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Your Patient Has Breast Cancer Until You Prove She Doesn't



M2 - Reproduction Sequence

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Clinical Professor of Surgery

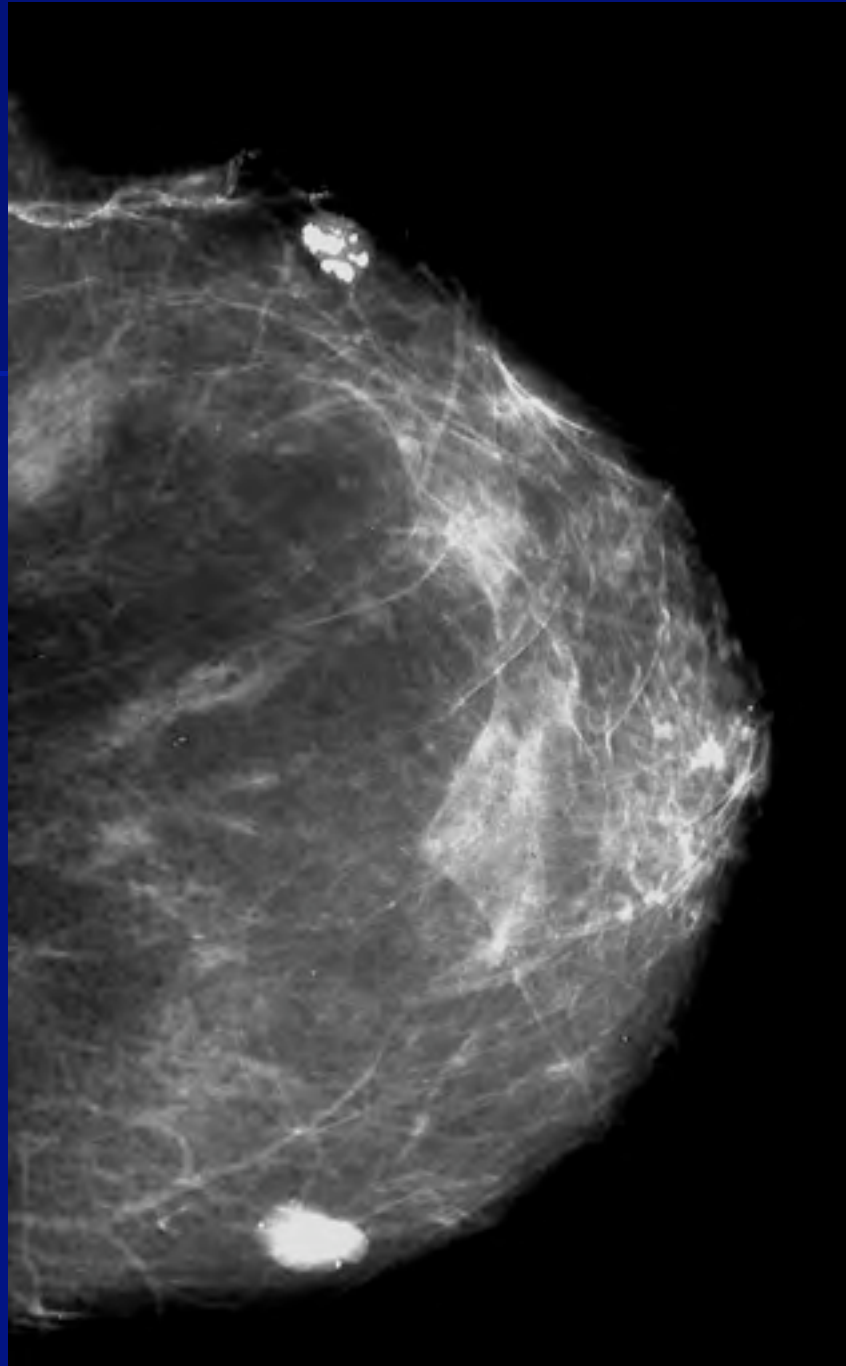
University of Michigan

Division of Surgical Oncology

The patient is a 25 year old female with a mass in the lower inner quadrant of the right breast.

