An Introduction to Breast Cancer: Biology, Pathology, and the Latest in Screening and Diagnostic Tools

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Disclosures

- **I have no relevant relationships to disclose**

Objectives

- To understand the epidemiology of breast cancer
- To understand the risk factors, natural history, and histopathology of breast cancer
- To learn the current guidelines for breast cancer screening
- To understand mammographic findings significant for breast cancer
- To understand when a Breast MRI is indicated

Epidemiology of Breast Cancer

- **Most common cancer in women**
- **2nd leading cause of cancer death in women**
- **In 2008, in the United States**
  - **182,460 new cases of invasive breast cancer in women**
  - **1,990 new cases in men**

American Cancer Society. Cancer Facts & Figures 2008. Atlanta: American Cancer Society: 2008.

Epidemiology of Breast Cancer

- **Incidence rates had been increasing from 1980-2000**
  - **Increased use of screening mammography**
  - **Detecting breast cancers in earlier stages of disease**
- **Incidence rates began decreasing by 3.5% per year between 2001-2004**
  - **Reduced use of hormone replacement therapy (HRT)**
    - **Publication of results from the Women's Health Initiative in 2002**
    - **HRT linked with increased r/o heart disease and breast cancer**
  - **Slight drop in mammography rates in women 40+ y/o**
    - **70.1% to 66.4% between 2000-2005**
- **Death rates from breast cancer have steadily decreased since the 1990's.**
  - **2.3% per year**
  - **Early detection**
  - **Improved treatment**

American Cancer Society. Cancer Facts & Figures 2008. Atlanta: American Cancer Society: 2008.

Question #1

- **What is a woman's lifetime risk of having invasive breast cancer?**

- **A) 0.5%**
- **B) 3.8%**
- **C) 6.7%**
- **D) 12.5%**
- **E) 25%**

Question #1

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- **Risk of invasive breast cancer is strongly associated with age**
  - **≤ 39 y/o: 1 in 210**
  - **40-59 y/o: 1 in 26**
  - **60-69 y/o: 1 in 28**
  - **≥ 70 y/o: 1 in 15**
  - **Lifetime risk: 1 in 8 (12.5%)**

Jemal A, et al. CA Cancer J Clin 58:71-96, 2008

Epidemiology of Breast Cancer

- **Considerable geographic, ethnic, and racial variability in breast cancer**

- **National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program:**

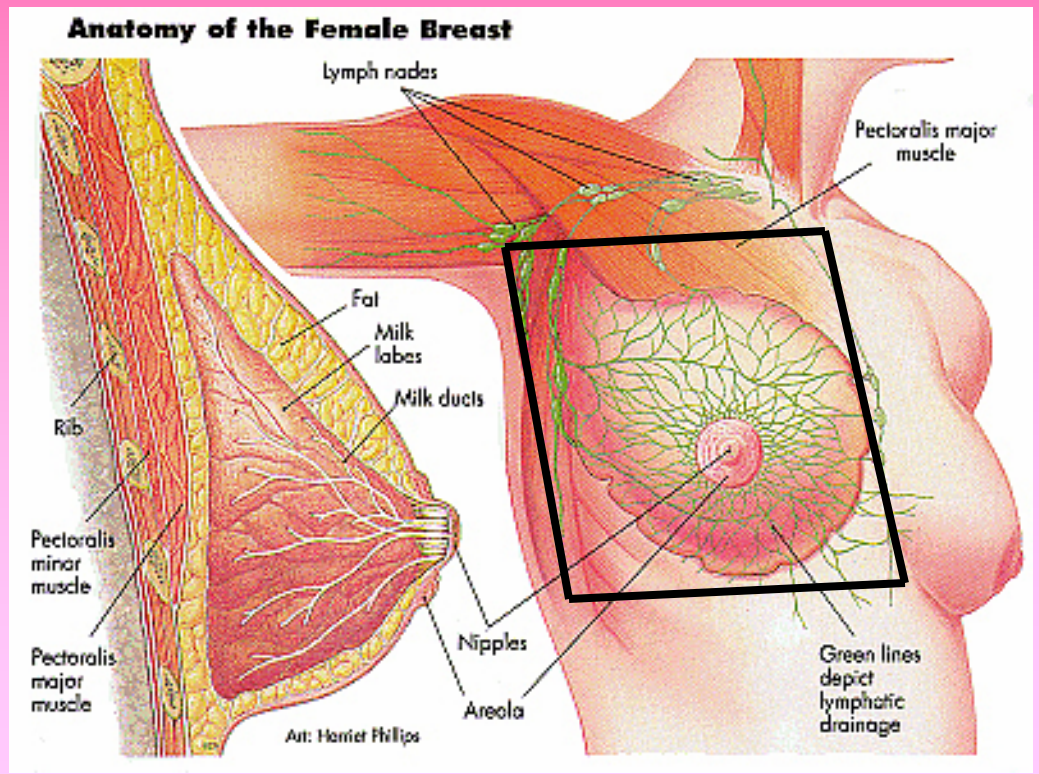
	Incidence per 100,000 cases
White women	141
African Americans	122
Asian Pacific Islanders	97
Hispanics	90
American/Alaskan Natives	58

- **Lower incidence in African American women, but**
  - **Age of onset ~10 yrs younger than in white women**
  - **Diagnosed at a more advanced stage**
  - **More aggressive biology**
  - **Poorer overall prognosis**

American Cancer Society. Cancer Facts & Figures 2008. Atlanta: American Cancer Society: 2008.

Breast Anatomy

- **Anterior chest wall**
- **Superficial to pectoralis major muscle**
- **Borders**
  - **Medial: Midline chest wall**
  - **Lateral: mid-axillary line**
  - **Superior: 2nd anterior rib**
  - **Inferior: 6th anterior rib**

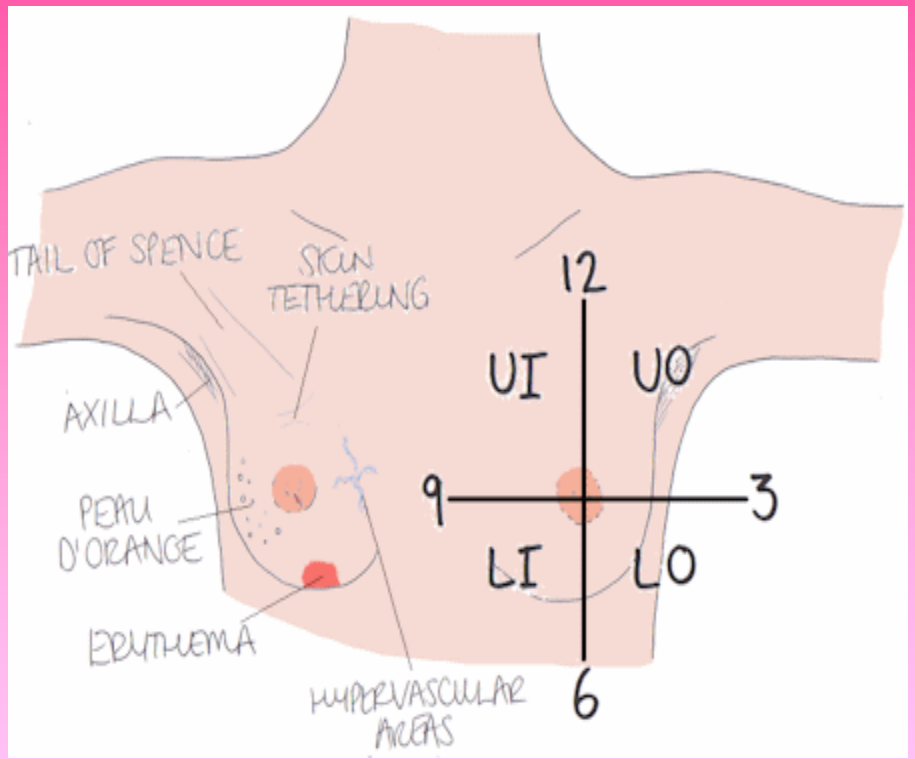


Halperin E, Perez C, Brady L, Ed. Perez and Brady's Principles and Practice of Radiation Oncology: Fifth edition. Lippincott Williams & Wilkins, Philadelphia: 2008. 1162-1317.

Breast Anatomy

- **4 Quadrants:**
  - **Upper Inner (UI)**
  - **Upper Outer (UO)**
  - **Lower Inner (LI)**
  - **Lower Outer (LO)**

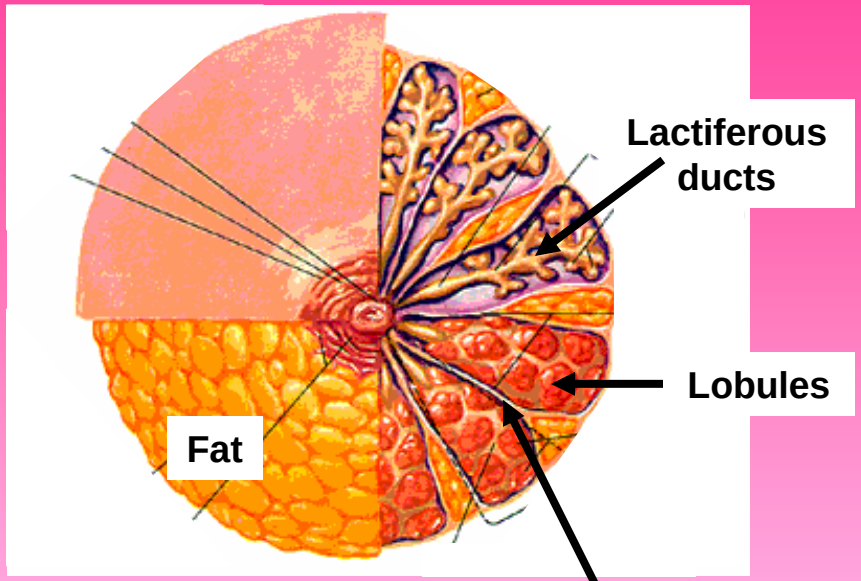
- **Upper Outer Quadrant**
  - **Extends into region of the low axilla (axillary tail of Spence)**
  - **Greater percentage of breast tissue**
  - **Greater percent of breast caners**



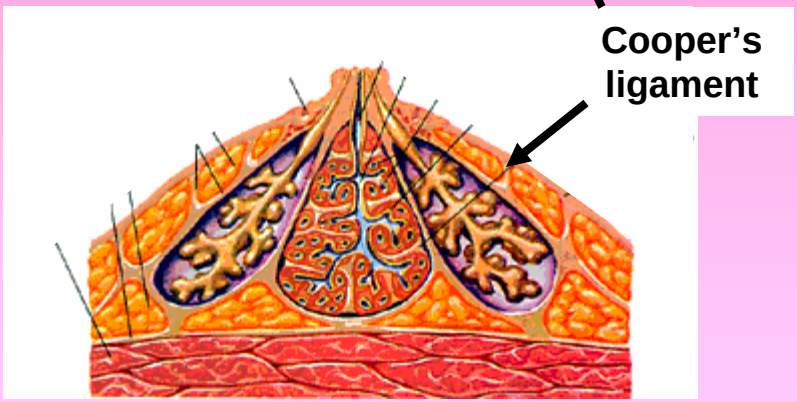
http://www.breastdiagnostic.com/images/anatomy1.gif.

Breast Anatomy

- Mammary glands
- Fat
- Blood vessels
- Nerves
- Lymphatics



- Cooper's ligament
  - Fibrous septa running between the superficial fascia (skin) and the deep fascia (covering muscles of the chest wall)

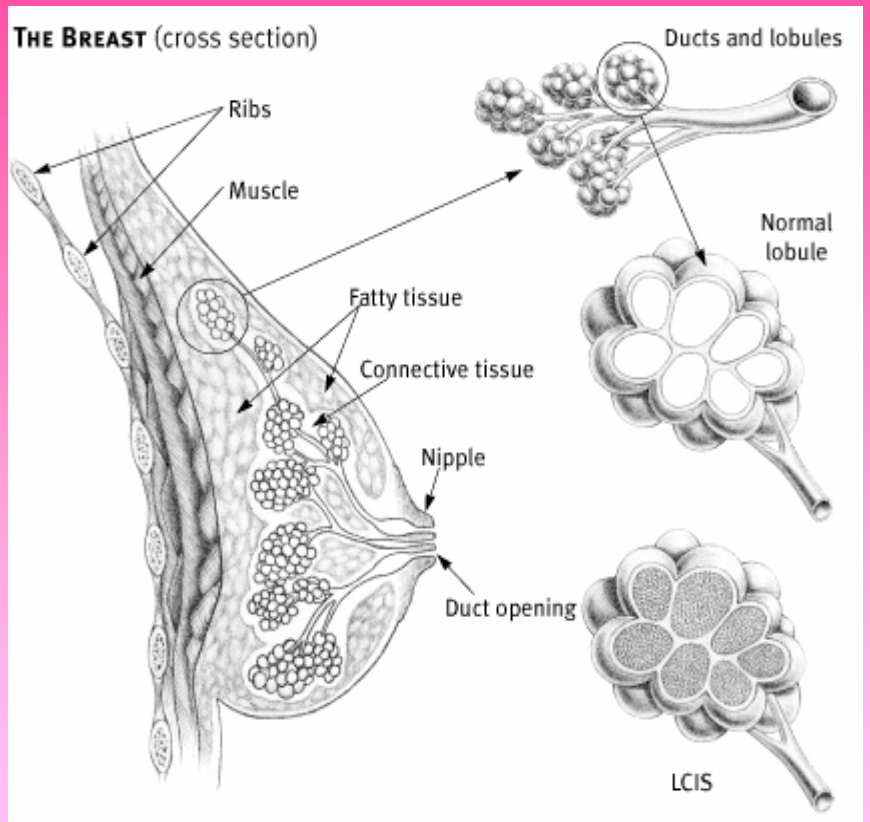


http://www.breastdiagnostic.com/images/anatomy1.gif

Breast Anatomy

- **Parenchyma:**
  - **Lobules**
    - **Produce Milk**
  - **Ducts**
    - **Function to transport lactation products to the nipple**
    - **Peripheral ducts converge into major lactiferous ducts, which communicate with the nipple-areola complex**

- **Most breast cancers develop at the terminal ducal lobular unit**
  - **Interface between ductal system and lobules**



