



# Overview of Breast Cancer & its Clinical Management

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**South Bend  
Indiana**

 *Michiana Hematology Oncology, PC*  
Advanced Centers for Cancer Care®







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## Summary of the talk

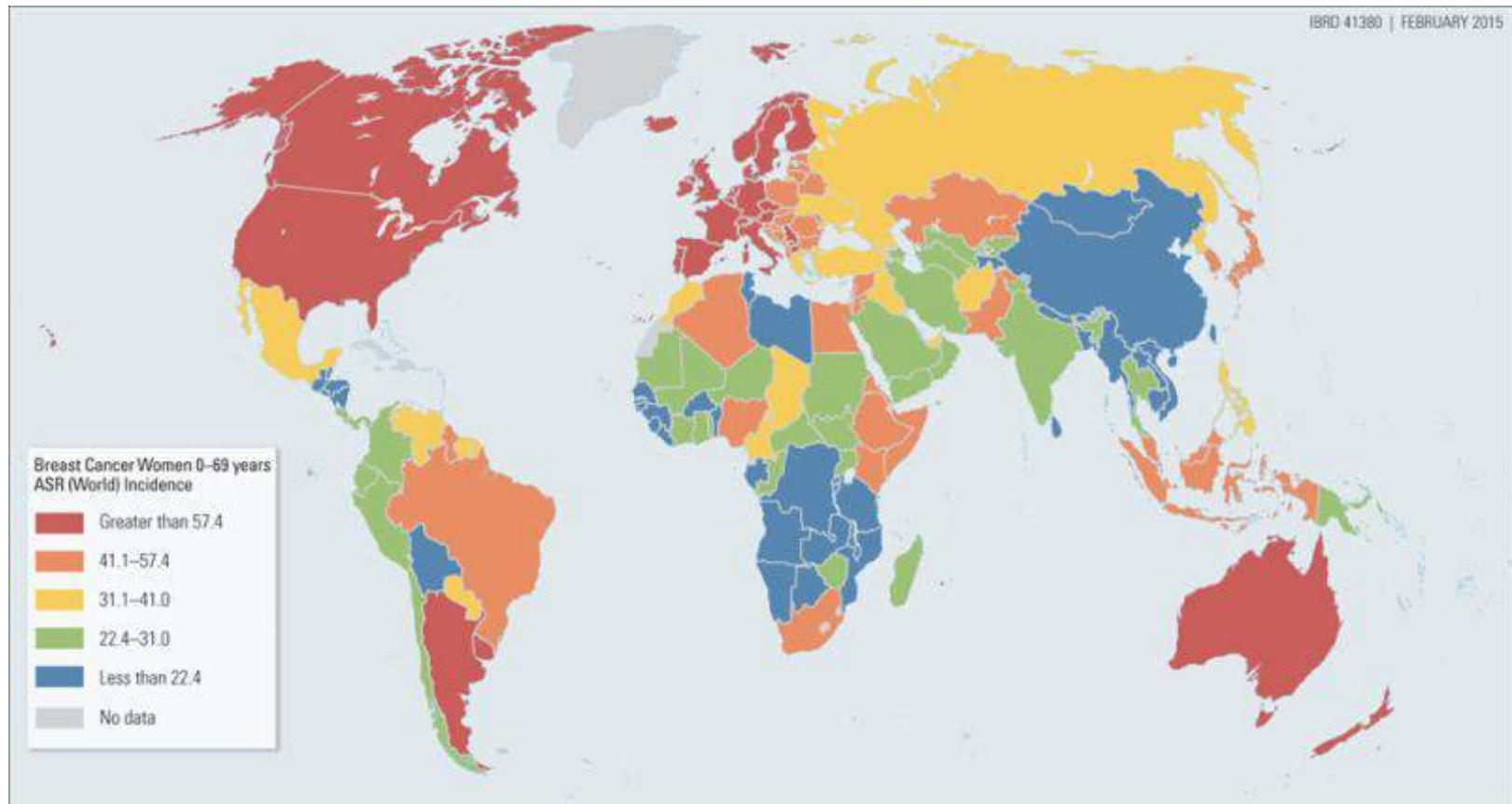
- Epidemiology of breast cancer
- Screening & diagnostic techniques
- Approach to newly diagnosed breast cancer
  - ✓ Multidisciplinary
  - ✓ Local therapy
  - ✓ Systemic therapy
- Approaches to systemic therapy for breast cancer
  - ✓ Based on stage
    - Early stage
    - Locally advanced
    - Metastatic
  - ✓ Based on biology
    - ER positive
    - Her-2 positive
    - Triple negative
- Questions

# Breast cancer: Basic concepts

- Global health concern
  - ✓ Most common cancer diagnosed in women
  - ✓ Leading cause of cancer death in women
  - ✓ Most common cause of death in women ages 40-49
- Clinical heterogeneity
- Opportunities for prevention
- Stage at diagnosis (in the US):
  - ✓ 95% early (stages I-II (T2N1) or locally advanced (T3N0 – stage III)
  - ✓ 5% stage IV



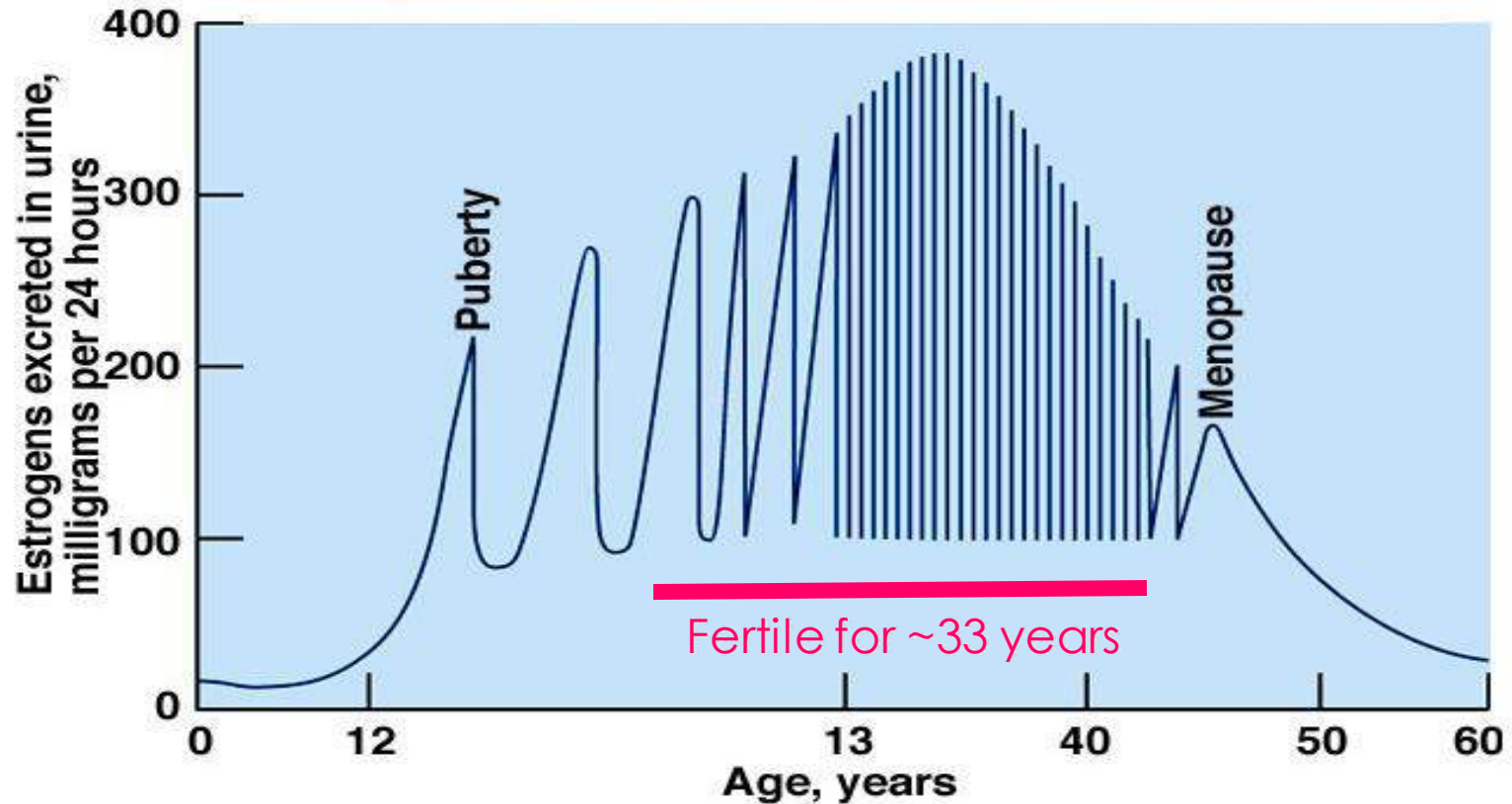
## Worldwide Incidence of Breast Cancer (2015)