Fibroadenoma

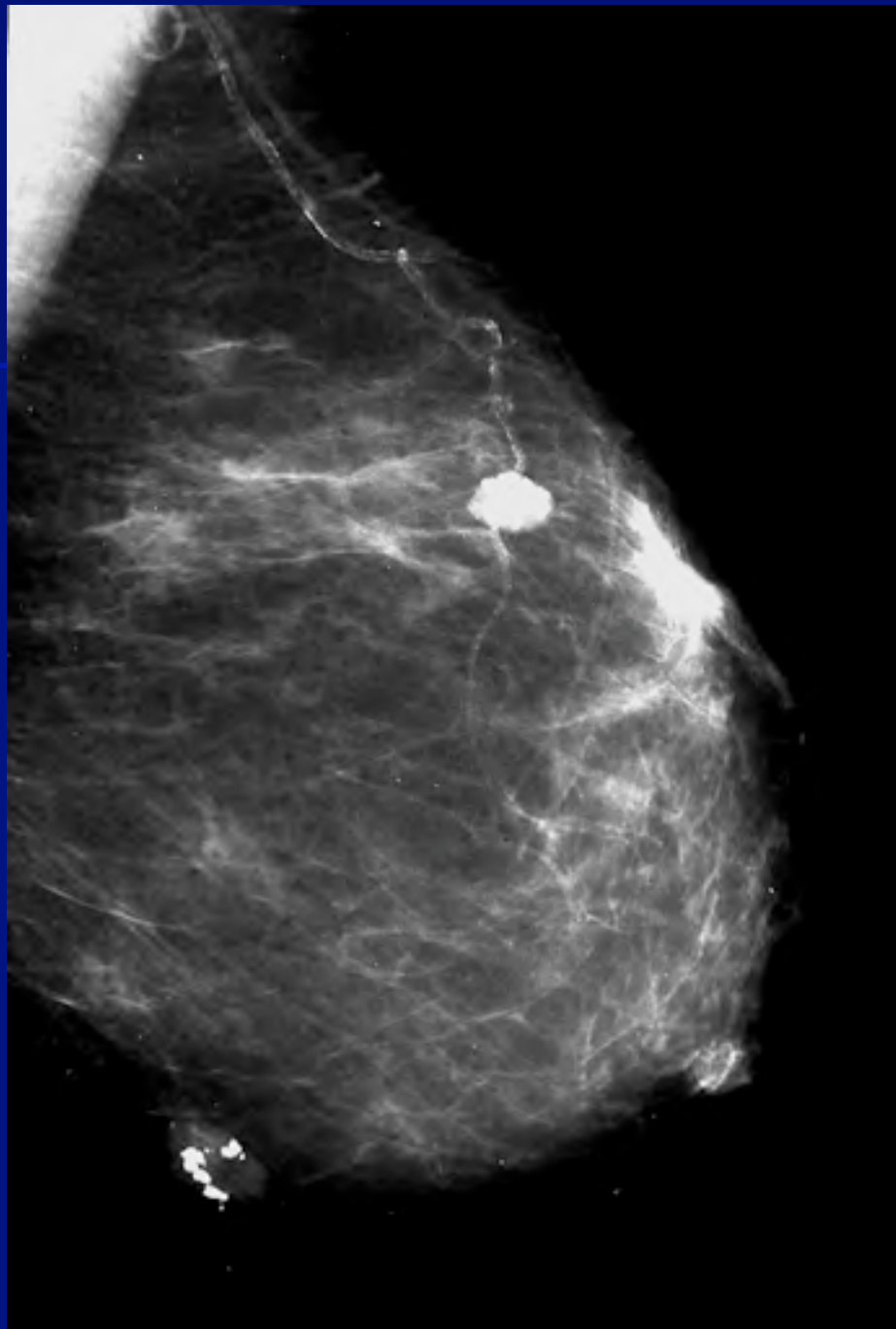
- Most common breast neoplasm in adolescents and young adult women.
- Usually presents as a solitary, painless, well-circumscribed, mobile mass.
- 25% are multiple.
- More common in African-Americans than Caucasians.