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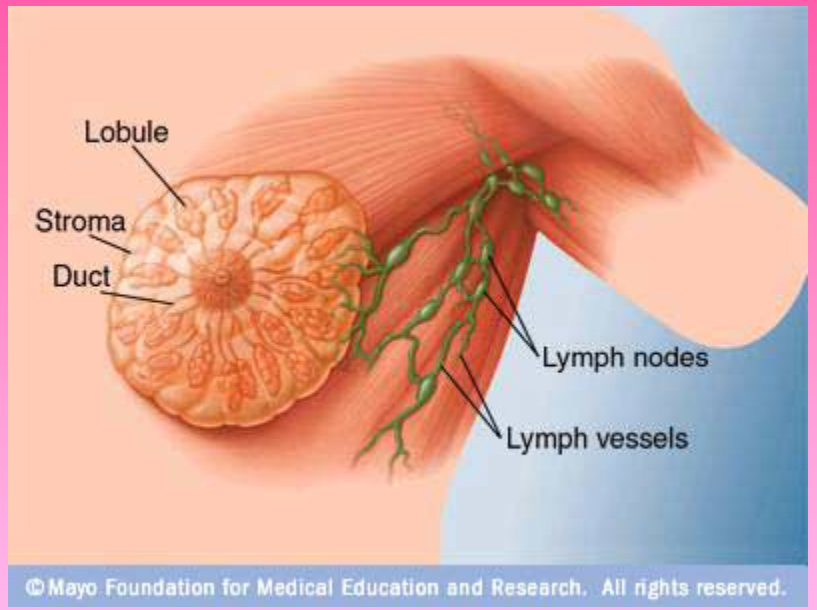
http://www.cancervic.org.au/images/content/breast_health/lcis.gif

Breast Anatomy

- **Lymphatics**
  - **Begin in the interlobular spaces**
  - **Travel along the ducts**
  - **End in the subareolar network of lymphatics of the skin**

- **Lymphatic drainage of the breast predominantly goes to the axillary lymph nodes**
  - **Axilla = most common site of lymphatic involvement with breast cancer**



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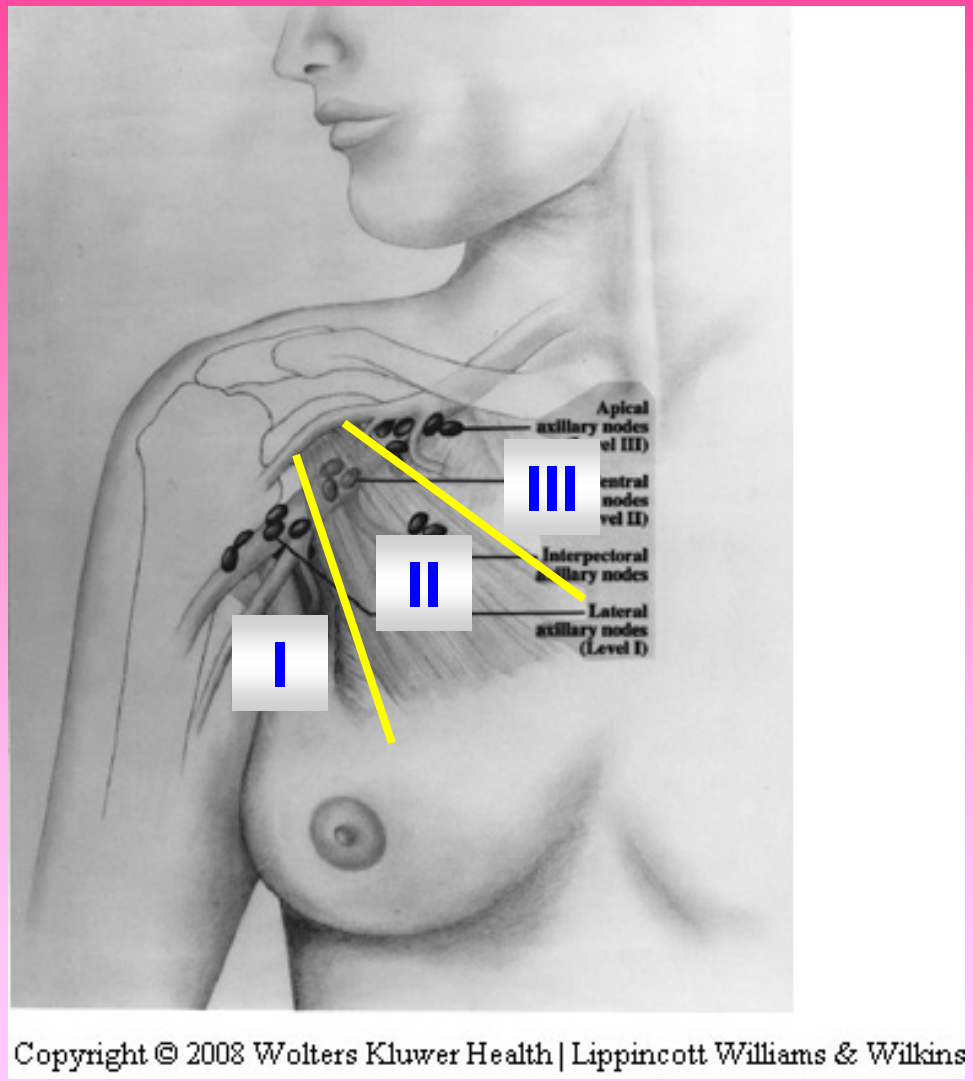
Breast Anatomy



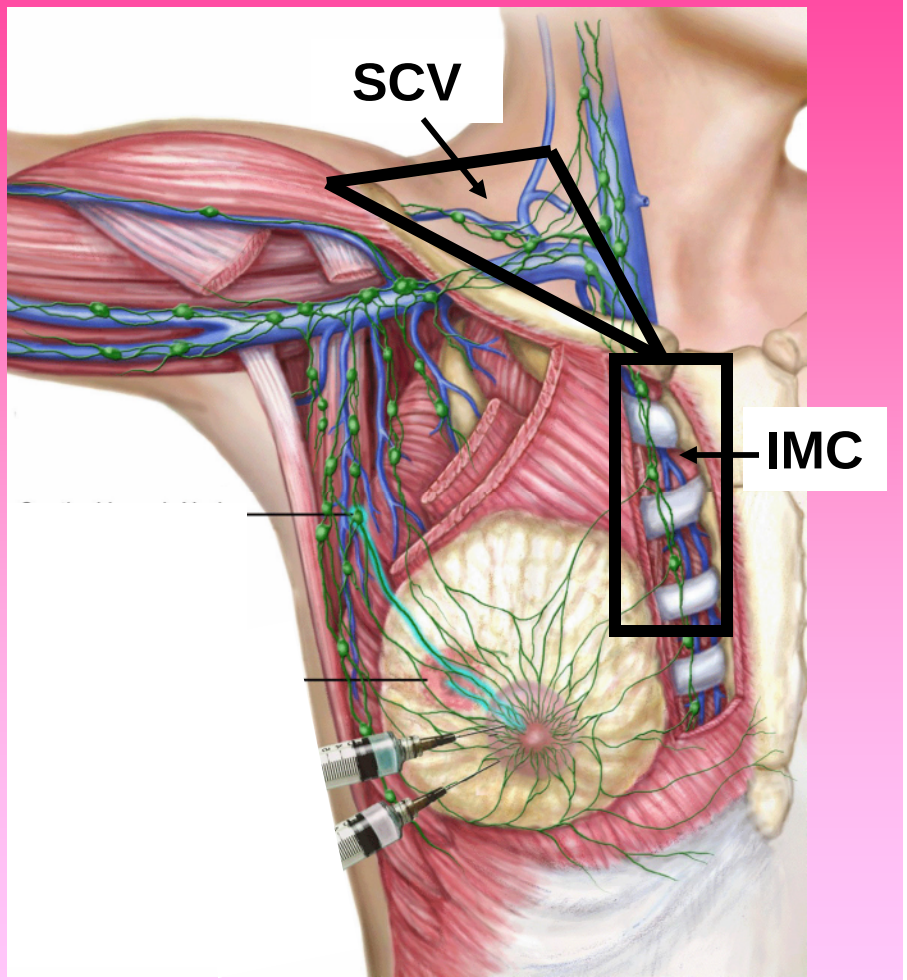
- Axillary lymph nodes
- 3 levels
  - Based on relationship to pectoralis minor muscle
- Level I axilla
  - Caudal and lateral to pectoralis minor m.
- Level II axilla
  - Beneath pectoralis minor m.
- Level III axilla
  - Infraclavicular region
  - Cranial and medial to pectoralis minor m.

Halperin E, Perez C, Brady L, Ed. Perez and Brady's Principles and Practice of Radiation Oncology: Fifth edition. Lippincott Williams & Wilkins, Philadelphia: 2008. 1162-1317.

Breast Anatomy

- **Supraclavicular (SCV) LNs**
  - **Axillary lymph nodes continue underneath the clavicle to become the SCV lymph nodes.**
  - **Locally advanced cancers**

- **Internal mammary chain (IMC) lymph nodes**
  - **Intrathoracic in the parasternal space**
  - **3-4 cm lateral to midline**
  - **1st 3 interspaces**
  - **More commonly seen with medial, central, or lower breast cancers**



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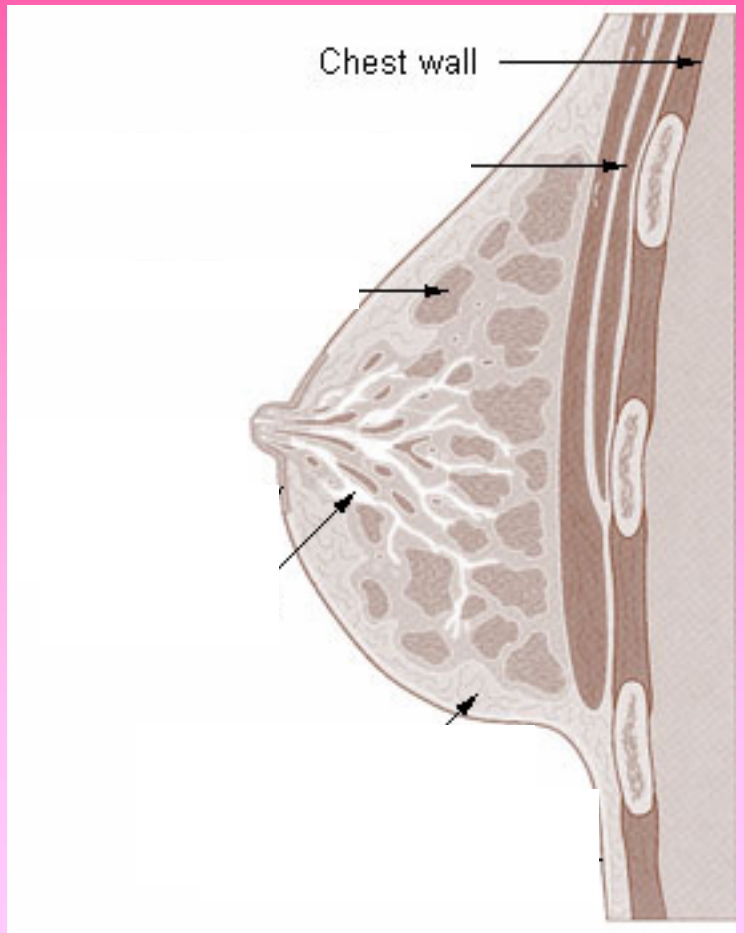
www.intra-medical.com/lymphatic.html

Breast Anatomy

- **Anatomy of the chest wall is important for staging purposes**

- **Chest wall:**
  - **Ribs**
  - **Intercostal muscles**
  - **Serratus anterior muscle**
  - **NOT the pectoral muscles**



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Question #2

- **What is the most significant risk factor for developing breast cancer (other than gender)?**

- **A) Prior history of breast cancer**
- **B) Alcohol consumption**
- **C) Obesity**
- **D) Use of hormone replacement therapy**
- **E) Increasing age**

Question #2

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- **E) Increasing age**

Jemal A, et al. “Cancer statistics, 2006.” CA Cancer J Clin 2006;56:106-130

Risk Factors for Breast Cancer

- Female gender
- Increasing age
- Age > 50 y/o
- Early menarche (< 12 y/o)
- Nulliparity
- Late age at first live birth (> 30 y/o)
- Late menopause (> 55 y/o)
- Prior breast biopsy
  - Hyperplasia
  - Atypical hyperplasia
- Personal history of invasive breast cancer
  - 10-15% r/o developing a new primary in the contralateral breast

- Alcohol consumption
  - 3-4 drinks per day increased relative risk 32%
  - > 4 drinks oer day increased relative risk 46%

Hamajima N, et al. Br J Cancer 2002;87:1234-1245.

Jemal A, et al. “Cancer statistics, 2006.” CA Cancer J Clin 2006;56:106-130

Risk Factors for Breast Cancer

- **Obesity, particularly after menopause**
- **High dose chest irradiation at a young age**
  - **E.g. Lymphoma**
- **Dense breast tissue (more glandular tissue)**
- **Use of Hormone Replacement Therapy (HRT)**
  - **Combined estrogen/progesterone therapy > estrogen alone**
  - **Oral contraceptive use is controversial as a RF**
- **Family history**
  - **1st degree relative**
    - **1: increases risk 2x**
    - **2: increase risk 5x**
  - **2nd degree relative: 1.5x**

Jemal A, et al. “Cancer statistics, 2006.” CA Cancer J Clin 2006;56:106-130

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Genetic and Familial Factors

- **Familial breast cancer**
  - **10% of patients**
  - **Germline mutations in tumor suppressor genes**
    - **p53, BRCA1, BRCA2**

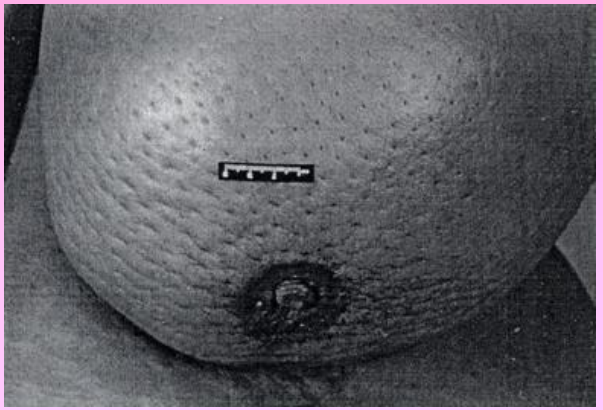
Halperin E, Perez C, Brady L, Ed. Perez and Brady's Principles and Practice of Radiation Oncology: Fifth edition. Lippincott Williams & Wilkins, Philadelphia: 2008. 1162-1317.