# Development of Breast Cancer



## Lifetime Estrogen Exposure: A major risk factor for breast cancer



# Factors that modify breast cancer risk in women

## High Risk Profile

- Early menarche
- Late menopause
- Never been pregnant
- Older age at first pregnancy
- No breast feeding
- Hormone replacement therapy
- Obesity
- Oral contraceptives (TNBC)

## Low Risk Profile

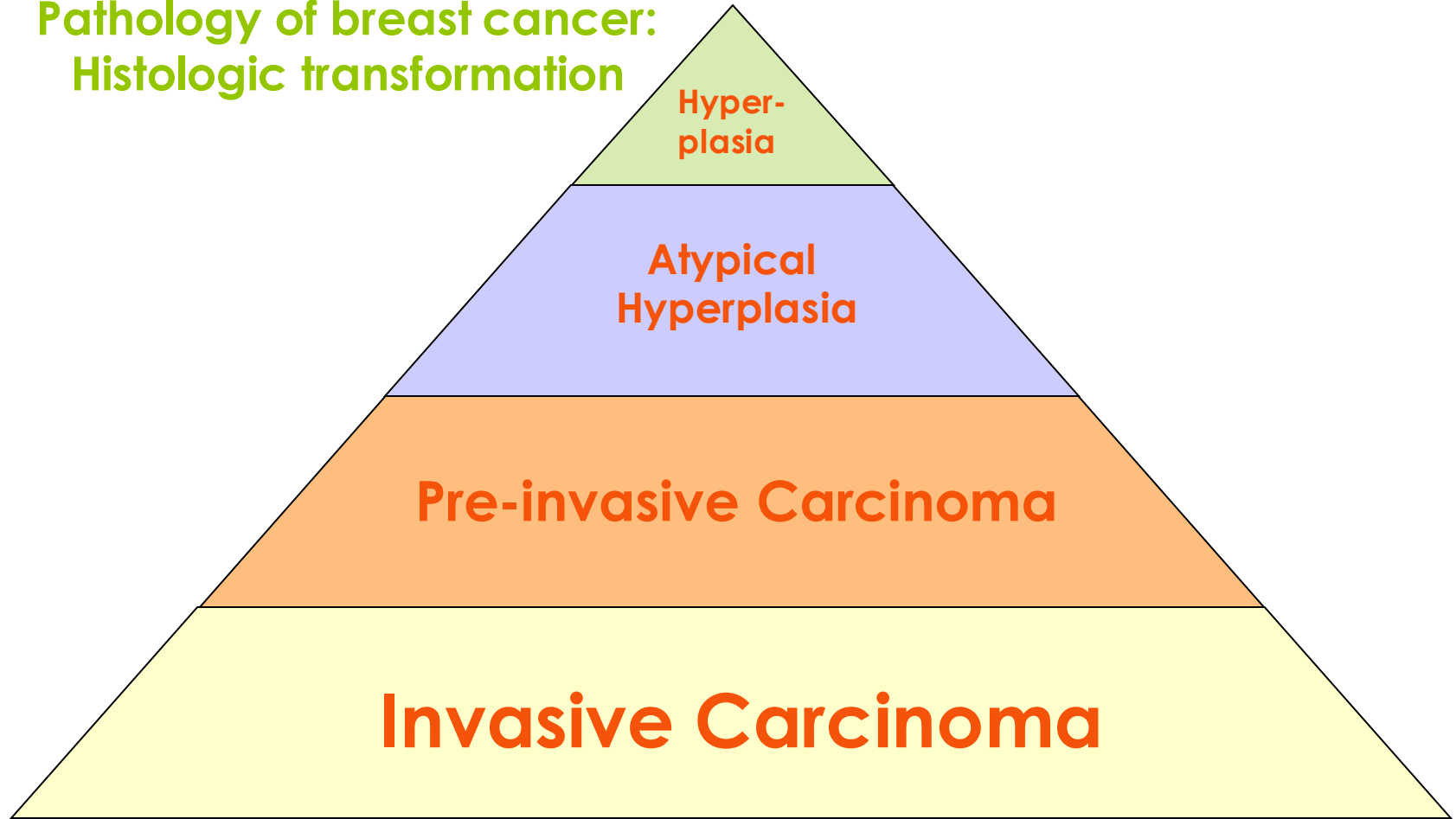
- Late menarche
- Early menopause
- Multiple pregnancies
- Younger age at first pregnancy
- Breast feeding > 6 months
- No hormone replacement therapy
- Non-obese



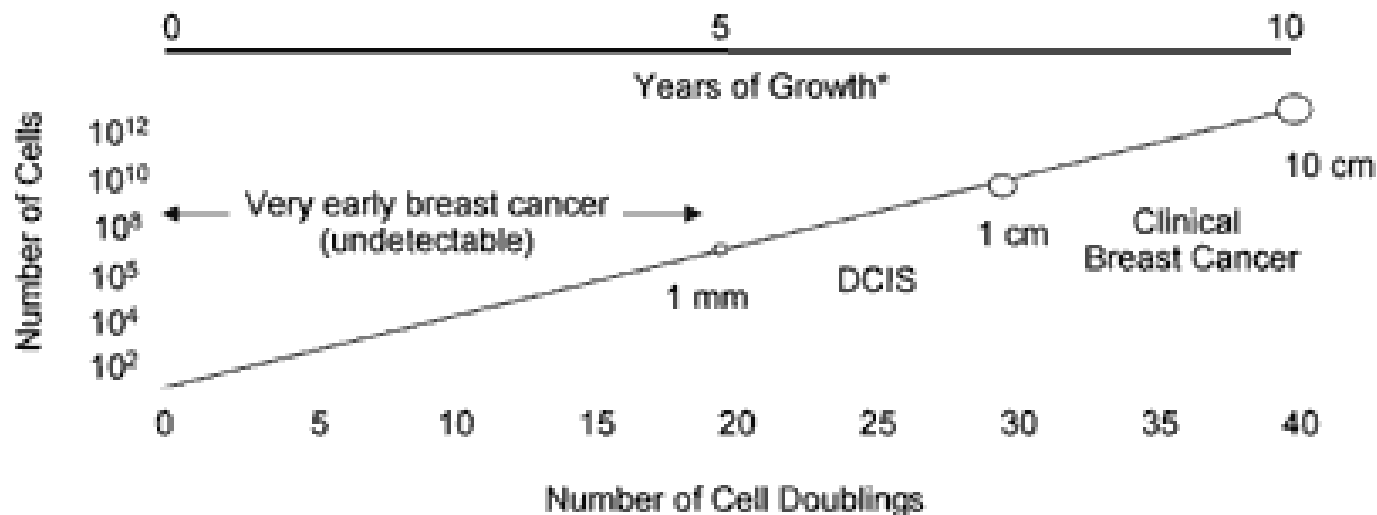
# Epidemiology of Breast Cancer

- Lifetime probability of developing invasive breast cancer 1 in 9 (SEER data)
- Breast cancer rates increased by 1.2 % per year from 1940 to 1980
- Breast cancer rates increased rapidly in the early 1980's, then constant since 1987

