Breast Cancer

Fall 2021

Clinical Laboratory Personnel Committee of the
Louisiana State Board of Medical Examiners

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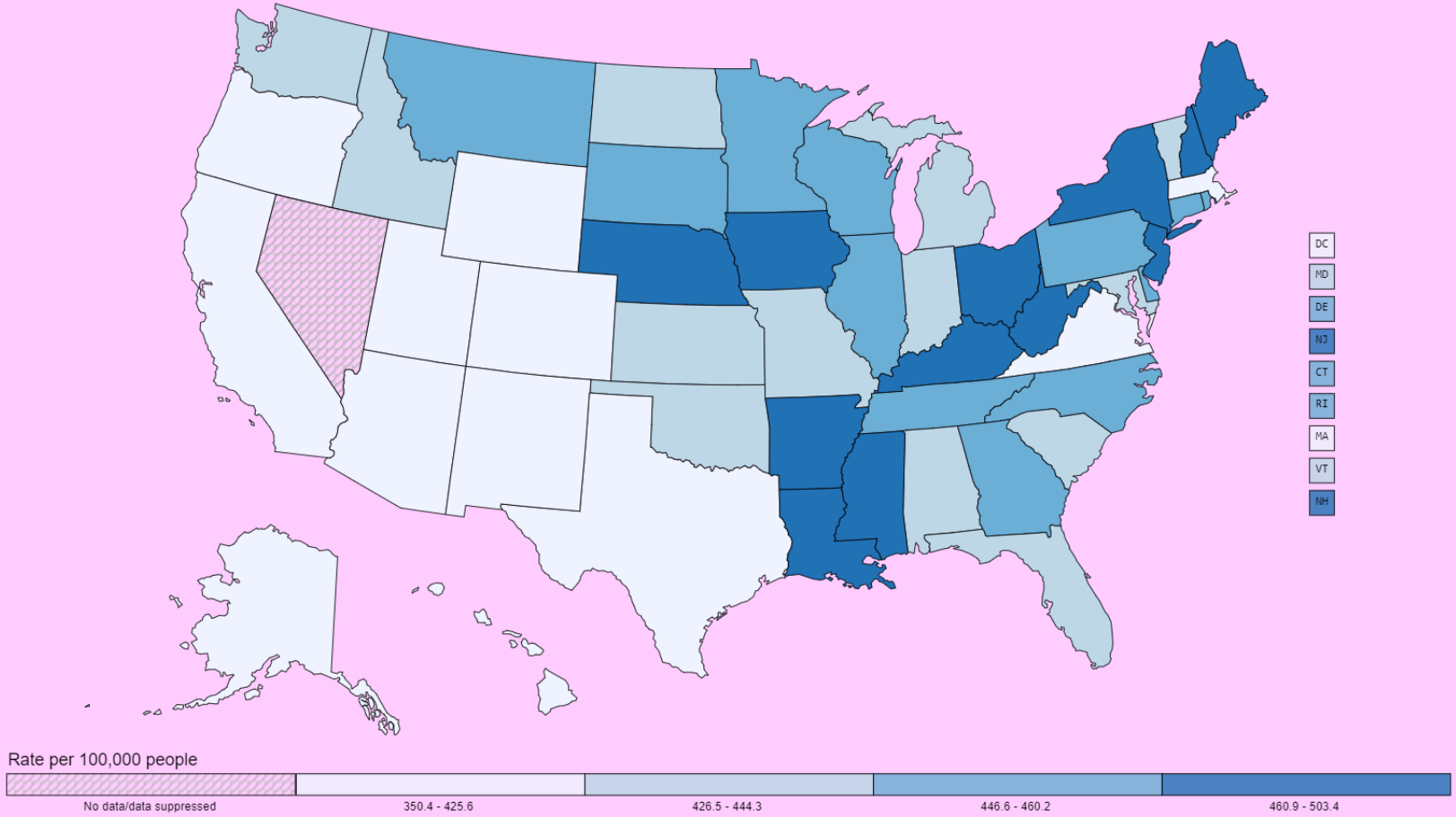
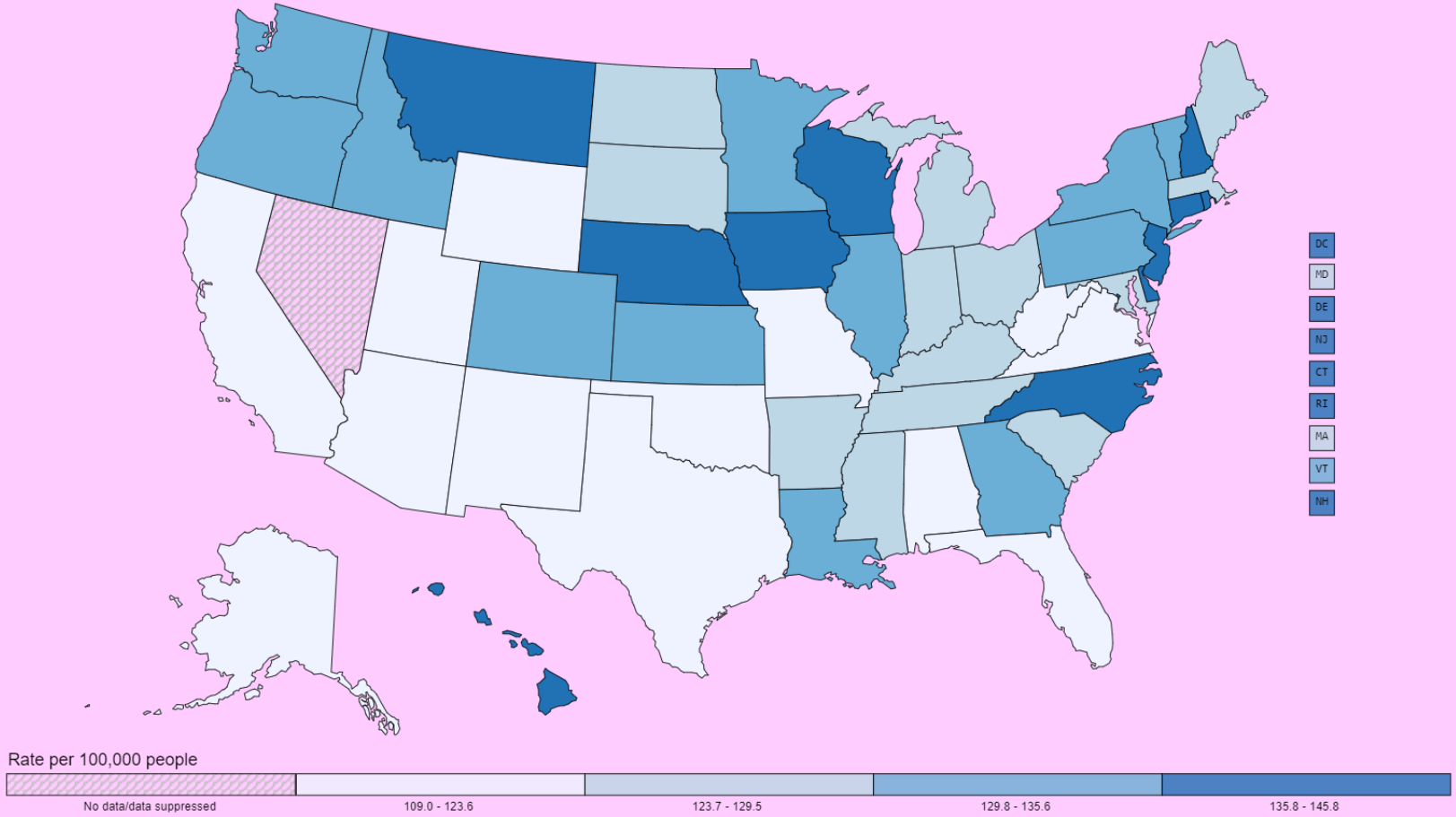
Introduction

- Breast cancer starts when cells in the breast begin to grow out of control. These cells form a tumor that may be seen on an x-ray or felt as a lump.
- If the tumor is **malignant**, the cells can grow into (invade) surrounding tissues and spread (**metastasize**) to distant areas of the body.
- Breast cancer occurs almost entirely in women, but men can get breast cancer.

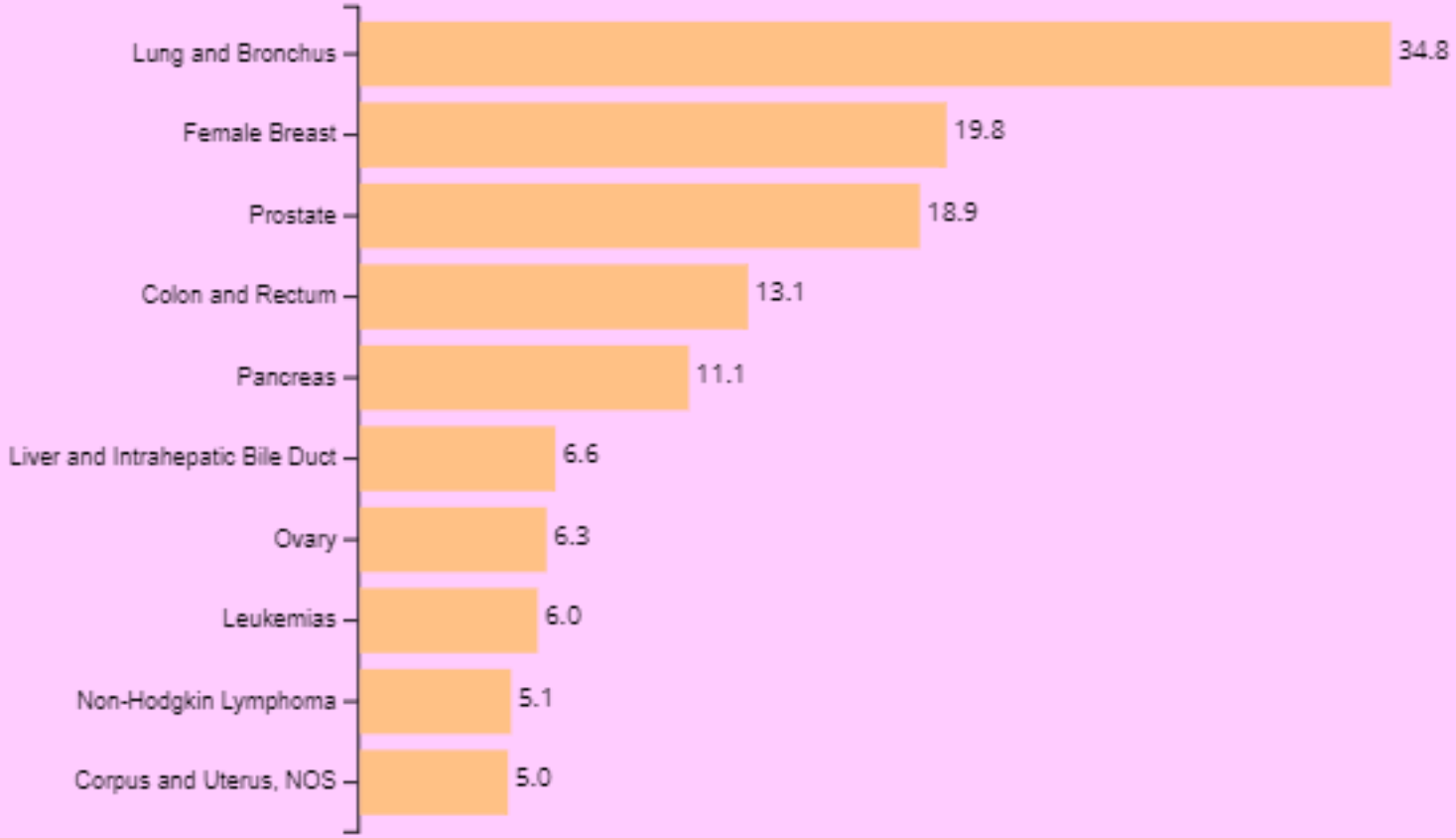
Rate of New Cancers in the United States
All Types of Cancer, All Ages, All Races and Ethnicities, Male and Female



Rate of New Cancers in the United States
Female Breast, All Ages, All Races and Ethnicities, Female



Top 10 Cancers by Rates of Cancer Deaths
All Types of Cancer, United States, 2018



Rate per 100,000 people

Data source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2020 submission data (1999-2018): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in June 2021.

1 IN 8

women will be diagnosed with breast cancer during her life.

11% OF WOMEN

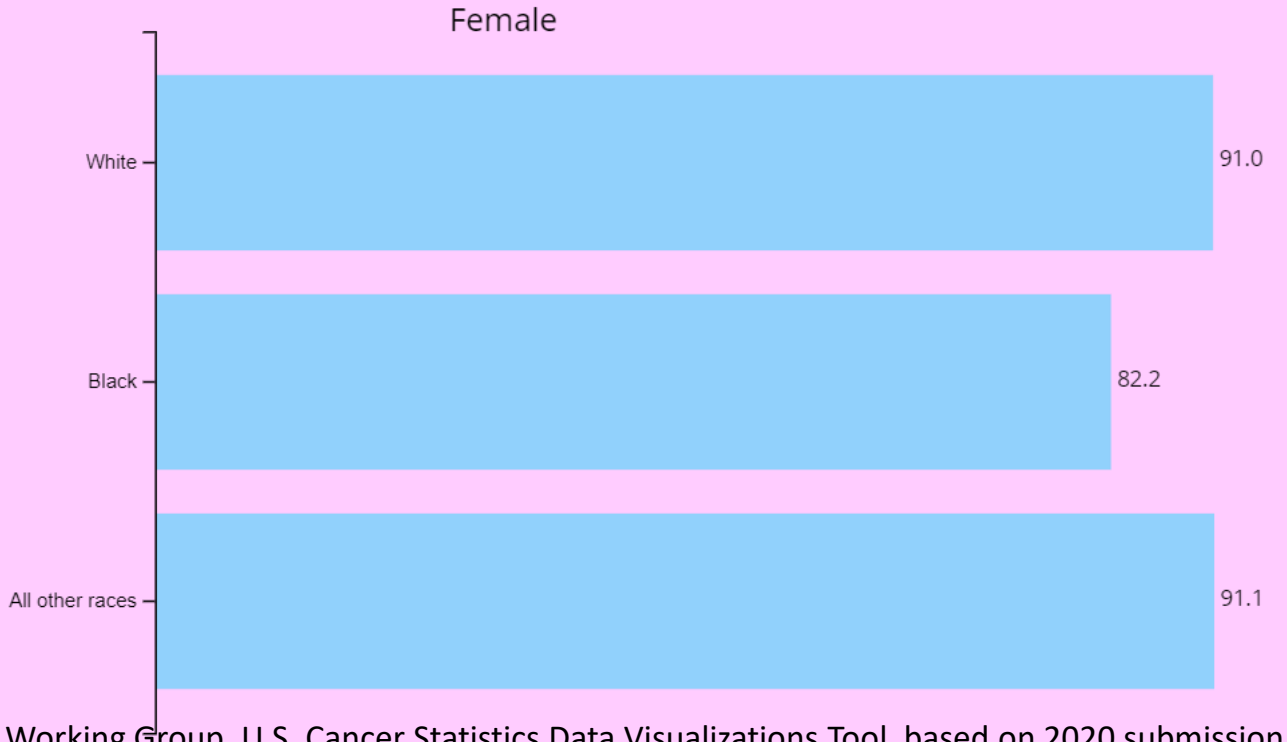
DIAGNOSED WITH BREAST CANCER IN THE US ARE YOUNGER THAN 45 YEARS OLD.

BRING YOUR brave.

www.cdc.gov/BringYourBrave
#BringYourBrave

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

5-year Survival (%) by Sex and All Races and Ethnicities
Female Breast, United States



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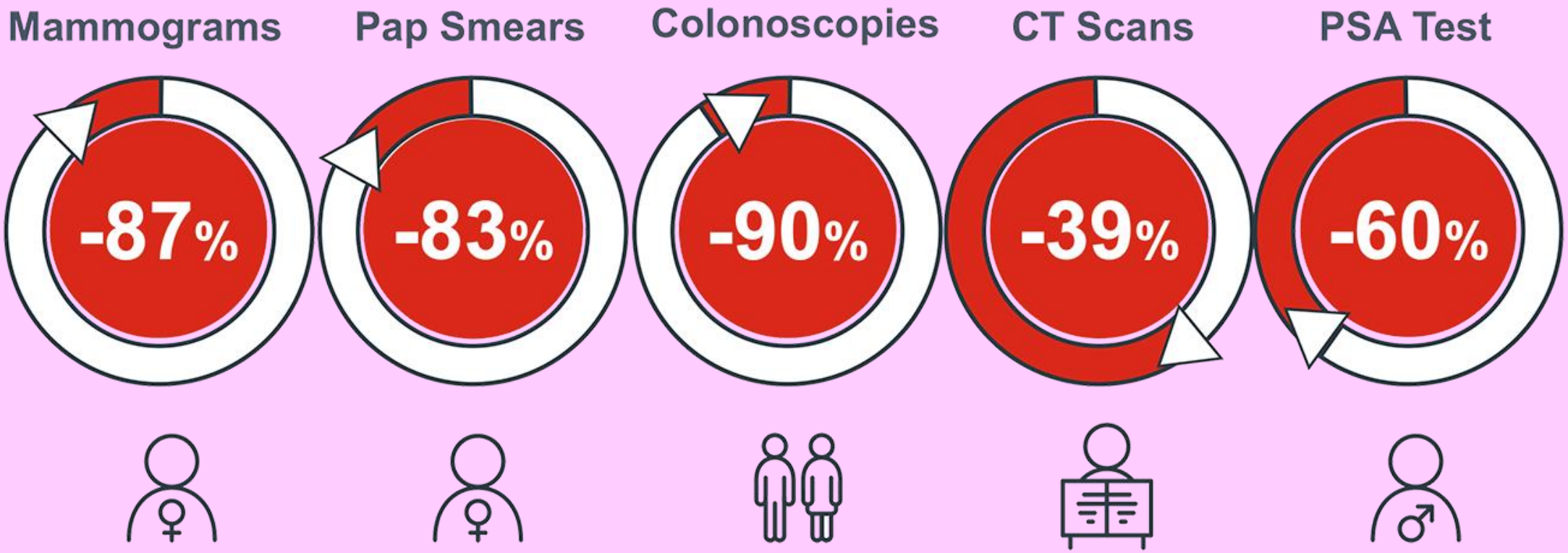
Sharp Declines in Breast and Cervical Cancer Screening

https://www.cdc.gov/media/releases/2021/p0630-cancer-screenings.html

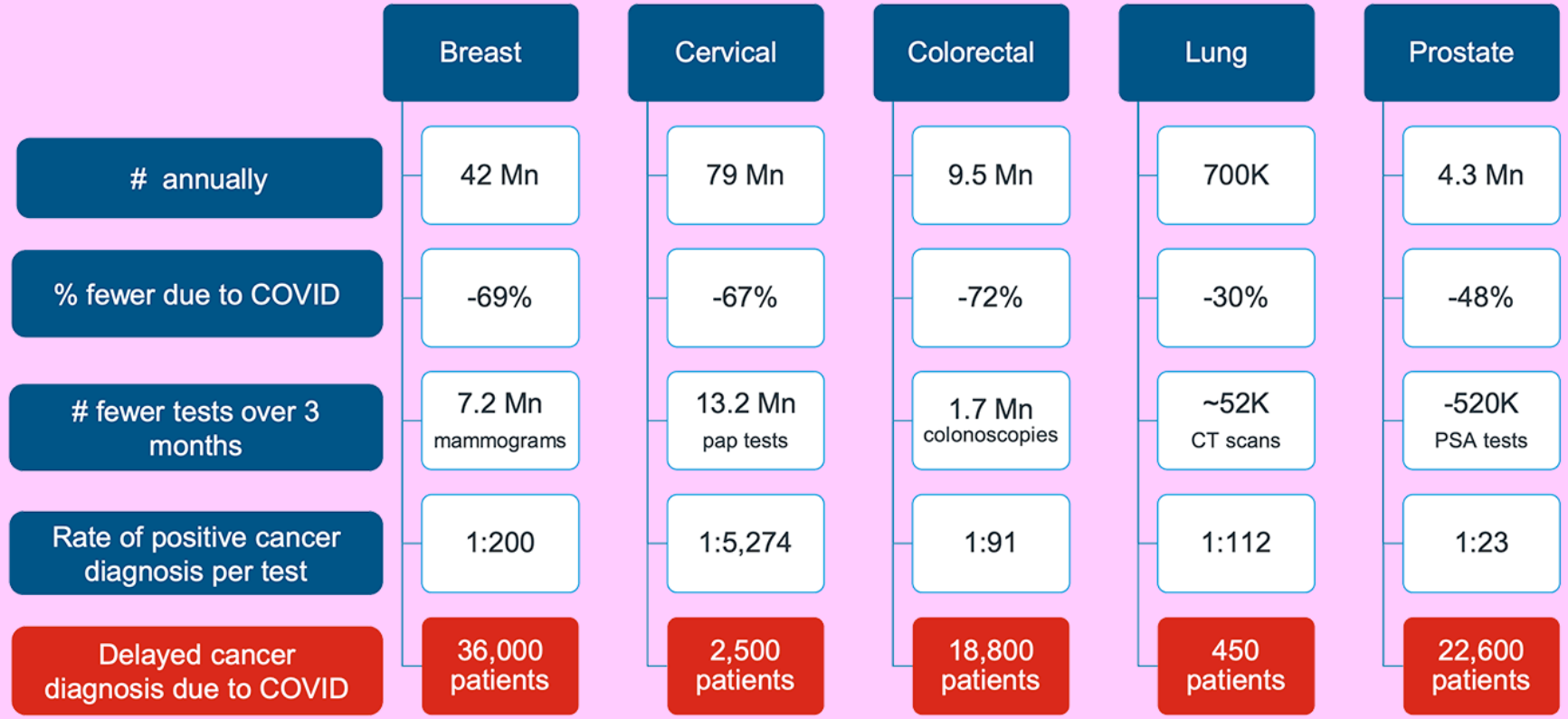
- Published: Preventive Medicine; Volume 151, October 2021, 106559
- In April,2020, the number of screening tests for breast cancer declined in metro (86%), urban (88%), and rural (89%) areas compared to the respective five-year averages.

Preventative care/testing losses during Covid



Source: IQVIA Real World Claims, April 17, 2020

Another way of looking at it



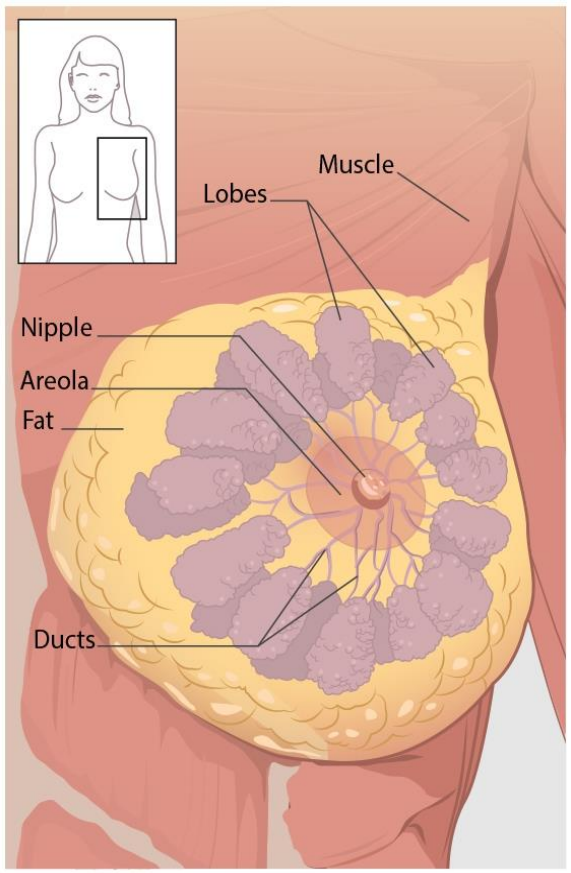
Source: IQVIA Institute, Apr 2020

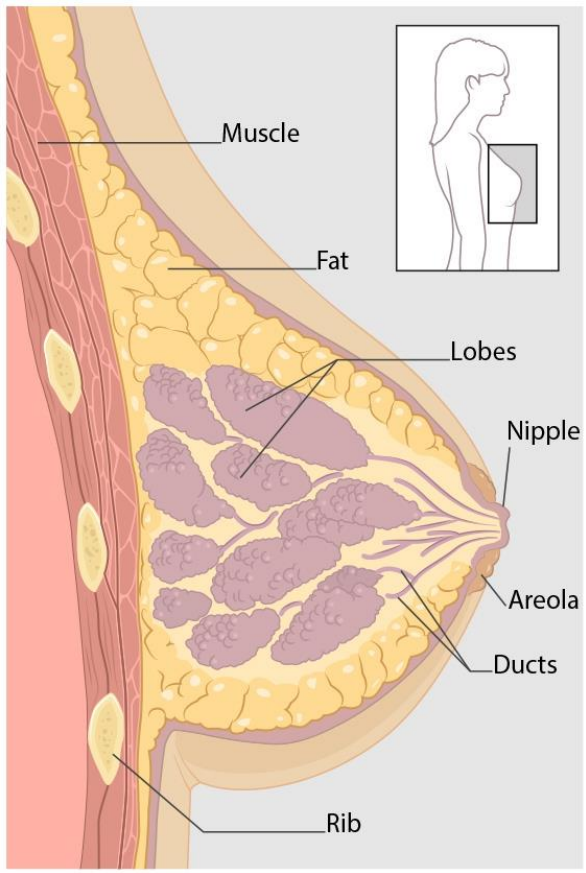
- Scenarios run by NCI and affiliated modeling groups predict that delays in screening for and diagnosis of breast and colorectal cancers will lead to a **1% increase in deaths through 2030**. This translates into 10,000 additional deaths, on top of the expected one million deaths resulting from these two cancers.