PD-TMCL

Source Undetermined





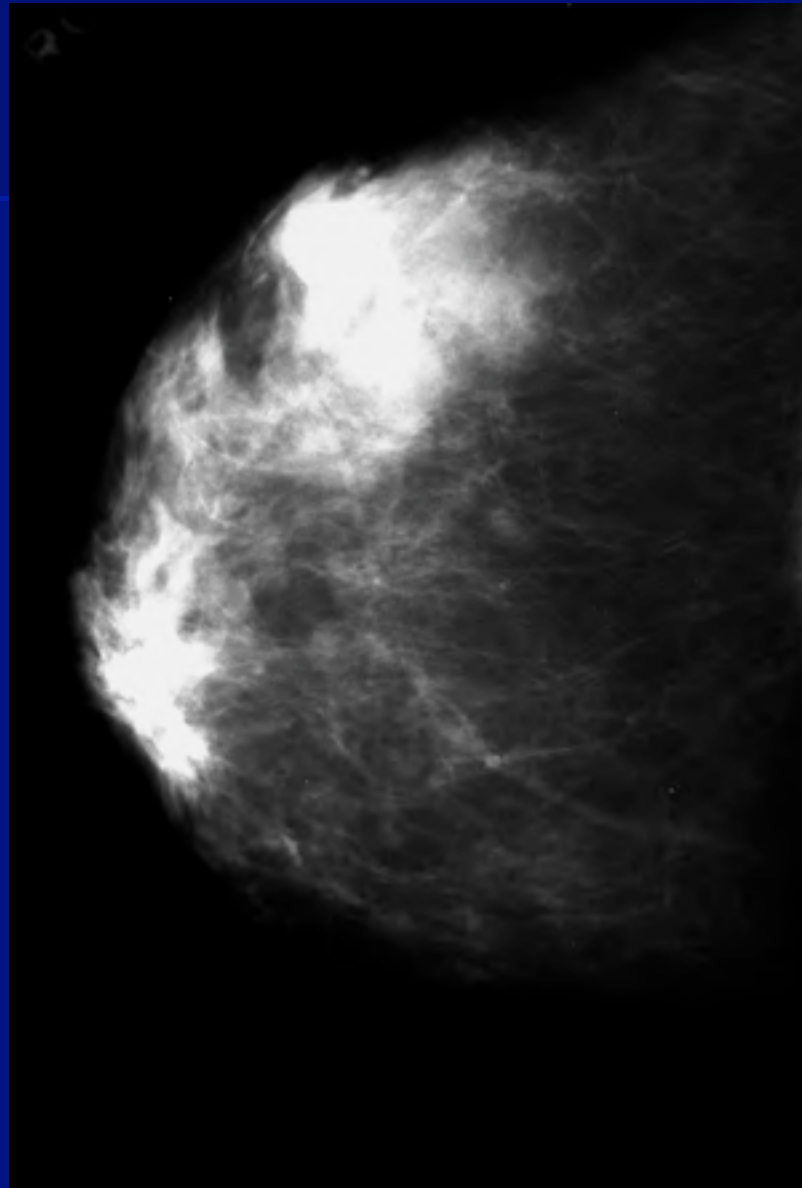
PD-TMCL Source Undetermined

The patient is a 37 year old female complaining of pain in both breasts but more pronounced prior to the beginning of her menses.