Genetic and Familial Factors

- **BRCA1 and BRCA2**
  - **< 1% of the population**
  - **< 7% of breast cancer patients**
  - **Mediate effects of cell response to DNA damage**
  - **BRCA1**
    - **Lifetime risk of breast cancer 65-85%**
    - **Lifetime risk of ovarian cancer 50%**
    - **Increased risk of colon and prostate cancer**
  - **BRCA2**
    - **Lifetime risk of breast cancer 65-85%**
    - **Increased lifetime risk of ovarian cancer, but less than that for BRCA1**
    - **Associated with pancreatic cancer and male breast cancer**

Signs and Symptoms of Breast Cancer

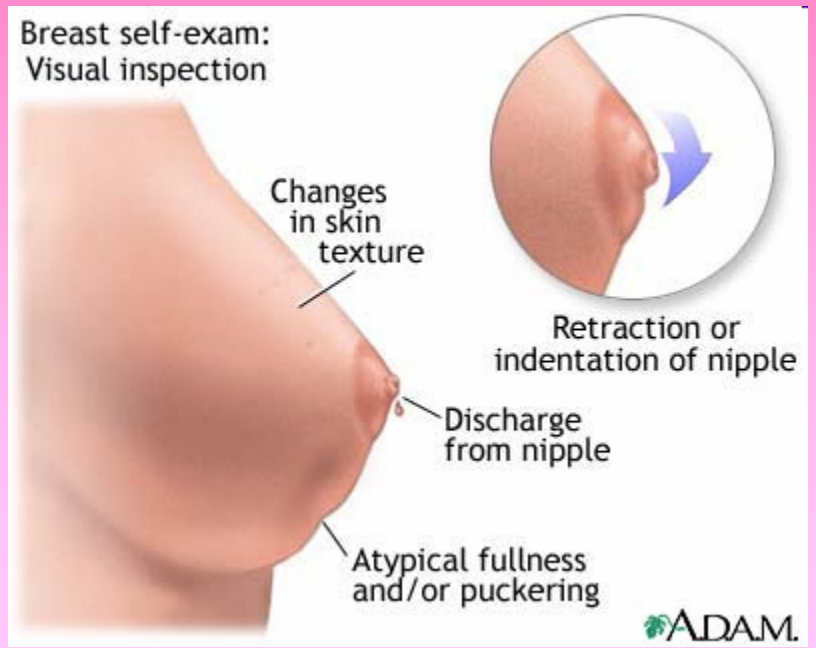
- **Often found as an abnormality on mammogram**
- **Painless firm mass**
- **Persistent changes to the breast**
  - **Thickening**
  - **Swelling**
  - **Dimpling**
    - **Cooper's ligament affected**
  - **Distortion**
  - **Tenderness**
  - **Skin irritation**
  - **Redness**
  - **Scaling**
  - **Prominent superficial veins**

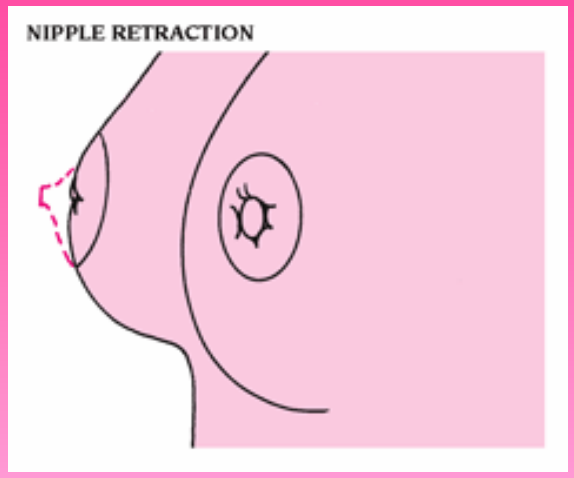


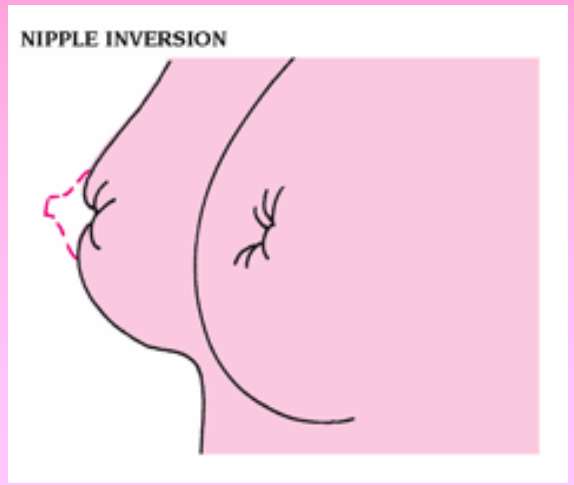
Giordano, SH. Update on locally advanced breast cancer. Oncologist 2003; 8:526.

Signs and Symptoms of Breast Cancer

- **Nipple changes**
  - **Ulceration**
  - **Retraction, inversion**
  - **Spontaneous discharge**



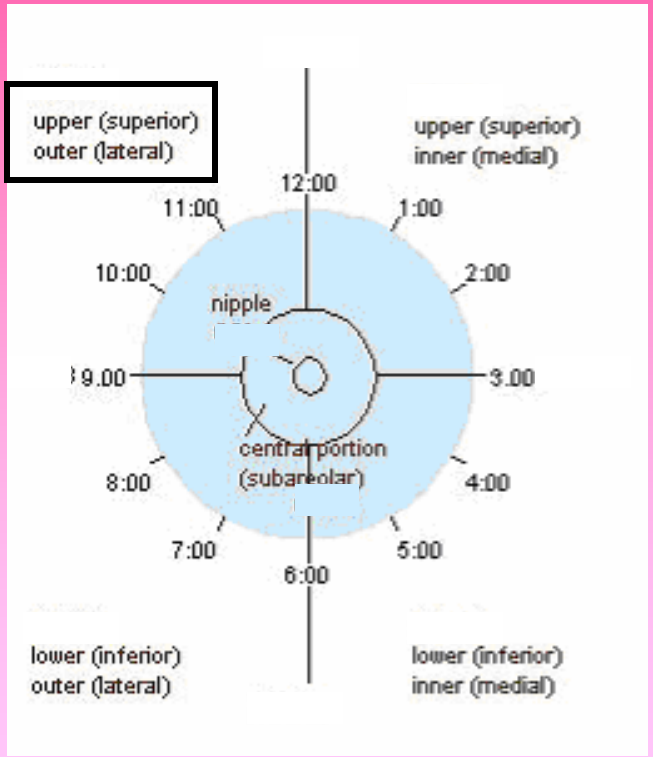




Natural History of Breast Cancer

- **Thought to be slow growing tumors, with an average of 5 yrs before a tumor becomes palpable.**

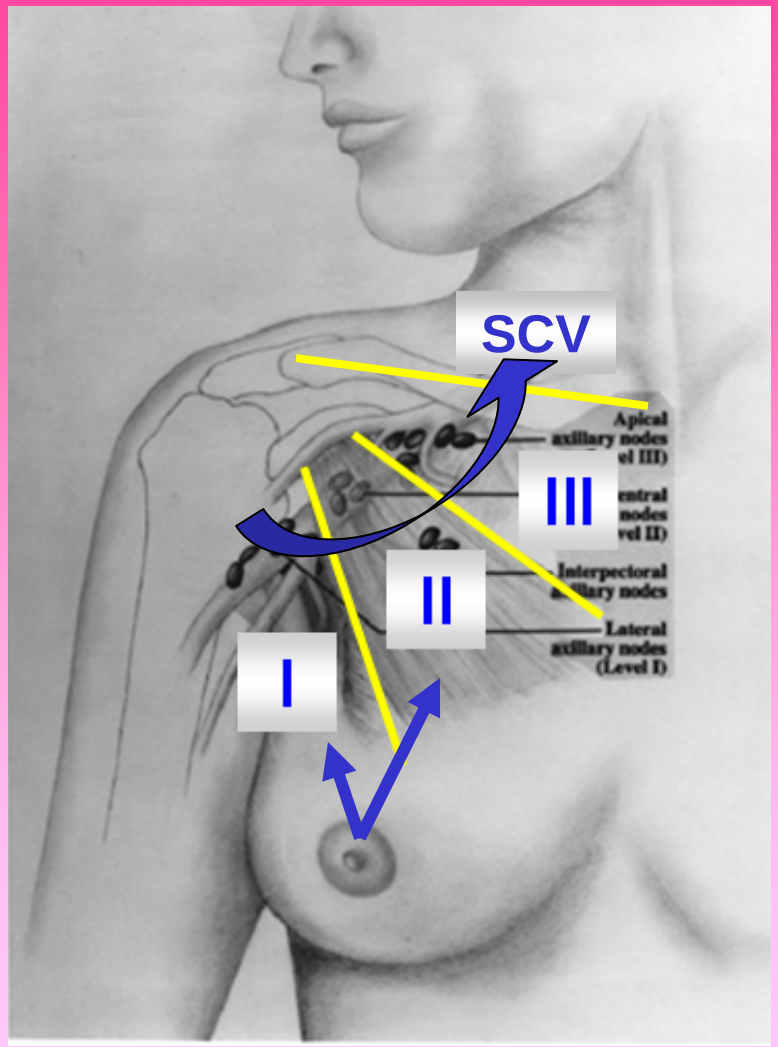
- **Most common sites of origin:**
  - **UOQ (38.5%)**
  - **Central area (29%)**
  - **UIQ (14.2%)**
  - **LOQ (8.5%)**
  - **LIQ (5%)**



Natural History of Breast Cancer

- **Spread of disease**
  - **Travels along the ducts (carcinoma *in situ*)**
  - **Eventually breaking through the basement membrane (invasive carcinoma)**
    - **Invades adjacent lobules, ducts, fascial strands, & mammary fat**
    - **Spreads through breast lymphatics into peripheral lymphatics**
  - **Can grow through blood vessel walls and spread into the deep lymphatics of the dermis (skin)**
    - **Edema and dimpling of the skin (*peau d'orange*)**
  - **Ulceration and infiltration of the overlying skin**

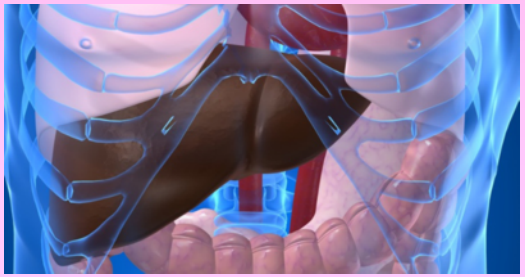
Natural History of Breast Cancer



- **Lymph node spread of disease**
  - **LN involvement increases with:**
    - **Increasing tumor size**
    - **Histological nuclear grade (moderate or poorly differentiated)**
    - **Presence of lymphovascular invasion**
    - **Age < 60y/o**
    - **African American race**
  - **Usually goes to axillary LN levels I and II, before reaching level III, the supraclavicular LNs, or the internal mammary LNs.**

Natural History of Breast Cancer

- **Distant spread of disease**
  - **Most common site**
    - **Bone**
  - **Other sites:**
    - **Lungs**
    - **Lung pleura**
    - **Liver**
    - **Brain/CNS**
  - **Local control of disease can impact systemic metastasis and survival, as well as cosmesis and quality of life**

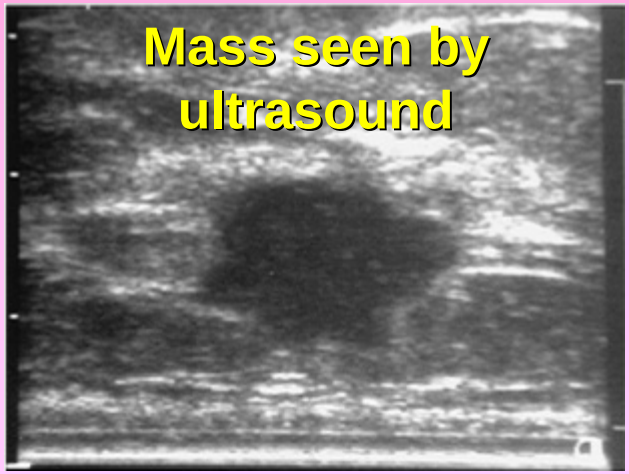


Work up

- Complete clinical and family history
- Physical exam
  - Sitting and supine
  - Size, symmetry, pigmentation, scaling or discharge from the nipple, dilated veins or edema of the skin
  - Location, size, consistency, tenderness, and mobility of a palpable tumor
  - Axillary, supraclavicular, and infraclavicular LNs

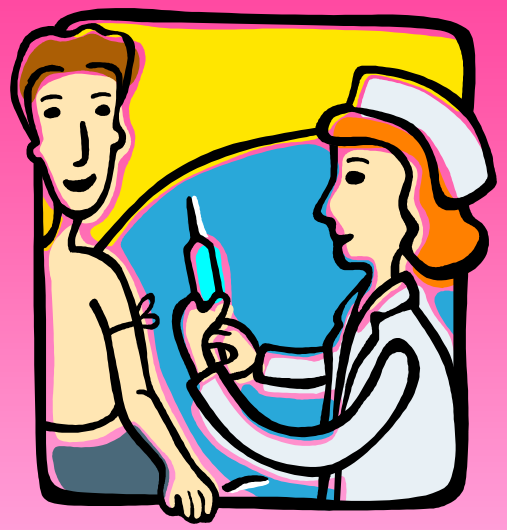
- Bilateral diagnostic mammogram
- +/- MRI

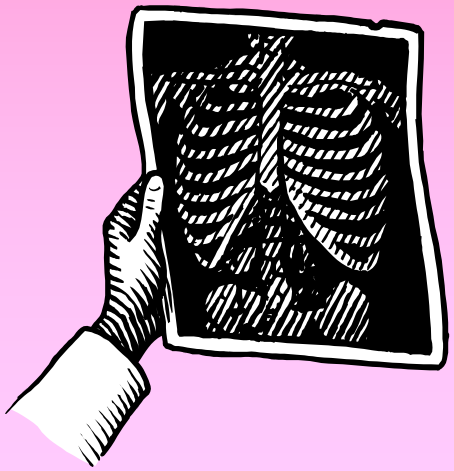
- Ultrasound with biopsy
  - Estrogen & progesterone receptor status
  - Her2/neu status



Work up

- CXR
- Labs
  - Complete blood cell count
  - General chemistries
  - LFTs
    - AST, ALT, Lactate dehydrogenase (LD), Bilirubin





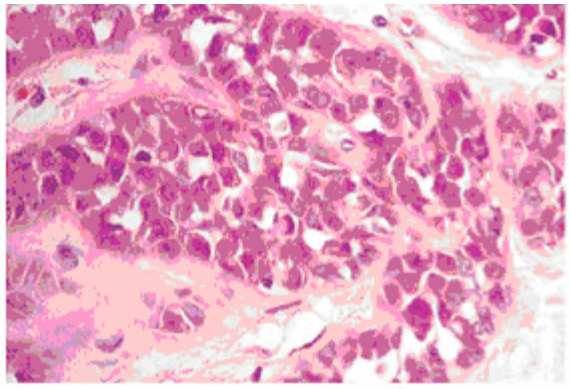
- +/- Bone scan
  - Clinical indication, stage II or III disease, or elevated alkaline phosphatase level
- +/- CT chest/abdomen/pelvis
  - Stage II or III disease, or elevated liver function tests