Some definitions

- Neoplasia – new tissue growth that is unregulated
- Neoplastic tumors – can be Benign (do not spread –metastasize) or Malignant (invade locally and have the ability to metastasize)
- Malignant = Cancer
- In situ (in the original place) vs. Invasive
- Tumor nomenclature is based on the cell lineage of the and whether it is benign or malignant
- Carcinoma = a malignant cancer of epithelial tissue
- *Breast cancers are usually carcinomas*

Breast anatomy





1- The breasts are made of fat, glands, and connective (fibrous) tissue

2- The breast has several lobes, which are divided into lobules and end in the milk glands

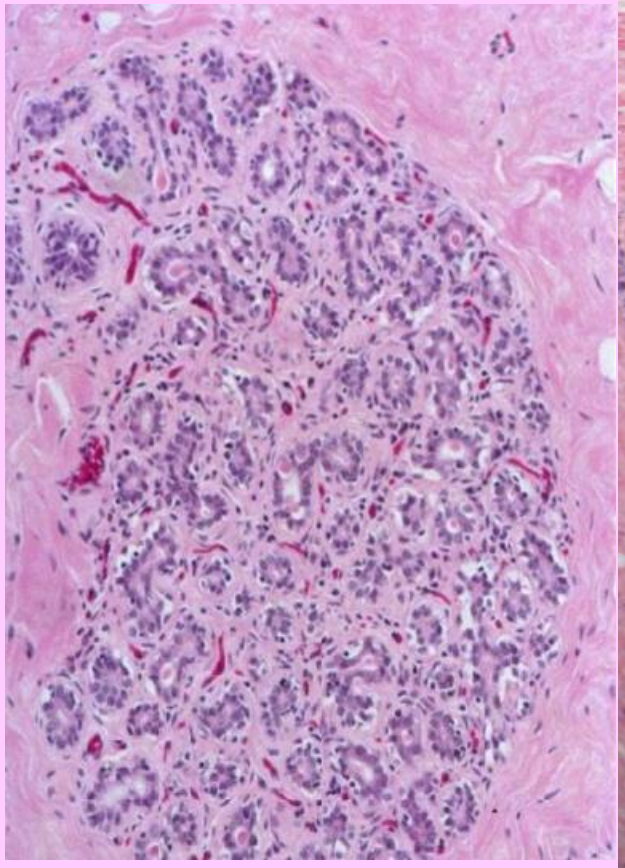
3- Tiny ducts run from the many tiny glands, connect together, and end in the nipple

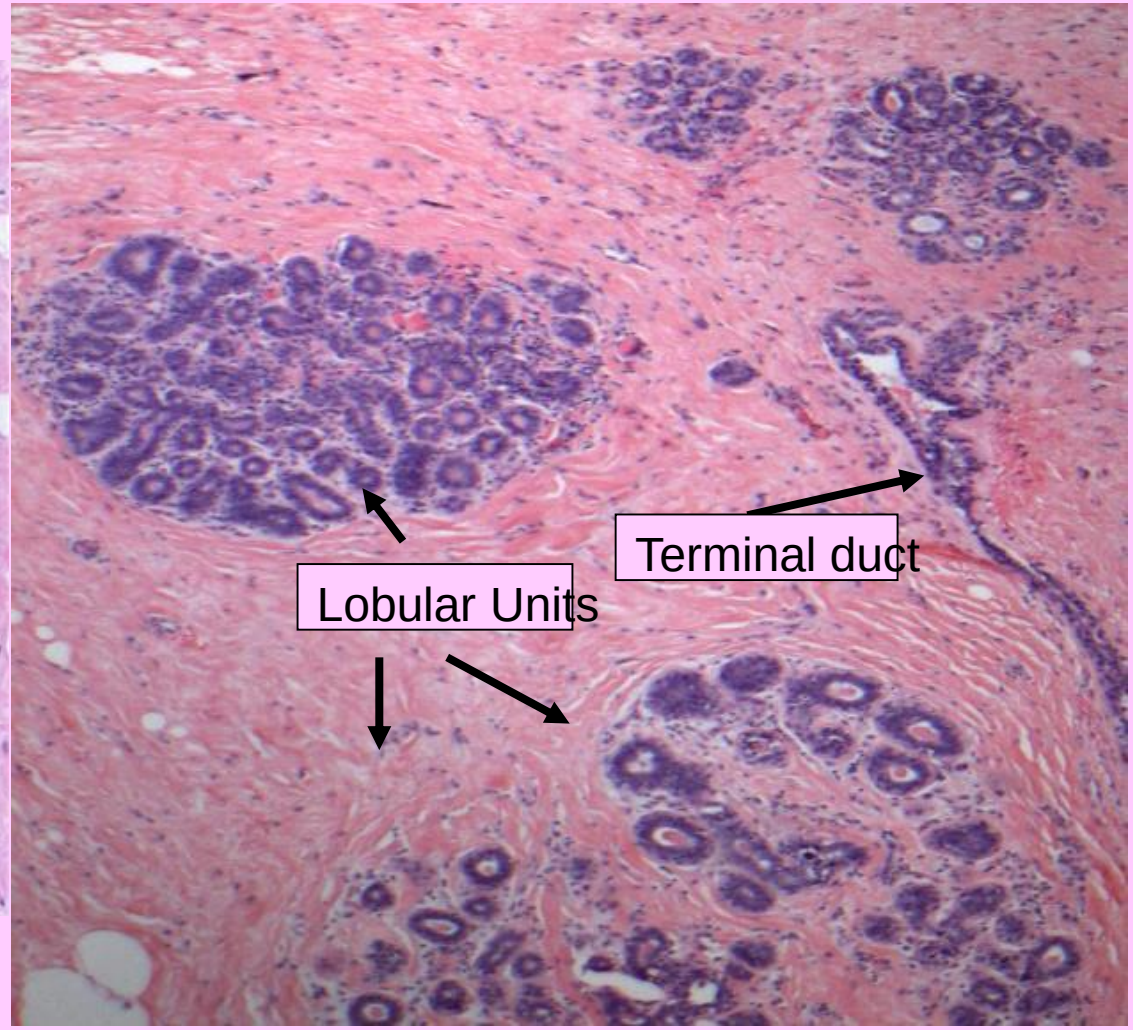
These ducts are where 78% of breast cancers occur. This is known as infiltrating ductal cancer.

4- Cancer developing in the lobules is termed infiltrating or invasive lobular cancer. About 10-15% of breast cancers are of this type.

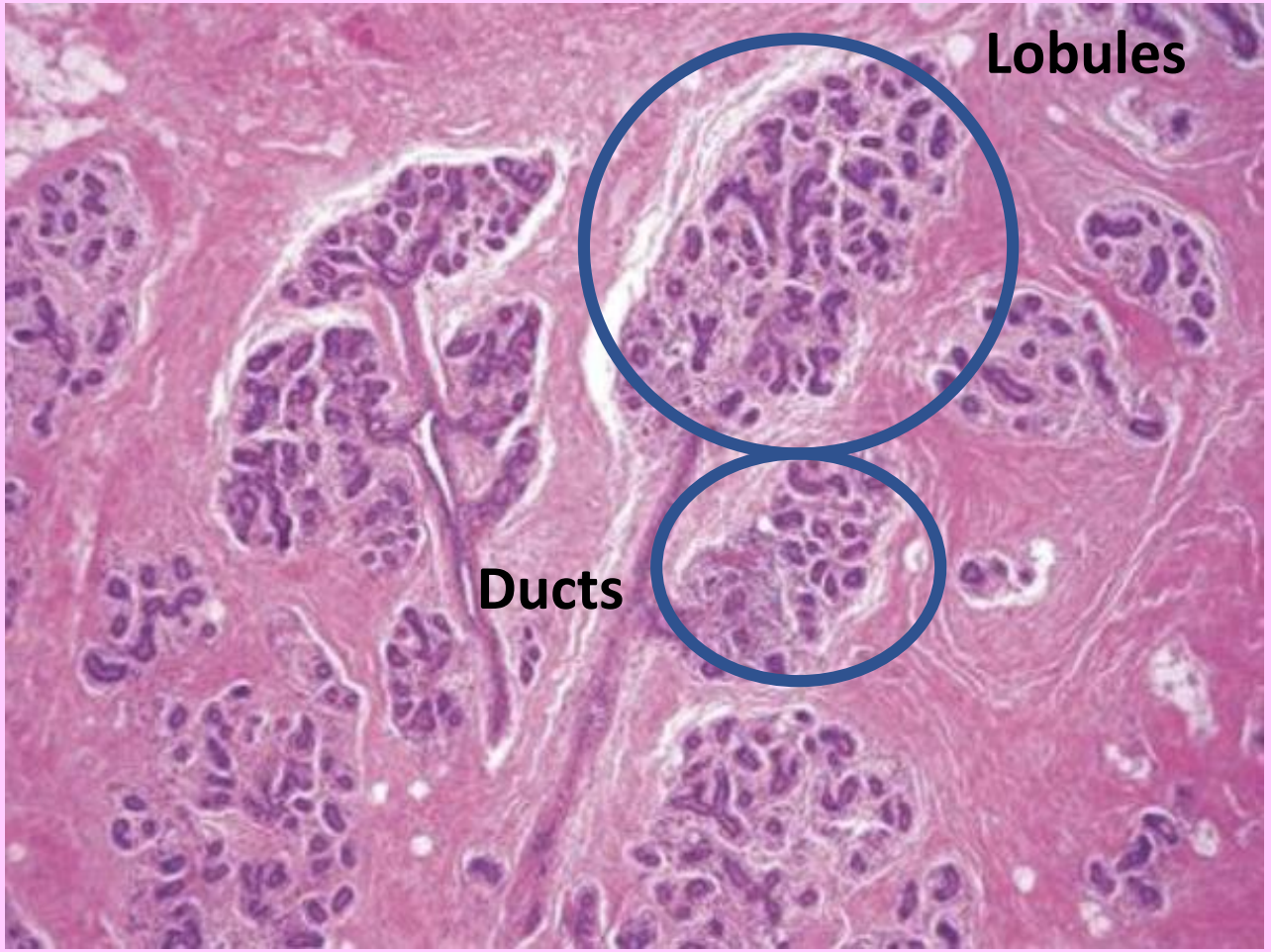
Normal Histology: Terminal Duct Lobular Unit (TDLU)

- Lobules –composed of tiny glands (acini)

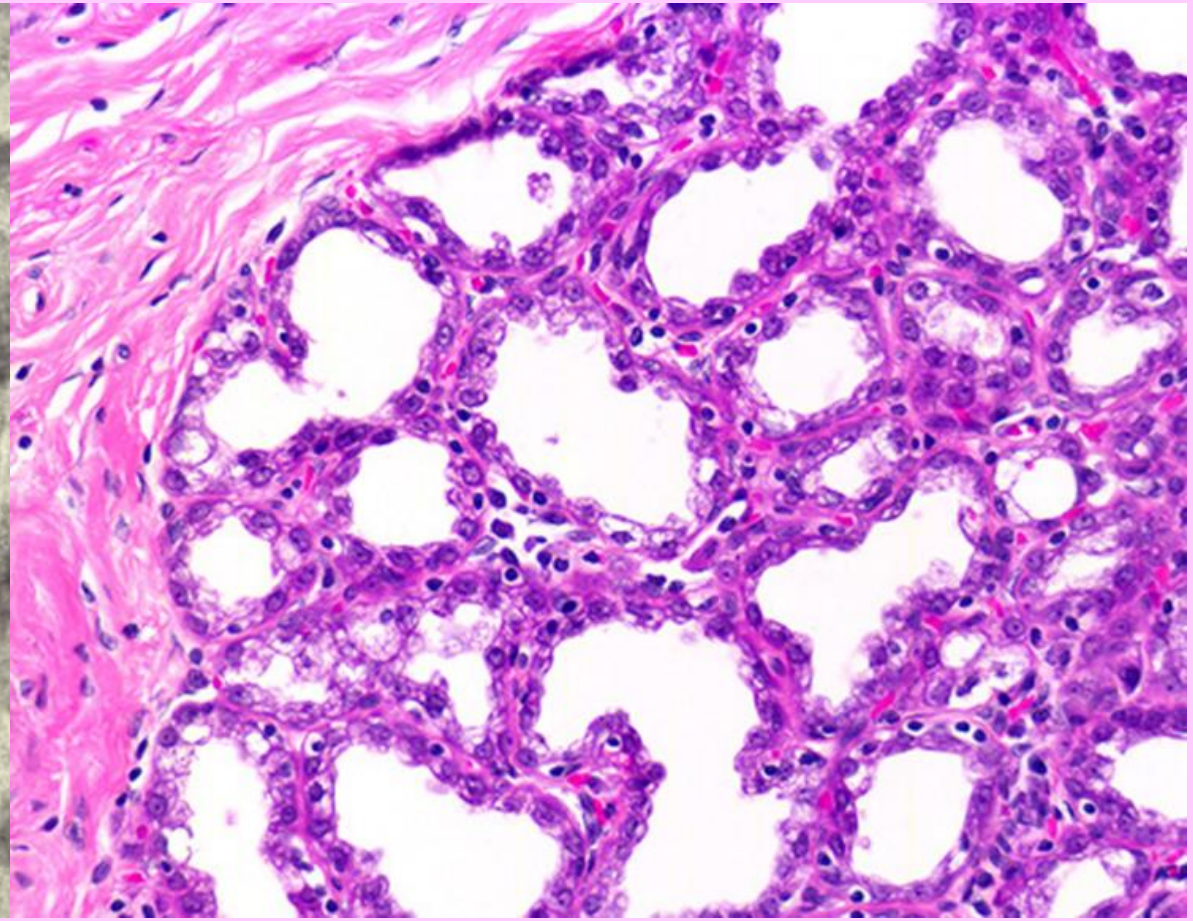




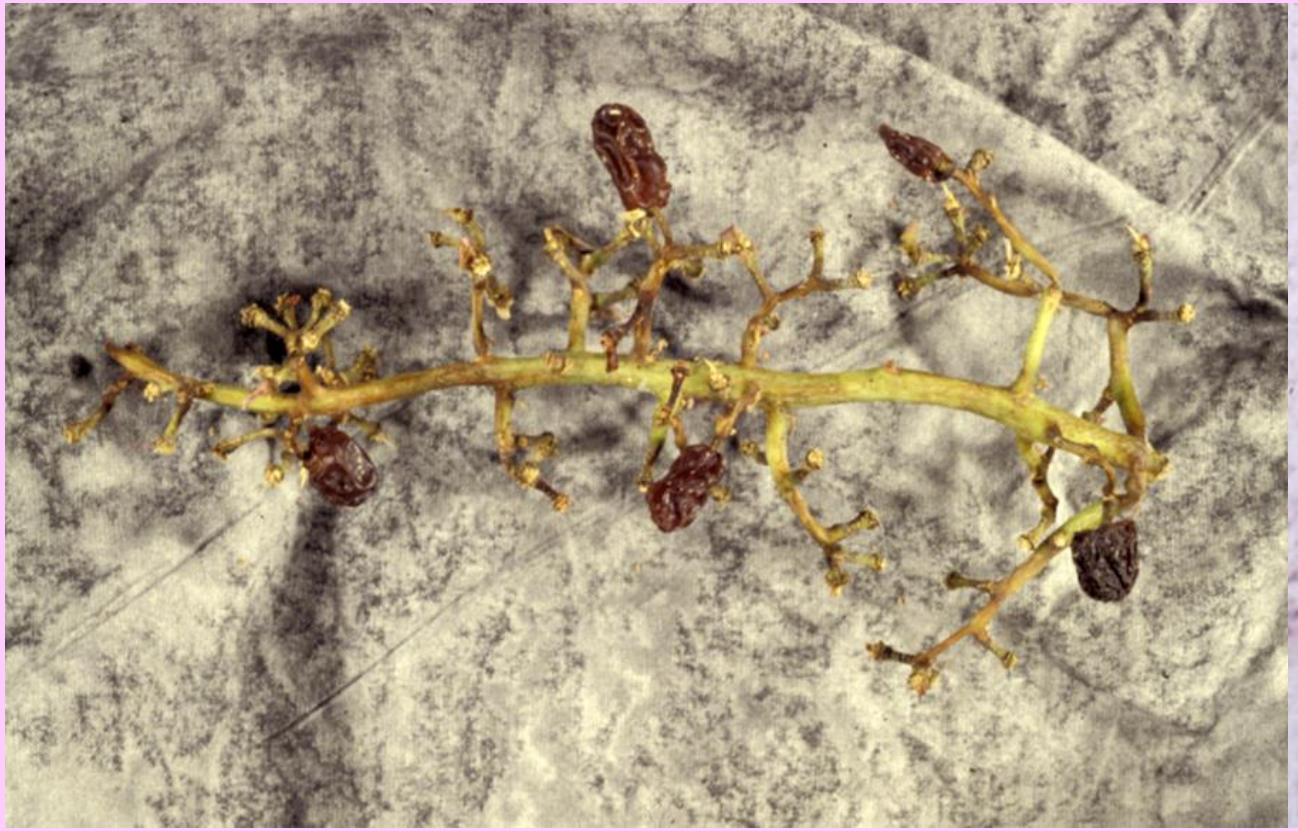
Terminal Duct Lobular Unit (TDLU)