Fibrocystic Changes

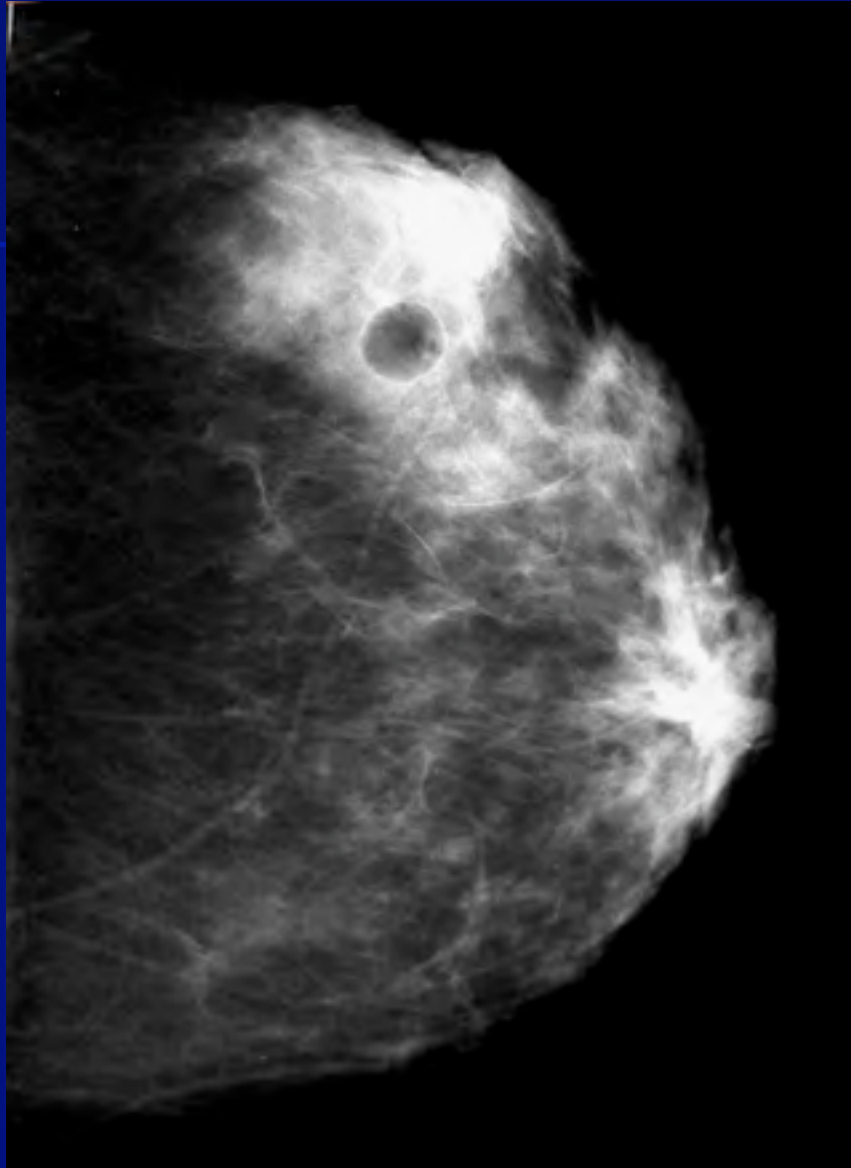
- Affect 30% to 35% of women between ages of 20 and 40 years.
- Usually multifocal and bilateral.
- Most common complaint is premenstrual swelling and tenderness.
- Symptoms gradually disappear after menopause.
- Not associated with an increased risk for cancer unless lobular or ductal atypical hyperplasia involved.
- Treatment involves use of NSAIDs, oral contraceptives, evening primrose oil or yam cream.