**Pathology of breast cancer:  
Histologic transformation**

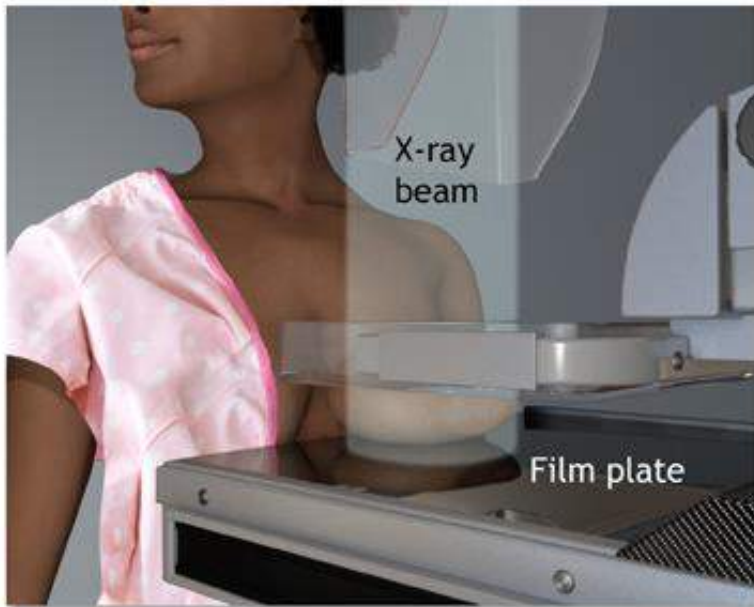


# Natural history of breast cancer



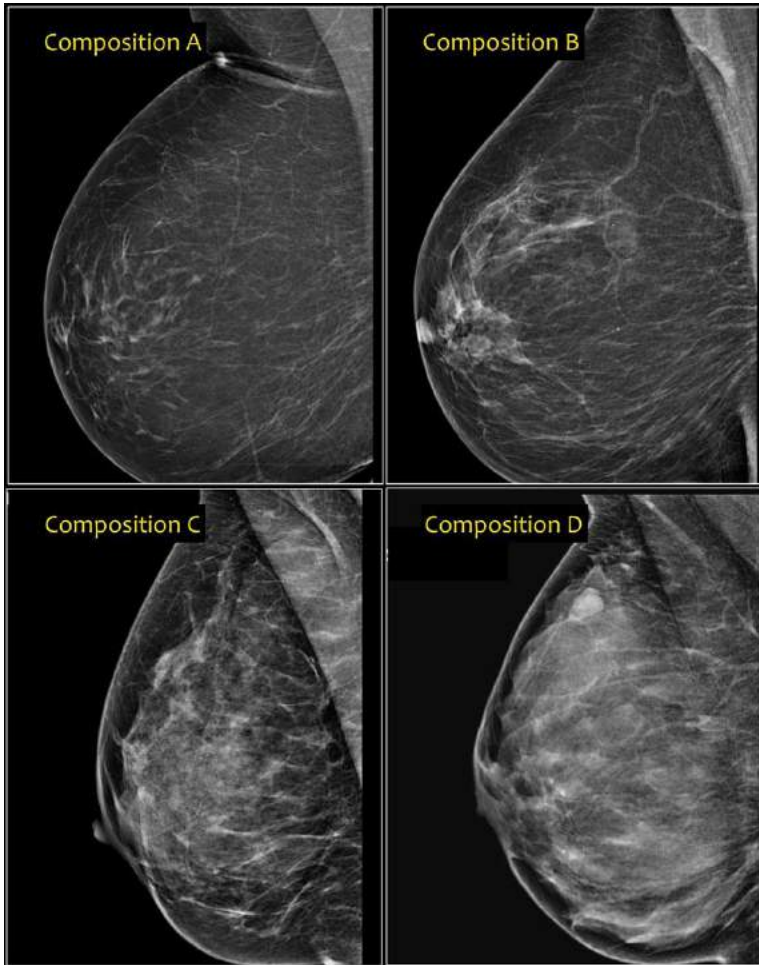
\*Note 90-day doubling time x 40 doublings = 3600 days (approximately 10 years)  
Harris et al. *Breast Diseases*, 2nd ed. 1991:165-189.