Breast Cancer Histology

- ***In situ* carcinomas**
  - **Confinement of malignant cells within the basement membrane**
  - **Ductal carcinoma *in situ* (DCIS)**
    - **15-20% of all breast cancer**
    - **Prognostic variables:**
      - **Large tumor size**
      - **Close or positive surgical margins**
      - **High nuclear grade (how abnormal cancer cells appear)**
      - **Presence of necrosis**
  - **Lobular carcinoma *in situ* (LCIS)**
    - **Marker for bilateral breast cancer**


Ductal Carcinoma in Situ

Lobular carcinoma *in situ*



Lakhani *Breast Cancer Res* 1999 **1**:31 doi:10.1186/bcr10

www.gastricbreastcancer.com/figures/figure3.htm

Breast Cancer Histology

- ***In situ* carcinomas**
  - **Paget's disease (with no tumor)**
    - **A rare form of breast cancer that begins in the milk passages (ducts) and spreads to the skin of the nipple and areola**
    - **The nipple may appear crusted, scaly, red, or oozing.**
    - **Prognosis is better if these nipple changes are the only sign of breast disease and no lump can be detected.**

Breast Cancer Histology

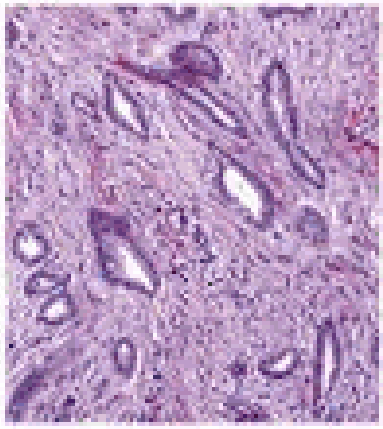
- **Microinvasion**
  - **Extension of cancer cells beyond the basement membrane with no focus more than 2mm in greatest dimension**

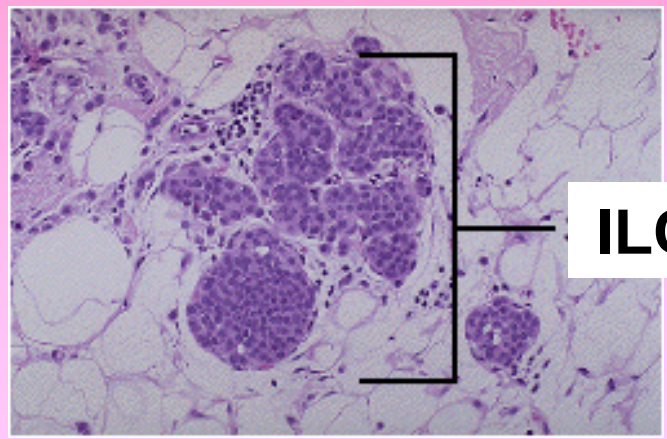
DCIS with microinvasion

http://www.bccancer.bc.ca/NR/rdonlyres/E74D74FF-9D8E-4FF1-8B39-92E61EFE5310/18064/ductal_carcinoma_range1.jpg

Breast Cancer Histology

- **Invasive carcinomas**
  - **Invasive ductal carcinoma (IDC)**
    - **Most common type (> 50% of cases)**
    - **Solid cords or groups of cells**
    - **Commonly associated with an *in situ* component**
  - **Invasive lobular carcinoma (ILC)**
    - **Cells appear singly or in small clusters in a target-like or single-file pattern**
    - **Tend to be aggressive and multicentric**
    - **Often not visualized mammographically**
    - **Increased risk of bilateral, multifocal breast cancer**


Invasive Carcinoma



Breast Cancer Histology

- **Invasive carcinomas**
  - **Inflammatory carcinoma**
    - **Rare (1-6% of cases in the U.S.)**
    - **Aggressive**
    - **Rapid onset of erythema, warmth, edema, and tenderness that does not resolve with antibiotics**
    - **Clinical diagnosis**
    - **Pathological findings: malignant cell invasion of dermal lymphatics**
    - **Poor prognosis**

Breast Cancer Histology

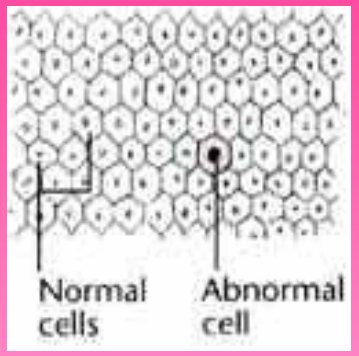
- **Other invasive carcinomas**
  - **Medullary carcinoma**
  - **Mucinous carcinoma**
  - **Tubular carcinoma**

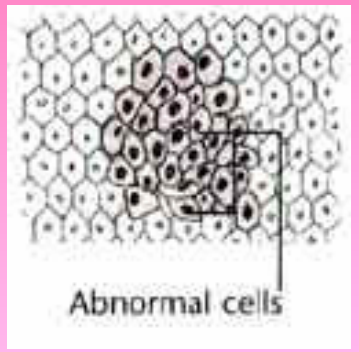
  } **Better prognosis**

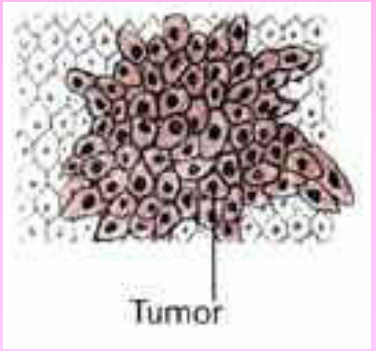
  - **Papillary or micropapillary carcinoma**
  - **Undifferentiated carcinoma**
  - **Squamous cell carcinoma**
  - **Adenoid cystic carcinoma**
  - **Secretory carcinoma**
  - **Cribiform carcinoma**

Breast Cancer Histologic Grading

- **Bloom-Richardson histologic grading system used for invasive carcinomas**
  - **Grade 1**
    - **Well differentiated**
    - **Relatively normal-looking cells that do not appear to be growing rapidly and are arranged in small tubules.**
  - **Grade 2**
    - **Moderately differentiated**
    - **Have features between grades 1 and 3**
  - **Grade 3**
    - **Poorly differentiated**
    - **The highest grade**
    - **Lack normal features and tend to grow and spread more aggressively**







- **Prognostic significance:**
  - **Grade 1 tumors tend to have a better prognosis than grade 2 or 3 tumors**

Hormone Receptor Status Testing

- Receptors are proteins on the surface of cells that can attach to certain substances circulating in the blood stream, like hormones.

- Normal breast cells and some breast cancer cells have receptors for the hormones estrogen and progesterone
  - Cancer cells positive for estrogen receptors = ER+
  - Cancer cells positive for progesterone receptors = PR+
  - In hormone receptor positive cells, the presence of estrogen or progesterone can fuel the growth of breast cancer cells

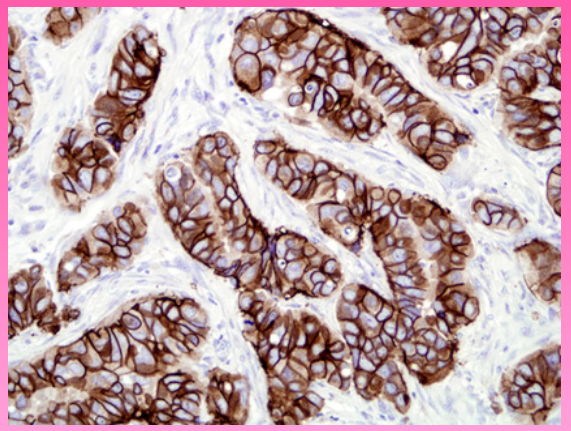
Hormone Receptor Status

- **Implications: Systemic therapy can be directed at blocking these hormone receptors (hormone therapy)**
  - **Selective Estrogen-Receptor Modulators (SERM)**
    - **Example: Tamoxifen**
    - **Blocks estrogen from attaching to receptors**
  - **Aromatase inhibitors**
    - **Examples: Arimidex and Femara**
    - **Blocks the effect of an enzyme that aids in production of estrogen**
  - **Aromatase inactivator**
    - **Example: Aromasin**
    - **Inactivates or destroys the enzyme that aids in estrogen production**

- **Women with hormone receptor-positive cancers tend to have a better prognosis and are much more likely to respond to hormone therapy than women with cancers without these receptors.**

HER-2/neu Testing

- **HER-2/neu gene**
  - **Proto-oncogene (also called c-erbB-2)**
  - **Codes for a transmembrane glycoprotein (p185)**
    - **Tyrosine kinase activity**
    - **Is a growth-promoting protein**
  - **Amplified and over-expressed in up to 30% of breast cancers**
  - **Over-expression is associated with**
    - **Tumor aggressiveness**
    - **Decreased disease-free survival in node-positive patients**
    - **Variable significance in node-negative patients**

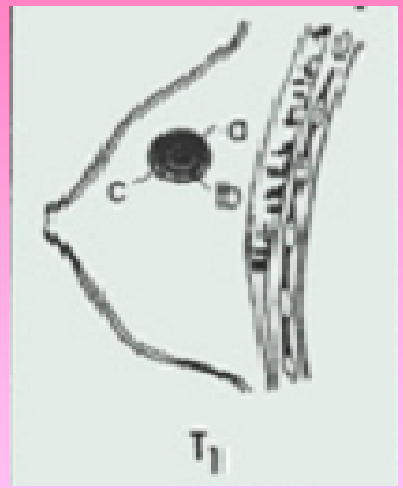


HER2-positive cancers are much more likely to benefit from treatment with drugs that target the HER2/neu protein, such as trastuzumab (Herceptin) and lapatinib (Tykerb)

Staging of Breast Cancer

- American Joint Committee on Cancer (AJCC)
- Primary tumor

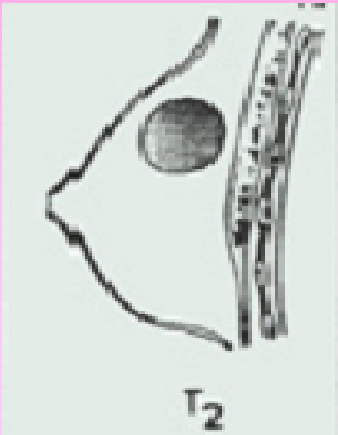
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple with no tumor
T1	Tumor 2cm or less
T1mic	Microinvasion ≤ 0.1cm
T1a	Tumor size > 0.1cm, but ≤ 0.5cm
T1b	Tumor size > 0.5cm, but ≤ 1cm
T1c	Tumor size > 1cm, but ≤ 2cm

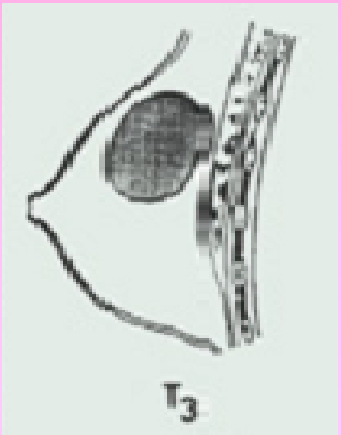


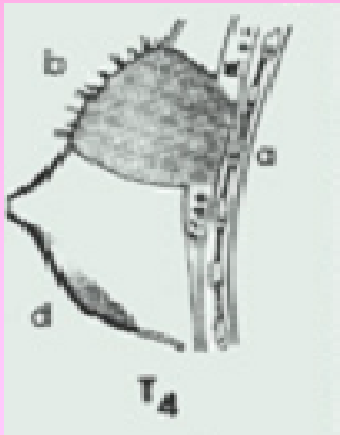
Staging of Breast Cancer

- **Primary Tumor**

T2	**Tumor size > 2cm, but ≤ 5cm**
T3	**Tumor size > 5cm**
T4	**Tumor of any size with direct extension to chest wall or skin**
T4a	**Extension to chest wall, not including pectoralis muscle**
T4b	**Edema (including *peau d'orange*), or ulceration of the skin, or satellite skin nodules confined to the same breast**
T4c	**Both T4a and T4b**
T4d	**Inflammatory carcinoma**







Staging of Breast Cancer

- **Clinical regional lymph node staging**

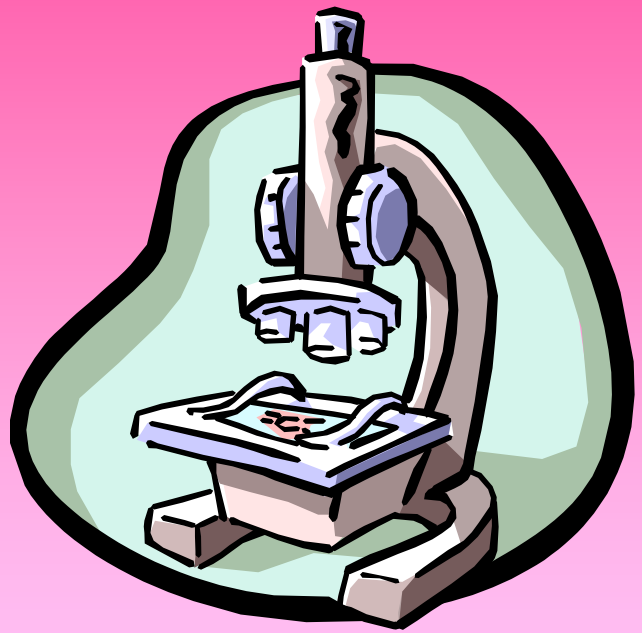
Nx	LNs cannot be assessed
N0	No regional LN metastasis
N1	Movable ipsilateral axillary LN(s)
N2	Fixed or matted ipsilateral axillary LNs, or ipsilateral internal mammary LN in the absence of axillary LNs
N2a	Ipsilateral axillary LNs fixed to one another (matted) or to other structures
N2b	Clinically apparent ipsilateral internal mammary LN in the absence of axillary LNs

N3	Ipsilateral infraclavicular LN(s) +/- axillary LN(s); or ipsilateral internal mammary LN(s) + axillary LN(s); or supraclavicular LN(s) +/- axillary or internal mammary LN(s)
N3a	Ipsilateral infraclavicular LN(s)
N3b	Ipsilateral internal mammary LN(s) + axillary LN(s)
N3c	Ipsilateral supraclavicular LN(s)