1-21-05

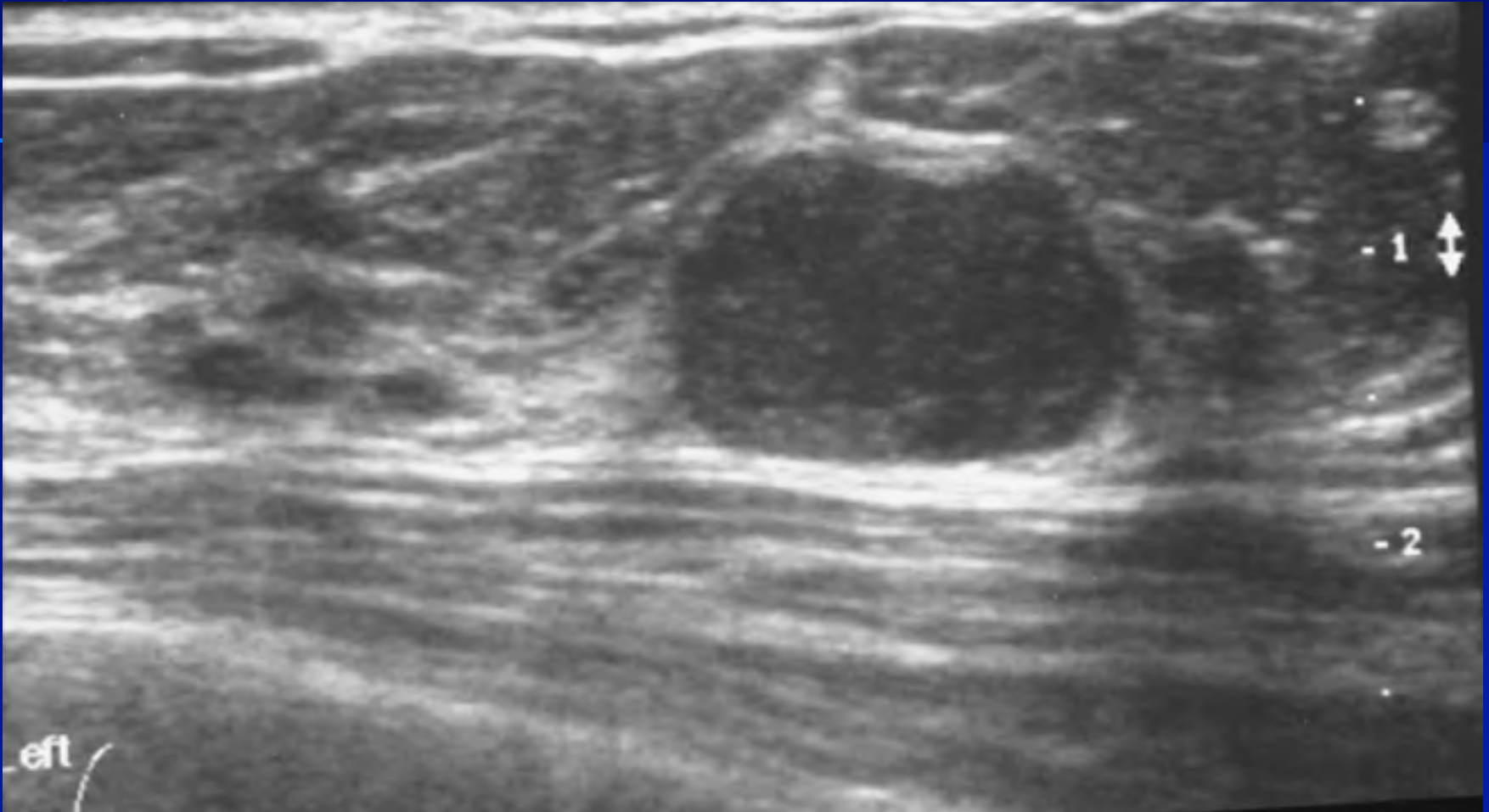


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 PD-TMEL Source Undetermined