# Screening for breast cancer: Mammography

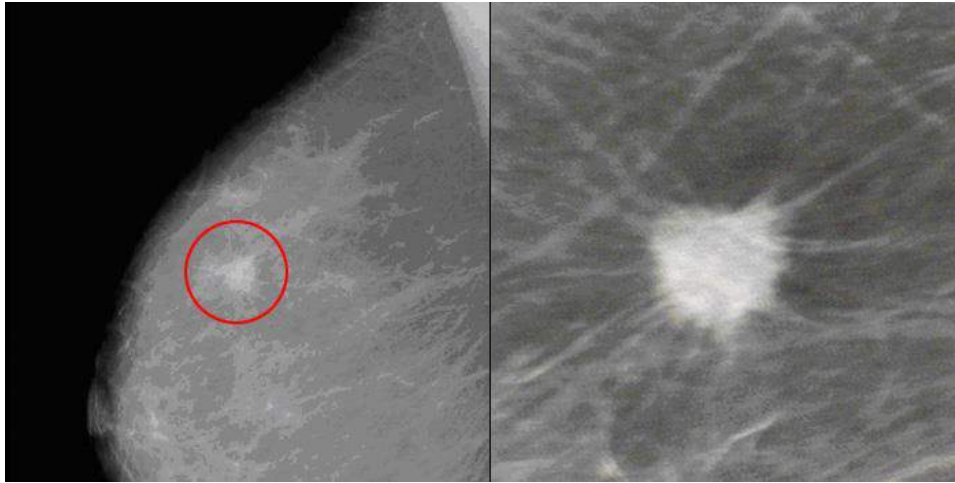


Early detection  
increases chances  
of cure



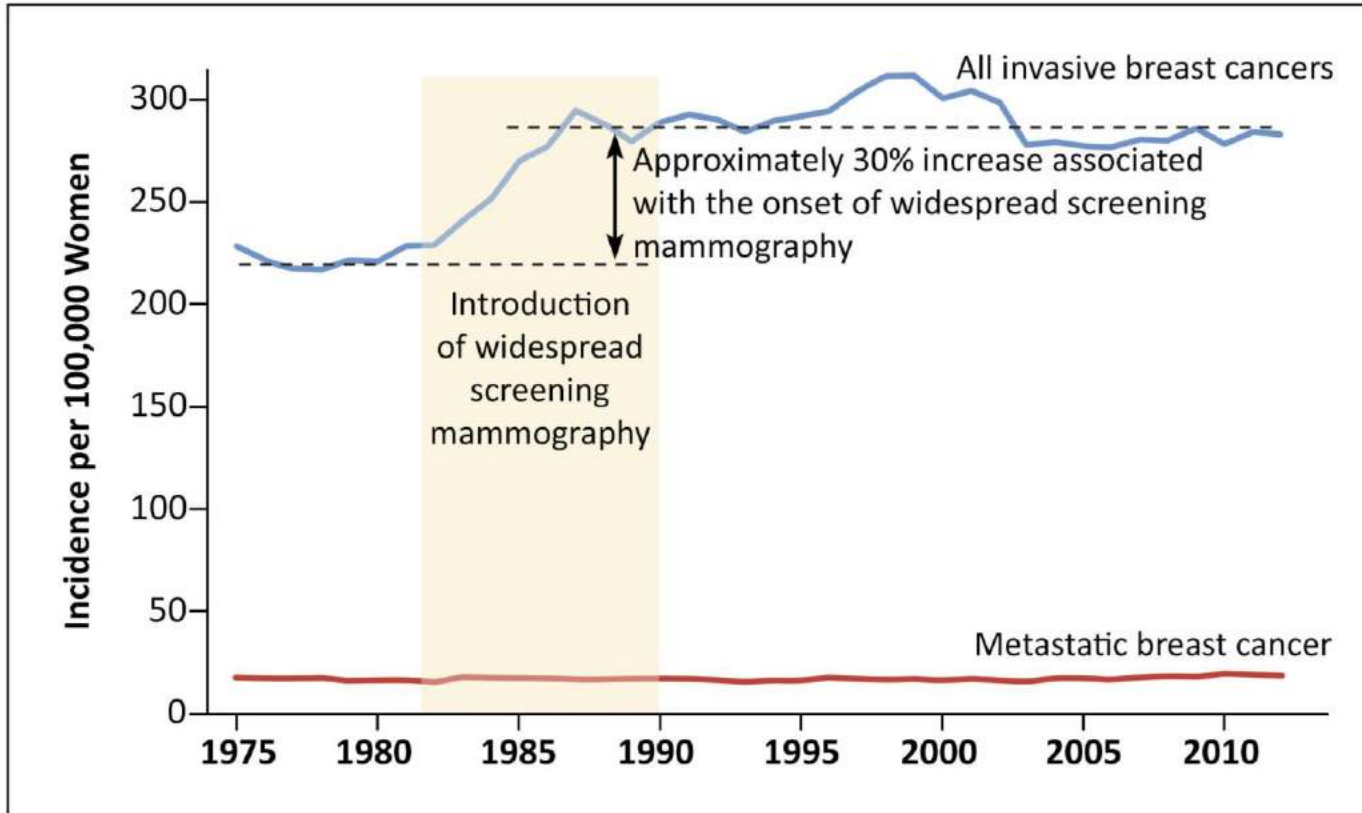


**Four normal  
mammograms  
varying by  
breast density**

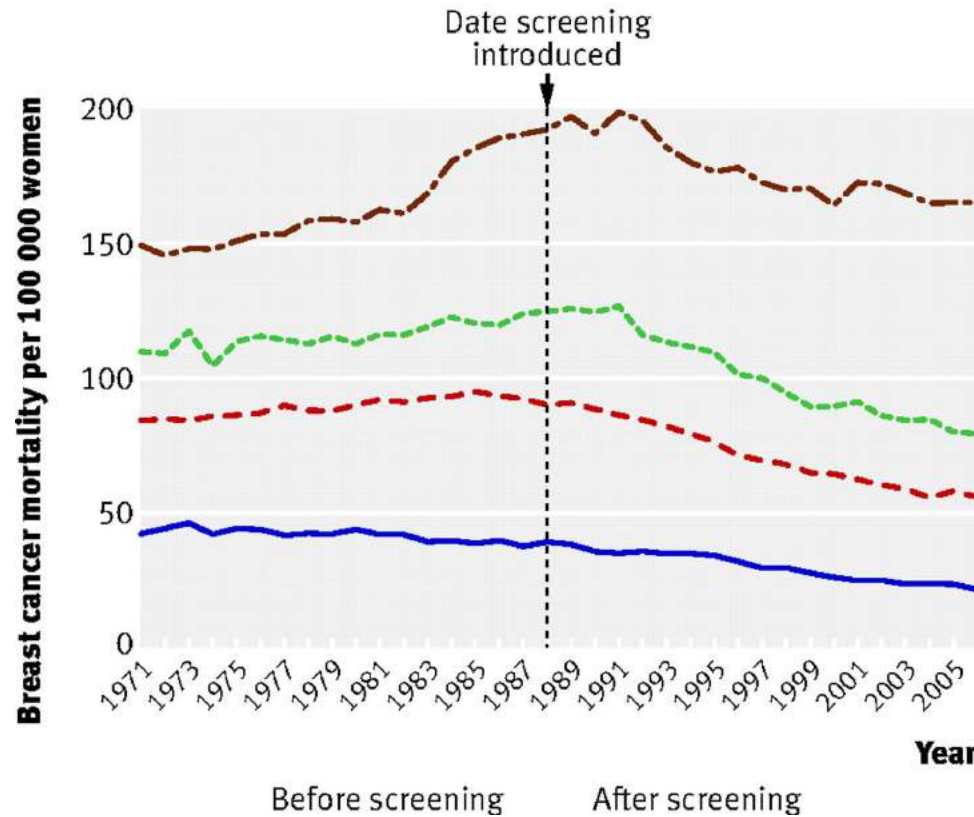


**Abnormal  
mammogram  
suspicious for  
cancer**

## Effect of mammographic screening on breast cancer INCIDENCE (USA)



Source: PDQ



## Effect of mammographic screening on breast cancer MORTALITY

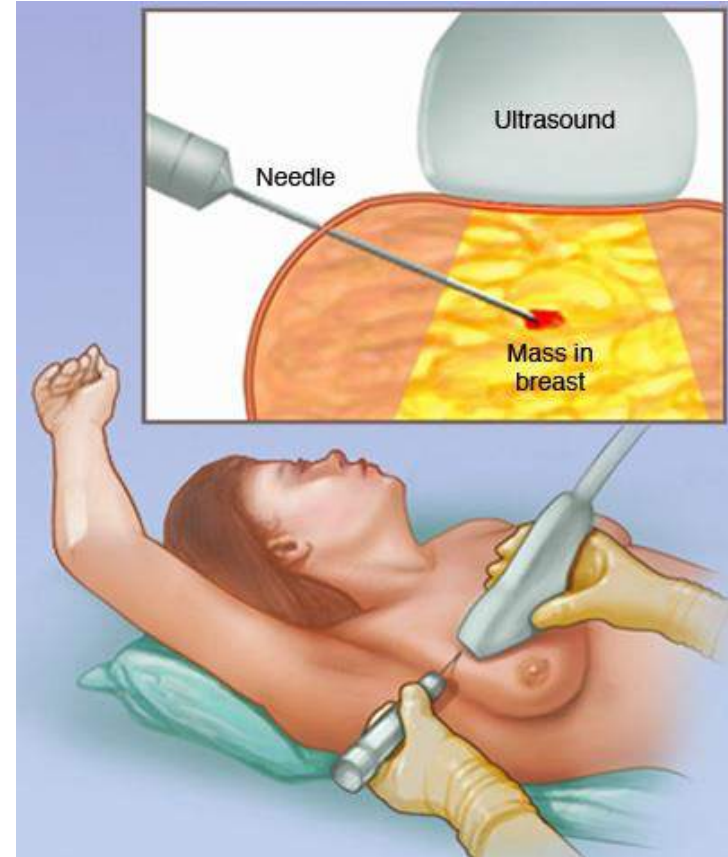
(Data from Denmark)