Staging of Breast Cancer

- **Pathologic regional lymph node staging**

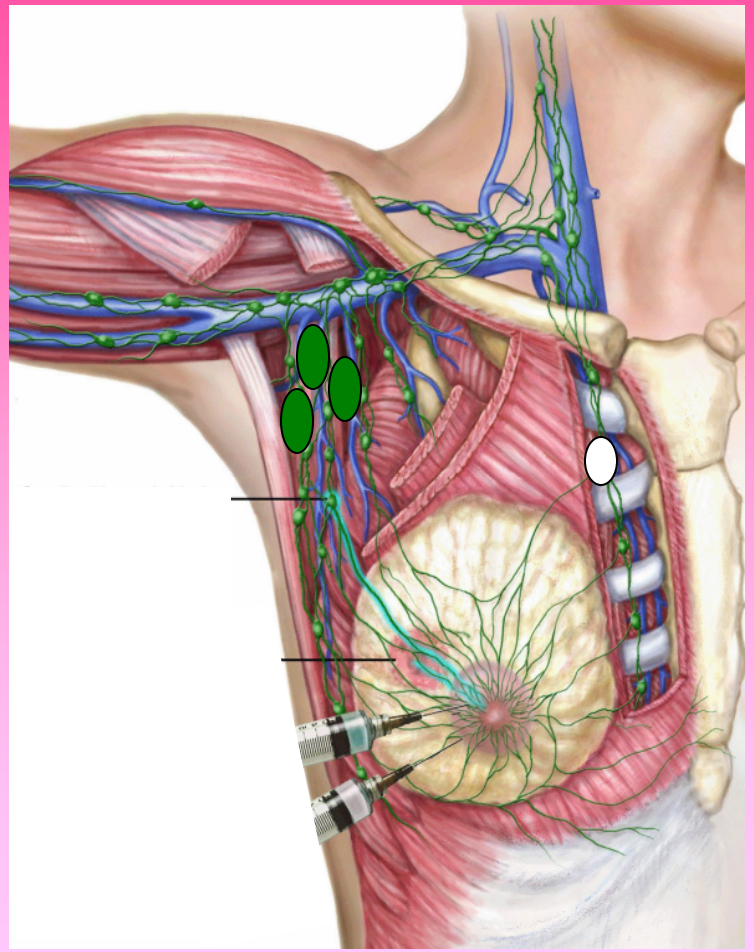
pNx	Cannot be assessed
pN0	No regional LN metastasis histologically, no additional examination for isolated tumor cells (ITC)
pN0(i-)	Negative histologically, negative immunohistochemically (IHC)
pN0(i+)	Negative histologically, positive IHC
pN0 (mol-)	Negative histologically, negative molecular findings (RT-PCR)
pN0 (mol+)	Negative histologically, positive molecular findings (RT-PCR)



Staging of Breast Cancer

- **Pathologic regional lymph node staging**

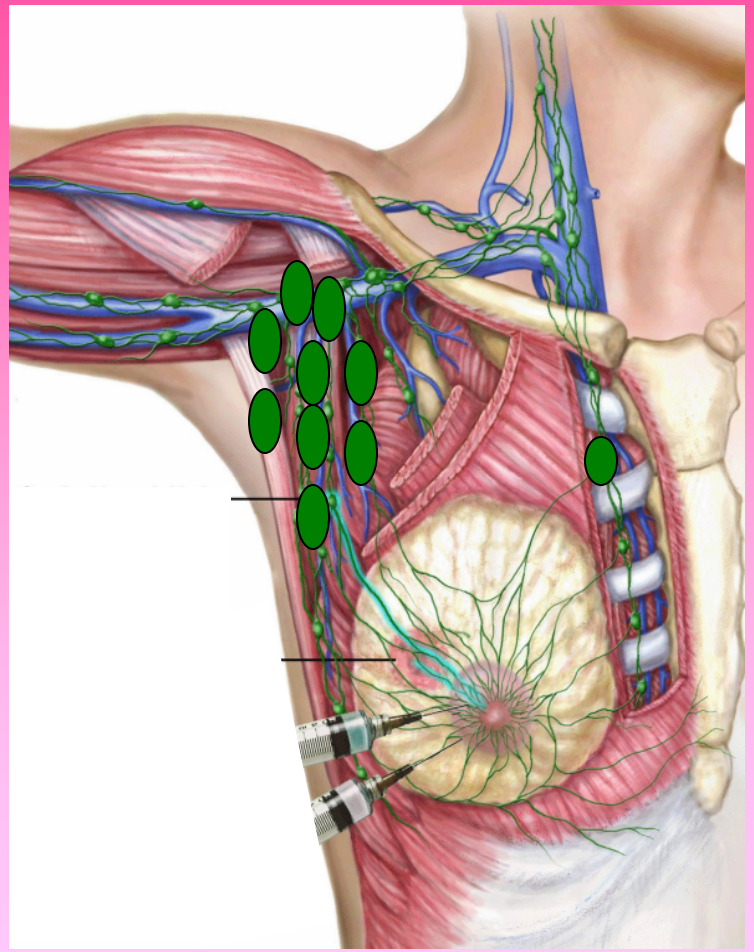
pN1	**1-3 axillary LNs, and/or microscopic disease in ipsilateral internal mammary (IM) LNs detected by sentinel LN dissection, but not clinically apparent**
pN1mic	**Micrometastasis (> 0.2mm, ≤ 2 mm)**
pN1a	**1-3 axillary LN(s)**
pN1b	**Microscopic disease in ipsilateral IM LN(s) detected by sentinel LN dissection, but not clinically apparent**
pN1c	**1-3 axillary LN(s) + microscopic disease in ipsilateral IM LN(s) detected by sentinel LN dissection, but not clinically apparent**



Staging of Breast Cancer

- **Pathologic regional lymph node staging**

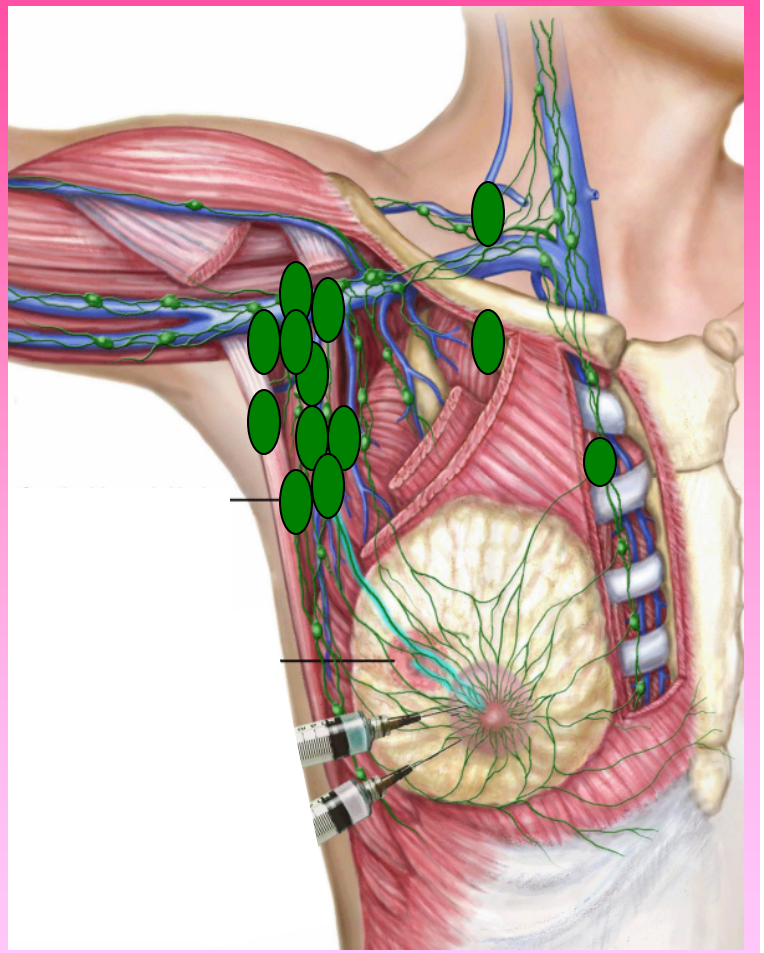
pN2	**4-9 axillary LNs, or in clinically apparent ipsilateral IM LNs in the absence of axillary LNs**
pN2a	**4-9 axillary LNs (at least one tumor deposit > 2mm)**
pN2b	**Metastasis in clinically apparent IM LNs in the absence of axillary LNs**



Staging of Breast Cancer

- **Pathologic regional lymph node staging**

pN3	≥ 10 axillary LNs, or in infraclavicular LNs, or in clinically apparent ipsilateral IM LNs, or in ipsilateral supraclavicular LNs
pN3a	≥ 10 axillary LNs (at least one tumor deposit > 2mm), or in infraclavicular LNs
pN3b	Clinically apparent ipsilateral IM LNs + ≥ 1 axillary LN(s), or in > 3 axillary LNs with microscopic disease in ipsilateral IM LNs detected by sentinel LN dissection but not clinically apparent
pN3c	Ipsilateral supraclavicular LNs



- **Distant metastatic disease staging**

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Staging of Breast Cancer

- **Stage grouping**

Stage	Tumor size	Nodal involvement	Distant Metastasis
0	Tis	N0	M0
I	T1	N0	M0
IIA	T2	N0	M0
	T1-0	N1	M0
IIB	T3	N0	M0
	T2	N1	M0
IIIA	T3	N1	M0
	T0-3	N2	M0
IIIB	T4	N0-2	M0
IIIC	any T	N3	M0
IV	any T	any N	M1

Pictures courtesy of http://www.faslodex.com/

Question #3

- **Beginning at what age does the American Cancer Society recommend annual mammogram screening in women of average risk for breast cancer?**

- **A) 30 y/o**
- **B) 35 y/o**
- **C) 40 y/o**
- **D) 45 y/o**
- **E) 50 y/o**

Question #3

- **Beginning at what age does the American Cancer Society recommend annual mammogram screening in women of average risk for breast cancer?**

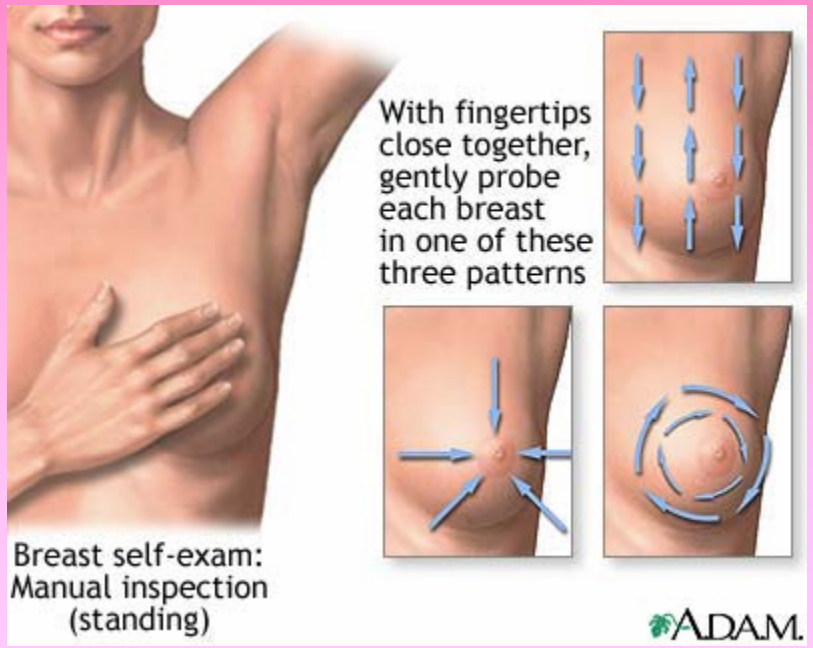
- **A) 30 y/o**
- **B) 35 y/o**
- **C) 40 y/o**
- **D) 45 y/o**
- **E) 50 y/o**

- **Woman ≥ 40 y/o of average risk for developing breast cancer**
  - **Annual screening mammogram**
  - **Annual Clinical Breast Exam**

"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?rnav=cri. Last revised on 09/04/2008.

Breast Cancer Screening

- **American Cancer Society**
- **Woman < 40 y/o**
  - **May begin Breast Self Exams (BSE) at 20 y/o**
    - **To recognize the normal texture of their breasts**
    - **To be able to report any breast changes to their physician**
  - **Clinical Breast Exam (CBE) every 3 yrs.**



"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?rnav=cri. Last revised on 09/04/2008.

Breast Cancer Screening

- **Women at moderate risk**
  - **15-20% lifetime risk of breast cancer**
    - **As defined by BRCAPRO or other models that are largely dependent on family history**
  - **Personal history of**
    - **Invasive breast cancer**
    - **Ductal carcinoma in situ (DCIS)**
    - **Llobular carcinoma in situ (LCIS)**
    - **Atypical ductal hyperplasia (ADH)**
    - **Atypical lobular hyperplasia (ALH)**
  - **Extremely dense breasts or unevenly dense breasts when viewed by mammograms**
  - **Recommendations:**
    - **Annual mammograms starting at age 40 y/o**
    - **Should discuss the benefits and limitations of adding an annual screening MRI**

"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?rnav=cri. Last revised on 09/04/2008.

Breast Cancer Screening

- **Women at high risk**
  - **> 20% lifetime risk of breast cancer**
  - **Proven mutation in BRCA1 or BRCA2**
  - **First-degree relative (parent, brother, sister, or child) with a BRCA1 or BRCA2 gene mutation**
  - **Radiation therapy to the chest between the ages of 10-30 years old**
  - **Personal history or family history in a first-degree relative of**
    - **Li-Fraumeni syndrome**
    - **Cowden syndrome, or**
    - **Bannayan-Riley-Ruvalcaba syndrome**
  - **Recommendations:**
    - **Begin screening at age 30 y/o**
    - **Annual mammogram and MRI**
    - **Annual Clinical Breast Exam**
    - **For patients who have BRCA1 or BRCA2 mutations**
      - **Annual pelvic exams with transvaginal U/S of the ovaries, and Ca-125**

"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?mav=cri. Last revised on 09/04/2008.

Question #4

- **On average, screening mammograms detect what percentage of malignancies?**

- **A) < 1%**
- **B) 4%**
- **C) 10%**
- **D) 20%**
- **E) 35%**

Question #4

- **On average, screening mammograms detect what percentage of malignancies?**

- **A) < 1%**
- **B) 4%**
- **C) 10%**
- **D) 20%**
- **E) 35%**

- **For every 1000 screening mammograms:**
  - **80 (8%) patients will be recalled for additional imaging**
  - **10 (1%) patients will require tissue diagnosis (biopsy)**
  - **3 (0.003%) patients will have a malignancy**

Harris J, et al. Diseases of the breast. Philadelphia: Lippincott Williams & Wilkins, 2004.