Lactation

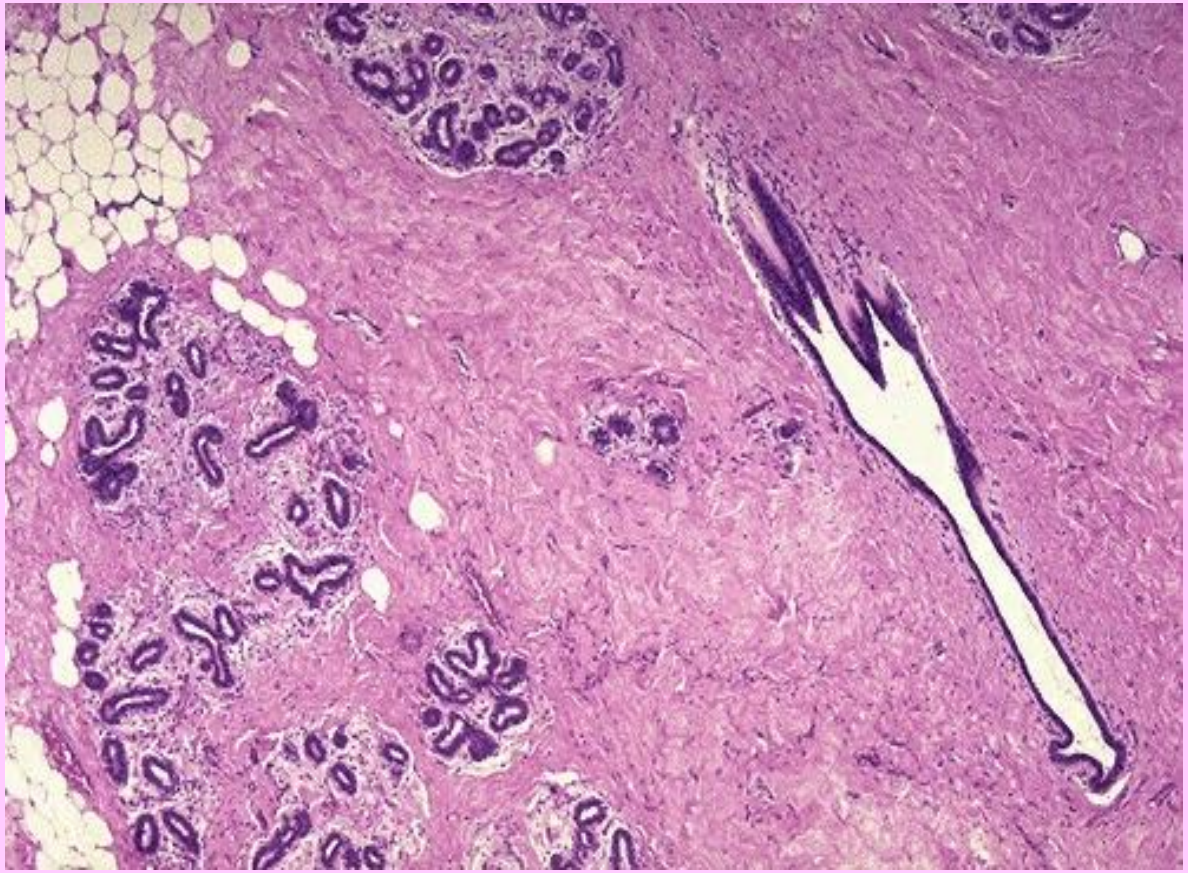


Atrophy of TDLU - Aging

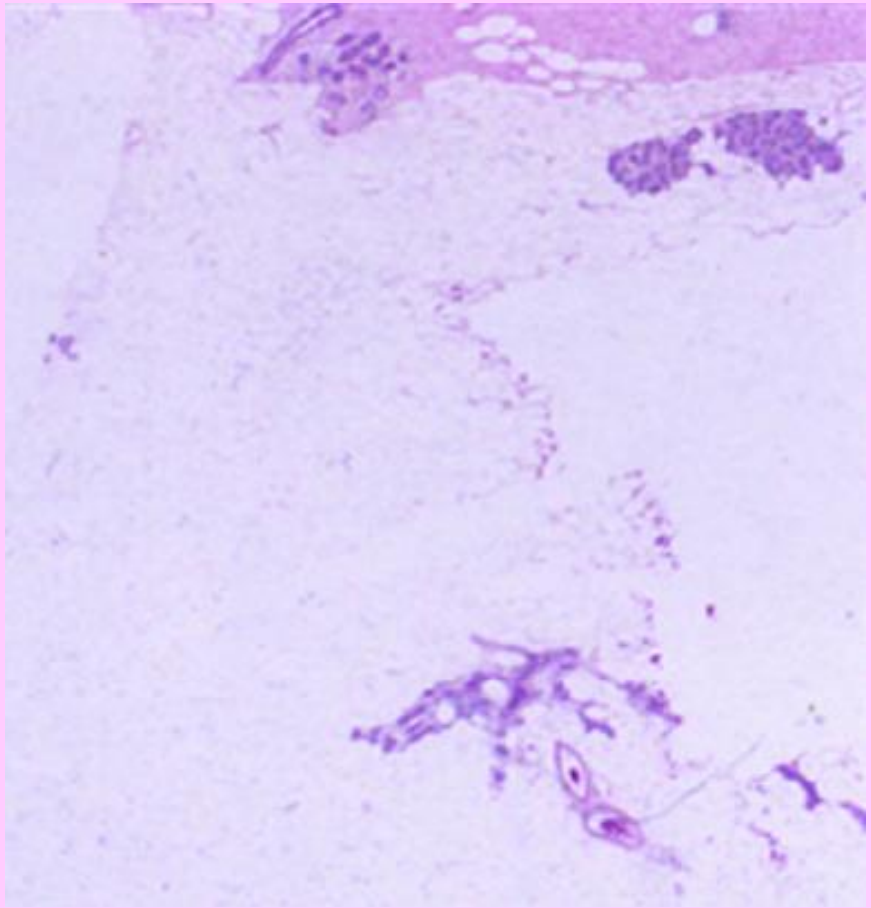


Variation in fibrous stroma and fat in breast

- Normal young breast



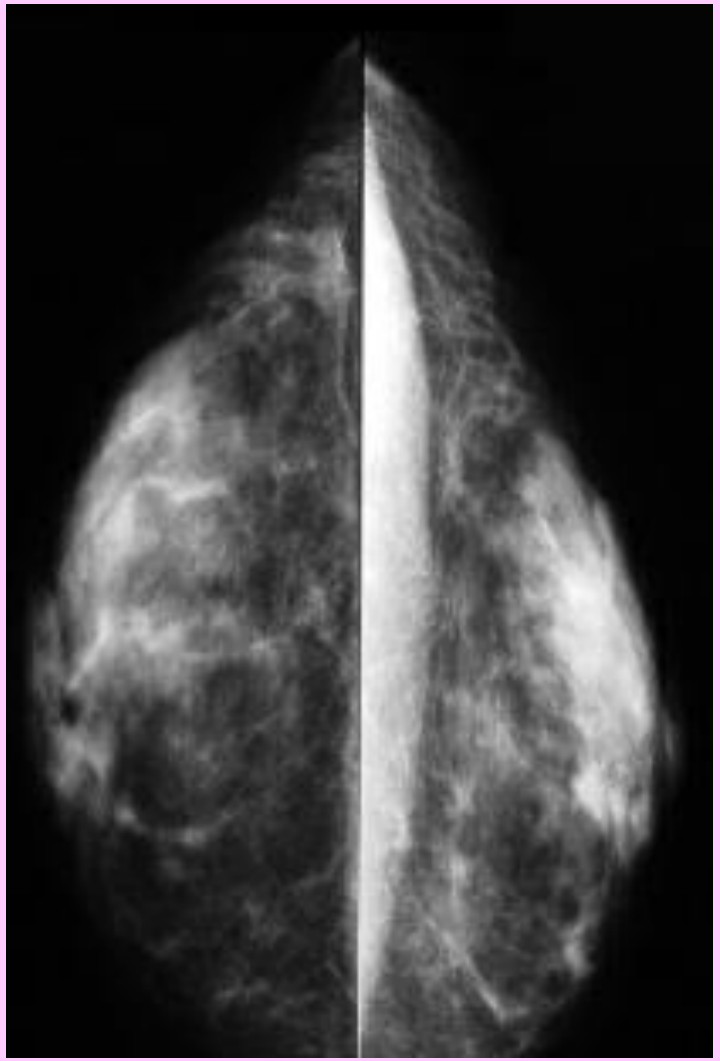
Older breast



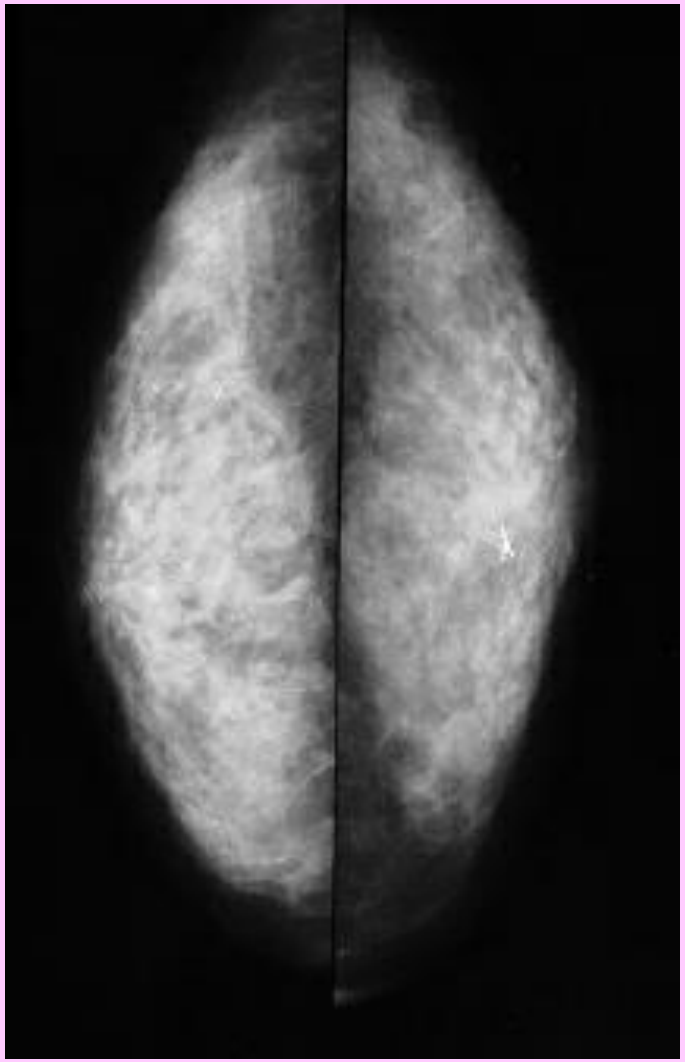
Mammography

Mostly fatty tissue – older women

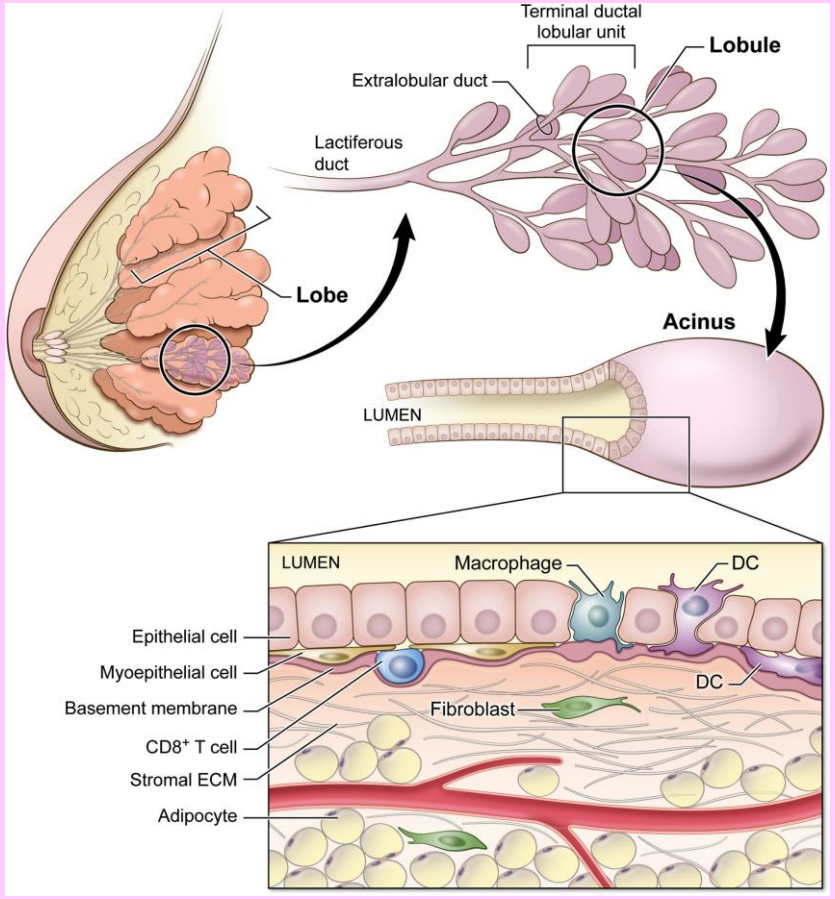
Breast cancer

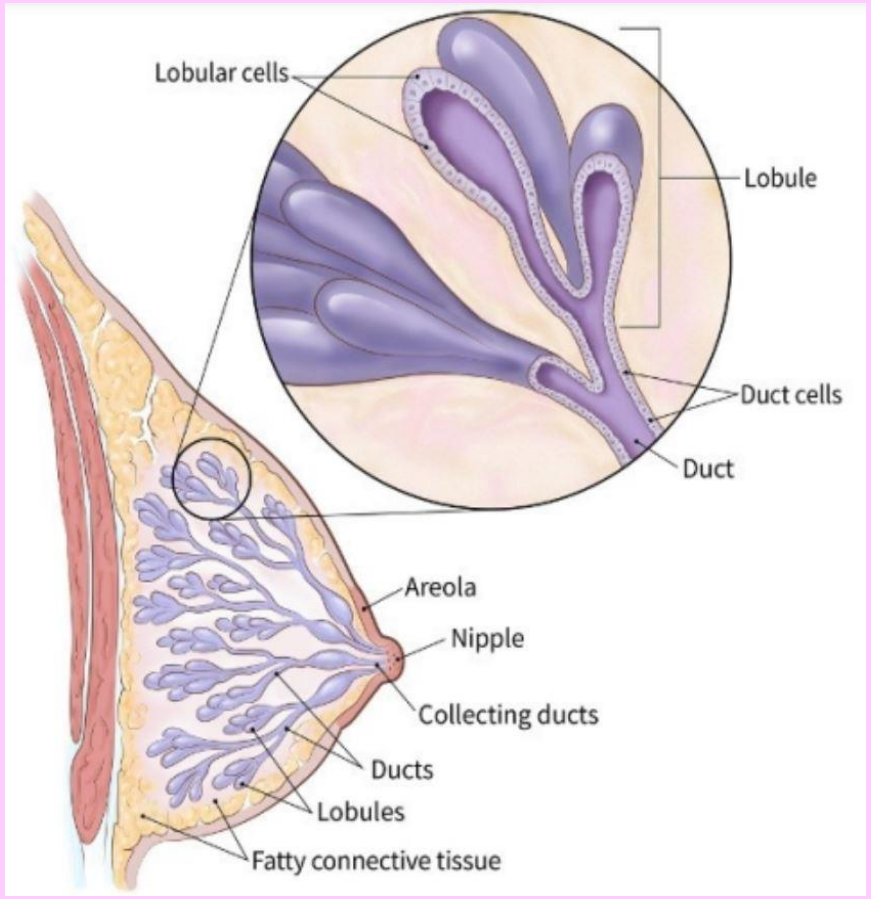


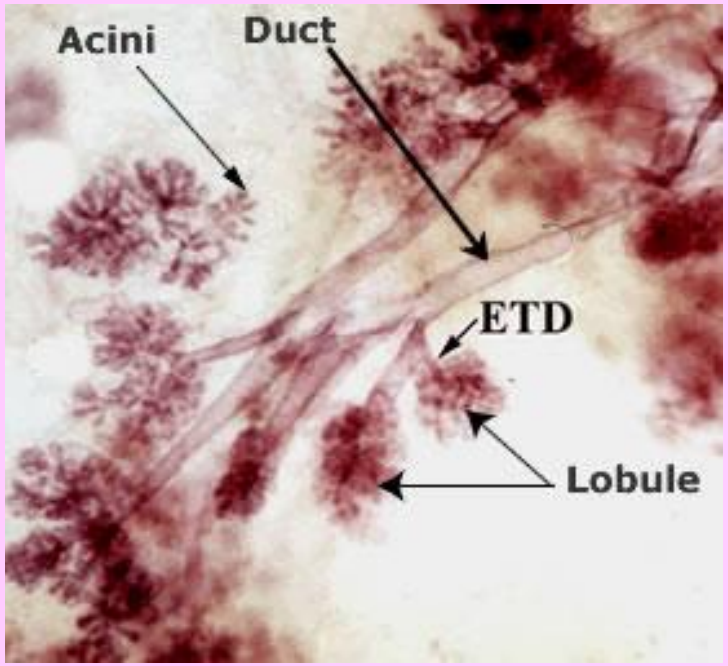
Dense fibrous tissue – young women



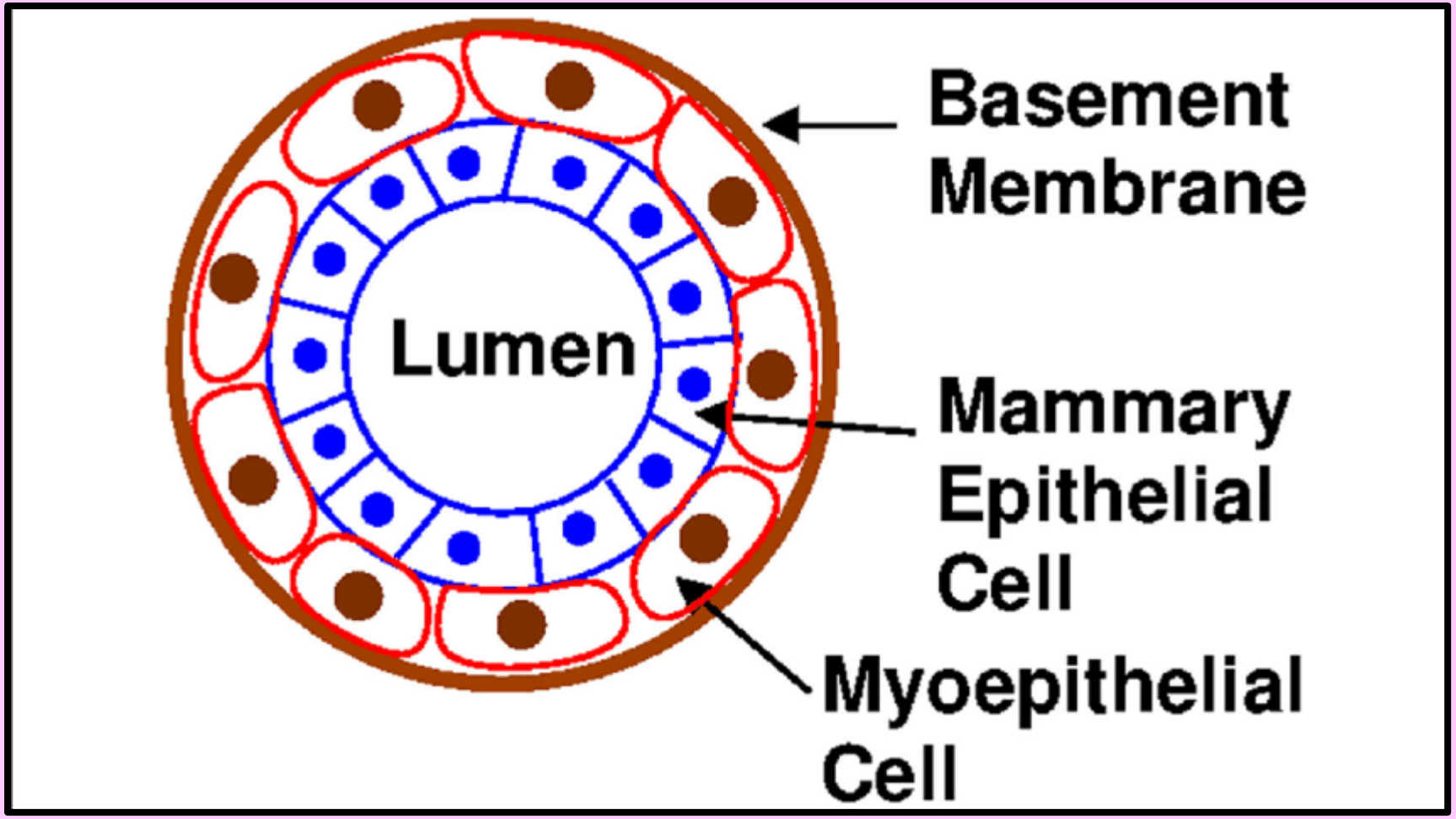
Ducts and Lobules







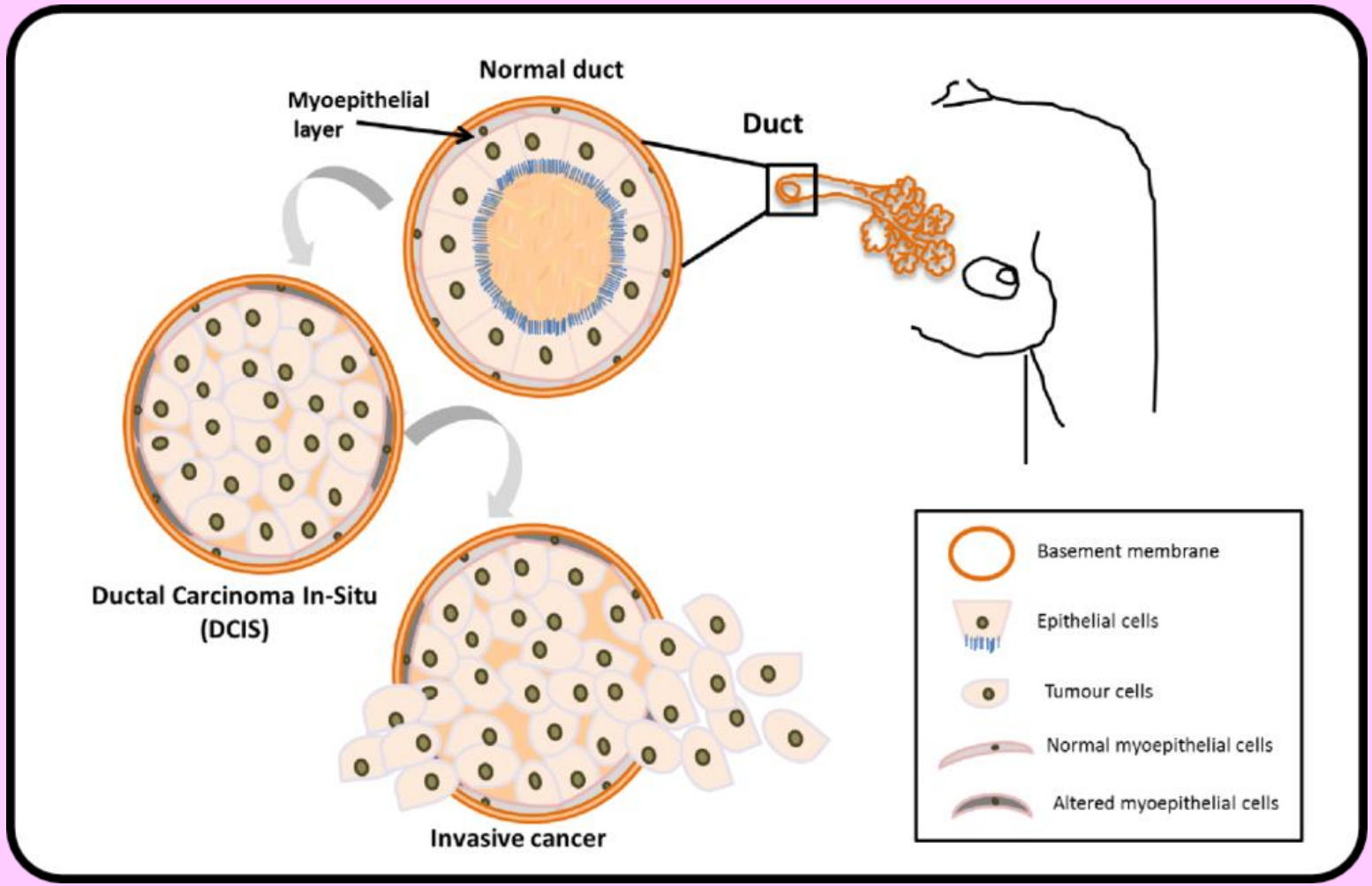
Normal Duct



Cross section of a normal milk duct showing the lumen, mammary epithelial cells, myoepithelial cells, and basement membrane

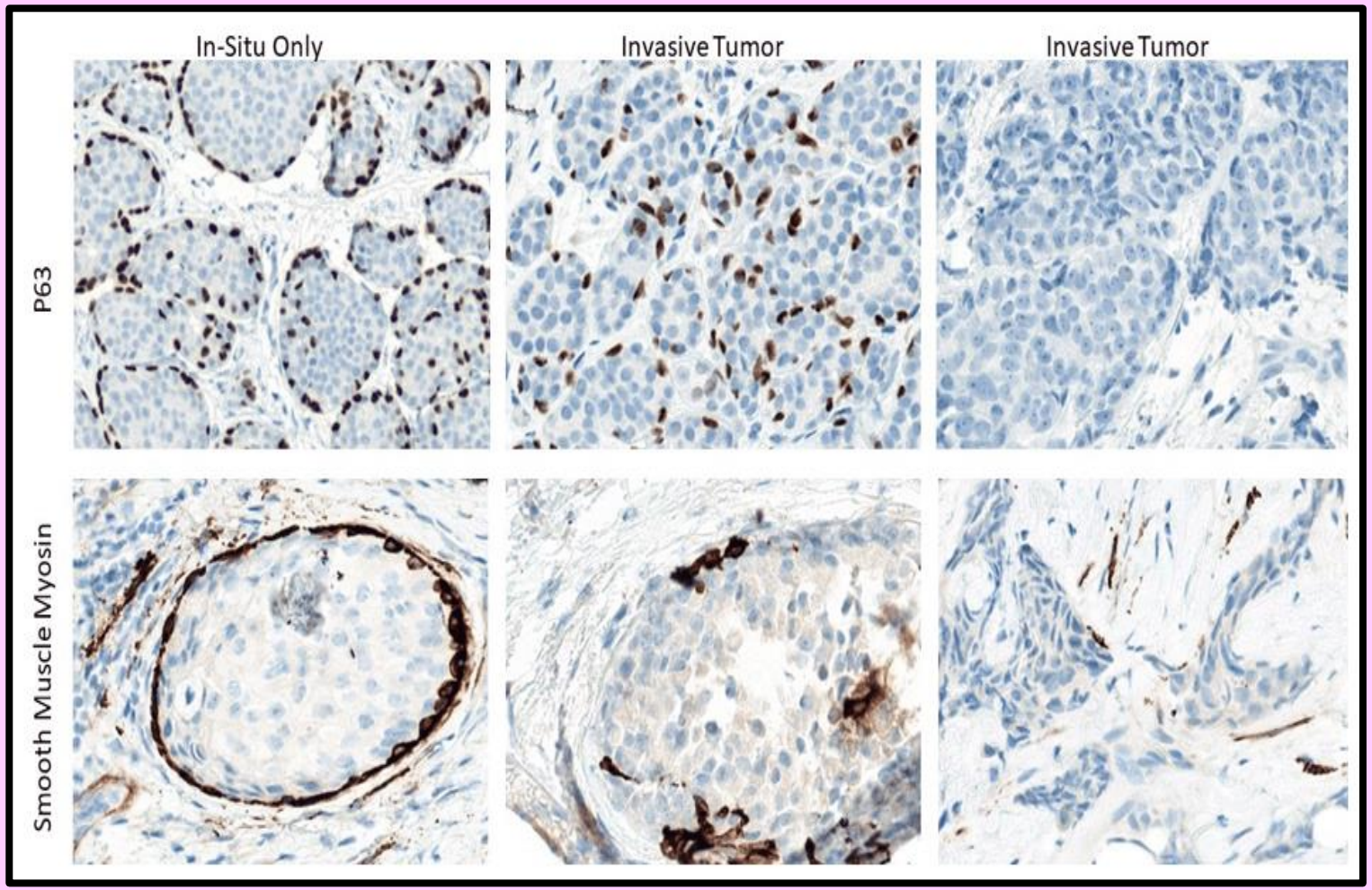
Histology: two cell layers around acini and ducts