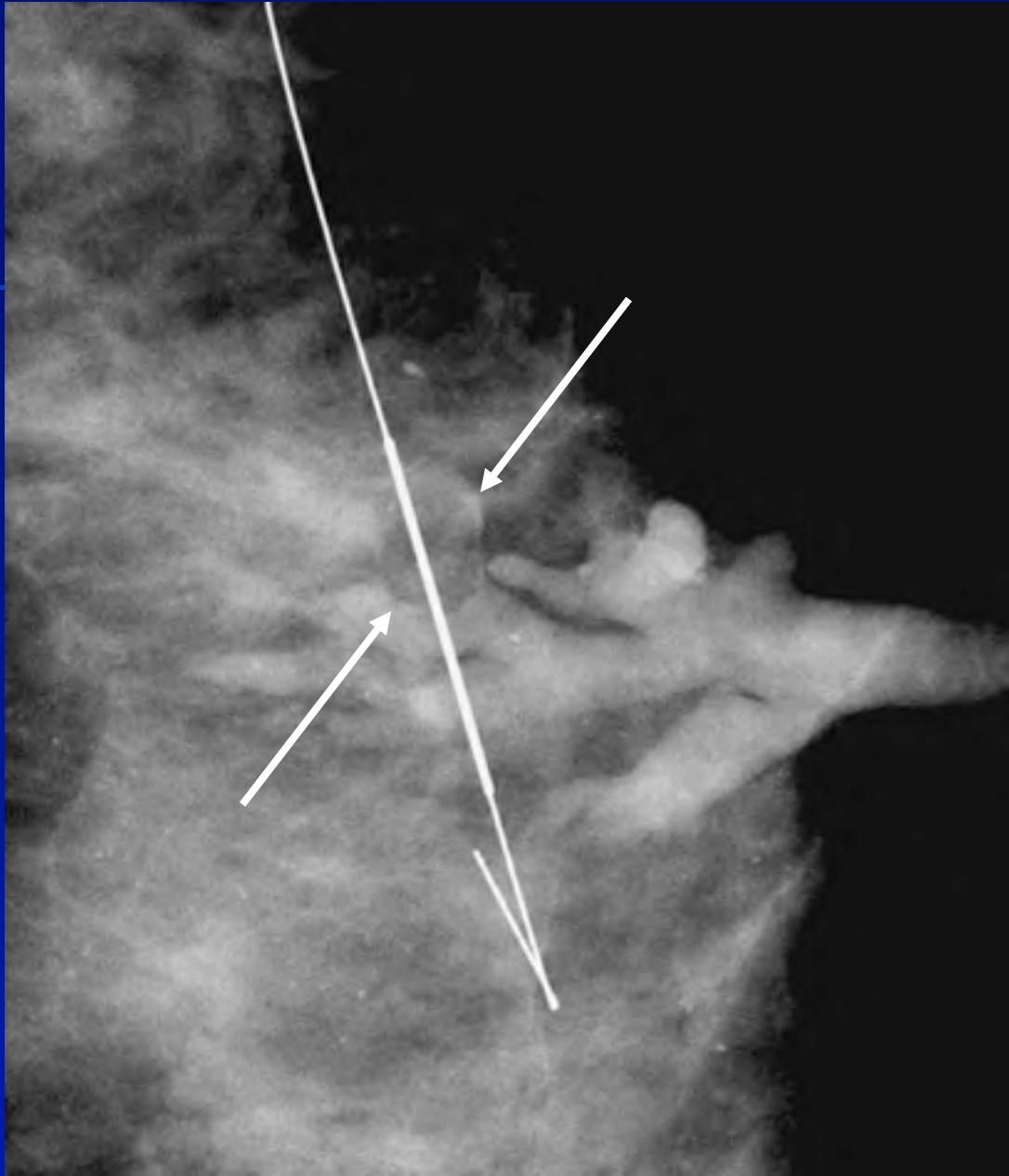


PD-INCL Source Undetermined

A 35 year old Caucasian female comes to your office and states that she has had a nipple discharge on the left for three months.

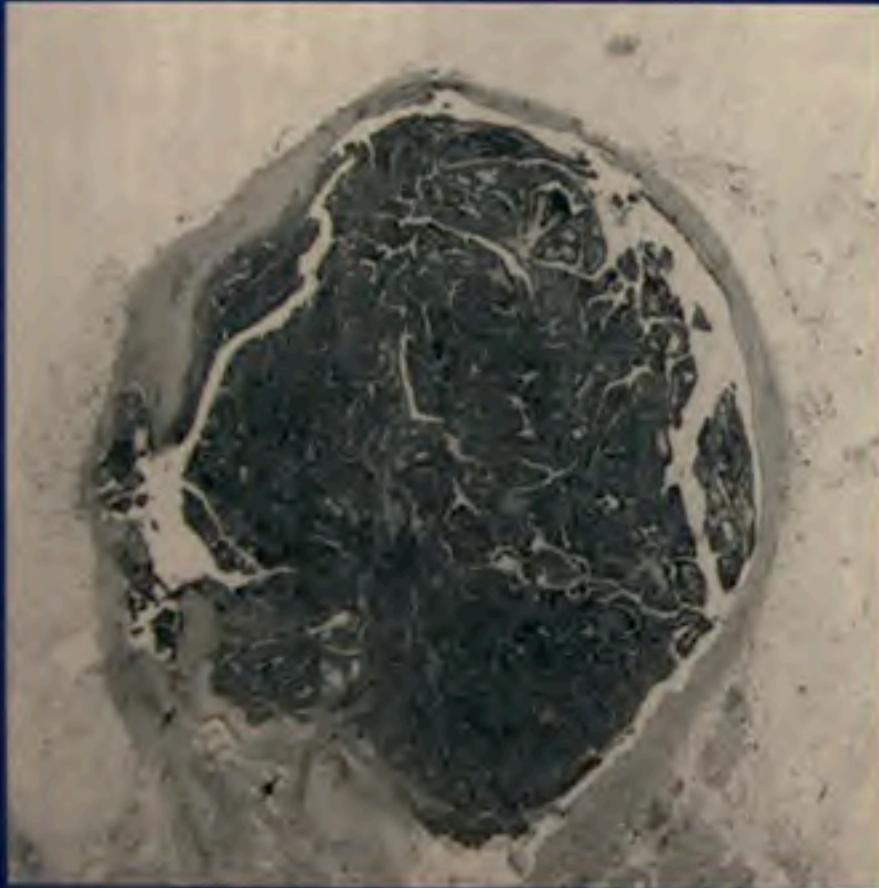
Intraductal Papilloma

- Benign local proliferation of ductal epithelial cells.
- Unilateral serosanguinous or bloody nipple discharge.
- Treatment:
 - Ductogram
 - Ductoscopy
 - Excise affected duct



Ductogram: dilated duct with intraluminal filling defect.

