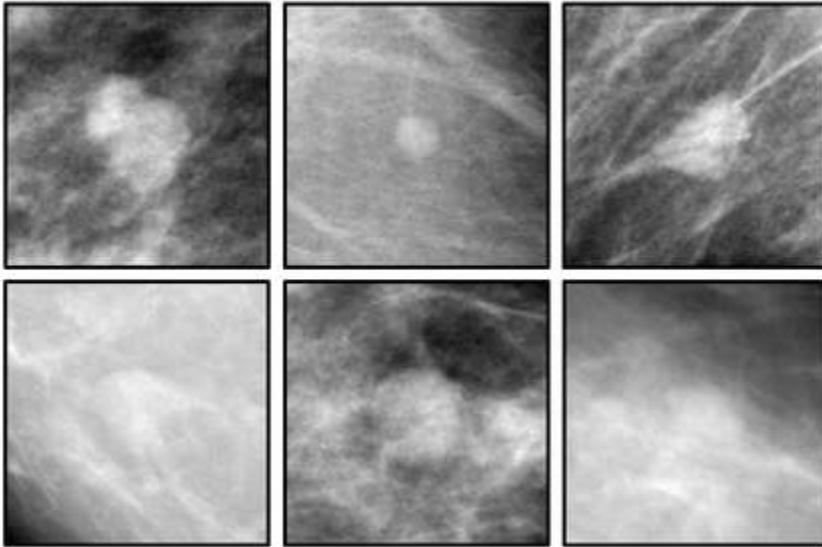
Benign microcalcifications: secretory change.



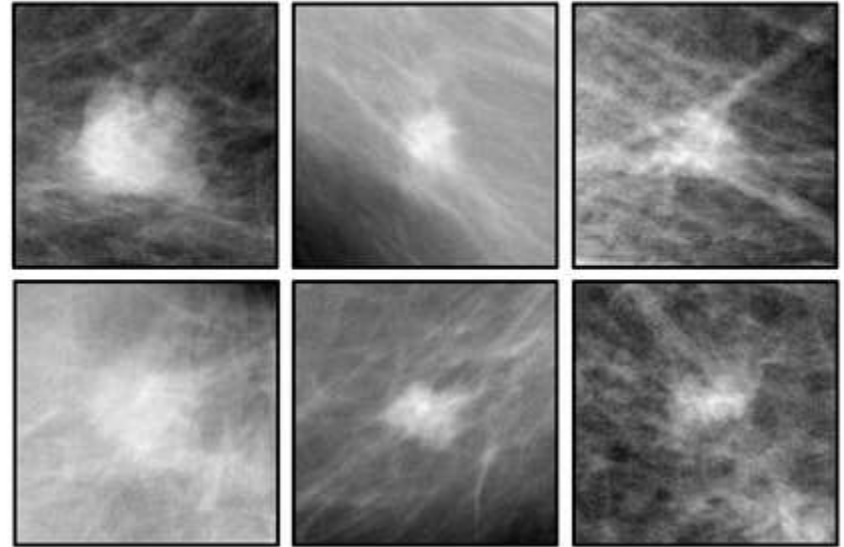
Traumatic fat necrosis. Mammogram shows traumatic fat necrosis following removal of a lesion. The stellate lesion has a halo center.



Benign masses

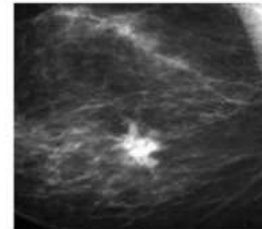


Malignant masses



- Characteristics of **malignant lesions** in mammography:

- architectural *distortion*
- *solid mass* with or without stellate features
- *microcalcifications*
- *stippled* calcifications
- *asymmetric thickening* of breast tissues
- nipple *retraction*