- 40-49 years
- - - 50-64 years
- · - · 65-69 years
- - - · 70 years

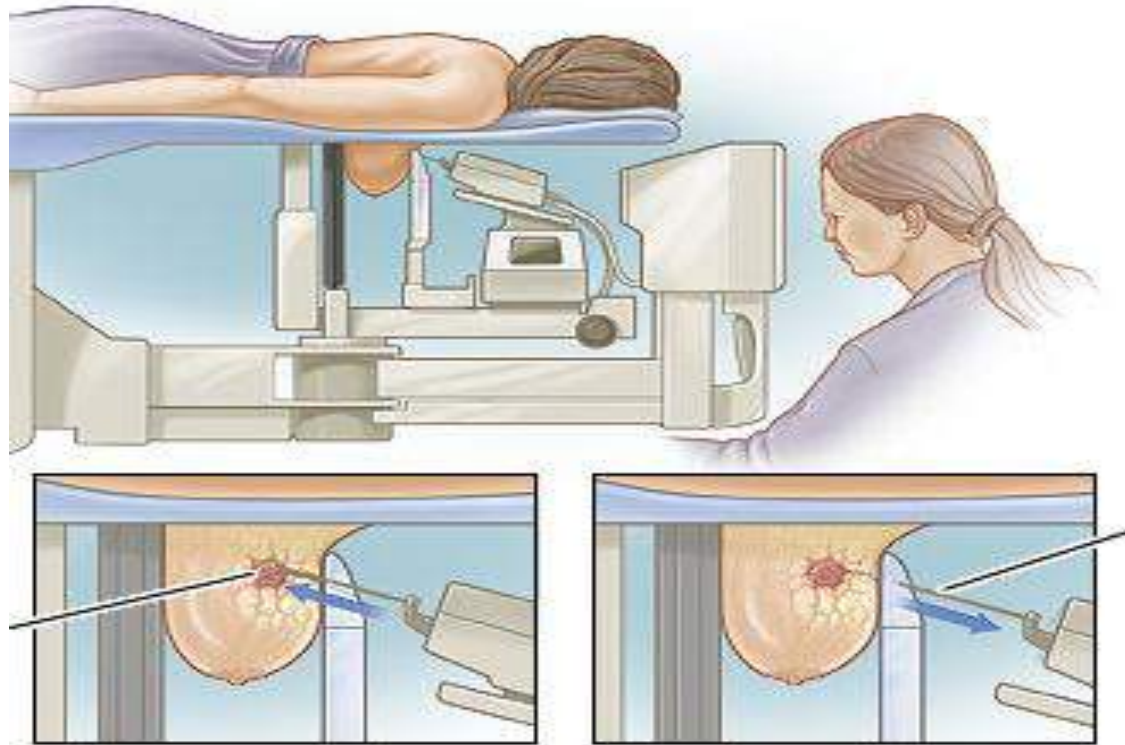


# Evaluation of suspected breast cancer

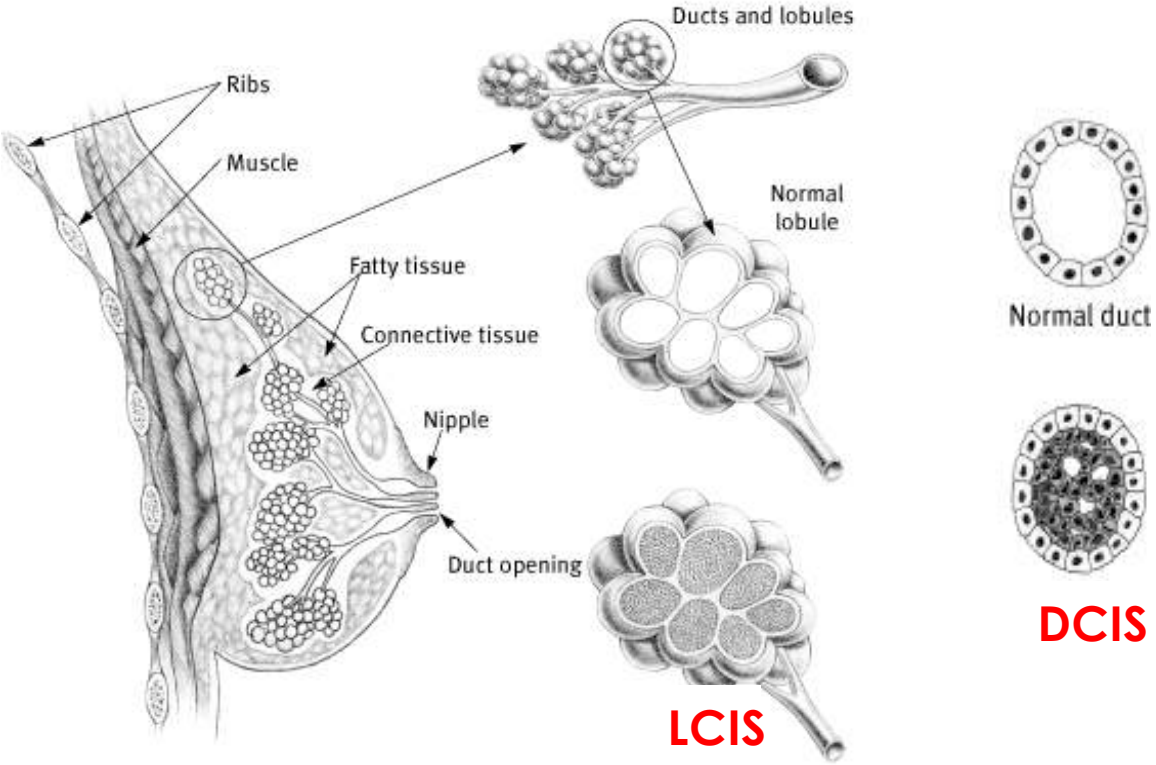
- Core biopsy
  - 8-14 gauge
  - Larger sample than FNA
  - Allows for ER/PR, Her2 testing
- Techniques
  - Palpation
  - Ultrasound-guided
  - Stereotactic