Mammogram

- **Mammography has been associated with:**
  - **Detection of earlier stage breast cancers**
  - **Reduction in breast cancer mortality rates**

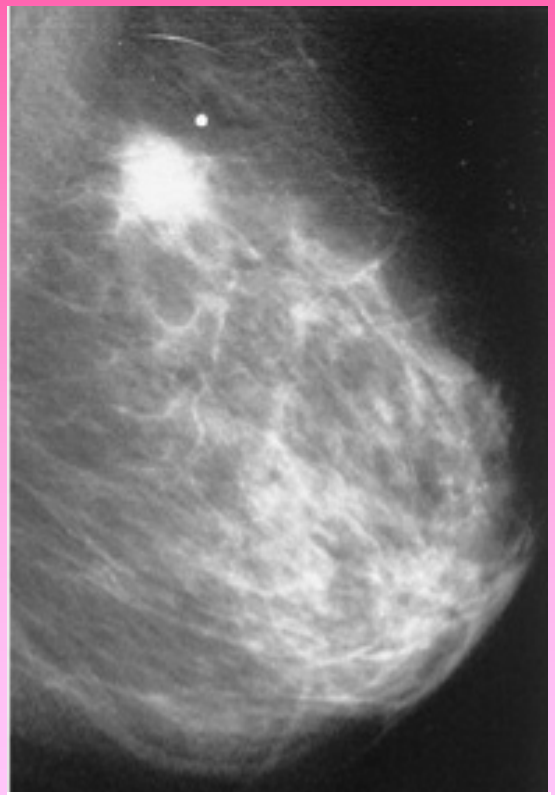
- **Mammography for all woman:**
  - **Sensitivity: ~90% (60-95%)**
  - **Specificity: ~94% (50-98%)**
  - **Positive Predictive Value: 8-14% for all screened patients, higher for symptomatic patients**

Harris J, et al. Diseases of the breast. Philadelphia: Lippincott Williams & Wilkins, 2004.

http://www.med.yale.edu/intmed/cardio/imaging/anatomy/breast_anatomy/graphics/breast_anatomy.gif

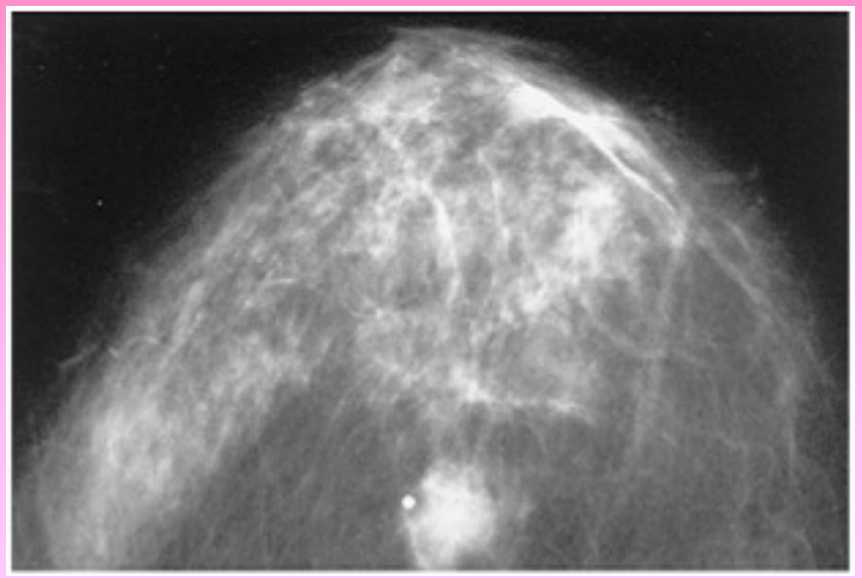
Mammogram

- **Screening Mammogram**
  - **Routine images in asymptomatic women**
  - **2 views: craniocaudal and mediolateral obliques of each breast**



Craniocaudal

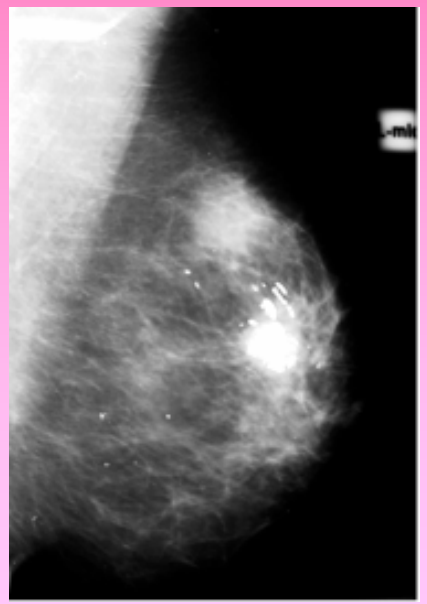
Mediolateral

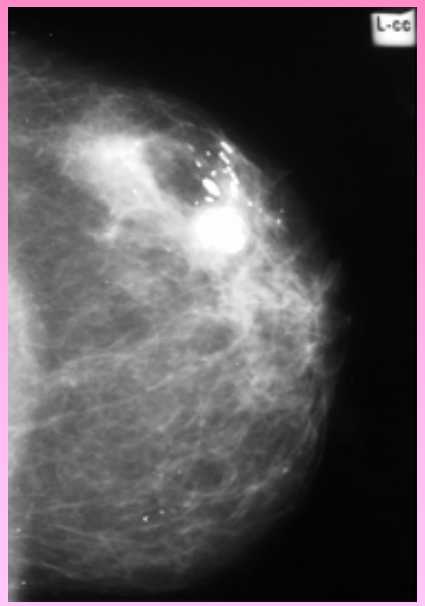


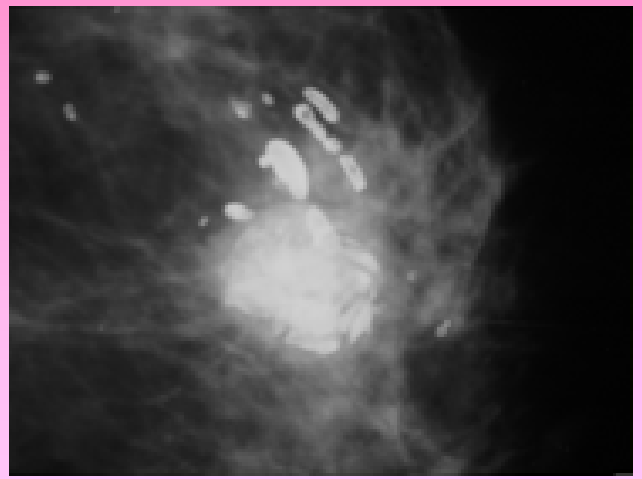
"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?rnav=cri. Last revised on 09/04/2008.

Mammogram

- **Diagnostic Mammogram**
  - **Used to characterize abnormalities detected at screening or in women with palpable masses**
  - **Additional magnification views**
  - **Generally done with the radiologist present to determine the need for additional views and/or follow-up studies.**







"American Cancer Society Guidelines for Early Breast Cancer Detection." http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_Can_breast_cancer_be_found_early_5.asp?rnav=cri. Last revised on 09/04/2008.

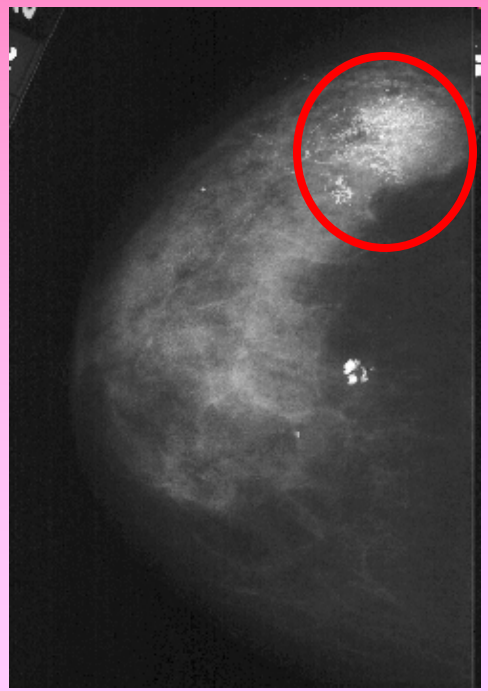
Mammogram Classification System

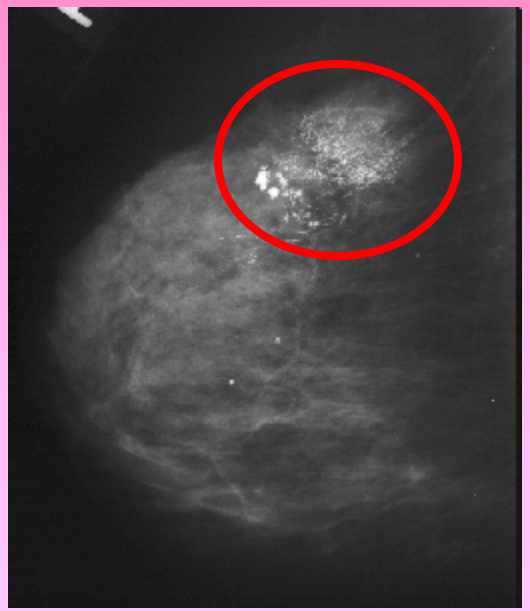
- **Breast Imaging Reporting and Data System (BI-RADS)**

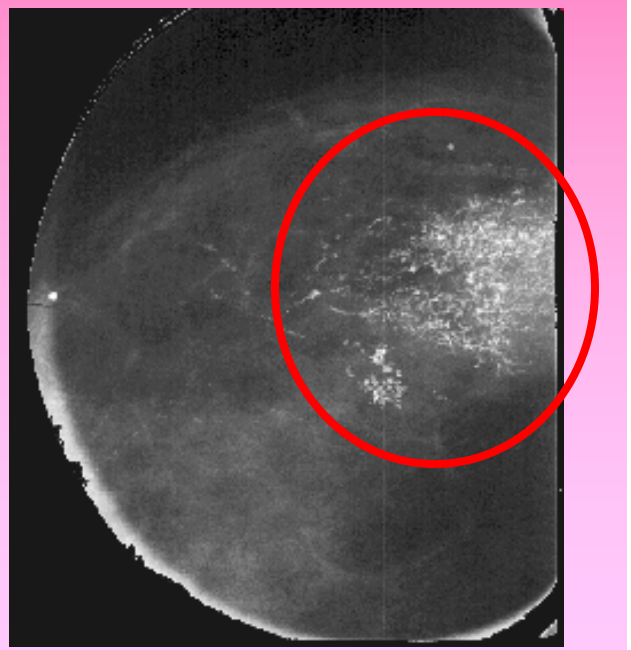
Category 0	**Need additional imaging evaluation**	**Screening situation. Need additional magnification views, spot compression, U/S, etc.**
Category 1	**Negative**	**No findings to comment on.**
Category 2	**Benign finding**	**Calcified fibroadenomas, secretory calcifications, cysts, lipomas, hamartomas, etc.**
Category 3	**Probable benign finding — short interval follow-up suggested**	**Not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability.**
Category 4	**Suspicious abnormality – biopsy should be considered**	**Do not have the characteristic morphologies of breast CA, but have definite probability of being malignant**
Category 5	**Highly suggestive of malignancy — appropriate action should be taken**	**Characteristic of breast cancer.**

Mammographic Findings

- **Ductal carcinoma in situ**
  - **Clusters of microcalcifications (> 5)**
  - **Calcifications**
    - **100-300 μm in size**
    - **Rod-like, tubular, branching, or punctate**