Important Cancer terminology : In Situ vs. Invasive



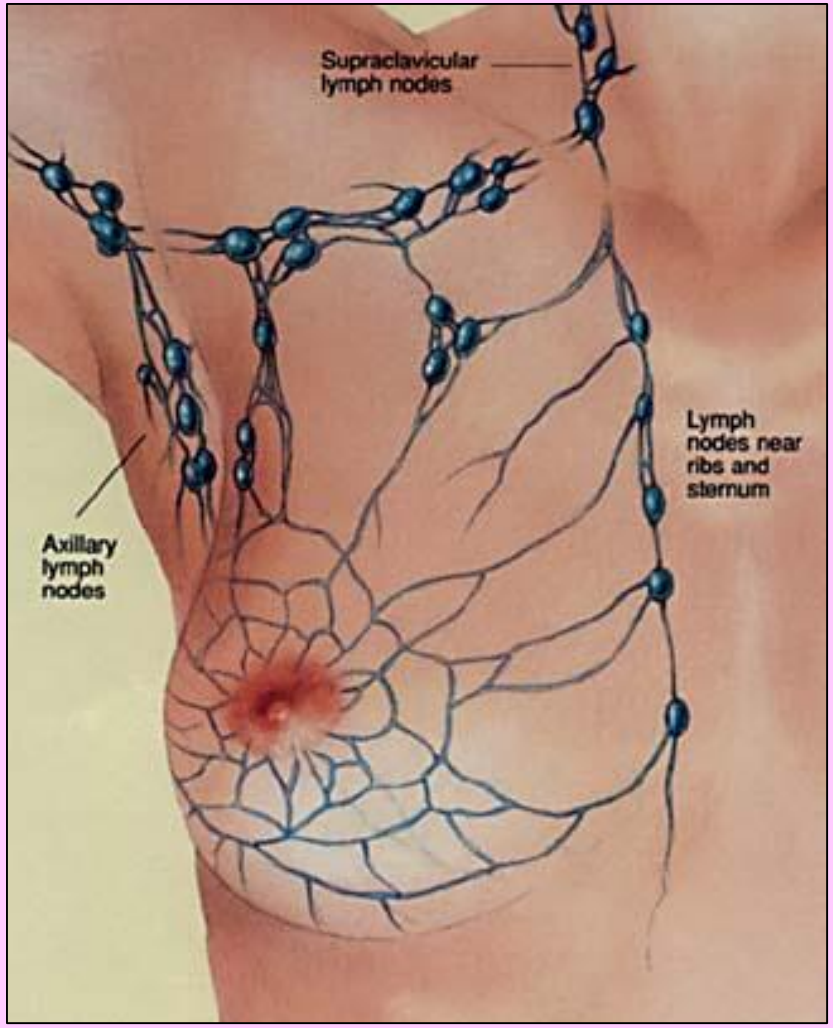
- In Situ –cancer cells do not cross the basement membrane
- Invasive cancer – cancer cells grow through the basement membrane – they are no longer contained

Immunohistochemistry – specific markers



- P-63 staining (myoepithelial cells)
- Smooth Muscle Myosin staining (basement membrane)

Lymph nodes (LN)



- Lymph nodes (LN) contain immune cells that can help fight infection by attacking and destroying germs that are carried in through the lymph fluid.
- If breast cancer spreads it typically goes to the LN under the arm and then to those near the collarbone or breastbone
- Examine LN for cancer cells
  - Biopsy
  - Dissection

Risk factors for Breast Cancer

- Personal or family history, esp. first degree relative
- Not having children
- Having first child after age 30
- Radiation therapy to chest/upper body
- Overweight or obese
- Age (Older)
- Late menopause
- Diets high in saturated fat; Alcohol
- Sex F>M
- Estrogen use/Replacement Therapy

Signs and Symptoms

- Early breast cancer has little or no symptoms; it is not painful
- Breast discharge, especially if only from one breast
- Sunken nipple
- Redness, changes in texture, and puckering (Usually caused by skin disease but sometimes can be associated with breast cancer).
- Lumps on or around breast; however, most lumps are not cancerous
- Other lumps around the under arm or collarbone which don’t go away

Benign breast lesions

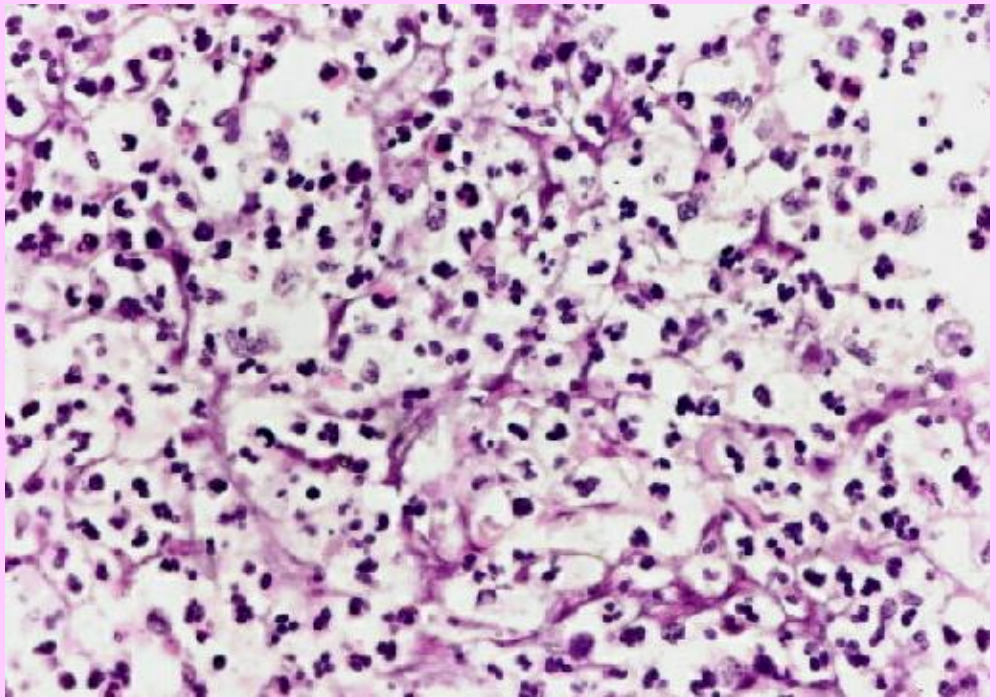
- May mimic malignancy
  - Palpable lumps on physical exam
  - Microcalcifications or masses on imaging
  - Nipple discharge
- Some have increased risk for future development of cancer
- **More** common than cancers

Inflammatory Conditions: Mastitis

Acute mastitis:

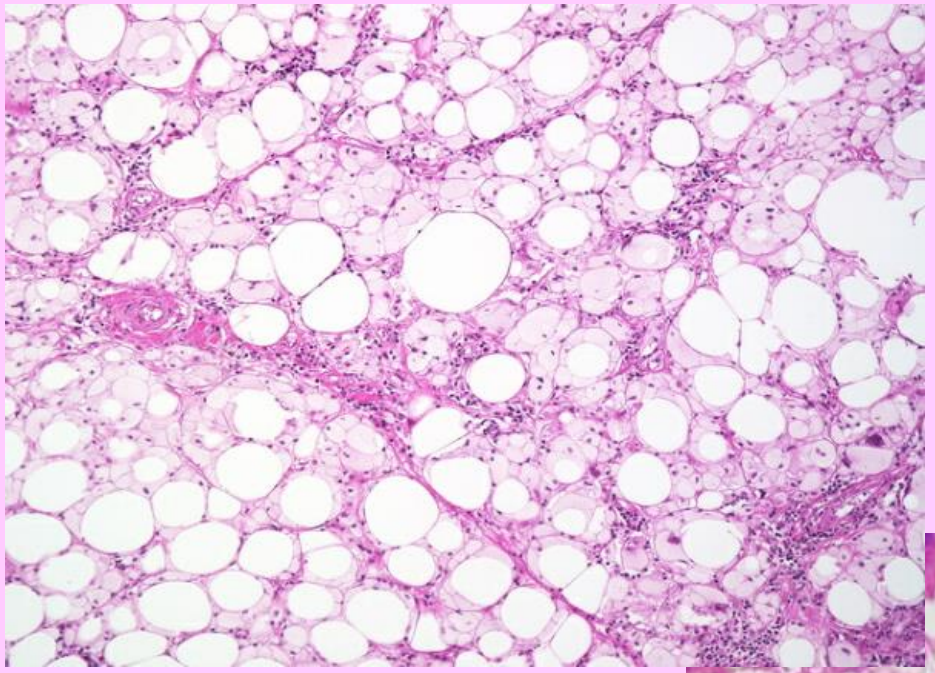
- Fever, breast pain, swelling, redness
- Associated with lactation in postpartum period
- Organisms:
  - *S. aureus* > *Streptococcus*
- Treatment:
  - Antibiotics
  - Continue breastfeeding

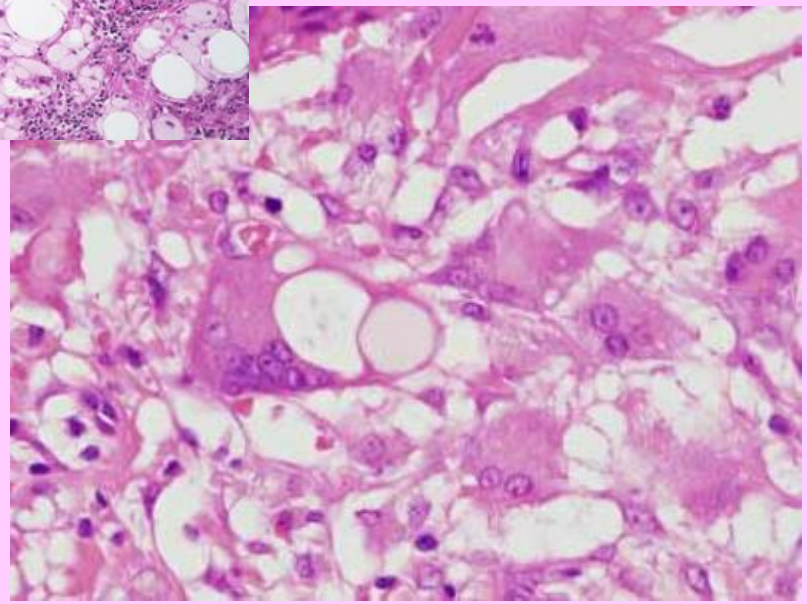
- LOOKS LIKE INFLAMMATORY BREAST CANCER

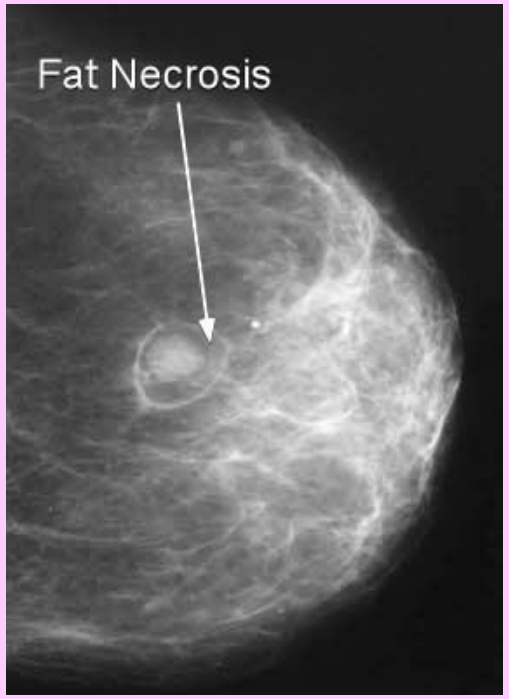


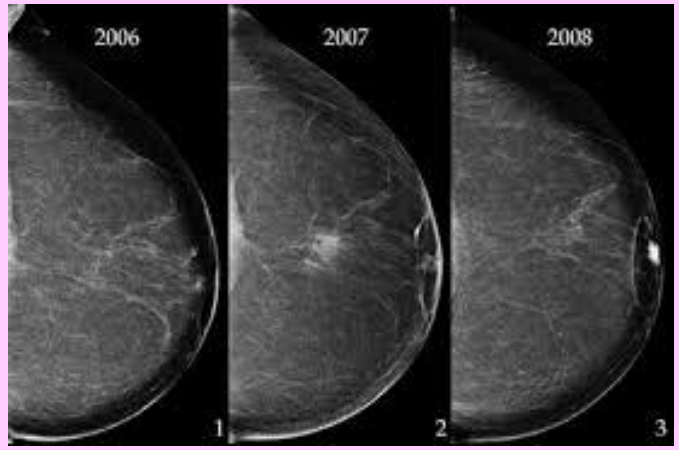
Fat Necrosis

- Physical trauma to breast – surgery, accident, biopsy
- Calcifications on mammography – looks bad





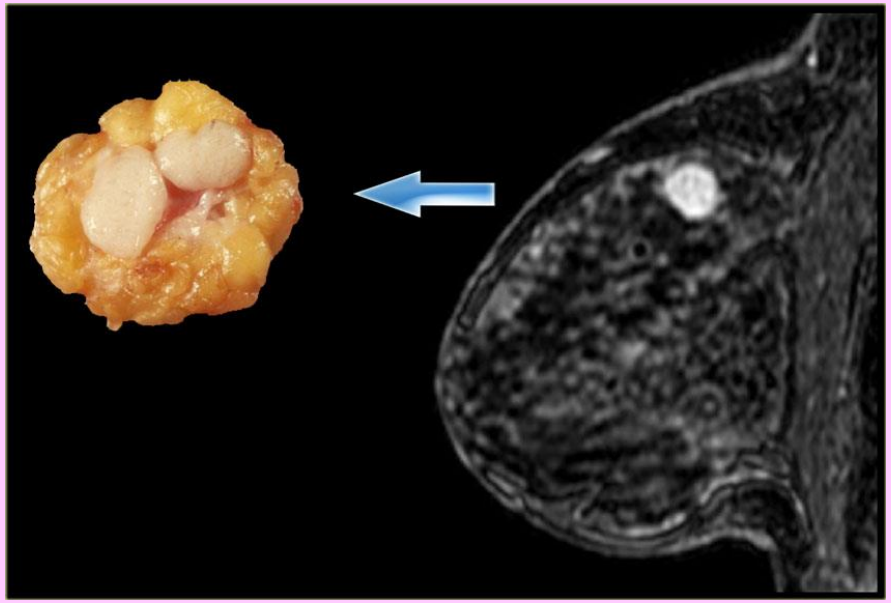


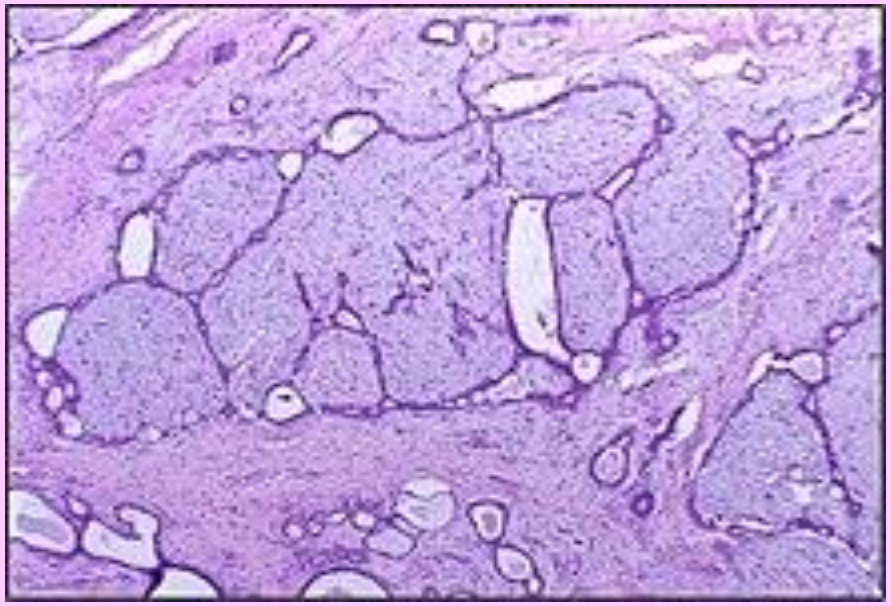


Fibrocystic Change

- Age 30-40
- Fibrosis
- Exaggerated response to hormonal stimulation
- Vague irregularity – Cysts, lumps
- Calcifications
- Benign but may increase risk for Invasive carcinoma if associated hyperplasia is seen

Fibroadenoma





- Most common benign neoplasm of breast –tumor of fibrous tissue and glands
- Pre-menopausal women
- Well circumscribed mass, mobile, “marble like”
- Estrogen-sensitive
- Benign, no increased risk

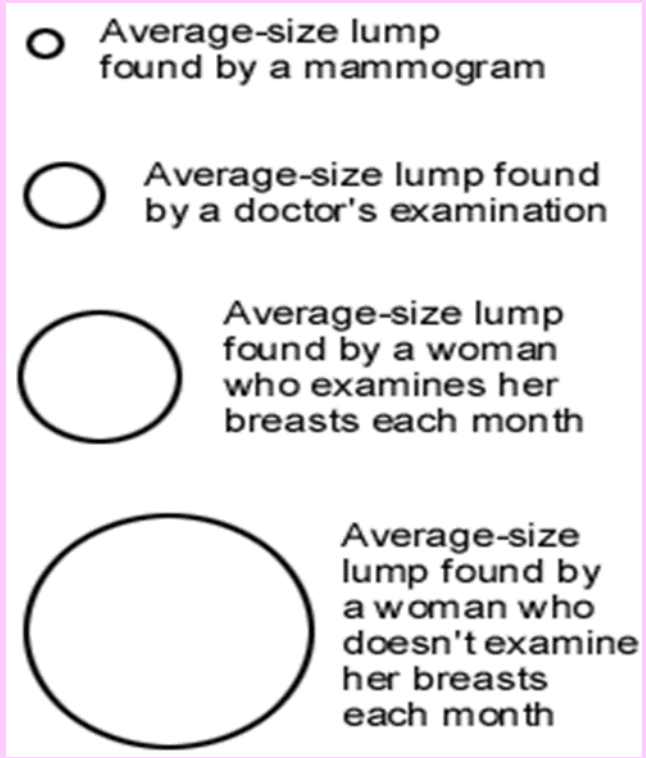
Where breast cancer occurs

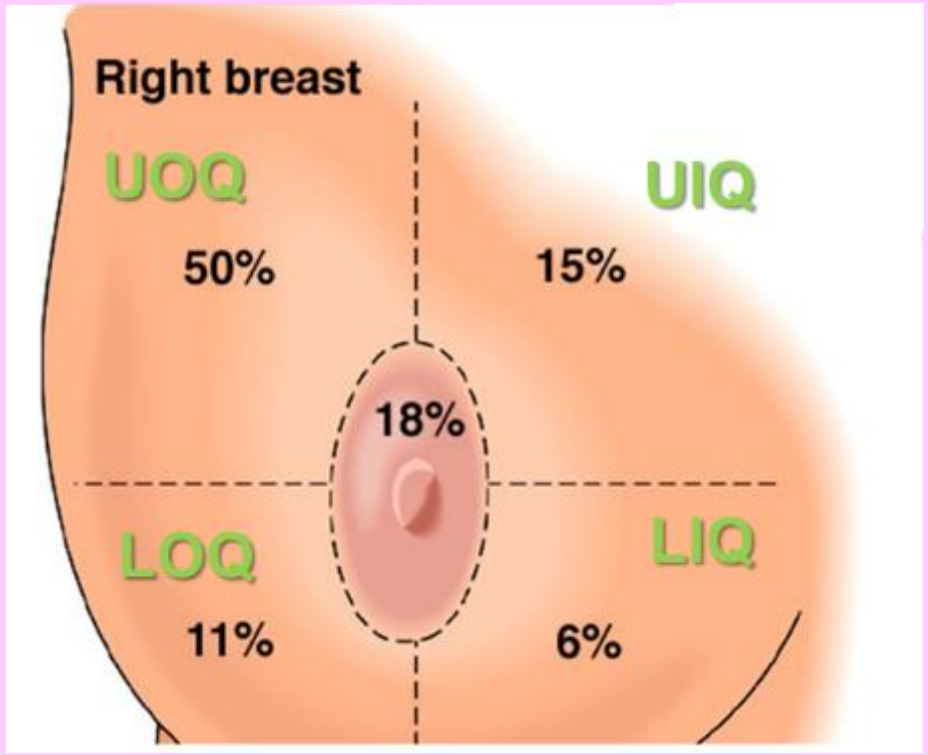
0.5 cm

1.0 cm

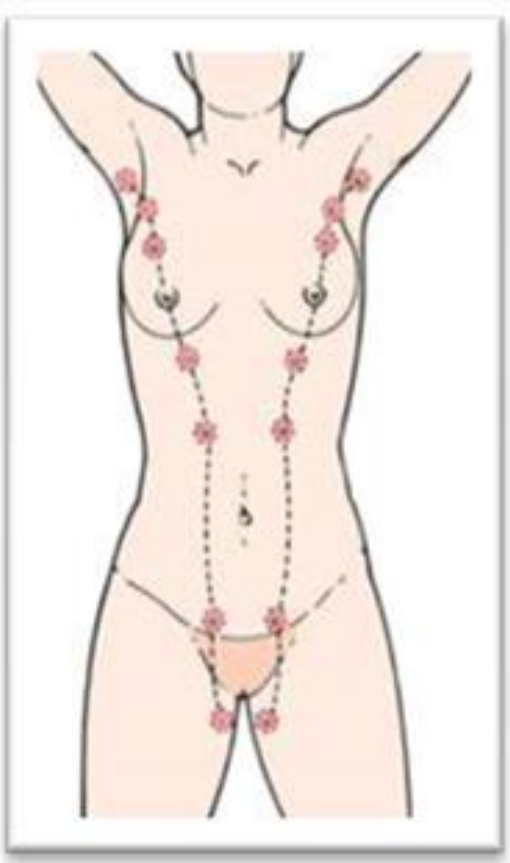
2.0 cm

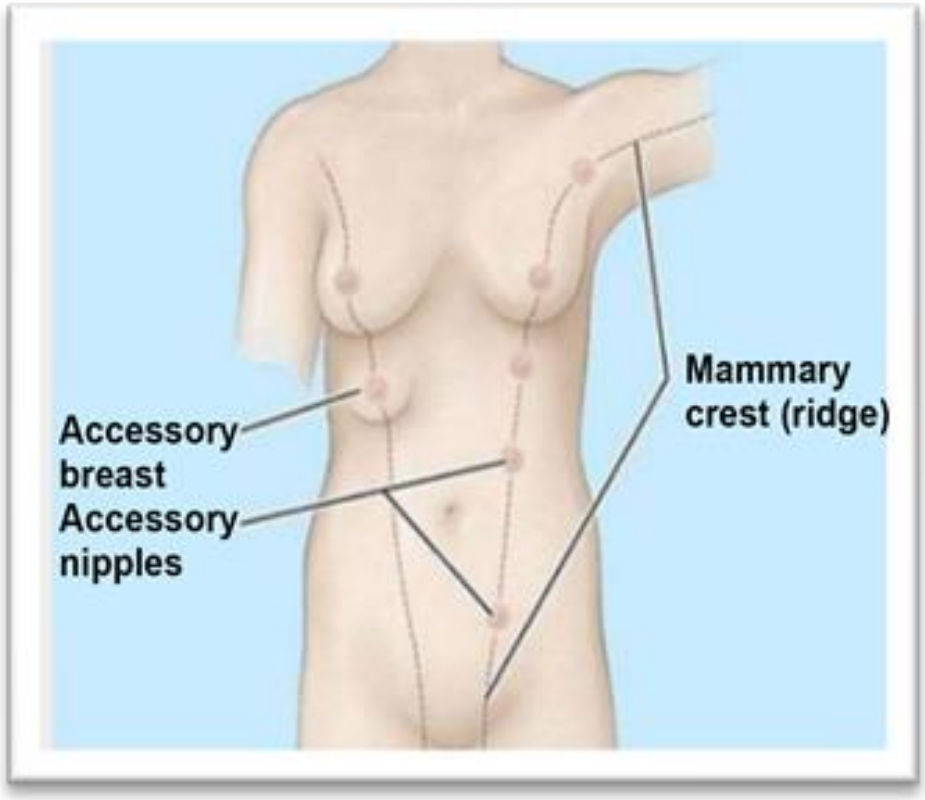
4.0 cm





Milk Lines



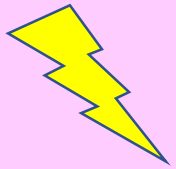


Screening recommendations (American Cancer Society) Women at “average” risk

- **Women between 40 and 44** have the option to start screening with a mammogram every year.
- **Women 45 to 54** should get mammograms every year.
- **Women 55 and older** can switch to a mammogram every other year, or they can choose to continue yearly mammograms.
- Screening should continue as long as a woman is in good health and is expected to live at least 10 more years.
- Clinical breast exams are not recommended for breast cancer screening among average-risk women at any age.

- Women with risk factors –start screening at age 30.