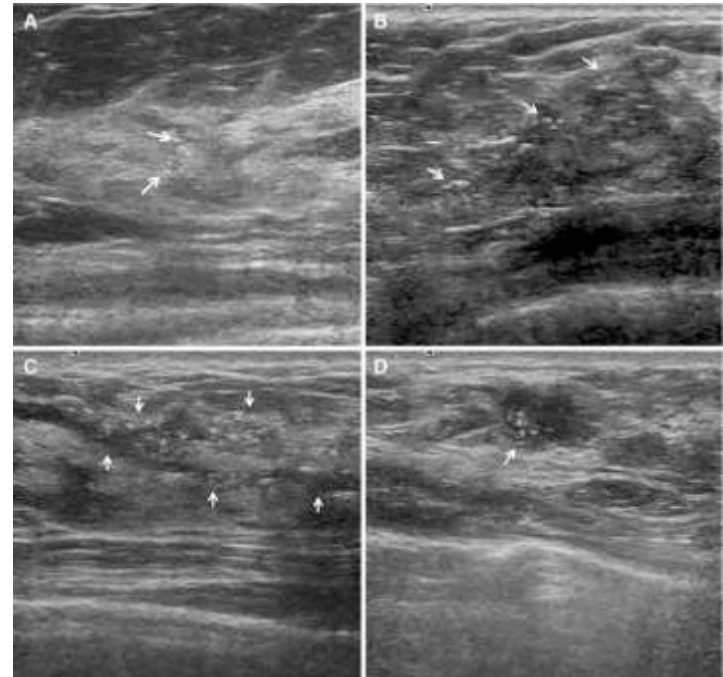
Summary of BI-RADS assessment categories

- **Category 0** - Need additional imaging evaluation
- **Category 1** - Negative
- **Category 2** - Benign finding, noncancerous
- **Category 3** - Probably benign finding, short-interval follow-up suggested
- **Category 4** - Suspicious abnormality, biopsy considered
- **Category 5** - Highly suggestive of malignancy, appropriate action needed
- **Category 6** - Known cancer, appropriate action should be taken

Category	Description	Risk of Malignancy	Care Plan and Comments
1	Negative	5 in 10000	Continue annual screening mammography for women 40 years of age or older.
2	Benign	5 in 10000	Continue annual screening mammography for women 40 years of age or older. This category is for cases with a characteristically benign finding (e.g., cyst, fibroadenoma).
3	Probably Benign	<2%	Usually, 6-month follow-up mammography is performed. Most category 3 abnormalities are not evaluated with biopsy.
4	Suspicious of malignancy	25-50%	Most category 4 abnormalities are benign but may require biopsy.
5	Hugely suggestive of malignancy	75-99%	Classic signs of cancer are seen on the mammogram. All category 5

Ultrasonography

- Useful adjunct to mammography
- Useful in the guidance of biopsies and therapeutic procedures
- As a screening tool- failure to detect microcalcifications and its poor specificity (34%)
- US showing Carcinoma
- Relatively inexpensive and effective method of differentiating cystic breast masses