# Stereotactic breast biopsy



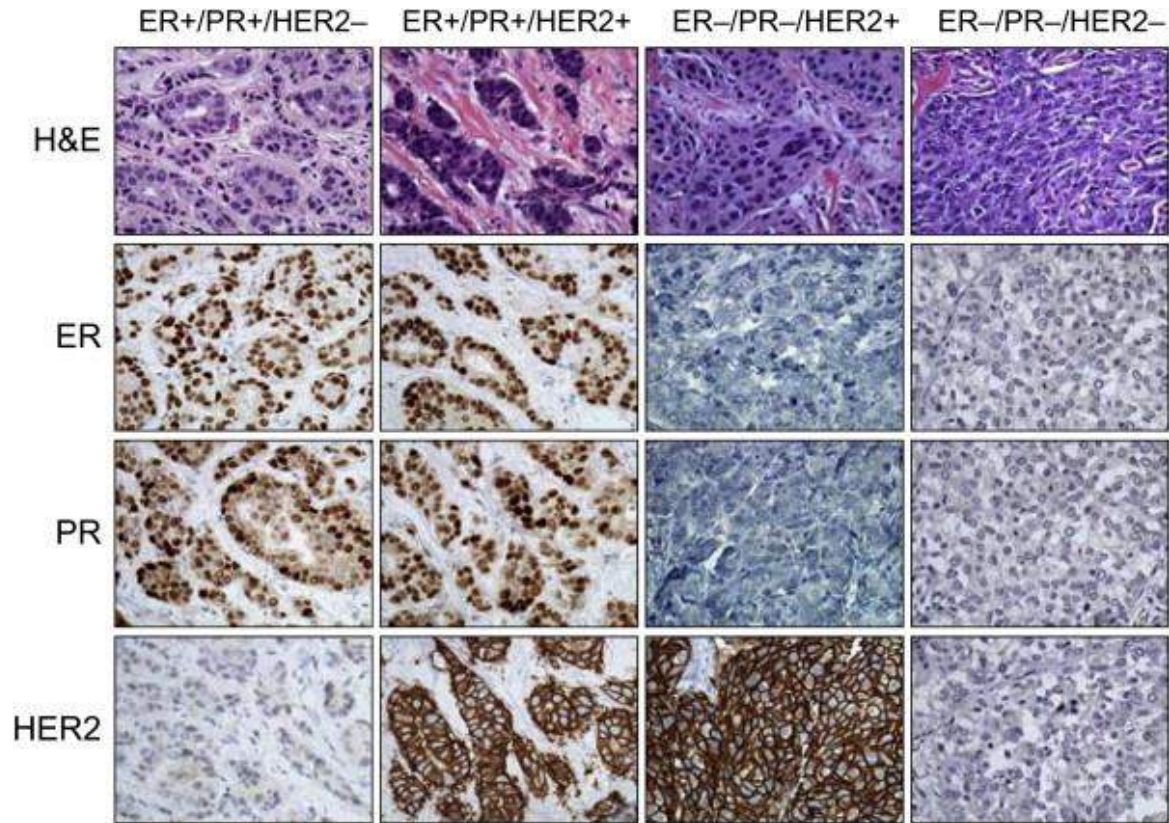
# Pathology of breast cancer



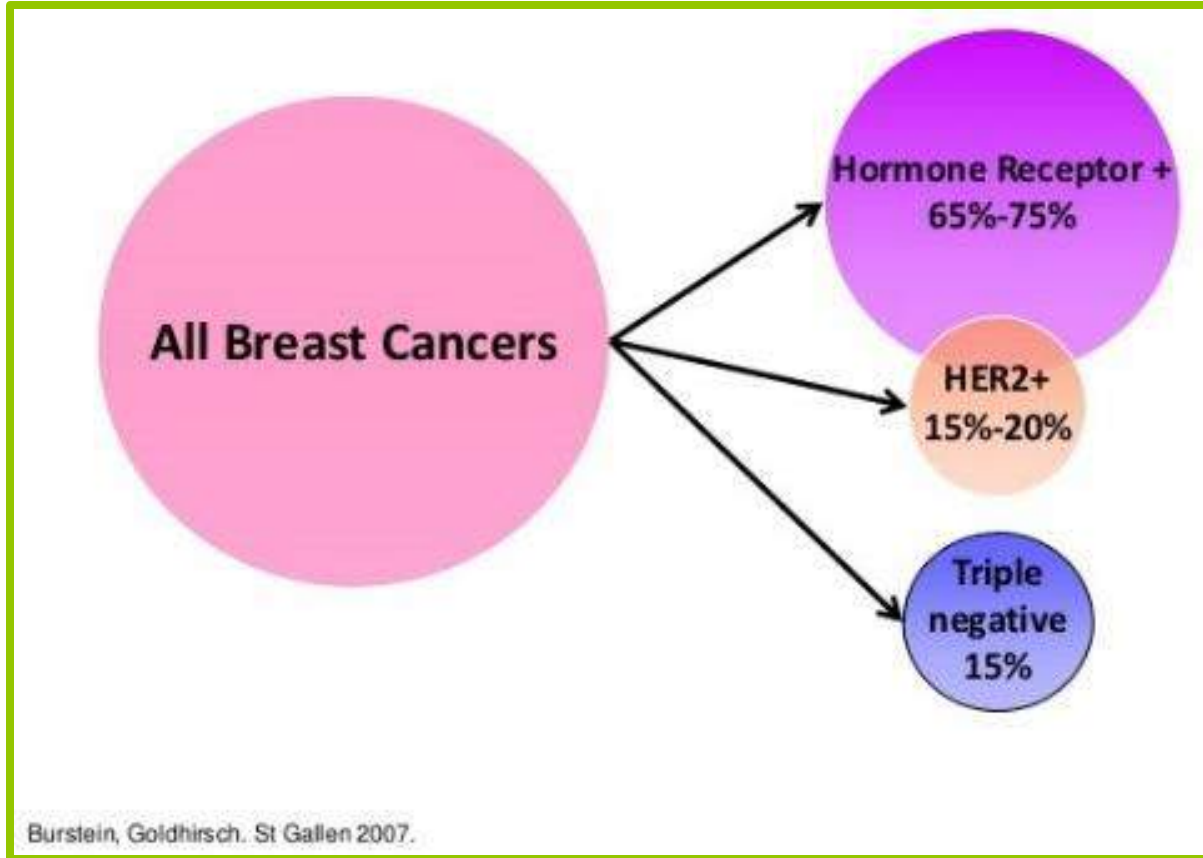
## Pathology of breast cancer

- Infiltrating ductal ~70-80%
- Infiltrating lobular ~5-10%
- Mixed ~5%
- Rare variants <5%

# Pathology of Breast Cancer: Immunostaining



# Clinical subtypes of breast cancer

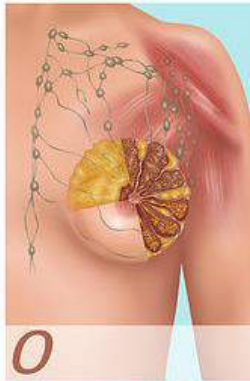




# Genomic subtypes of breast cancer

BC subtype	Luminal A	Luminal B	HER2-positive	Triple - negative
% of breast cancers	50%	25%	15%	10%
Phenotype <sup>a</sup>	ER+PR+	ER+PR+	HER2+	ER-PR-HER2-
Related molecular intrinsic subtype	<b>Luminal A</b> 90% ER+ 89% PR+ 14% HER2+	<b>Luminal B</b> 98% ER+ 82% PR+ 24% HER2+	<b>HER2-enriched</b> 38% ER+ 20% PR+ 72% HER2+	<b>Basal-like</b> 8% ER+ 7% PR+ 7% HER2+
Proliferation (GEPs)				
Prognosis				
Prognosis value of TIL (at diagnosis)				
Treatment				

# Stages of Breast Cancer



0

Abnormal cells in duct lining or sections of the breast. Increased risk of developing cancer in one or both breasts.

**100%**  
SURVIVAL RATE



1

Cancer in breast tissue. Tumor is less than one inch across in size.

**98%**  
SURVIVAL RATE



2

Cancer in breast tissue. Tumor is less than two inches across in size. Cancer may spread to the auxiliary lymph nodes.

**88%**  
SURVIVAL RATE



3

Tumor is larger than two inches across in size and cancer has spread to auxiliary lymph nodes. Possible dimpling, inflammation or skin color change.

**52%**  
SURVIVAL RATE



4

Cancer has spread beyond the breast to other nearby areas of the body.

**16%**  
SURVIVAL RATE

# Thinking about breast cancer treatment

- **Local therapy (the chest)**

- ✓ Surgeon
- ✓ Radiation therapist

- **Systemic therapy (the rest)**

- ✓ Medical Oncologist

# Local therapy of breast cancer

- **Surgical approaches**

- ✓ Breast conservation
- ✓ Mastectomy

- **Radiation therapy**

- ✓ Whole breast radiation
- ✓ Accelerated partial breast radiation (Mammosite)
- ✓ Radiation to the axilla?