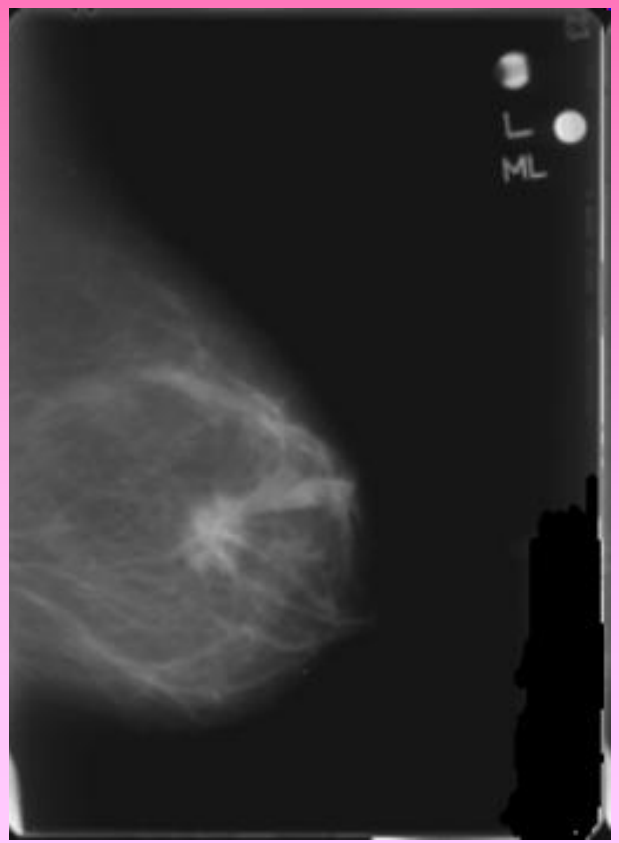


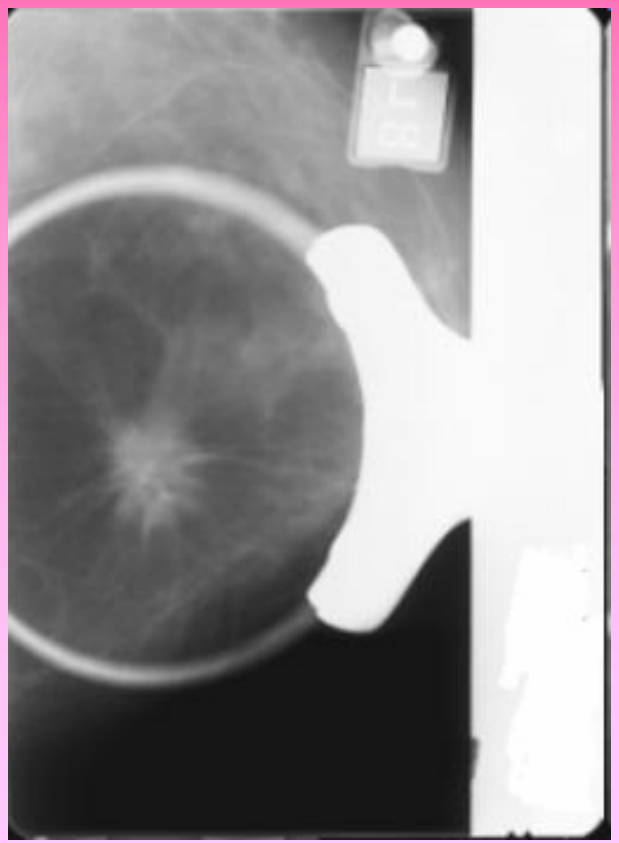




Mammographic Findings

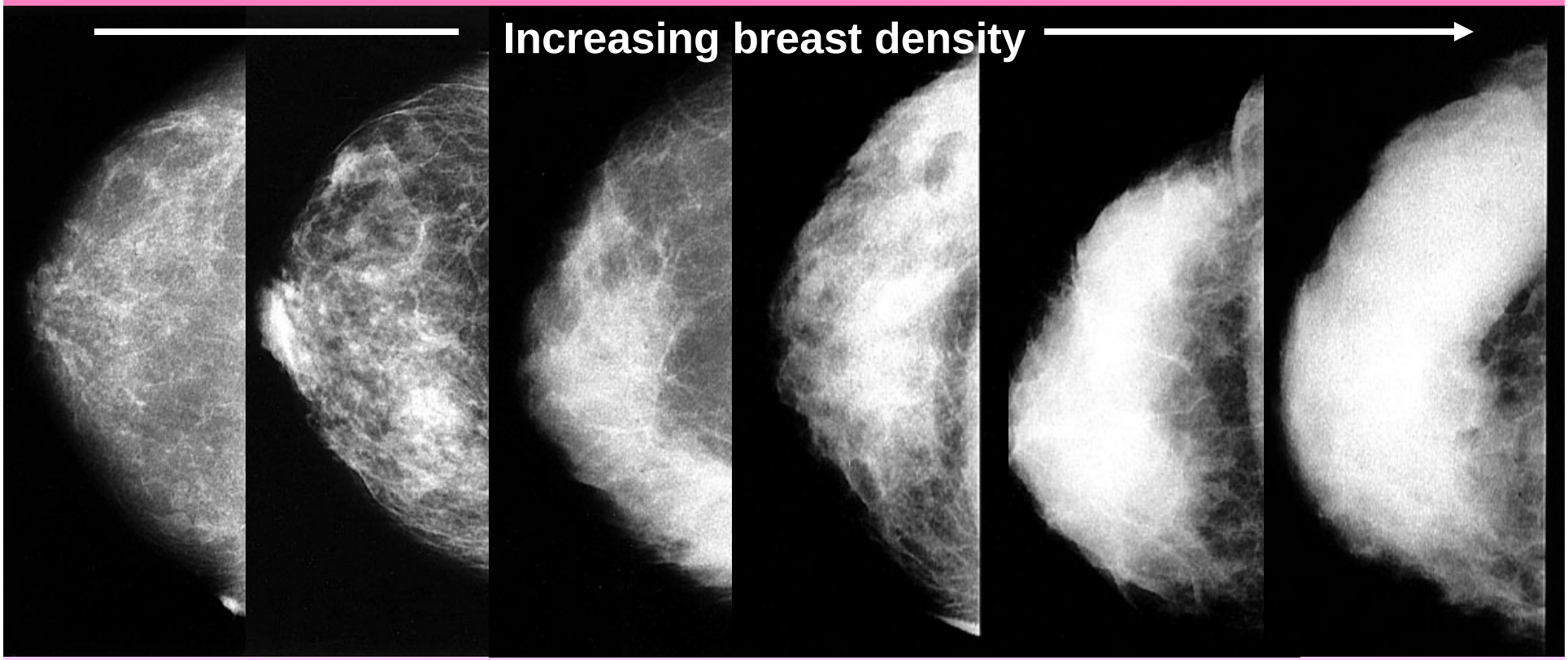
- **Invasive carcinoma**
  - **Ill-defined mass with spiculated margins**
  - **Linear, radiated, or spiculated changes around a central focus**





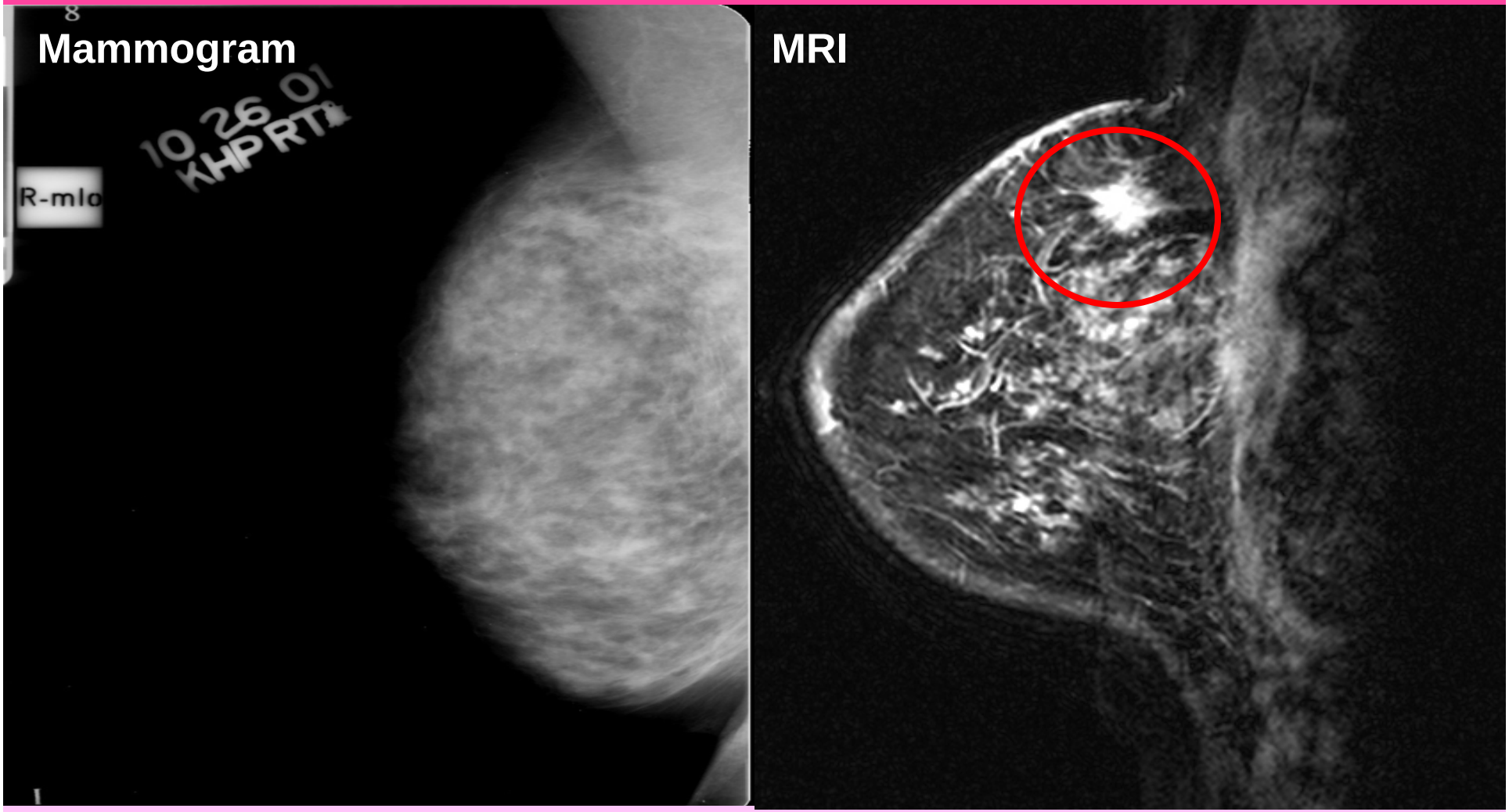
Limitations of Mammography

- **Reduced sensitivity for dense breasts**
- **Sometimes difficult to determine extent of disease in the breast**
- **May miss small lesions and certain histologies**
  - **E.g. Invasive lobular carcinoma**



Boyd NF *Curr Oncol Rep* 3:314-321, 2001

Mammography vs. MRI

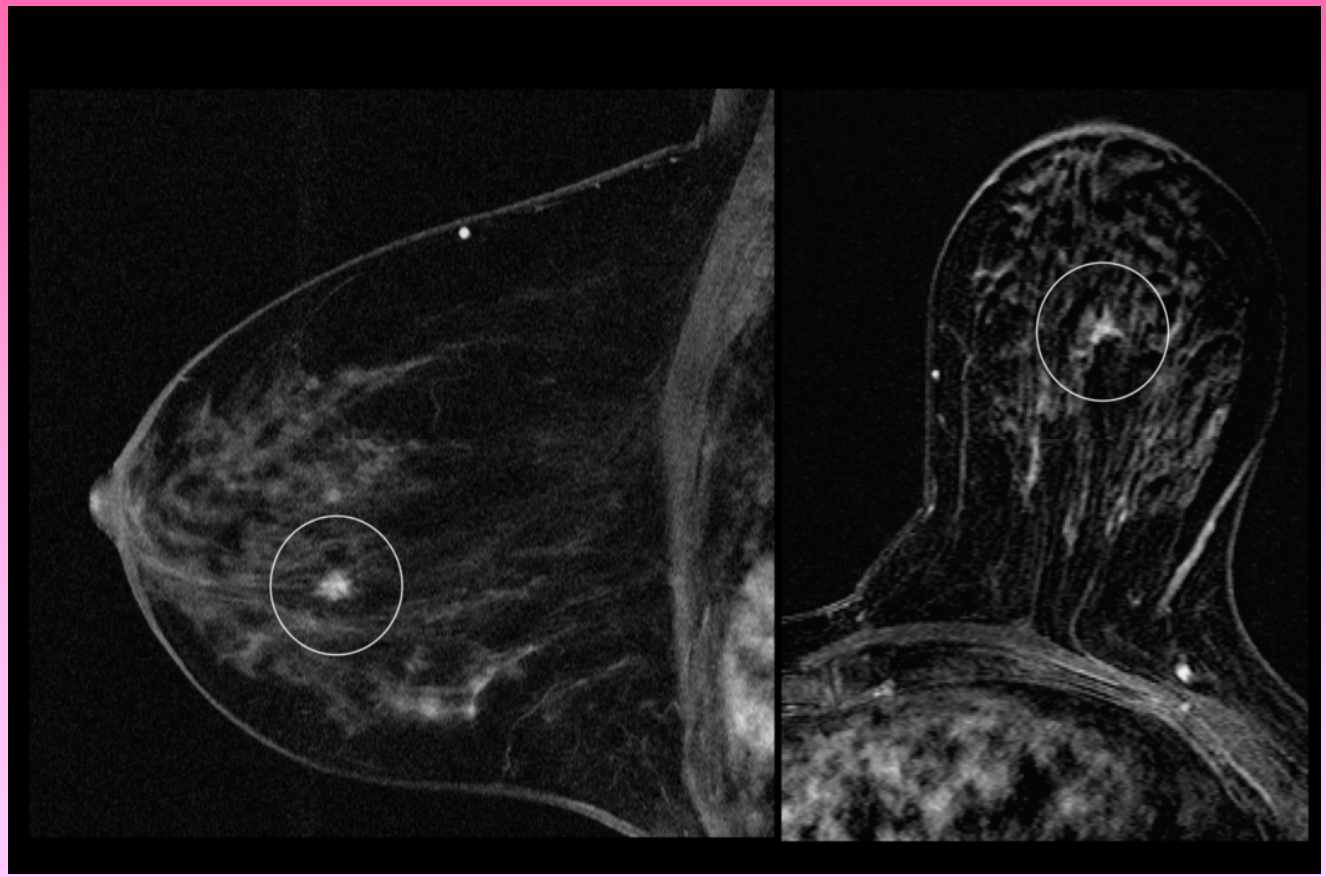


- **Increased density decreases sensitivity of mammography**

Courtesy of Bernard J R, Mayo Clinic Jacksonville

Magnetic Resonance Imaging (MRI)

- **MRI has been found to be more sensitive than mammogram and clinical breast exams in detecting invasive breast cancer in women at high risk for familial breast cancer**



Kriege M, et al. "Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition." N Engl J Med 2004;351:427-437.

Courtesy of Bernard J R, Mayo Clinic Jacksonville

Question #5

- **Magnetic Resonance Imaging (MRI) detects what percentage of contralateral otherwise occult malignancies?**

- **A) < 1%**
- **B) 3-4%**
- **C) 10-15%**
- **D) 20-25%**
- **E) 35%**

Question #5

- **Magnetic Resonance Imaging (MRI) detects what percentage of otherwise occult contralateral malignancies in women of any age, recently diagnosed with breast carcinoma?**

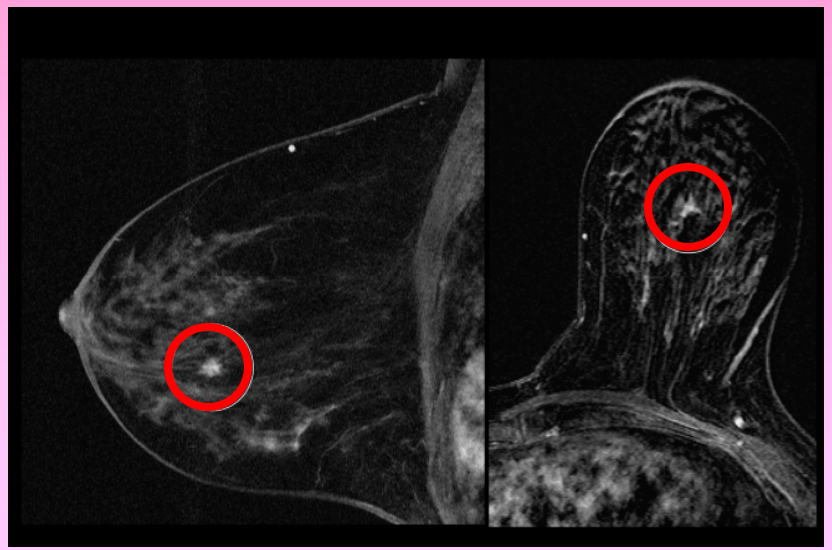
- **A) < 1%**
- **B) 3-4%**
- **C) 10-15%**
- **D) 20-25%**
- **E) 35%**

- **Mayo Clinic experience**
- **Review of 401 women with newly diagnosed breast carcinoma who underwent MRI**
- **13 patients (3.2%) were found to have pathologically confirmed, otherwise occult malignancies in the contralateral breast.**

Bernard J R, Vallow L A, et al. “Identification of Risk Factors in Mammographically Occult Contralateral Breast Carcinoma Detected by Magnetic Resonance Imaging (MRI).” J Clin Oncol, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No.18S (June 20 Supplement), 2007:614.

Magnetic Resonance Imaging (MRI)

- **Mayo Clinic Jacksonville**
- **Increased age is an independent risk factor for breast cancer**
- **Further evaluation of the value of MRI in detecting occult malignancies in the contralateral breast in women > 70 y/o**
  - **Retrospective review**
  - **159 women > 70 y/o, with newly diagnosed breast cancer**
  - **9 (5.7%) women were found to have synchronous, pathologically confirmed, otherwise occult malignances in the contralateral breast.**



Bernard J R, Vallow L A, et al. “Mammographically Occult Contralateral Breast Carcinoma Detected by Magnetic Resonance Imaging in the Elderly.” J Clin Oncol 26:2008 (May 20 supplement; abstr 500).