Oct 20, 2021 FB post from a friend



- It's been a habit for me to say something for breast cancer awareness month. I found my breast cancer in 2015 by self exam which is officially discouraged, but encouraged by women and every doctor I have spoken to, including radiologists and oncologists. I know 3 women who found their own breast cancers, one of them soon after mammography. If you are in that certain age bracket where 1:8 women have a breast cancer, check. Have your mammos. Early detection counts. I was very fortunate - grade 2 stage 1, hormone receptors positive and EGF receptor negative. Now it's in the distant past. Sorry this post is so long. What I really wanted to say is the most rewarding thing about saying this stuff in public is hearing the stories of my friends out there who are dear-to-me survivors. Thank you my sisters!

Diagnosis - Imaging

- **Mammogram -** low-dose detailed X-ray gives doctors a better view of lumps and other problems
- **Ultrasound** uses sound waves to make a picture of your breast
- **Digital breast tomosynthesis (DBT) 3D mammography**
- **Magnetic resonance imaging** uses a magnet linked to a computer to create detailed images of the insides of your breasts.

Diagnosis – Biopsy

- **Fine-needle aspiration.** This is for easy-to-reach lumps or those that might be filled with fluid.
- **Core-needle biopsy.** This type uses a bigger needle to remove a piece of tissue.
- **Image-guided biopsy.** The doctor uses imaging to guide the needle.
- **Surgical (open) biopsy.** A surgeon removes the entire lump along with nearby breast tissue.
- **Lymph node biopsy.** The doctor removes a part of the lymph nodes under your arm to see if the cancer has spread.
-

Testing on biopsy

- **Tumor features (TNM)** Is it invasive or in situ, ductal, or lobular? Has it spread to your lymph nodes? The pathologist examines the margins or edges of the tumor for the presence or absence of tumor cells.
- **Grade** The pathologist notes how different the cancer cells look compared to healthy cells
- **Markers for gene expression (by immunohistochemistry &/or molecular techniques):**

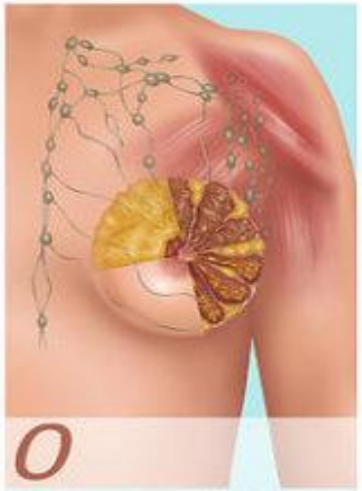
  Estrogen receptors (ER) and progesterone receptors (PR)

  HER2/neu

Newer Molecular Tests on biopsy

- **Oncotype Dx** This test evaluates 16 cancer-related genes and five reference genes to estimate the risk of the cancer coming back within 10 years of diagnosis. Gives a Breast Recurrence Score.
- **MammaPrint** This test uses information from 70 genes to predict the risk of the cancer coming back.
- **PAM50 (Prosigna)** This test uses information from 50 genes to predict if the cancer will spread.

Stages of Breast Cancer



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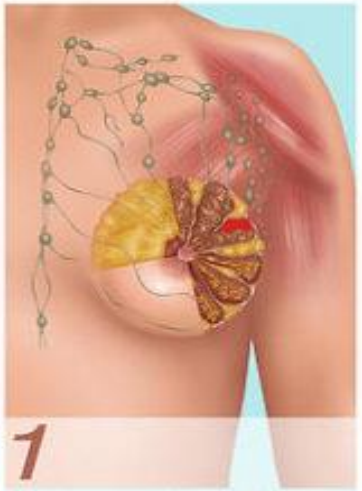
Abnormal cells in duct lining or sections of the breast. Increased risk of developing cancer in one or both breasts.

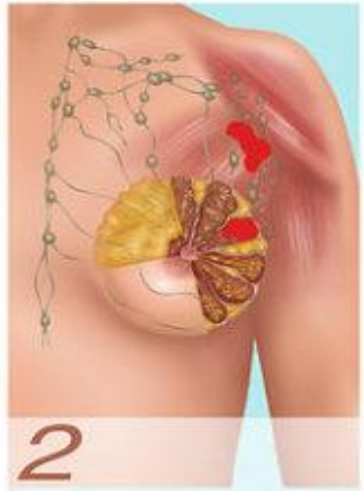
100%
SURVIVAL RATE



1

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

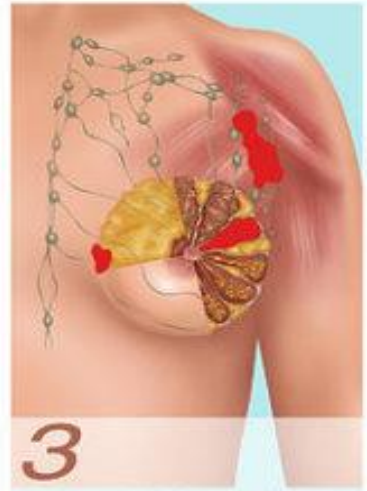
98%
SURVIVAL RATE



2

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

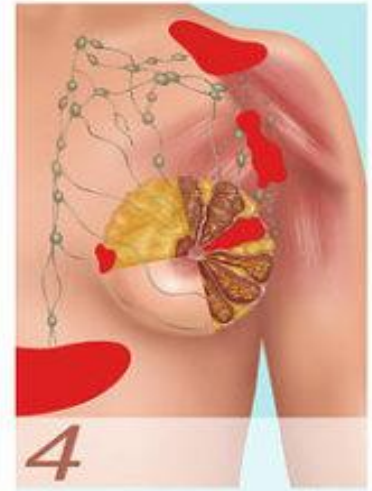
88%
SURVIVAL RATE



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

Prognosis – Classic TNM staging

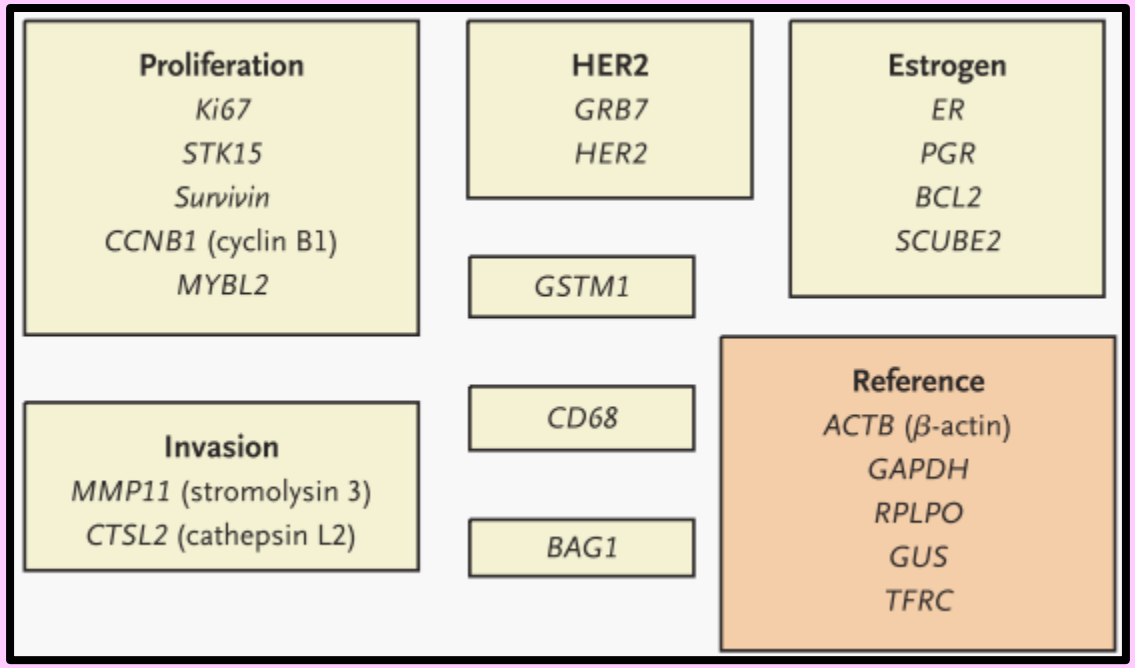
- Extent (size) of the tumor **(T)**
  - **T1 <2cm**
  - **T2 <2cm ≤ 5cm**
  - **T3 > 5cm**
  - **T4 – any size but extension to chest wall/skin**
- Spread to nearby lymph nodes **(N)**
  - **N0-N4**
- Spread (metastasis) to distant sites **(M)**
  - **M0 – M1**

Prognosis: TNM + (2018 updates AJCC)

- Estrogen Receptor (ER) presence
- Progesterone Receptor (PR) presence
- Her2/neu (HER2) presence
- Histopathologic grade (G) of tumor
  - G1
  - G2
  - G3
- Gene Expression Panels - Oncotype DX® - Recurrence Score

Oncotype Dx

- An individualized assessment of risk of distant recurrence.
- Prediction of absolute benefit from chemotherapy.
- Quantitative ER values by RT-PCR clarify the magnitude of hormonal therapy (tamoxifen) benefit.
- Quantitative PR and HER2 values by RT-PCR provide additional information.



Oncotype DX Breast Recurrence Score Results for Patients Younger Than 50 Years

Score	Treatment Discussion with All Receiving Hormone Therapy
0-15	No benefit from adding chemotherapy
16-20	1.6% benefit from adding chemotherapy
21-25	6.5% benefit from adding chemotherapy
26-100	Substantial benefit from chemotherapy

Oncotype DX Breast Recurrence Score Results for Patients Older Than 50 Years

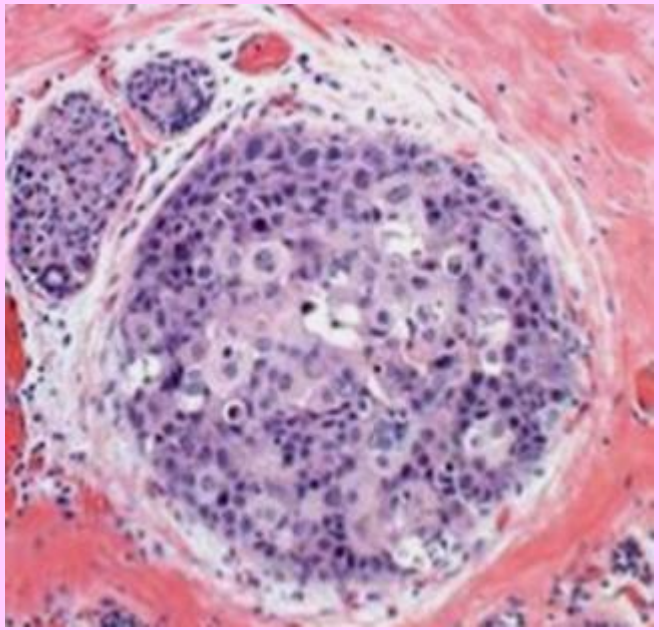
Score	Treatment Discussion
0-25	No benefit from chemotherapy
26-100	Substantial benefit from chemotherapy

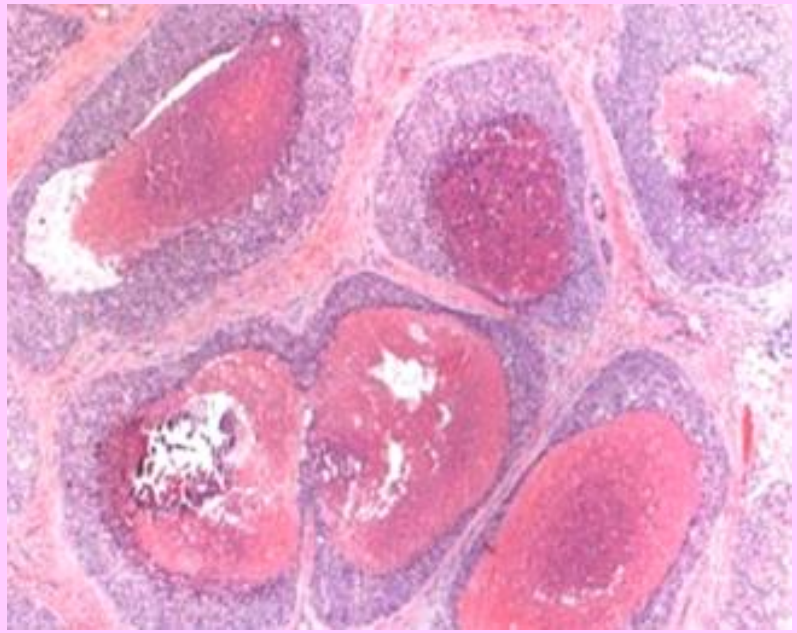
Breast Cancer – is usually a carcinoma a tumor of epithelial tissue

- Occurs predominantly in
  - Ducts
    - Ductal Carcinoma in Situ (DCIS)
    - Invasive Ductal Carcinoma
  - Lobules
    - Lobular Carcinoma in Situ (LCIS)
    - Invasive Lobular Carcinoma
- Rare cancers in other types of breast tissue

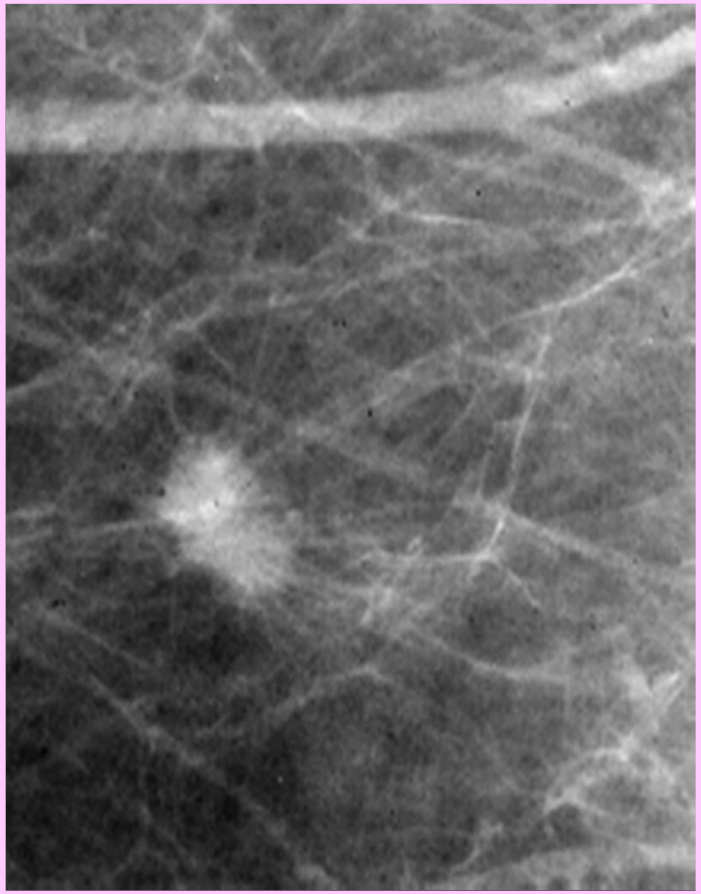
Ductal Carcinoma In Situ (DCIS)

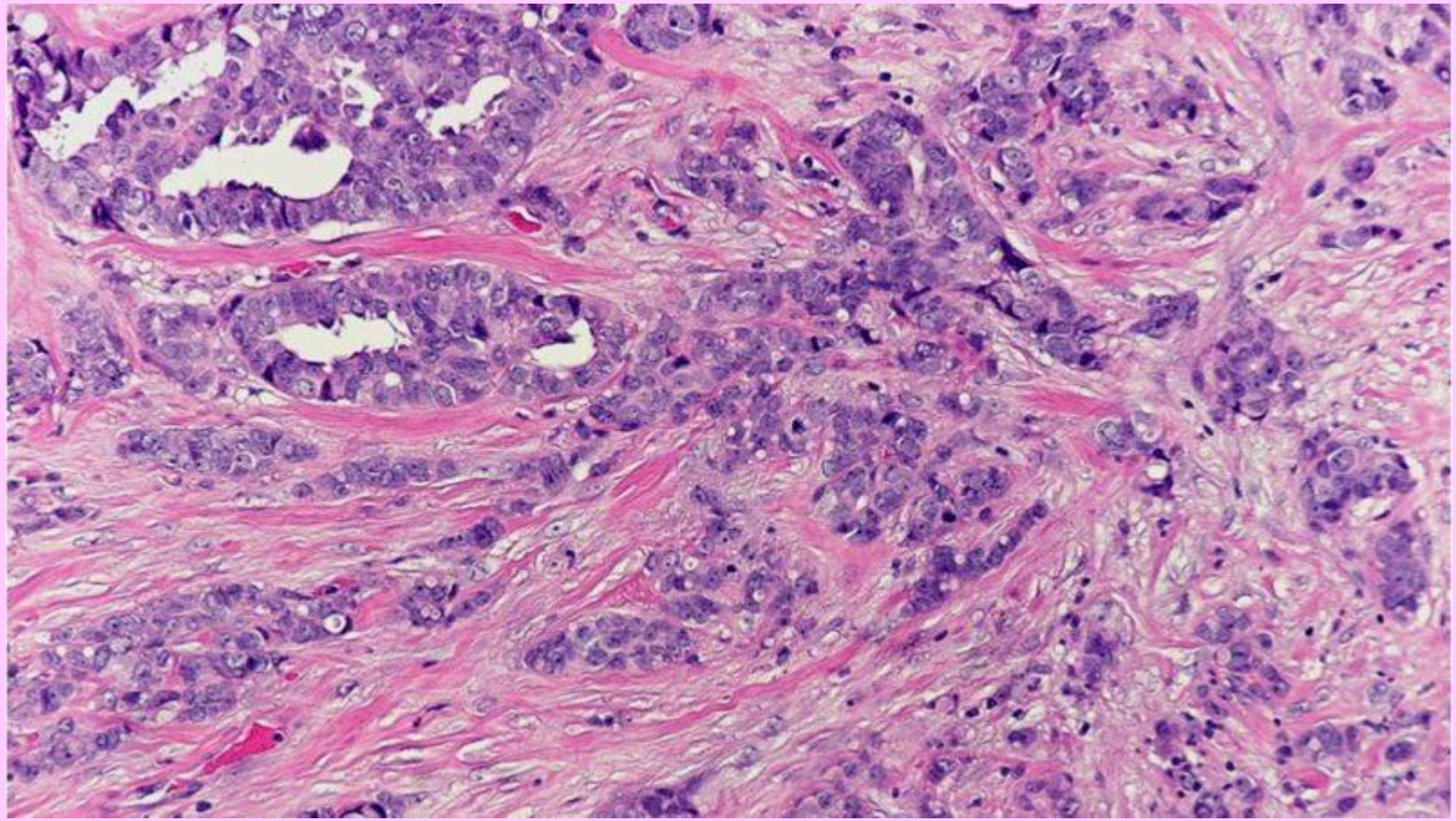
- 80% of Carcinoma In Situ of the Breast
- 15% bilateral
- Usually detected by mammogram – calcifications
- ~30% progress to invasive carcinoma
  - Higher risk in ipsilateral breast
- Cohesive cells, express E-cadherin

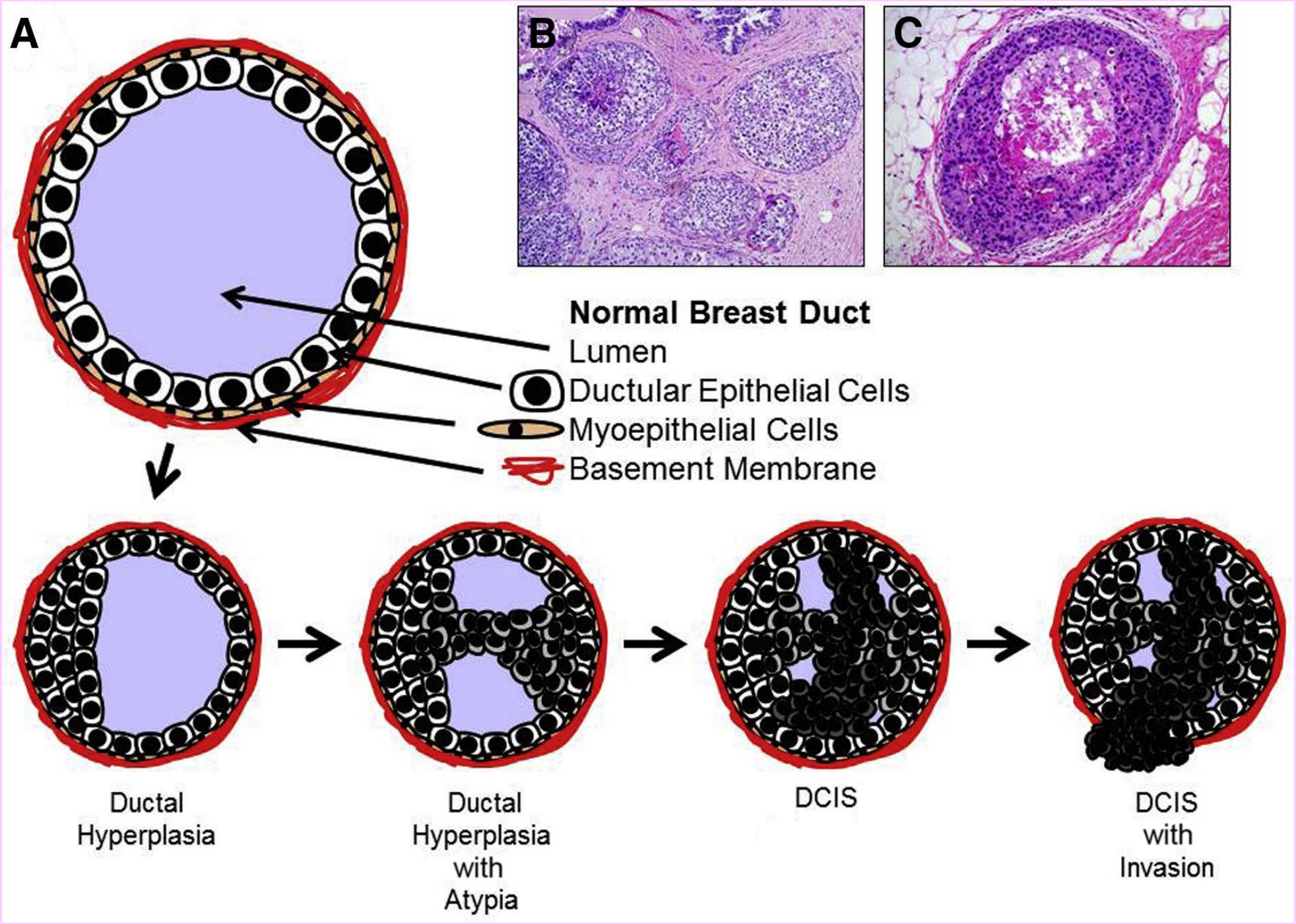




Invasive ductal carcinoma –most common type of breast cancer





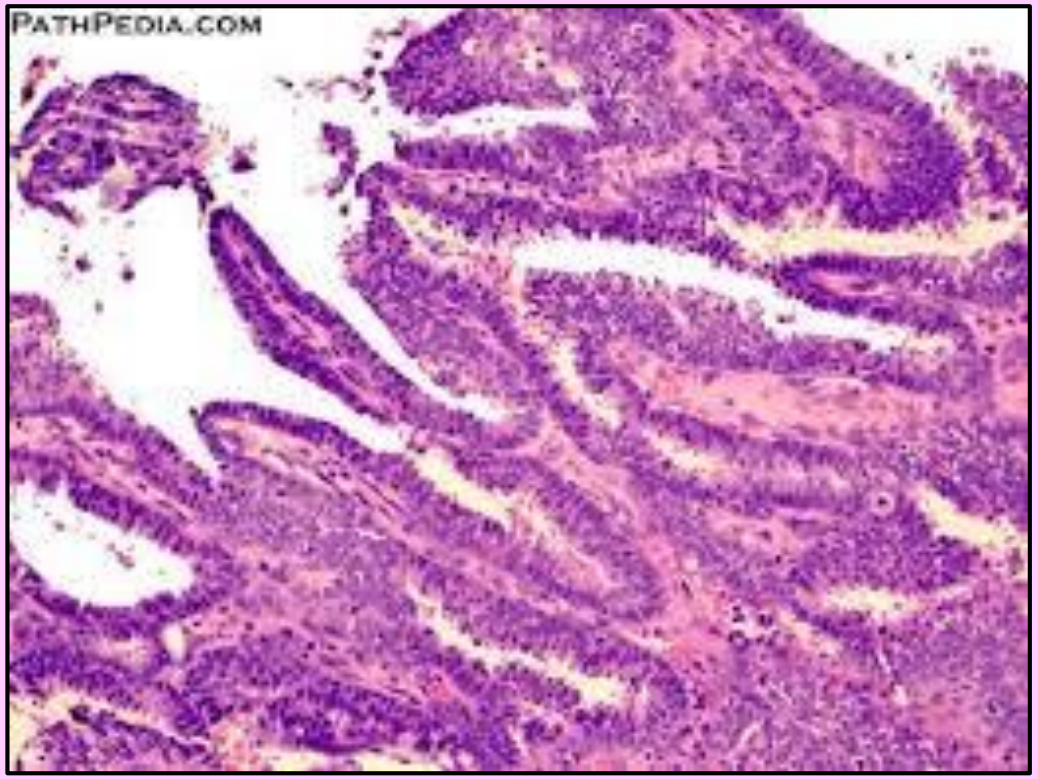

A
B
C
Normal Breast Duct
Lumen
Ductular Epithelial Cells
Myoepithelial Cells
Basement Membrane
Ductal Hyperplasia
Ductal Hyperplasia with Atypia
DCIS
DCIS with Invasion