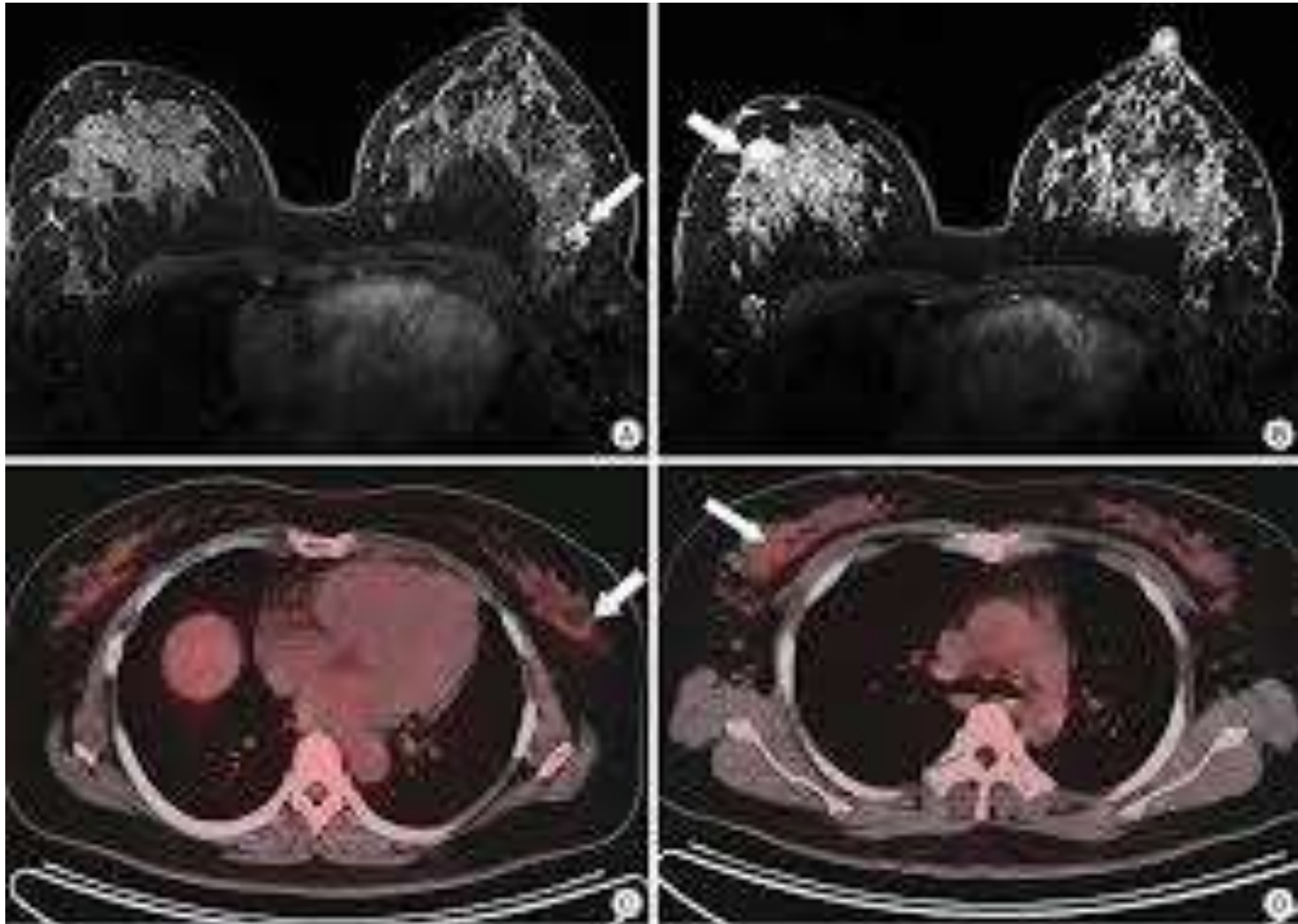


Magnetic resonance imaging (MRI)

Indications

- Indeterminate lesion
- Occult breast carcinoma with carcinoma in an axillary lymph node
- Suspected multifocal or bilateral tumor
- Invasive lobular carcinoma, which has a high incidence of multifocality
- Evaluation of suspected extensive high-grade intraductal carcinoma
- Detection of occult primary breast carcinoma in the presence of metastatic adenocarcinoma of unknown origin
- Monitoring of the response to neoadjuvant chemotherapy
- Detection of recurrent breast cancer