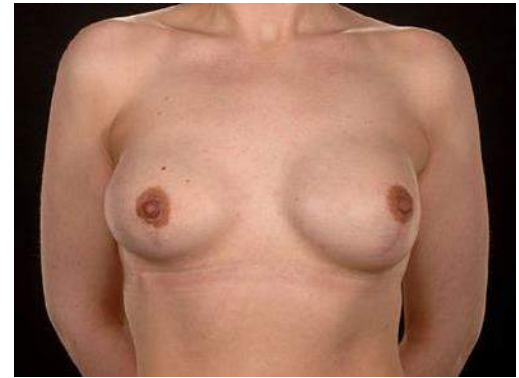
## Breast cancer surgery: Less is best



**Halsted Radical Mastectomy  
1890-1970**



**Modified Radical Mastectomy  
1970-present**



**Skin-sparing Mastectomy  
with reconstruction**

# Contraindications to Breast Conservation

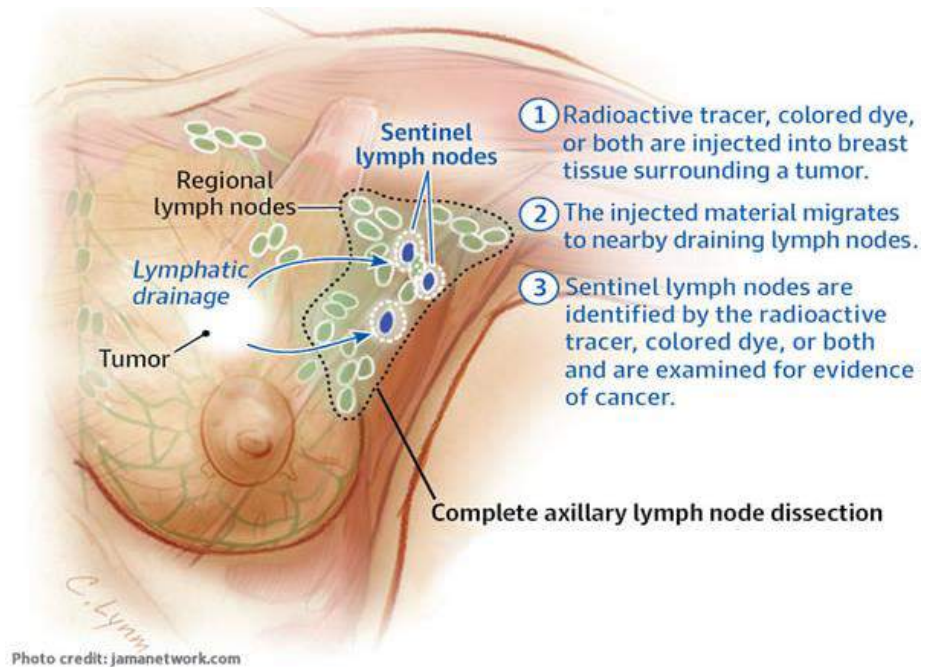
- Multicentric cancer
- Large tumor relative to breast size (“neo-adjuvant therapy)
- Persistently positive margins
- Difficult-to-interpret mammogram
- Pregnant at diagnosis
- Prior radiation therapy to chest (Hodgkin)



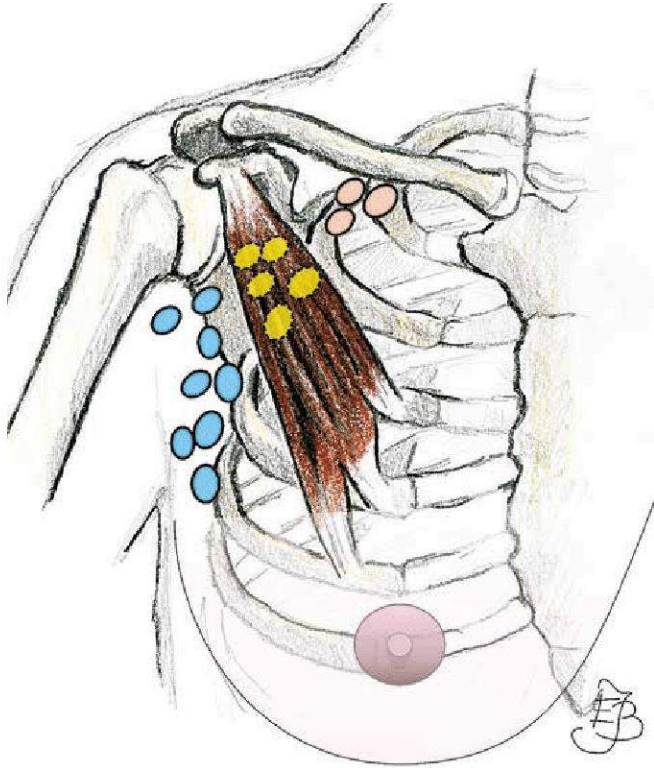
# Local therapy of breast cancer: “conservation”

## Partial mastectomy or “lumpectomy”

- Remove the tumor + normal surrounding tissue
- Sample “sentinel” lymph nodes
- Radiation therapy usually required after surgery



## Limited role for complete axillary dissection axilla



- Not required for patients with NEG SLN
- Not required for patients with positive SLN who are having RT to breast / axilla
- ?? For patients with positive SLN not having RT