Magnetic Resonance Imaging (MRI)

	MRI	Mammogram
Sensitivity	**77-100%**	**16-40%**
Specificity	**81-99%**	**93-99%**

- **Limitations of Breast MRI:**
  - **Expensive**
  - **Higher recall rates**
  - **Higher false positive rates because of lower specificity than mammography**

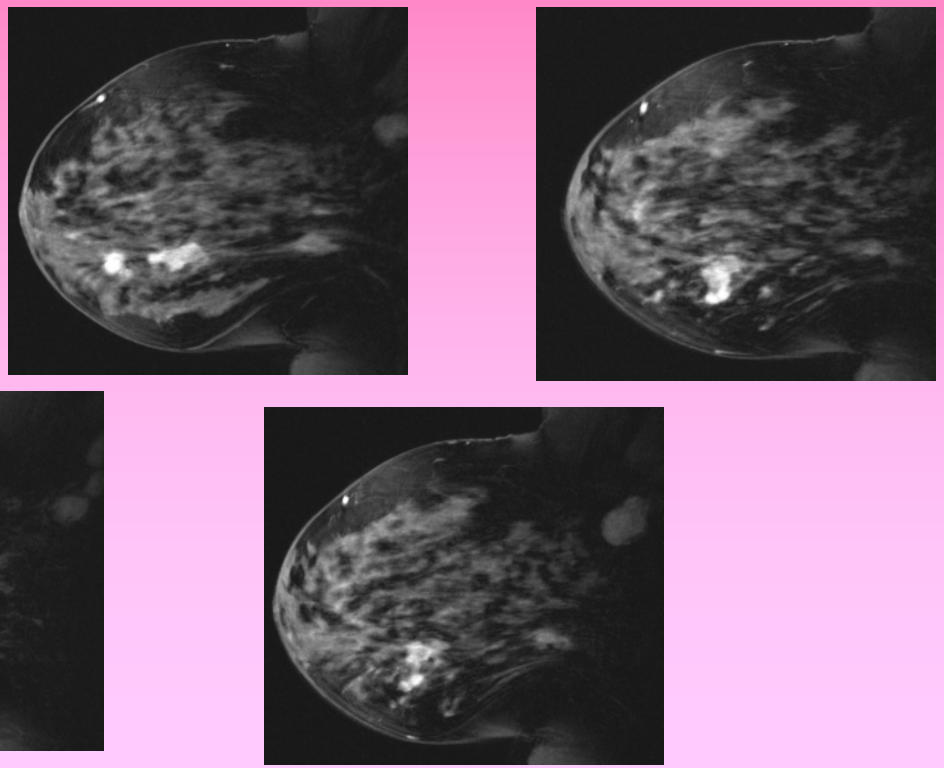
Saslow D, et al. "American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography." *CA Cancer J Clin* 2007;57;75-89.

Indications for Breast MRI

- **Screening for breast cancer in certain moderate to high risk patient populations (American Cancer Society)**

- **Evaluation of breasts with increased density**
  - **More sensitive than mammography**

MRI

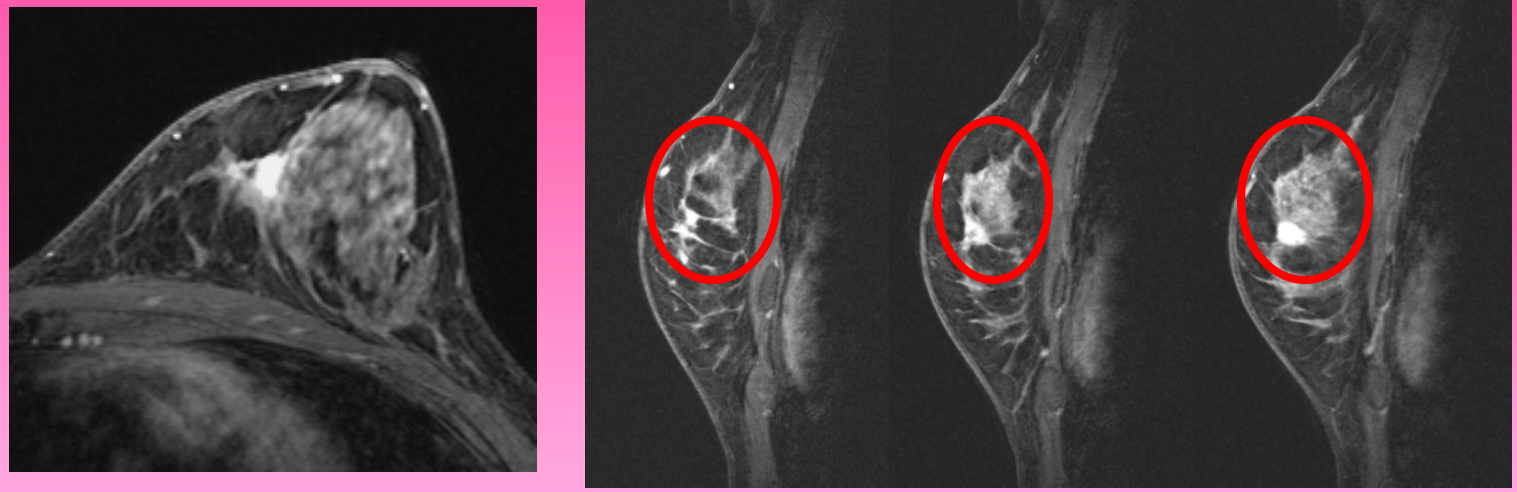


Courtesy of Bernard J R, Mayo Clinic Jacksonville

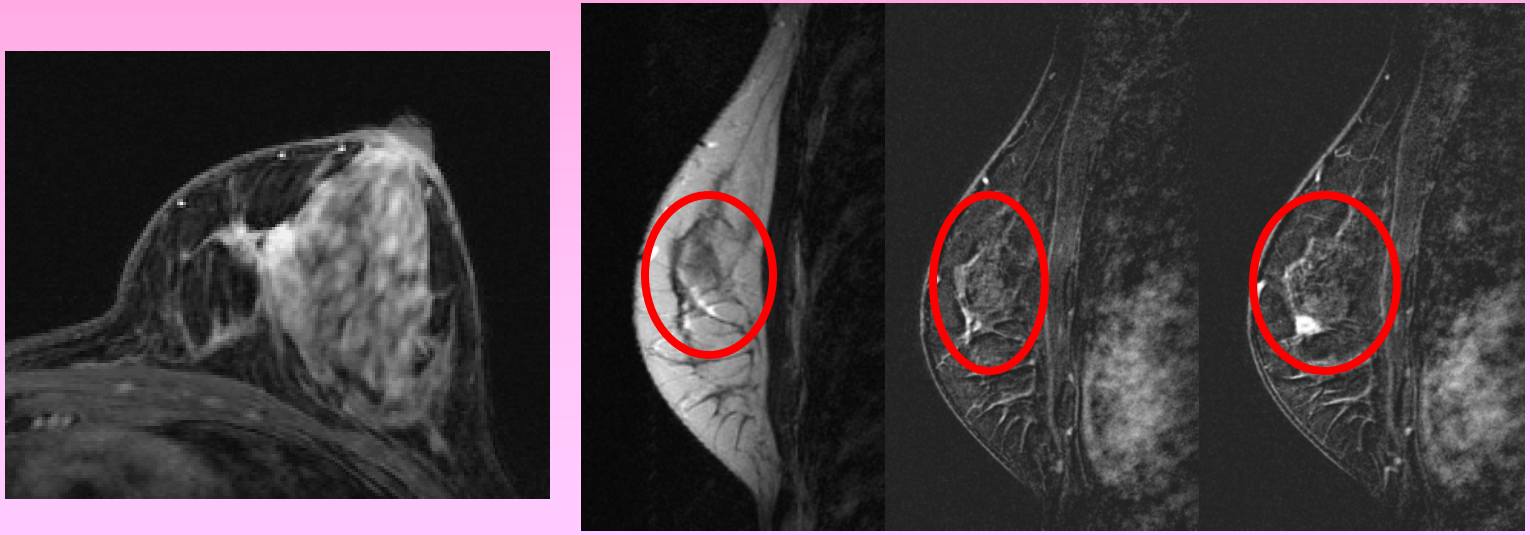
Indications for Breast MRI

- **Monitoring treatment response to neoadjuvant chemotherapy**

Post Cycle 1



Post Cycle 2



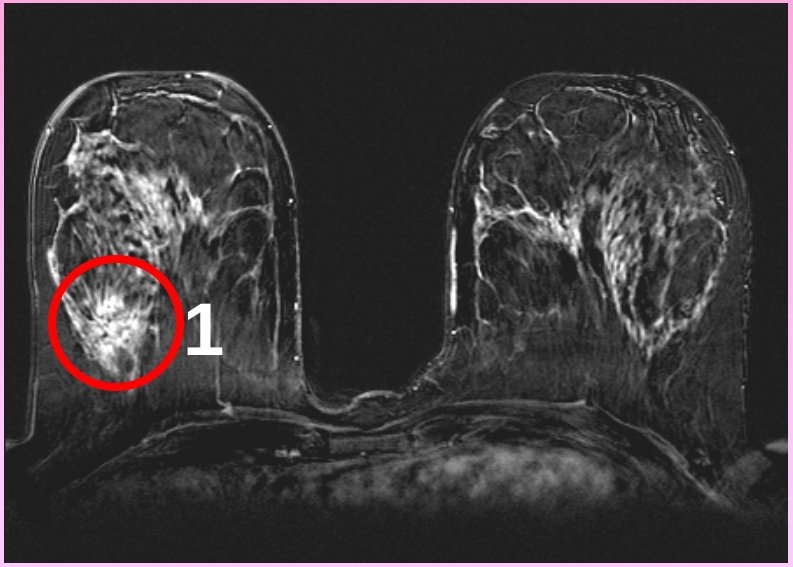
Courtesy of Bernard J R, Mayo Clinic Jacksonville

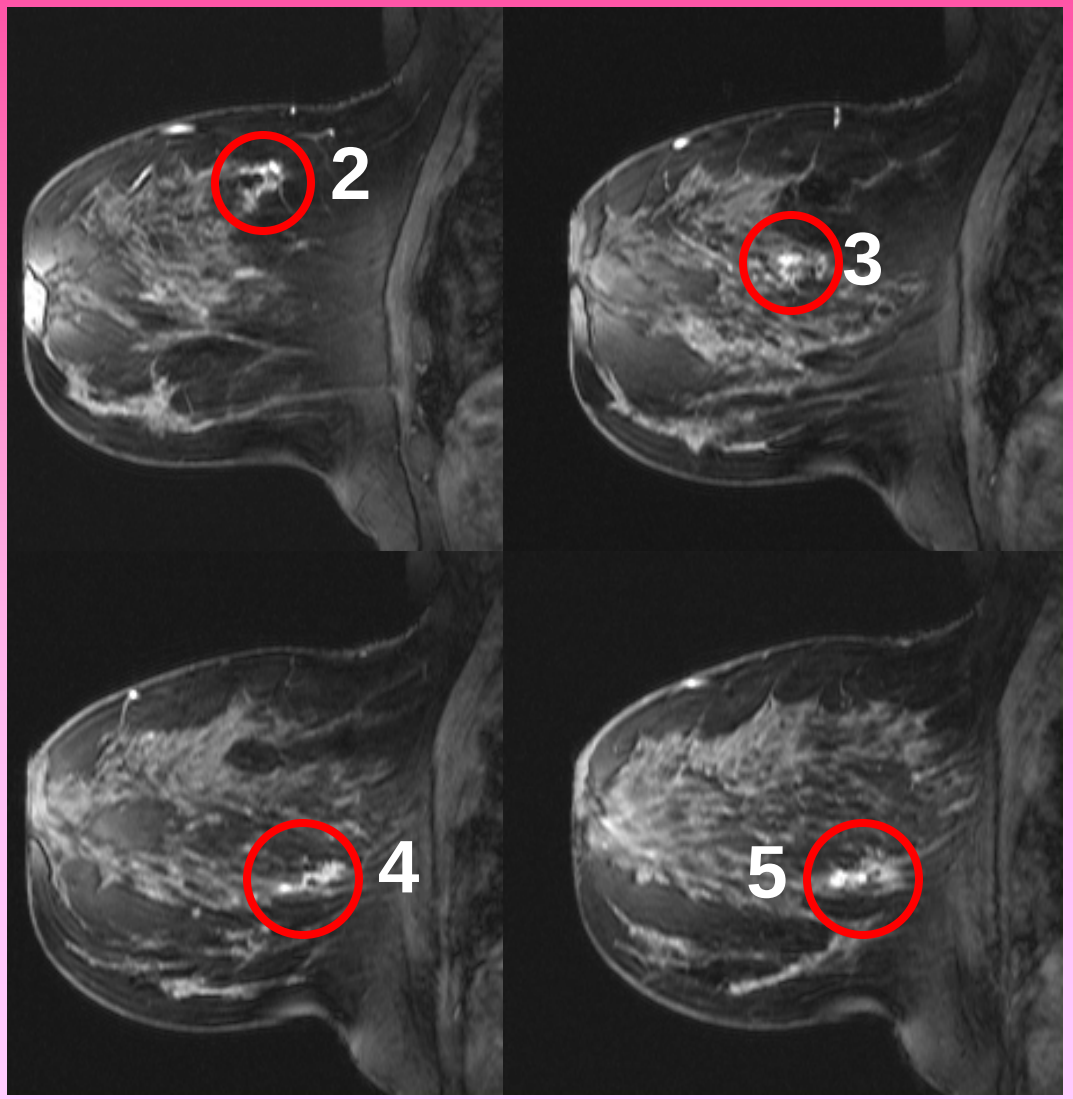
Indications for Breast MRI

- **Monitoring women with a personal history of breast cancer**
  - **Evaluate the extent of disease in the ipsilateral breast**
  - **Evaluate the presence of disease in the contralateral breast**

Indications for Breast MRI

- **Aid in surgical planning for breast cancer treatment**
  - **Evaluate for the presence of disease in multiple quadrants of the same breast (multicentric)**
  - **Breast conserving therapy (BCT) vs. mastectomy**





Courtesy of Bernard J R, Mayo Clinic Jacksonville

Summary

- **Breast cancer is a highly prevalent disease**
- **Improvements in screening have lead to an increase in detection of early stage breast cancers**
- **Detection of earlier stage breast cancers has allowed patients more treatment options and has decreased mortality rates**
- **Breast cancer is generally thought to be a slow growing disease with a propensity to spread lymphatically to the axilla and distantly to bones.**
- **The greatest risk factor for breast cancer development is increasing age**

Summary

- **American Cancer Society recommends**
  - **Women ≥ 40 y/o:**
    - **Annual mammogram**
    - **Annual clinical breast exam**
  - **Women with a moderate risk profile for developing breast cancer:**
    - **Should discuss the benefits and limitations of adding an annual screening MRI**
  - **Women with a high risk profile for developing breast cancer:**
    - **Begin screening at age 30 y/o**
    - **Annual mammogram and MRI**
    - **Annual Clinical Breast Exam**

- **MRI does not reliably detect calcifications, so it should not be used to replace mammography screening**

Summary

- **Breast MRI should be used for**
  - **Screening in select groups of moderate to high risk women**
  - **Evaluation of breasts with increased density**
  - **Monitory neoadjuvant treatment response**
  - **Evaluation of extent of disease in women with a personal history of breast cancer**
  - **Surgical planning for breast cancer treatment**
    - **Breast conservation vs. mastectomy**

Thank You

Questions?