MRI & 18F-FDG



Contraindications for MRI

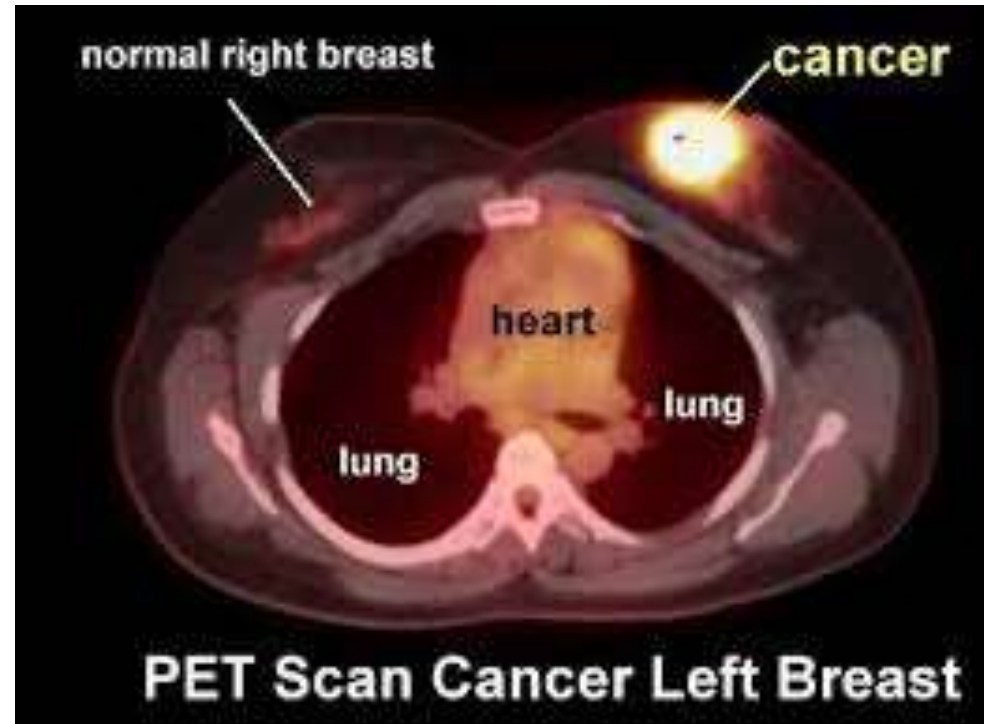
- Contraindication to gadolinium-based contrast media (e.g., allergy or pregnancy)
- Patient's inability to lie prone
- Marked kyphosis or kyphoscoliosis
- Marked obesity
- Extremely large breasts
- Severe claustrophobia

Nuclear imaging

- May play a role in
- Nondiagnostic
- Difficult mammography
- .
- Evaluation of high-risk patients, tumor response to chemotherapy, and metastatic involvement of axillary lymph nodes

Positron Emission Tomography

- Combined with CT can assist in
- Localization of axillary & non-axillary nodal metastasis
- Before initiation of neoadjuvant therapy and restaging high-risk patients for local or distant recurrences



Modality	Sensitivity	Specificity	PPV	Indications
Mammography	63-95% (>95% palpable, 50% impalpable, 83-92% in women older than 50 y; decreases to 35% in dense breasts)	14-90% (90% palpable)	10-50% (94% palpable)	Initial investigation for symptomatic breast in women older than 35 y and for screening; investigation of choice for microcalcification
Ultrasonography	68-97% palpable	74-94% palpable	92% (palpable)	Initial investigation for palpable lesions in women younger than 35 y
MRI	86-100%	21-97% (< 40% primary cancer)	52%	Scarred breast, implants, multifocal lesions, and borderline lesions for breast conservation; may be useful in screening high-risk women
Scintigraphy	76-95% palpable, 52-91% impalpable	62-94% (94% impalpable)	70-83% (83% palpable, 79% impalpable)	Lesions >1 cm and axilla assessment; may help predict drug resistance
PET	96% (90% axillary metastases)	100%		Axilla assessment, scarred breast, and multifocal lesions





MRI = magnetic resonance imaging; PET = positron emission tomography; PPV = positive predictive value

Breast Biopsy

- Percutaneous vacuum-assisted large-gauge core-needle biopsy
- Excisional biopsy