Paget’s Disease of the Nipple

- > age 50
- Skin on and around the nipple to become red, sore, and flaky, or scaly and spreads to the areola
- Over time gets worse – itching, burning sensation, pain, yellow or bloody nipple discharge
- 97% of women with Paget's disease also have either DCIS or invasive ductal cancer

Papillary DCIS & carcinoma

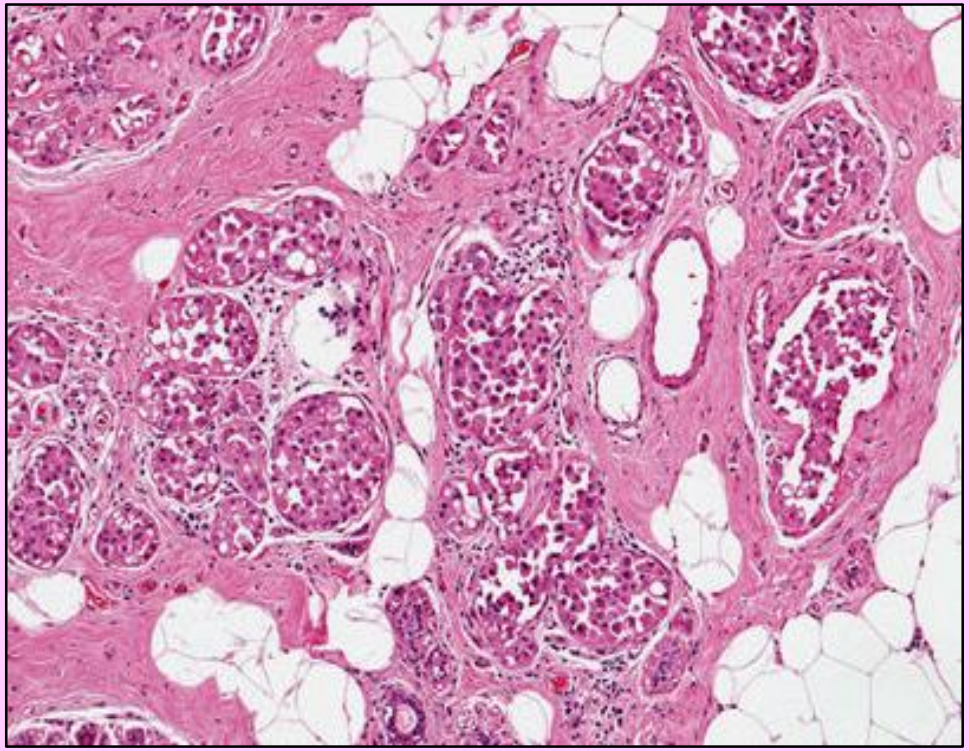
- Post menopausal women
- Rare cancer in ducts
- “arborescent fibrovascular stalks lined by epithelial cells”
- Usually ER+, PR+ and HER2 negative
- Less likely to spread to lymph nodes

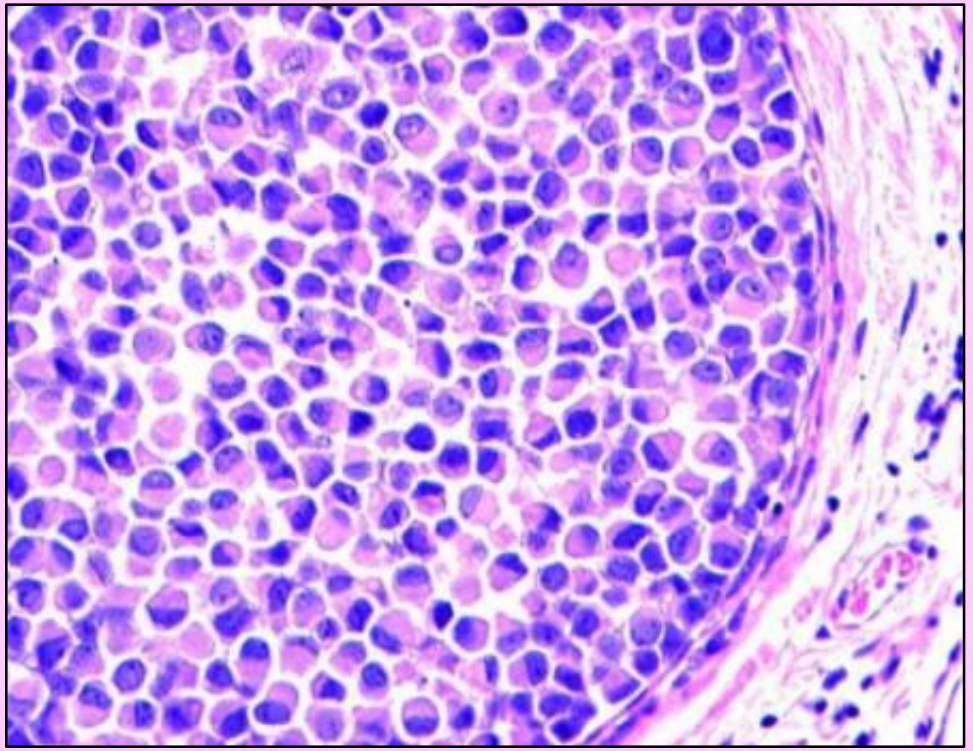


Lobular Carcinoma In Situ (LCIS)

- 20% of Carcinoma In Situ of the Breast
- 30% bilateral
- Not detected mammographically (usually incidental finding)
- Considered risk factor rather than direct cancer precursor
- 7-10x increased risk of invasive carcinoma
  - Absolute risk 1% per year, persists long-term
  - Bilateral breasts
- Loss of E-cadherin protein expression (Discohesive cells)

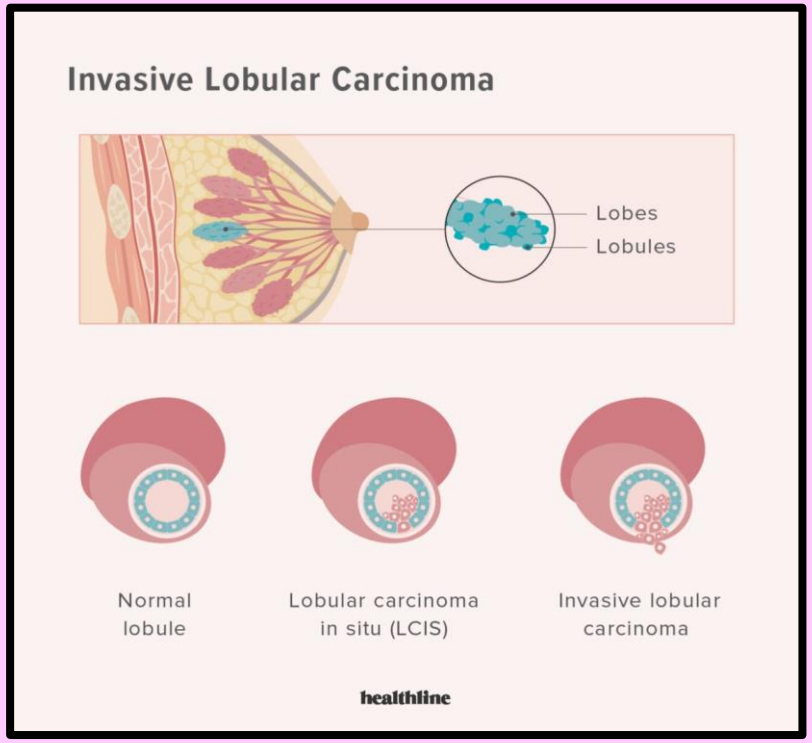
LCIS

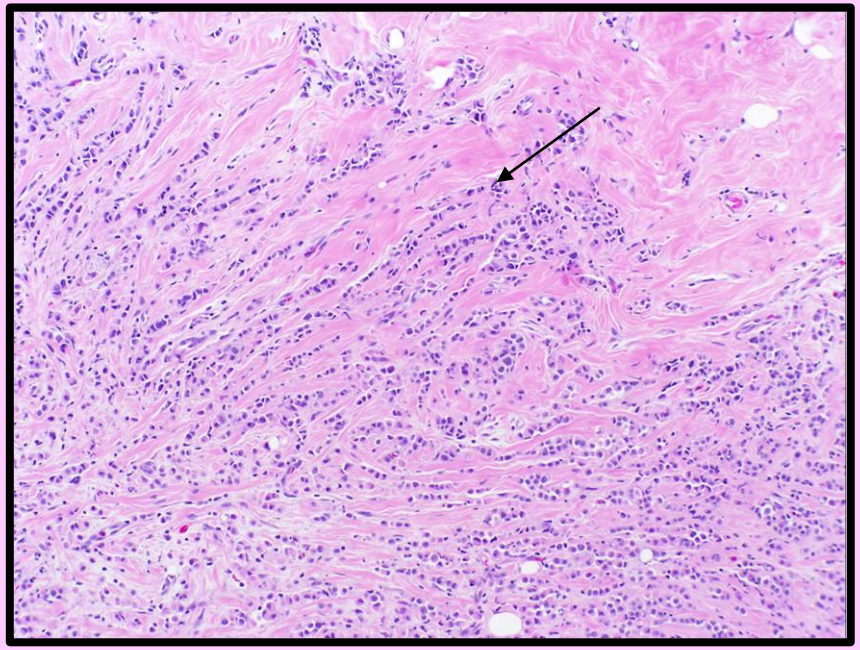




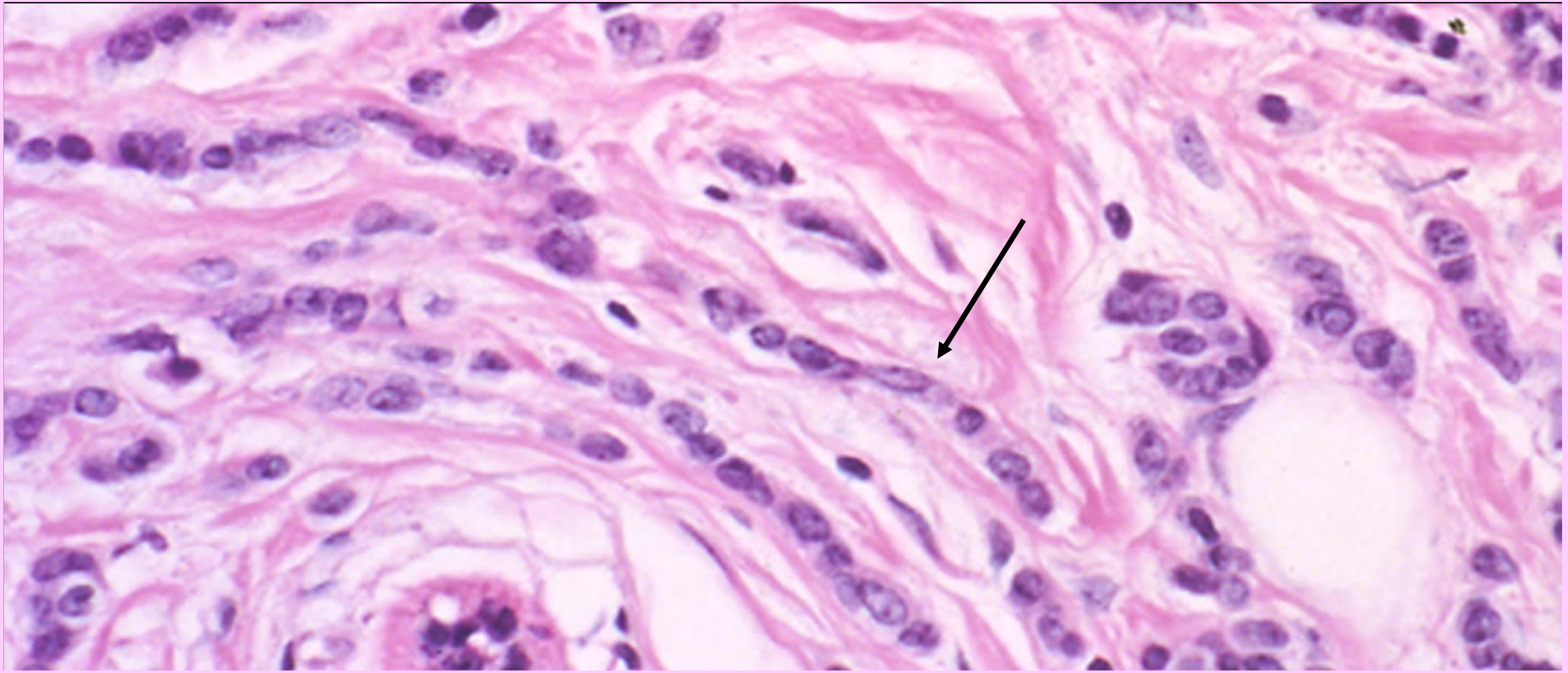
Invasive Lobular Carcinoma (ILC)

- 5-10% of breast cancer
- Originates in TDLU
- May not incite a fibrous/desmoplastic response
  - Maybe no detectable mass lesion
- Single-file cellular arrangement

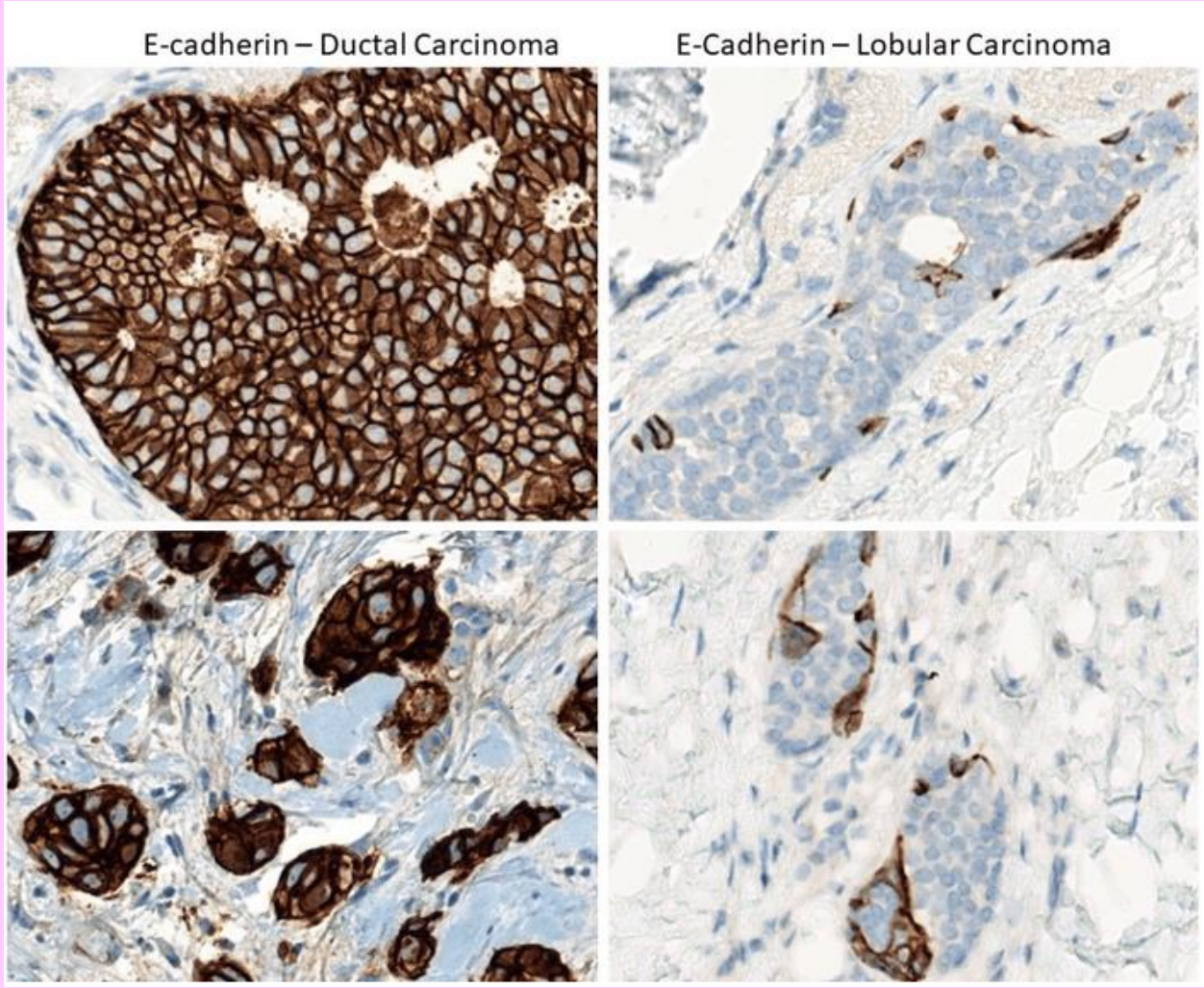




Invasive Lobular Carcinoma

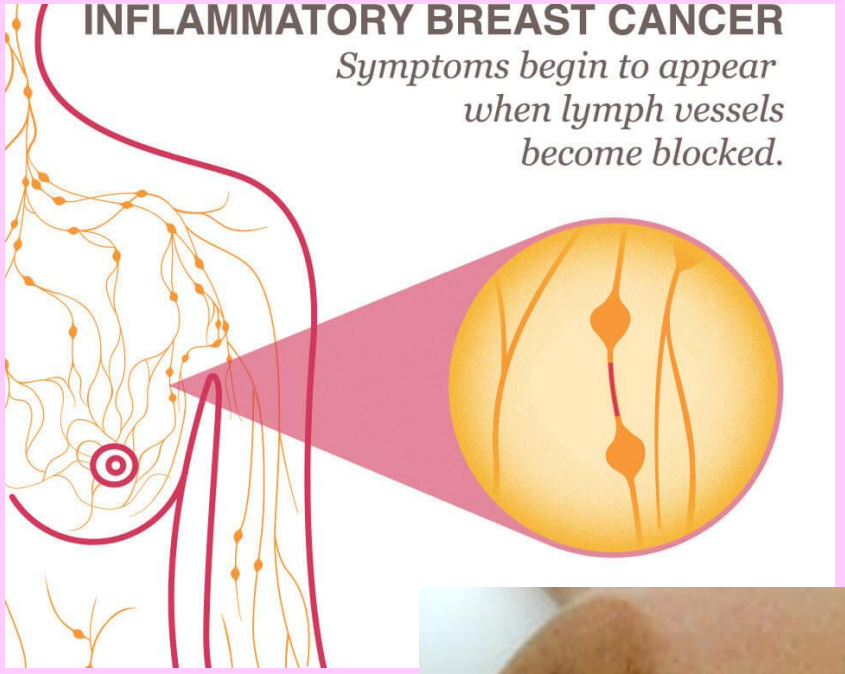


E-cadherin marker (IHC) to differentiate IDC vs. ILC



Other rare types of Breast Cancer, not carcinoma

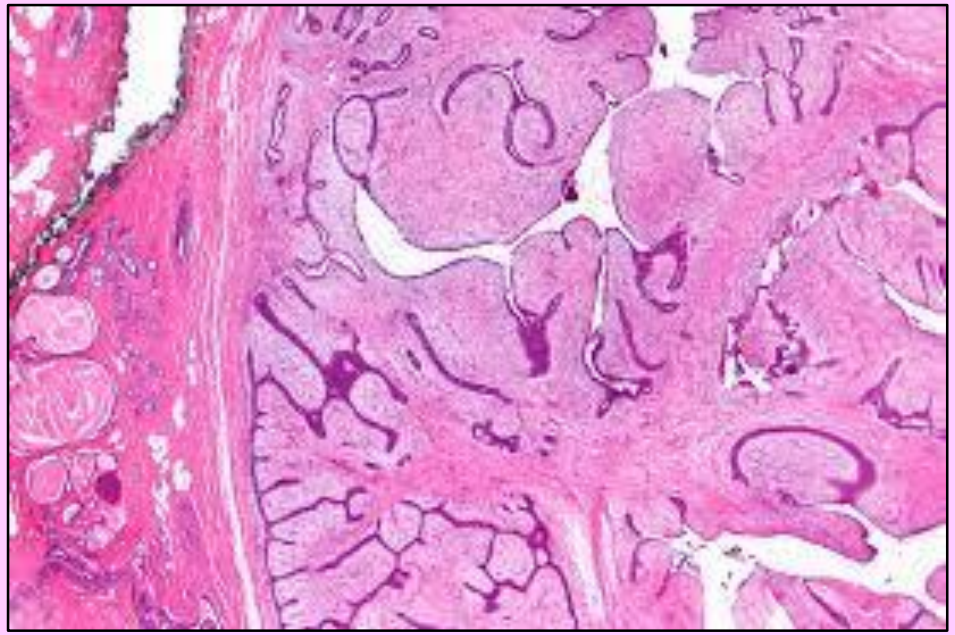
Inflammatory Breast Cancer

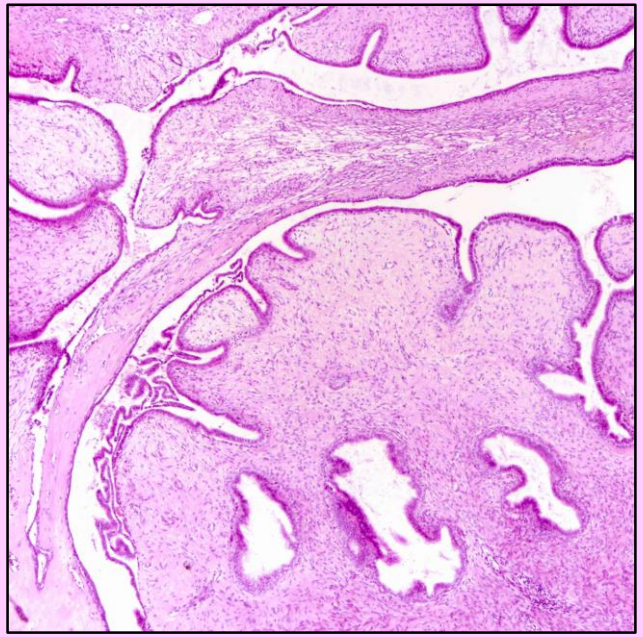


- Rare, aggressive
- Breast is red, swollen, and tender
- Cancer cells block the lymphatic vessels in skin covering the breast,
- Red, swollen breast –occurs in days to weeks; “peau de orange” skin
- Can be confused with infection
- Five-year survival rate around 40%

Phyllodes tumors of the breast

- Grow in the connective tissue (stroma) of the breast
- Large & fast growing, leaf like pattern
- Benign, borderline, or malignant, depending on histologic features
- Most common in age 40’s
- Treatment –surgical excision. Chemotherapy is not useful
- Radiation post surgery to prevent local reoccurrence