# Radiation therapy for breast cancer

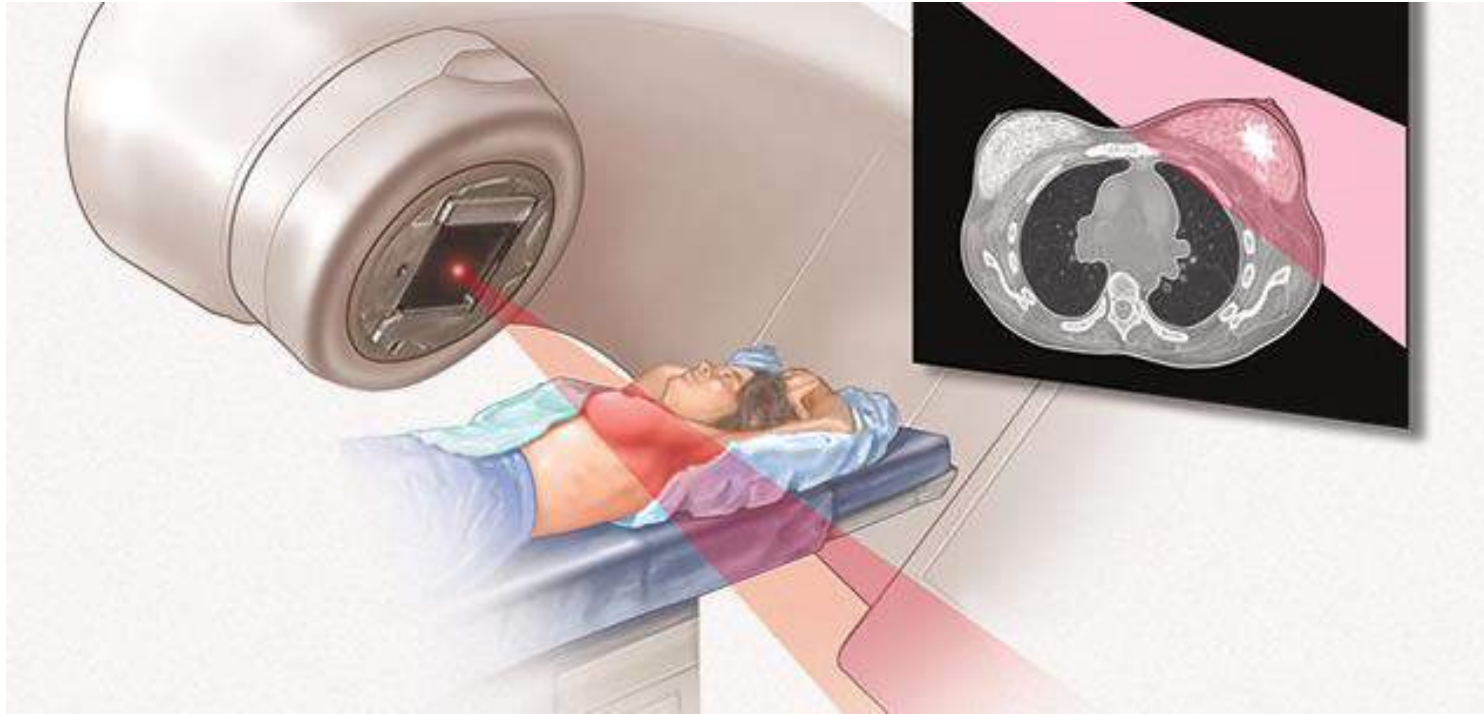
- **Following “lumpectomy”**

- ✓ Whole breast radiation with boost
- ✓ Accelerated partial breast radiation

- **Following mastectomy**

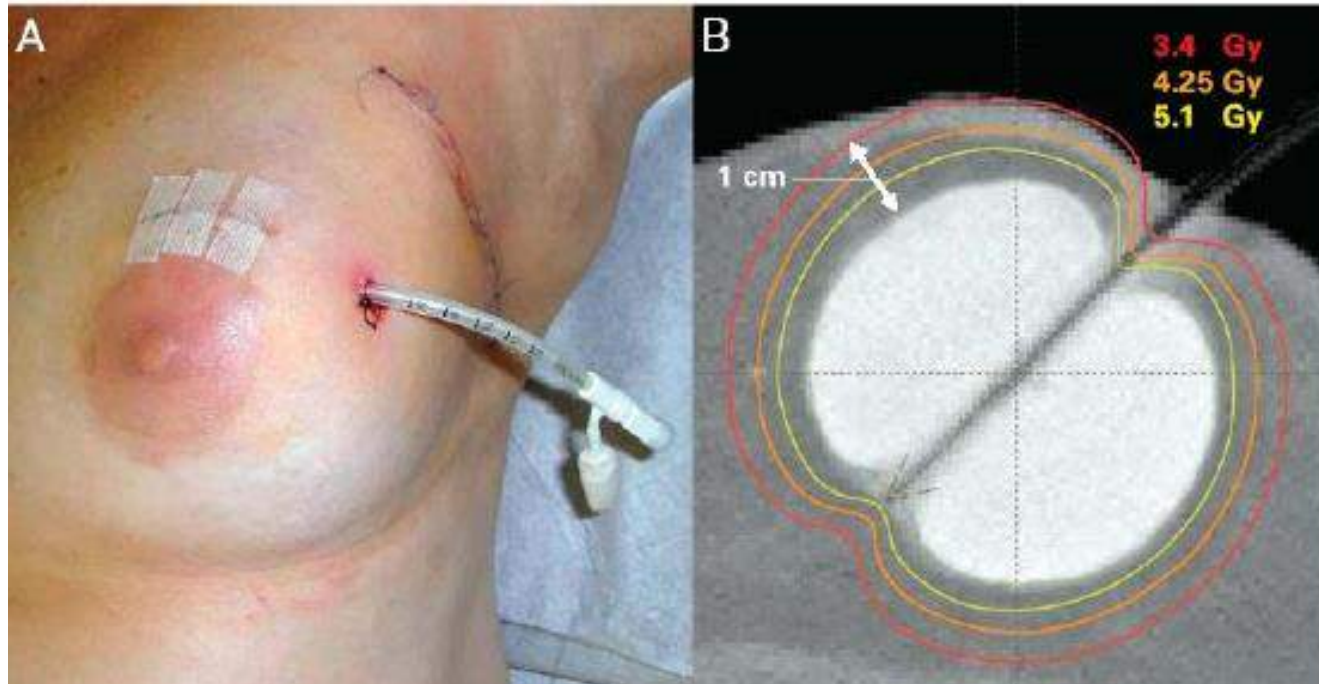
# Post-lumpectomy radiation (1)

## External beam whole breast radiation



# Post lumpectomy radiation (2)

## Accelerated partial breast radiation



- Age > 45
- Node neg
- Margins neg
- NSABP B-39
- RTOG 0413

## Breast conservation: good “cosmesis”





## Post-mastectomy radiation



- Usually required in patients with LABC
- Usually includes regional nodal beds
- Tumor > 4 cm
- Positive ALN > 3
- Extracapsular extension of tumor
- Persistent tumor after pre-op chemo

# Systemic therapy of breast cancer

	Early	Locally Advanced	Metastatic
ER (+)			
Her-2 (+)			
Triple negative			

## Rationale for Systemic Adjuvant Rx of Early Breast Cancer

- To eliminate micro-metastases: seeds of cancer that may have spread beyond the breast and axillary lymph nodes but are not yet detectable
- Treatments chosen based on ER (+), Her 2(+), Triple negative
- Check “[adjuvantonline.com](http://adjuvantonline.com)” for guidance
- Challenge: ER positive tumor with high risk features or low risk features but with 1-3 positive SLN's:
  - ✓ Oncotype DX
  - ✓ Mammosite

# Adjuvant treatment of ER (+) early breast cancer

## Definition of menopause

- Age > 60 years
- Age < 60 years and...
  - ✓ Prior bilateral oophorectomy
  - ✓ No menstrual bleeding in last 6 months + menopausal levels of estradiol

# Locally advanced breast cancer

- Stage IIB (T3N0) and Stage III
- No distant metastases after imaging
- Clinical features
  - ✓ Palpable breast or axillary mass
  - ✓ Inflammation or edema of skin
  - ✓ Ulceration (fungating tumor)
  - ✓ Attached to chest wall
  - ✓ No pain!

# Physical findings sometimes seen in LABC



Inflammation



Retraction

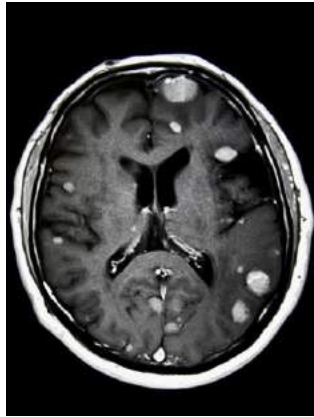
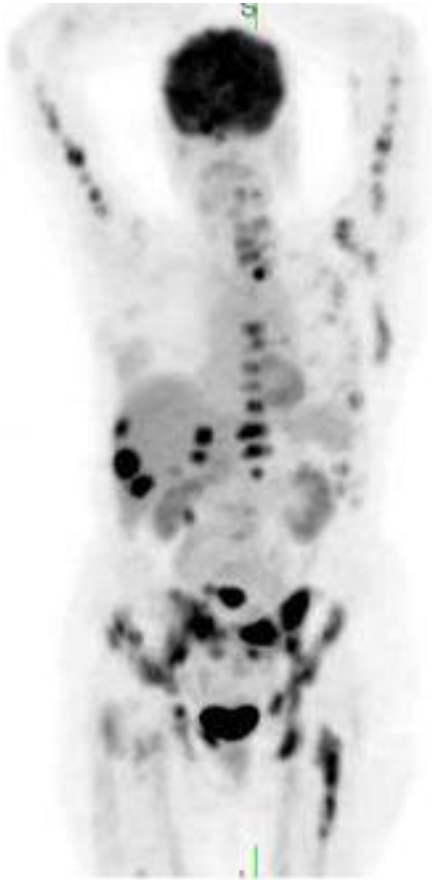


Ulceration



Edema





## Approach to Locally Advanced Breast Cancer

- Involves pre-operative or “neo-adjuvant” chemotherapy
  - ✓ Decrease size of tumor before surgery
  - ✓ Possible breast conservation
  - ✓ Decrease the risk of local recurrence
  - ✓ Decrease the risk of distant recurrence
- Chemo Regimens
  - ✓ ER (+) – AC-T then endocrine therapy based on menopausal status
  - ✓ Her-2 (+) – TCH then Herceptin x 1 year
  - ✓ TNBC – AC-T +/- carboplatin
- Local therapy employed after chemo
  - Sampling of tumor and axillary nodes allows assessment of therapeutic effect
  - If no CR achieved, consider additional post-op therapy
    - ER (+) patients should get hormonal therapy
    - TNBC patients may get Capecitabine

# Approach to metastatic breast cancer

## Role of repeat biopsy

- Rates of discordance between primary tumor and metastasis ~3-30%
  - ✓ ER from positive to negative
  - ✓ Her-2 from positive to negative
- Biopsy of newly metastatic cancer is recommended always

# Approach to Metastatic Breast Cancer

- Goals: Palliate symptoms + prolong life
- Metastatic pattern matters
  - ✓ Visceral predominant and # of sites
  - ✓ Bone predominant
  - ✓ Oligometastases
- Interval between initial therapy and relapse
- Age and comorbidities matter
- Specific choices based on biology: ER (+), Her-2 (+), Triple negative phenotype
  - ✓ Chemo: single agents sequentially
  - ✓ Hormonal agents +/-
  - ✓ Targeted agents

**Murakoze!**