TNM Classification for Breast Cancer

<p>Tumor size</p> <p>T</p>	<p>Tumor size < 2 cm</p>  <p>T1</p>	<p>Tumor size 2-5 cm</p>  <p>T2</p>	<p>Tumor size > 5 cm</p>  <p>T3</p>	<p>Tumor extends to skin or chest wall</p>  <p>T4</p>
<p>Lymph Nodes</p> <p>N</p>	<p>N0 No lymph node metastasis</p>	<p>N1 Metastasis to ipsilateral, movable, axillary LNs</p>	<p>N2 Metastasis to ipsilateral fixed axillary, or IM LNs</p>	<p>N3 Metastasis to infraclavicular/supraclavicular LN, or to axillary and IM LNs</p>
<p>Metastasis</p> <p>M</p>	<p>M0 No distant metastasis</p>	<p>M1 Distant metastasis</p>	<p>LN= Lymph Nodes; IM= Internal Mammary</p>	

Primary Tumor (T)

- **T1:** ≤ 2 cm (20 mm)
 - **mi:** ≤ 1 mm
 - **a:** 1-5 mm
 - **b:** 5-10 mm
 - **c:** 10-20 mm
- **T2:** 2-5 cm
- **T3:** >5 cm
- **T4:** Direct extension to chest wall and/or skin
 - **a:** Chest wall (exclude only pectoralis muscle adherence/invasion)
 - **b:** Ipsilateral ulceration, satellite nodules or peau'd orange
 - **c:** Both a and b
 - **d:** Inflammatory carcinoma



Stage 0



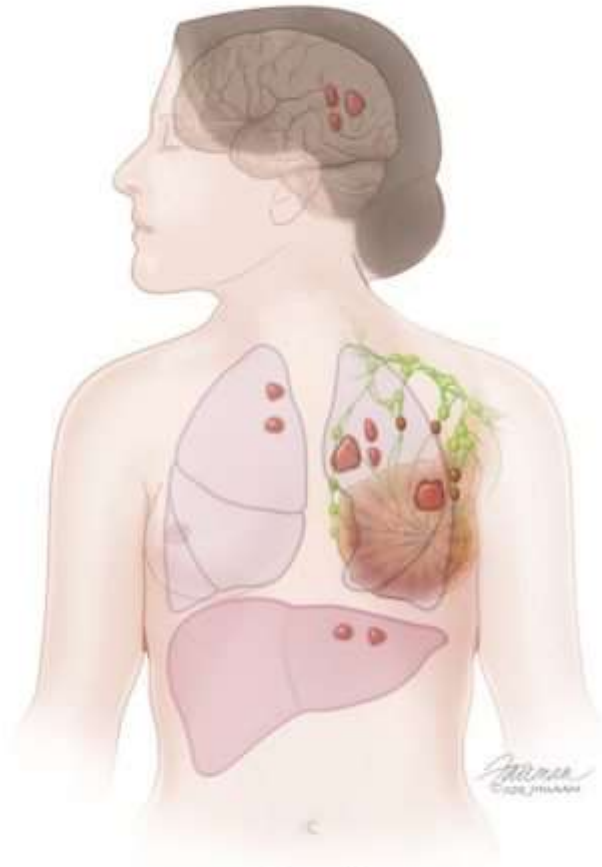
Stage I



Stage II



Stage III



Stage IV

Regional Lymph Node (N)

- **N1:** Ipsilateral and mobile level I and II axillary nodes
- **N2:**
 - **a:** Ipsilateral and matted level I and II axillary nodes
 - **b:** Ipsilateral internal mammary nodes only
 -
- **N3:a:** Ipsilateral level III axillary nodes (infraclavicular node)
- **b:** Ipsilateral internal mammary nodes + level I, II nodes
- **c:** Ipsilateral supraclavicular nodes

Distant Metastasis (M)