Treatment of Breast Cancer

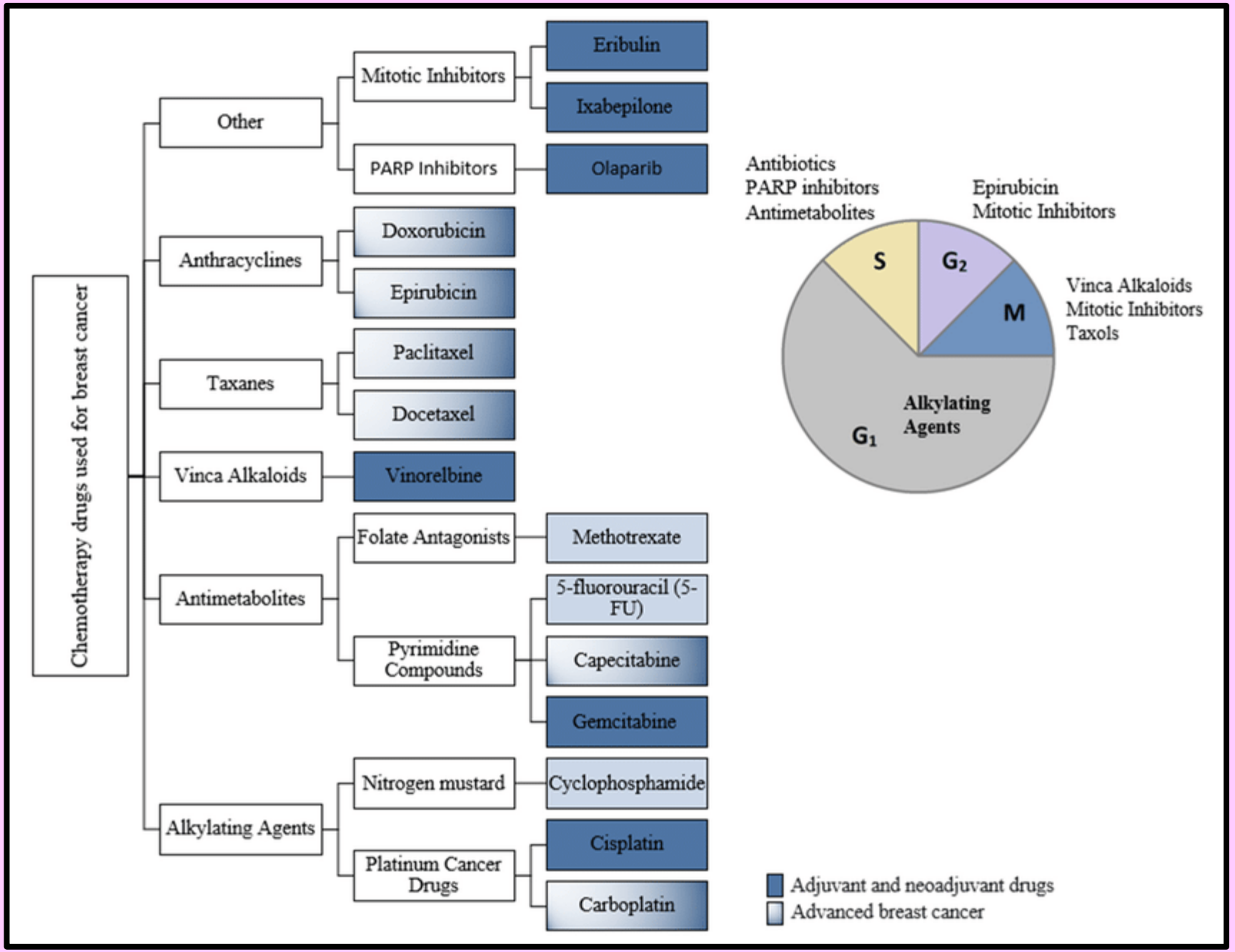
- Radiation
- Chemotherapy
- Surgery
- Hormonal therapy (Aromatase inhibitors, SERMs, ERDs)
  - ❖Tamoxifen is the most commonly prescribed hormone treatment.
- Other targeted
- Vaccines (?)
- Bisphosphonates

Radiation

- **External beam radiation.** This type comes from a machine outside your body. You generally get it 5 days a week for 5 to 6 weeks. Some
  - **Hypofractionated radiation therapy.** You get larger doses using fewer treatments, typically only 3 weeks.
  - **Intraoperative radiation therapy (IORT).** In this approach, you get a single large dose of radiation in the operating room right after breast conservation surgery (before the wound is closed).
  - **3D-conformal radiotherapy.** You get radiation from special machines that can better aim it at the area where the tumor was. You'll get treatments twice a day for 5 days.
- **Internal radiation (brachytherapy).** In this type, your doctor puts something radioactive inside your body for a short time.
  - **Interstitial brachytherapy.** The doctor inserts several small, hollow tubes called catheters into the breast around the area where the cancer was. They stay in place for several days. Doctors put radioactive pellets into them for short periods every day.
  - **Intracavitary brachytherapy.** This is the most common type of brachytherapy for women with breast cancer. The doctor uses a small catheter to put a device inside your breast. The device is widened and stays in place during the treatment. The other end sticks out of the breast. The doctor uses a tube to put radiation sources (often pellets) into the device. You usually get this twice a day for 5 days as an outpatient. After the last treatment, the doctor collapses and removes the device.

Systemic Chemotherapy

- You might take these drugs as pills or get them injected into a vein.
- It might be your main treatment if you have advanced breast cancer.
- Or you could get it before surgery (neoadjuvant chemotherapy) or after surgery (adjuvant chemotherapy).


Chemotherapy drugs used for breast cancer
Other
Mitotic Inhibitors
Eribulin
Ixabepilone
PARP Inhibitors
Olaparib
Anthracyclines
Doxorubicin
Epirubicin
Taxanes
Paclitaxel
Docetaxel
Vinca Alkaloids
Vinorelbine
Antimetabolites
Folate Antagonists
Methotrexate
Pyrimidine Compounds
5-fluorouracil (5-FU)
Capecitabine
Gemcitabine
Alkylating Agents
Nitrogen mustard
Cyclophosphamide
Platinum Cancer Drugs
Cisplatin
Carboplatin
Antibiotics
PARP inhibitors
Antimetabolites
Epirubicin
Mitotic Inhibitors
Vinca Alkaloids
Mitotic Inhibitors
Taxols
S
G2
M
G1
Alkylating Agents
Adjuvant and neoadjuvant drugs
Advanced breast cancer

Chemotherapy

Neoadjuvant & Adjuvant

- Anthracyclines, such as doxorubicin (Adriamycin) and epirubicin (Ellence)
- Taxanes, such as paclitaxel (Taxol) and docetaxel (Taxotere)
- 5-fluorouracil (5-FU) or capecitabine
- Cyclophosphamide (Cytoxan)
- Carboplatin (Paraplatin)

Advanced Breast cancer

- Taxanes, such as paclitaxel (Taxol), docetaxel (Taxotere), and albumin-bound paclitaxel (Abraxane)
- Anthracyclines (Doxorubicin, pegylated liposomal doxorubicin, and Epirubicin)
- Platinum agents (cisplatin, carboplatin)
- Vinorelbine (Navelbine)
- Capecitabine (Xeloda)
- Gemcitabine (Gemzar)
- Ixabepilone (Ixempra)
- Eribulin (Halaven)

Surgery

- Lumpectomy, removal of the cancerous tissue and a surrounding area of normal tissue
- Simple mastectomy, removes the entire breast but no other structures
- Modified radical mastectomy, removes the breast and the underarm lymph nodes
- Radical mastectomy, removal of the breast and the underlying chest wall muscles, as well as the underarm contents.
- Reconstructive surgery

breastcancer.org

Expert Quote

"Breast cancer surgery is not the radically deforming surgery that you may have seen in your grandmother's day. We do skin-sparing incisions, we try to make the incisions low enough that you can wear anything you want, we're not taking muscle out. You don't end up with a concave area where the ribs are showing and the scars run to the collarbone. It's a different era. I think the sooner you get back to seeing what your scar looks like the better off you are. I like to take a look at a patient's scar early in the healing process, to let her know that I think it looks okay.“

Thomas G. Frazier, M.D

Mastectomy may cause

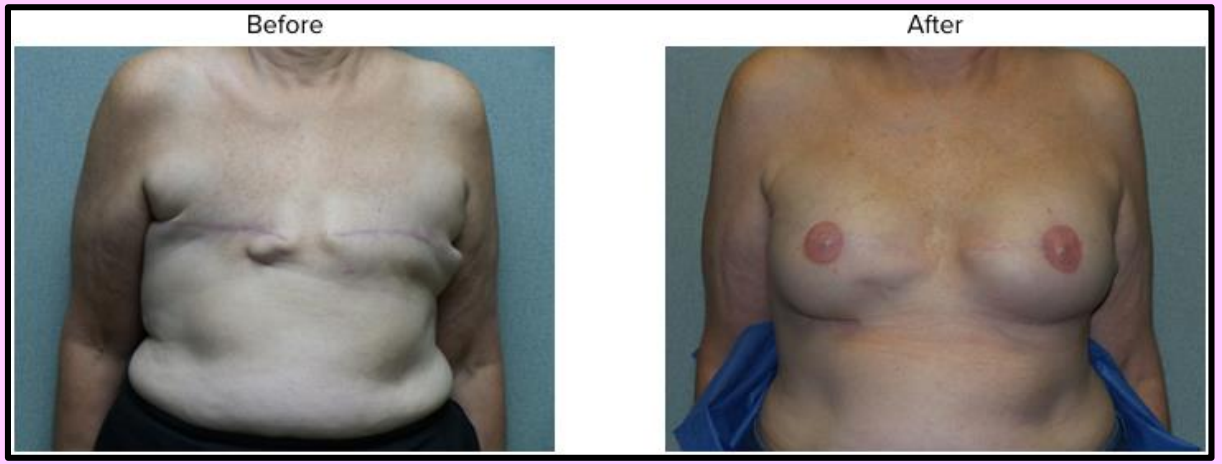
- Psychological stress
- Mood disturbance & anxiety
- Increased consciousness about clothes
- Negative body image
- Decreased sexual interest and satisfaction

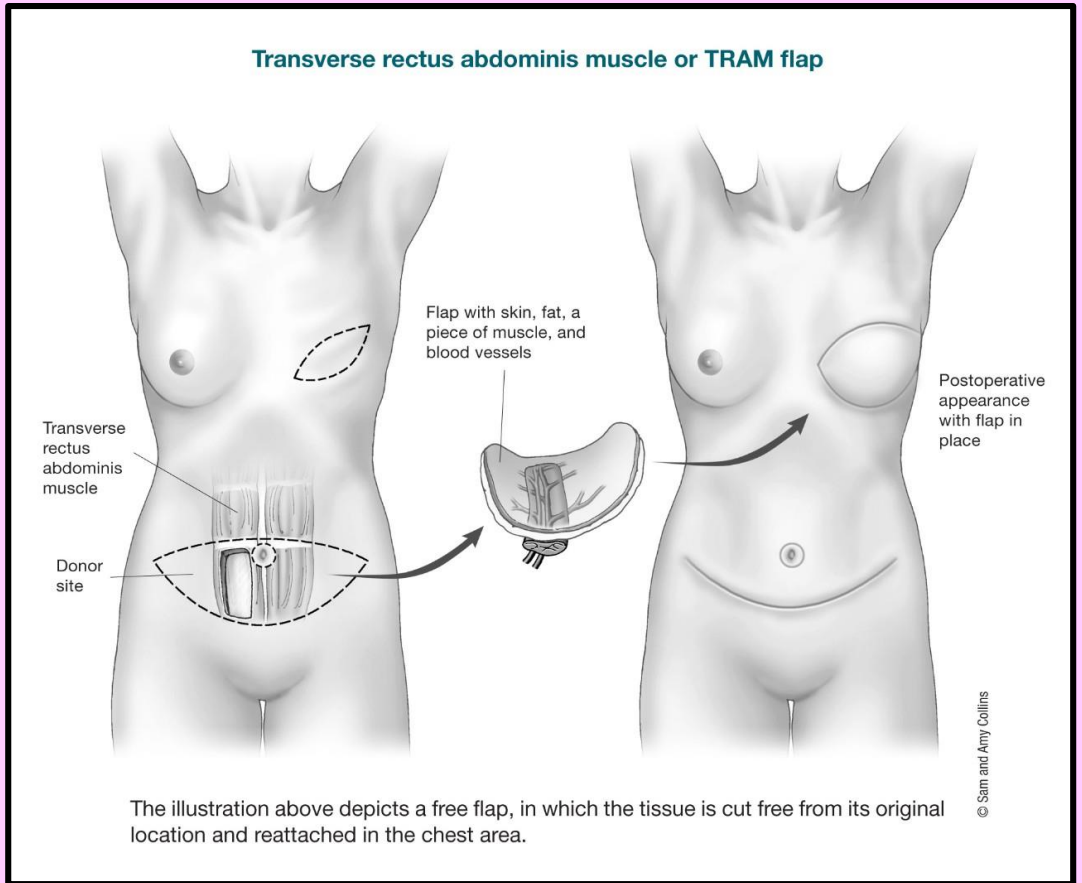
Breast Reconstruction

- Regain shape of breast
- Look balanced
- No need for prosthesis
- Improved mood and self confidence ; feeling “whole” again

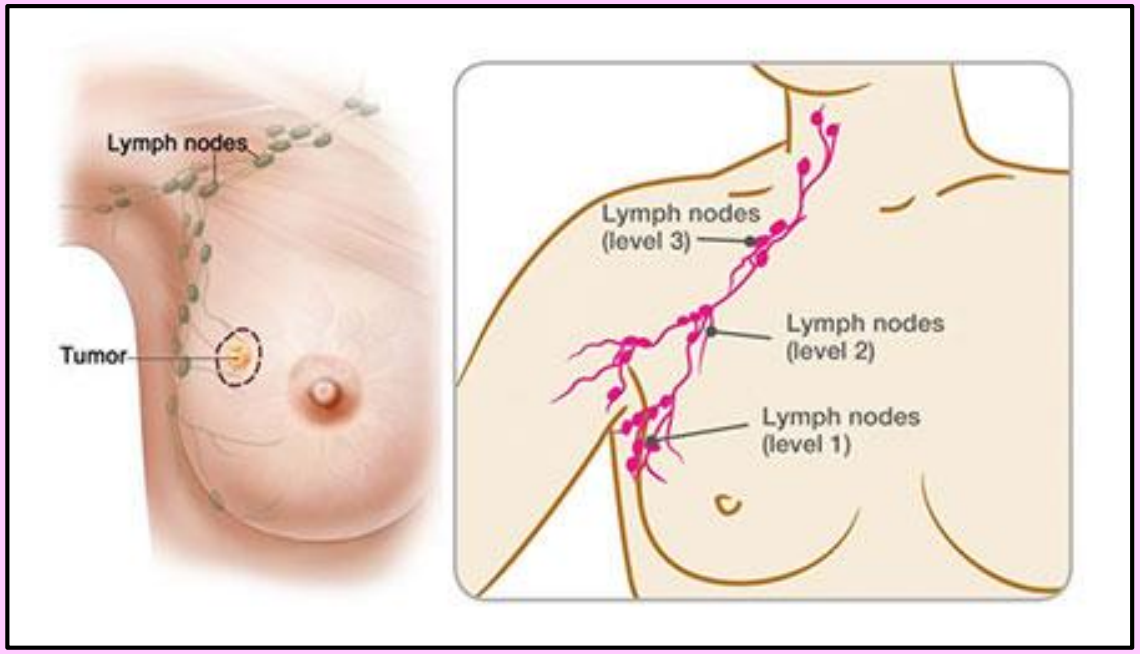
Breast Reconstruction surgery

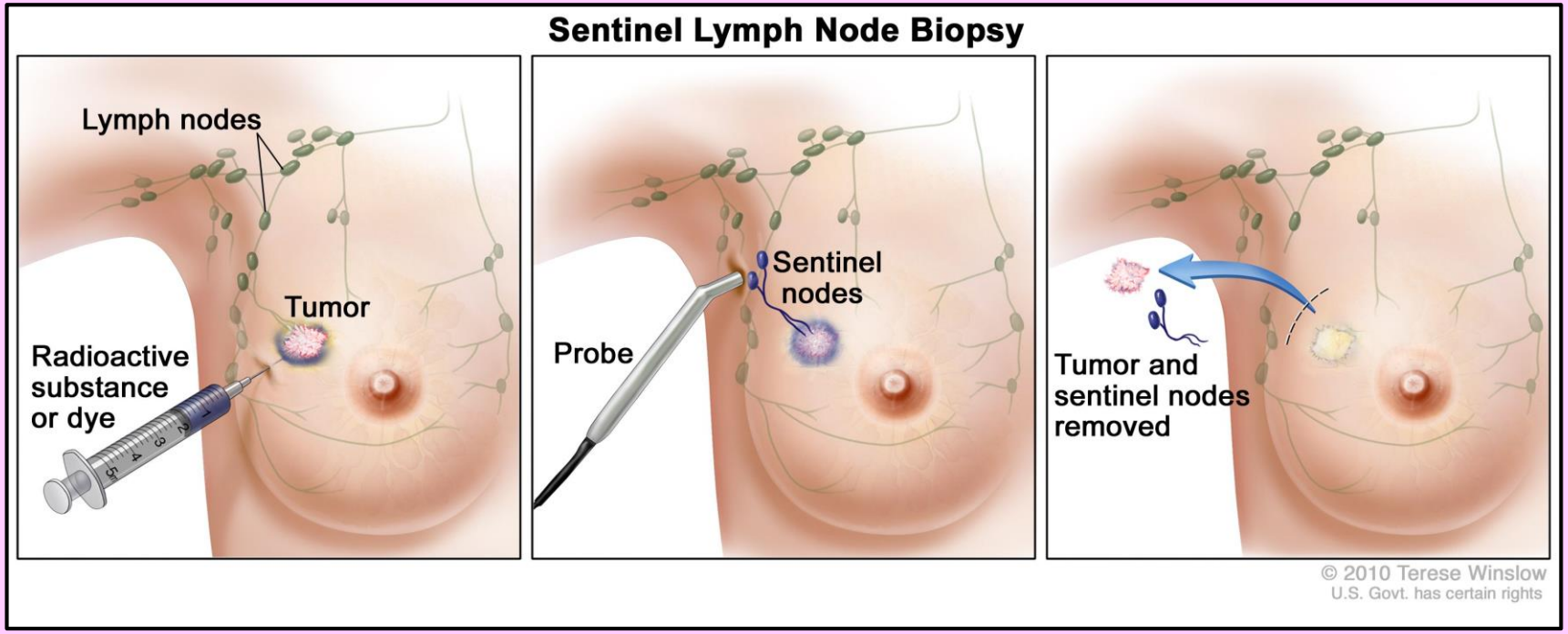
- Many women are now are now opting to have breast reconstruction
- Achieved with
  - Implants
  - Autologous tissue flaps with





Sentinel Lymph Node Biospy





Surgery to remove nearby lymph nodes

- To find out if the breast cancer has spread to underarm (axillary) lymph nodes, one or more of these lymph nodes will be removed and looked at in the lab
- Lymph nodes may be removed either as part of the surgery to remove the breast cancer or as a separate operation.
- **Sentinel lymph node biopsy (SLNB)**
- **Axillary lymph node dissection (ALND)** - removes many (usually less than 20) underarm lymph nodes. Not done as often…..major side effect: Lymphedema

A side effect of LN removal -Lymphedema

- Build-up of fluid in soft body tissues when the lymph system is damaged or blocked
- Most likely to happen within 1-5 years after treatment; It can appear in any area of the upper body on the same side as the breast cancer — areas that were accustomed to draining lymph through any of the vessels or nodes that were removed or damaged during treatment
- Causes:
  - Cancer itself blocks lymphatic vessels
  - Radiation treatment can cause scarring and inflammation of lymph nodes and vessels
  - Surgery – lymph nodes removed (to see if cancer is spread)
  - Parasitic worms can clog lymphatics

Diagnosis of Lymphedema

- **MRI scan.** Using a magnetic field and radio waves, an MRI produces 3D, high-resolution images of the involved tissue.
- **CT scan.** This X-ray technique produces detailed, cross-sectional images of the body's structures. CT scans can reveal blockages in the lymphatic system.
- **Ultrasound.** This test uses sound waves to produce images of internal structures. It can help find obstructions within the lymphatic system and vascular system.
- **Lymphoscintigraphy.** During this test, the person is injected with a radioactive dye and then scanned by a machine. The resulting images show the dye moving through the lymph vessels, highlighting blockages.

Lymphedema

Complications of Lymphedema

- **Skin infections (cellulitis)** The trapped fluid provides fertile ground for germs, and the smallest injury to the arm or leg can be an entry point for infection. Affected skin appears swollen and red and is typically painful and warm to the touch. Your doctor may prescribe antibiotics to keep on hand so that you can start taking them immediately.
- **Sepsis** Untreated cellulitis can spread into the bloodstream and trigger sepsis — a potentially life-threatening condition that occurs when the body's response to an infection damages its own tissues. Sepsis requires emergency medical treatment.
- **Leakage through the skin** With severe swelling, the lymph fluid can drain through small breaks in the skin or cause blistering.
- **Skin changes.** In some people with very severe lymphedema, the skin of the affected limb can thicken and harden so it resembles the skin of an elephant

Lymphedema Treatment – there is **NO** cure

- **Exercises.** Gentle contraction of the muscles in the arm or leg can help move the excess fluid out of the swollen limb.
- **Manual lymph drainage.** Therapists trained in this massage-like technique use very light pressure to move the trapped fluid in the swollen limb toward an area with working lymph vessels. People should avoid manual lymph drainage if they have a skin infection, blood clots or active cancer in the affected limb.
- **Compression bandages.** Using low-stretch bandages to wrap the entire limb encourages lymph fluid to flow back toward the trunk of the body.
- **Compression garments.** Close-fitting elastic sleeves or stockings can compress the arm or leg to encourage lymph fluid drainage. These garments often require a prescription to ensure that the proper amount of compression is used. You may need to be measured by a professional to ensure proper fit.
- **Sequential pneumatic compression.** A sleeve worn over the affected arm or leg connects to a pump that intermittently inflates the sleeve, putting pressure on the limb and moving lymph fluid away from the fingers or toes.

Mayo Clinic https://www.mayoclinic.org/diseases-conditions/lymphedema/diagnosis-treatment/drc-20374687

Lymphedema Treatment – surgical options

- **Lymph node transplant.** Lymph nodes are taken from a different area of the body and then attached to the network of lymph vessels in the affected limb. Many people with early-stage lymphedema see good results from this surgery and can decrease the amount of compression needed.
- **New drainage paths.** Another option for early-stage lymphedema, this procedure creates new connections between the lymph network and blood vessels. The excess lymph fluid is then removed from the limb via blood vessels.
- **Removal of fibrous tissue.** In severe lymphedema, the soft tissues in the limb become fibrous and hardened. Removing some of this hardened tissue, often through liposuction, can improve the limb's function. In very severe cases, hardened tissue and skin may be removed with a scalpel.