- **cMo (i+)**: Clinically and radiologically normal but ≤ 0.2 mm tumor cells in blood, bone marrow or other nonregional nodal tissues
- **M1**: >0.2 mm metastases

Trick or Mnemonic to remember AJCC Breast Cancer Staging

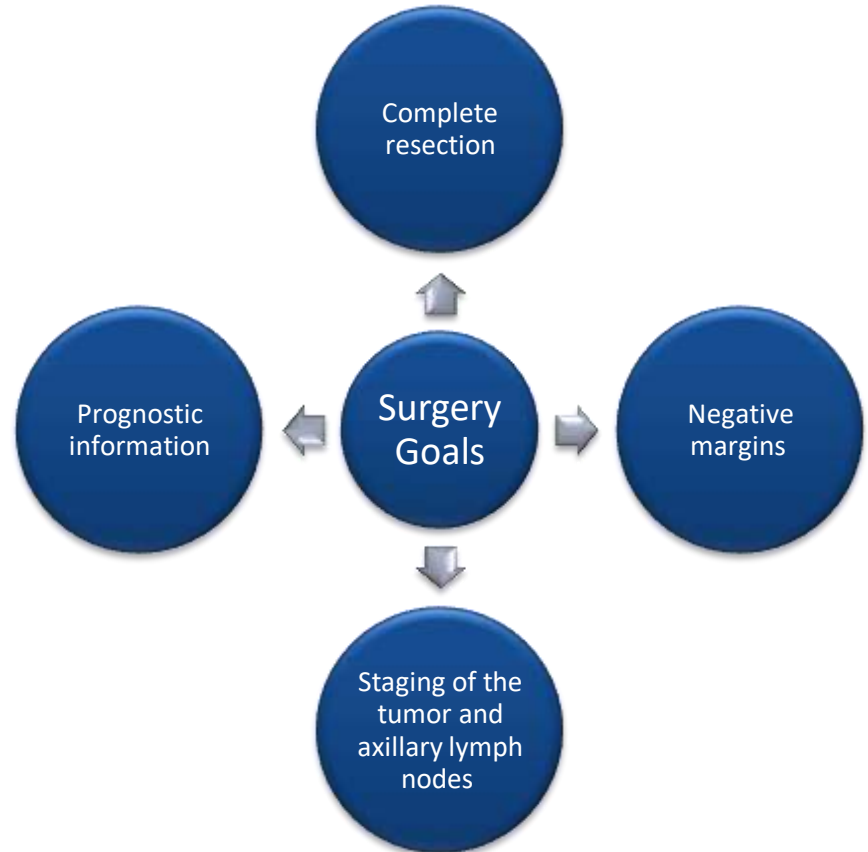
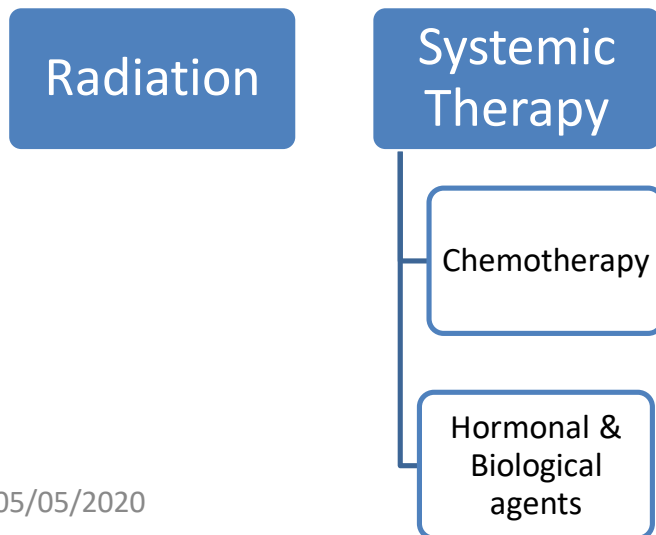
	N0	N1	N2	N3	M1
T1	I	IIA	IIIA	IIIC	IV
T2	IIA	IIB	IIIA	IIIC	IV
T3	IIB	IIIA	IIIA	IIIC	IV
T4	IIIB	IIIB	IIIB	IIIC	IV

Trick or Mnemonic to remember AJCC Breast Cancer Staging

- **M1** = Stage IV
- **T4** = Stage III – b or c
- **N3** = Stage III – c
- **N2** = Stage III – a or b
- From above, we know that T4 is either Stage III – b or c (cannot be “a” and cannot be “c”)
 - T4N2 = Stage IIIb
- Remaining T 1-3 is Stage IIIa
 - T 1,2,3 N2 = Stage IIIa
- **With remaining T 1-3 and N0-1, add them up:**
- Add up to make **1**: Stage I (T1No)
- Add up to make **2**: Stage **IIa** (T1N1 or T2N0)
- Add up to make **3**: Stage **IIb** (T3N0 or T2N1)
- Add up to make **4**: Stage **IIIa** (T3N1)

Treatment

- Surgery primary treatment for early-stage breast cancer
- Adjuvant treatment for micrometastasis



Treatment of Invasive Breast Cancer

- Lumpectomy or total mastectomy.
- Clinically negative nodes, surgery typically includes SLN dissection for staging the axilla
- Systemic Adjuvant Therapy for Breast Cancer- for micrometastasis
- Postmastectomy radiation therapy If
- Positive postmastectomy margins
- Primary tumors >5 cm
- Involvement of ≥ 4 lymph nodes

Treatment of Ductal carcinoma in situ

- Surgical resection with or without radiation
- Adjuvant radiation and hormonal therapies are often reserved for younger women, patients undergoing lumpectomy, or those with the comedo subtype.

Treatment of Lobular carcinoma in situ

- Options are
- Observation and close follow-up care with or without tamoxifen
- Or
- Bilateral mastectomy with or without reconstruction

Treatment of Locally Advanced and Inflammatory Breast Cancer

- Locally advanced disease means technically operable but have large primary tumors (>5 cm).
- IBC is a clinical diagnosis presentation with signs of inflammation involving the breast
- IBC younger age than LABC
- Neoadjuvant therapy for intent of cure

Locally advanced breast cancer

- LABC is more common in USA than IBC
- Associated with lower socioeconomic class
- LABC has a better long-term outcome than IBC



Evaluation of Lymph Nodes & Response

- Pts. LABC & IBC with +ve nodes need core biopsy before chemotherapy
- Ultra Sound most accurate to measure size of tumor
- Sentinel nodes in –ve nodes before chemotherapy
- Or Sentinel nodes delayed before chemotherapy

Systemic Treatment of Metastatic Breast Cancer

- No cure once distant metastases
- May benefit by surgical resection or radiation
- In general two main interventions: hormone therapy and chemotherapy.
- Hormone therapy in general better than chemotherapy

Surgical Treatment of Metastatic Breast Cancer

- As modern systemic chemotherapy has become more effective
- Increasing interest in the role of surgical intervention for the intact primary tumor of these metastatic breast cancer patients
- Several single-institution cohort and retrospective studies have concluded that surgical resection of the intact primary tumor may provide a survival advantage.
- ***Please see notes***

Follow-up Recommendations for Breast Cancer Survivors

History and physical examination	<p>Year 1-3, every 3-6 months</p> <p>Year 4-5, every 6-12 months</p> <p>Year 6+, annually</p>
Breast self-examination	Counseled to perform monthly breast self-examination
Mammography	<p>6 months after definitive radiation therapy</p> <p>Every 6-12 months for surveillance of abnormalities</p> <p>Annually if stability of abnormalities is achieved</p>
Pelvic examination	<p>Regular gynecologic follow-up</p> <p>Patients on tamoxifen should be advised to report any vaginal bleeding</p>
Routine blood tests/ Mammogram/ Tumor	Not needed