Another classification of Breast Cancer using genetic status and treatments

- Group 1, Luminal A: ER+, PR+, HER2 =
  - *Hormone therapy, chemo*
- Group 2, Luminal B: ER+, PR=,HER2+
  - *Hormone therapy, HER2 therapy*
- Group 3: ER=, PR=, HER2+
  - *Chemo, HER 2 therapy*
- Group 4, basal like: ER=, PR=, HER2=. (Triple negative)
  - *Chemo*

Treatment of Estrogen Receptor (ER+) and Progesterone Receptor (PR+) Positive tumors

- **Aromatase Inhibitors**
- Postmenopausal women
- Aromatase inhibitors work by blocking the enzyme aromatase, which turns the hormone androgen into small amounts of estrogen in the body. Less estrogen is available to stimulate the growth of hormone-receptor-positive breast cancer cells
  - Arimidex (chemical name: anastrozole)
  - Aromasin (chemical name: exemestane)
  - Femara (chemical name: letrozole)
- A pill taken once a day

Treatment of ER+ and PR+ tumors

- **Selective Estrogen Receptor Modulators (SERMs)**
- Block the effects of estrogen in the breast tissue. SERMs work by sitting in the estrogen receptors in breast cells. If a SERM is in the estrogen receptor, there is no room for estrogen and it can't attach to the cell. If estrogen isn't attached to a breast cell, the cell doesn't receive estrogen's signals to grow and multiply.
- There is a spectrum of response to SERMs

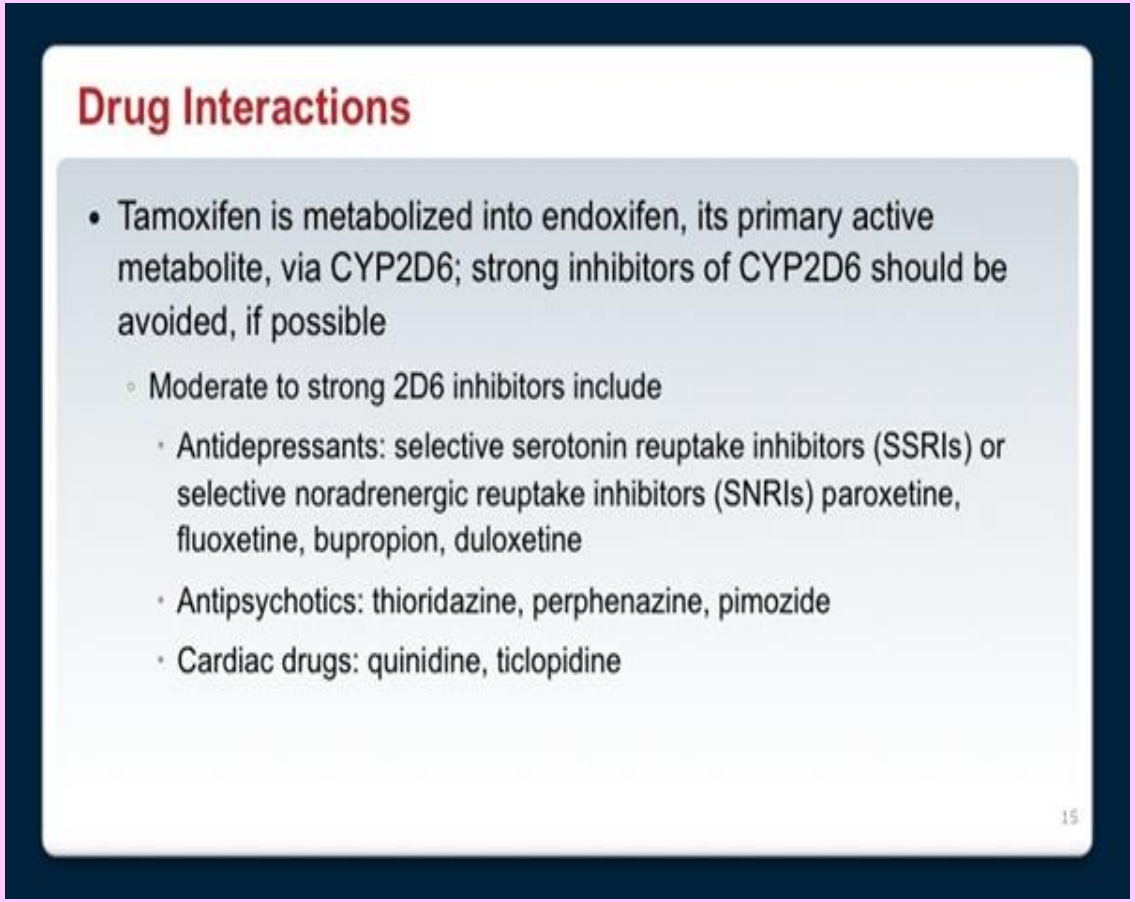
    - **Tamoxifen in pill or liquid form**
    - Evista (chemical name: raloxifene)
    - Fareston (chemical name: toremifene)

Tamoxifen

Side effects

- Blood clots, stroke
- Endometrial cancer
- Abnormal vaginal bleeding or discharge
- Pain or pressure in the pelvis
- Leg swelling or tenderness
- Chest Pain
- Shortness of breath
- Weakness, tingling, numbness
- Dizziness
- Vision problems
- Difficulty speaking or understanding

Drug interactions



BOTTOM LINE – these drugs prevent Tamoxifen from being metabolized to the active form –BLOCKS the therapeutic benefit

Foods/supplements to avoid when on Tamoxifen

- Grapefruit/Tangerines
- Turmeric/Curcumin
- Black cohosh
- St. John’s Wort
- Ginseng
- Chamomile
- Soy
- Flaxseed

Treatment of ER+ and PR+ tumors

- **Estrogen Receptor Downregulators (ERDs)**

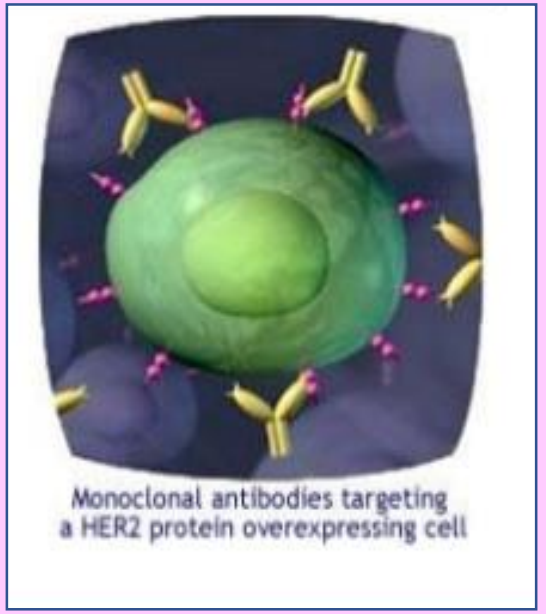
- Block the effects of estrogen in breast tissue
- Reduce the number of estrogen receptors
- Change the shape of breast cell estrogen receptors so they don't work as well
- Faslodex (chemical name: fulvestrant)

HER-2/Neu + tumors

- Human epidermal growth factor receptor 2
- Other names Receptor tyrosine-protein kinase erbB-2; CD340; ERBB2: neu –found in a neural tumor glioblastoma
- Found on surface of many cells involved in growth
- Overexpressed in cancers
- Used as a marker of certain breast cancers (~30%)

Herceptin (Trastuzumab)

- Monoclonal Antibody (biologic)
- Binds to and blocks HER-2 receptor
- Effective in metastatic HER-2/neu positive breast cancer
- Little effect with HER-2/neu negative breast cancer
- IV
- Side effects – reduced heart function, lung problems, nausea, headache, decreases RBC and WBC


Monoclonal antibodies targeting a HER2 protein overexpressing cell

HER-2/neu Vaccine

- Targets Her-2/neu
- Made from small protein pieces likely to trigger an immune response
- Helps to increase white blood cell counts
- Monthly shots for six months

- No serious side effects

Treatment -Triple Negative (TNBC)

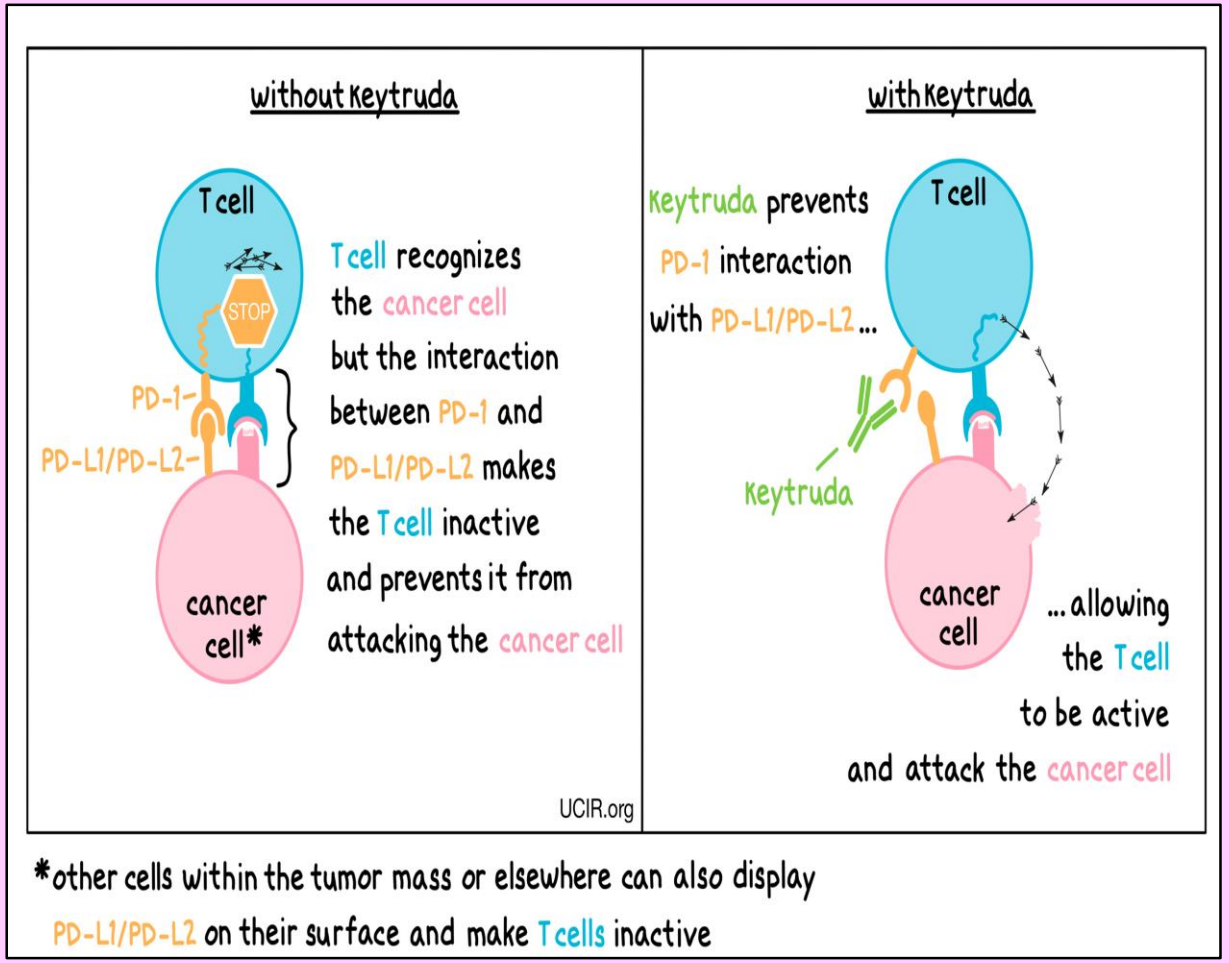
- 10-20% of breast cancers
- Younger women < 50 years
- Black and Hispanic women 3 x more likely
- Heterogenous, difficult to diagnose
- Not responsive to hormone therapies
- Neoadjuvant and adjuvant chemotherapy
  - Anthracyclines (DNA intercalators; impedes topoisomerase)
  - Taxanes –disrupt microtubules (inhibit mitosis)
  - Platinum agents –crosslink DNA
- PARP inhibitors – interferes with cancer cells repairing damaged DNA, helpful in BRCA+ Breast Cancer
- Immunotherapy (Keytruda)

Keytruda

Triple Negative Breast Cancer

Keytruda plus chemotherapy	Placebo plus chemotherapy
The disease did not get worse for a median of 10 months	The disease did not get worse for a median of 6 months
53% of patients had a response - 17% had their tumors completely disappear - 36% had partial shrinkage of their tumors	40% of patients had a response - 13% had their tumors completely disappear - 27% had partial shrinkage of their tumors
Responses lasted for a median of 19 months	Responses lasted for a median of 7 months

Mechanism



https://www.ucir.org/immunotherapy-drugs/pembrolizumab

Other Targeted Therapies

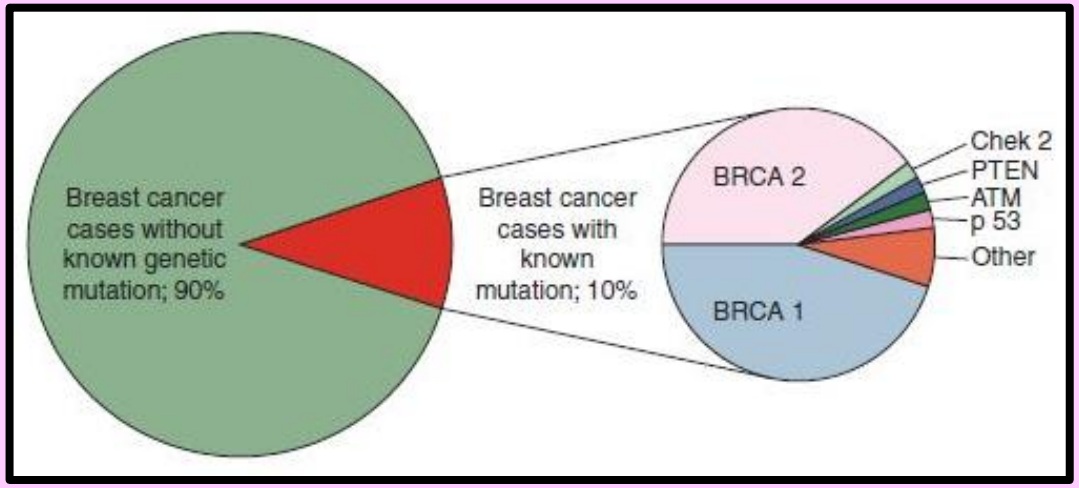
- CDK4/6 Inhibitors
- PI3K Inhibitors
- Everolimus (mTOR Inhibitor) slows cell growth, anti-angiogenic and immunosuppressant. Useful in hormone +, HER2Neg
- Antibody-drug conjugates (monoclonal antibody linked to a chemotherapy drug)

Bisphosphonates

- Bone-targeting drugs
- Used for treatment of Osteoporosis -limits the activity of osteoclasts, that contribute to the bone weakening and breakdown that leads to osteoporosis
- Taken to prevent bone lesions caused by metastasis
- Given to women at high risk after surgery for 3-5 years
- Research –given to those with DCIS can keep from getting invasive disease

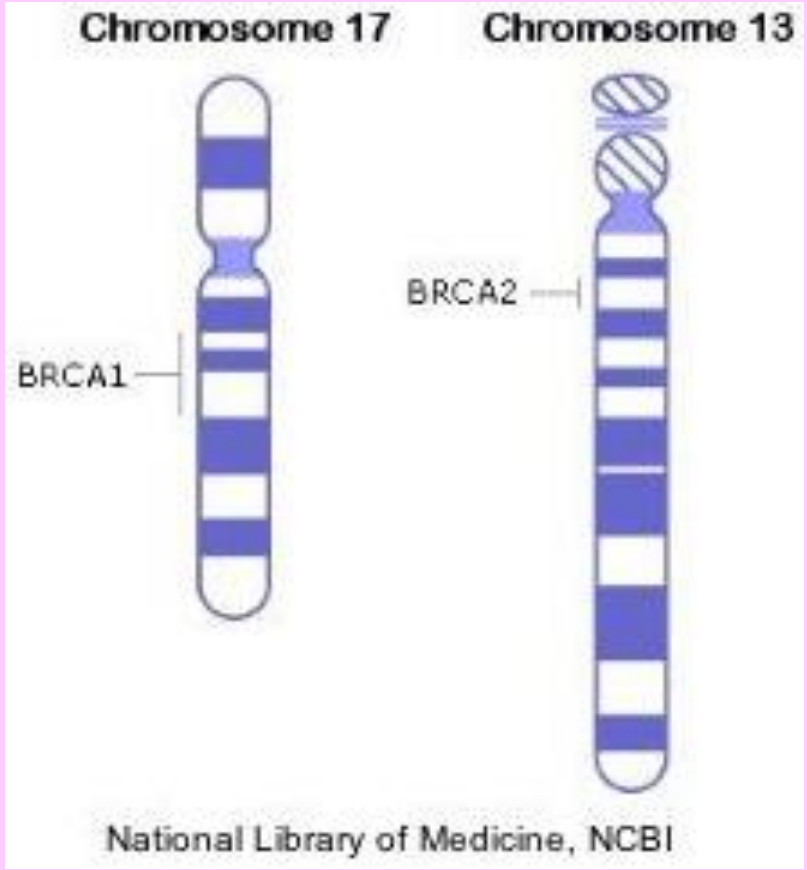
Hereditary Breast Cancer

- 10% of all breast cancer cases
- Causal gene is unknown for most hereditary cases
- Most common KNOWN implicated gene is BRCA
  - 25% of hereditary cases
  - 1-2% of all breast cancer cases
- 10% of hereditary cases due to other KNOWN genes
  - *CHEK2* (Li-Fraumeni)
  - *ATM* (Ataxia telangiectasia)



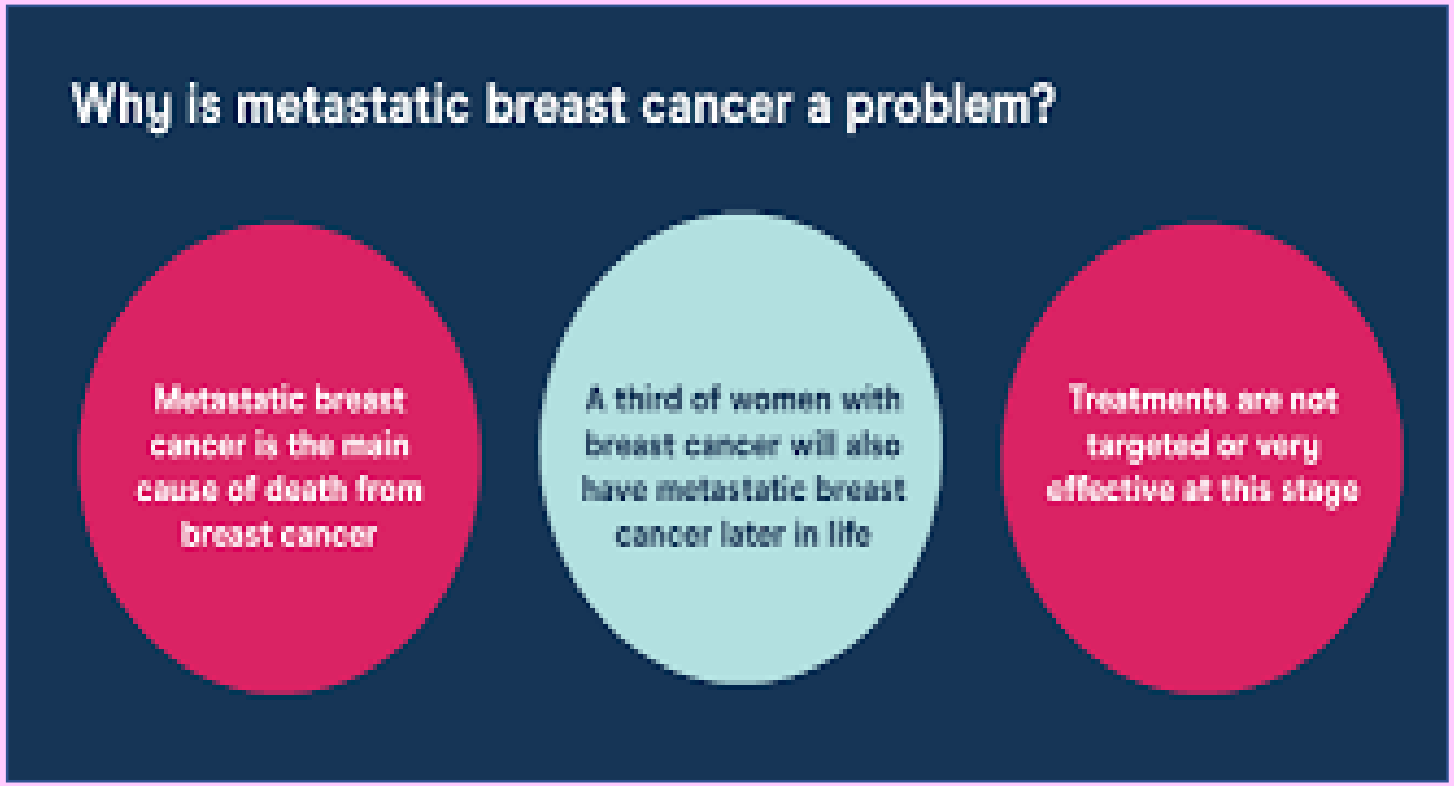
BRCA-related breast cancer (BRCA mutations)

- Lifetime breast cancer risk 30-80%
- BRCA genes –part of DNA Damage Response system
- BRCA1 mutations:
  - More common than BRCA2
  - **Younger patients (age 40-50)**
  - Ashkenazi Jewish association
  - Triple Negative Breast Cancer
  - Increased risk of other cancers:
    - Ovarian (30%)
    - Colon, prostate, pancreatic
- BRCA2 mutations:
  - **Slightly older patient group (50s)**
  - **Male breast cancer**
  - Increased risk of other cancers:
    - Ovarian (15%)
    - Melanoma, gastric, colon, prostate, pancreatic
- Bilateral Mastectomy – decreases risk



(MBC) Metastatic Breast Cancer

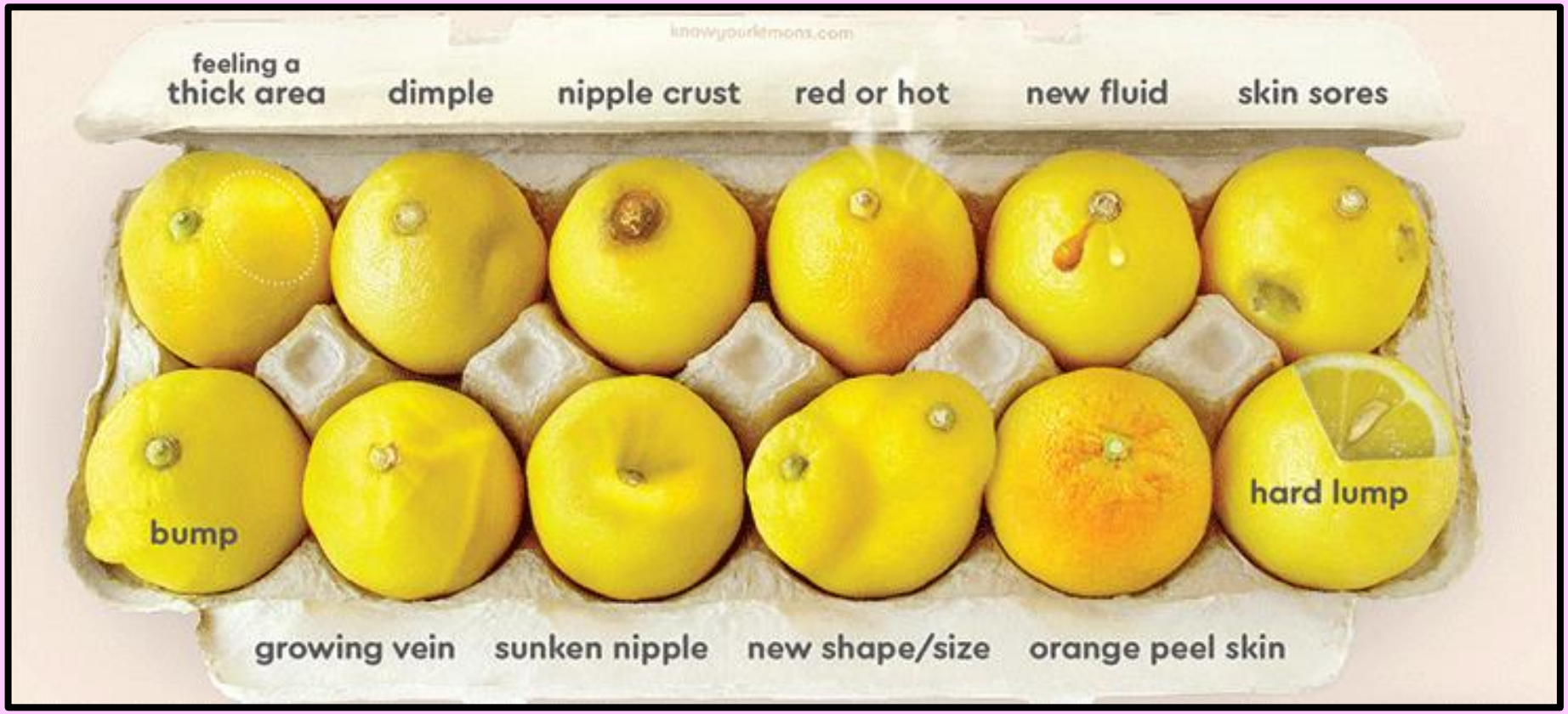
- Brain, Bones, Liver, Lung
- Generalized symptoms:
  - Anorexia
  - Weight Loss
  - Fatigue
- Bone pain, spinal cord compression
- Seizures, falls
- Jaundice, bleeding
- Pneumonia, shortness of breath, effusions



The End
Questions?

https://www.breastcancer.org/

https://www.cancer.org/



September 14, 21

- Let's talk murder boobs.
- I'm very fortunate to have caught my tumor when I did, because while I do have invasive ductal carcinoma, my oncotype score is only 15.
- So with my bilateral mastectomy in the rear view mirror, it's on to tamoxifen! And y'all - get those screenings. Please.