Intraductal Papilloma



A papillary lesion distends a single duct. The arborescent nature of the proliferation and its point of attachment or origin (arrow) from the duct wall are apparent.

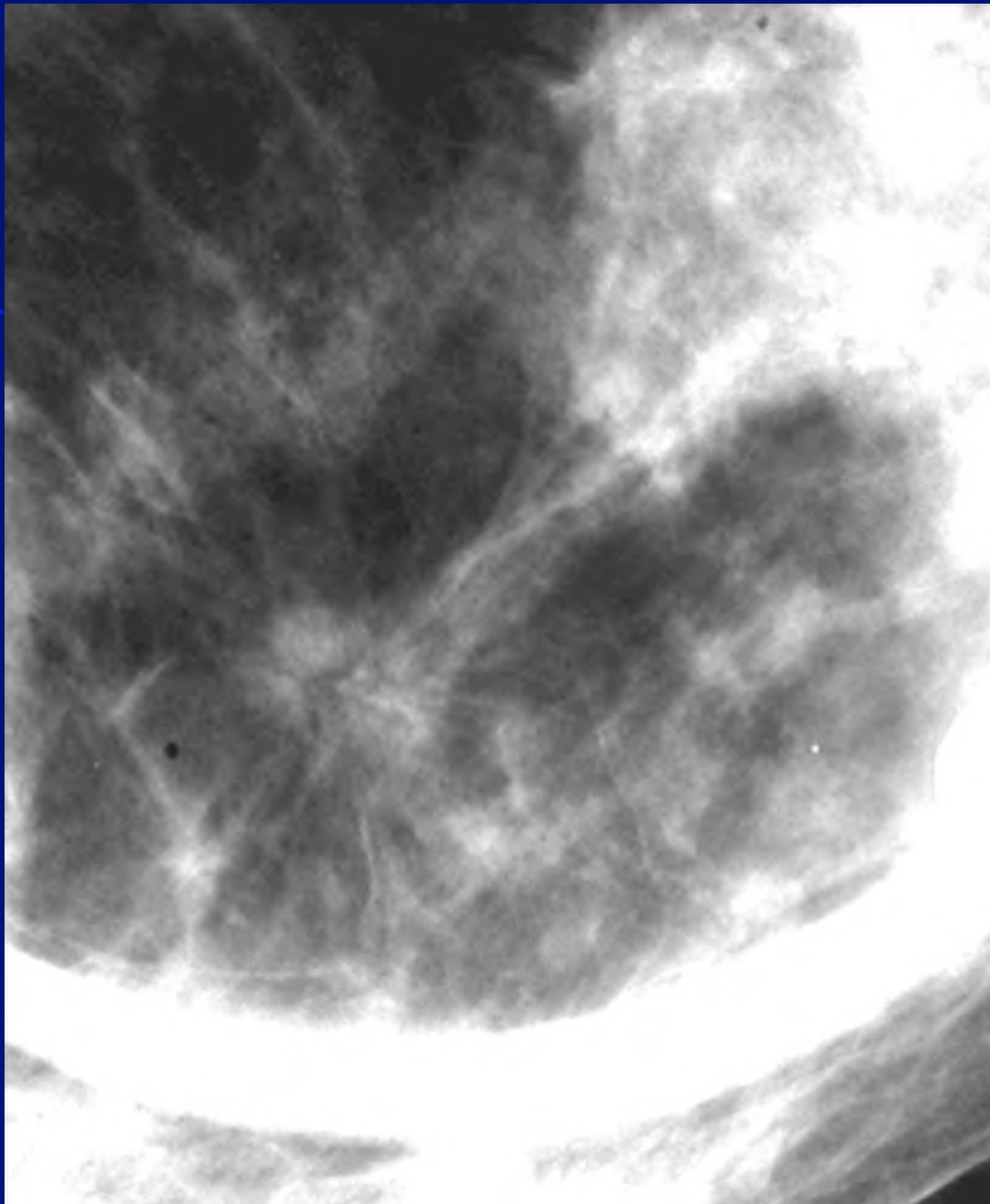
A 40 year old female strong history of fibrocystic breast disease comes to your office and states that she had a mammogram done two weeks ago which showed a suspicious lesion in her right breast.

ALND Controversy

- To do or not to do
- Er+ Pr+ H2N-
- T1 and T2 tumors
- Sentinel lymph node positive
- Patients to undergo radiation and/or chemotherapy
- Volume of metastasis in lymph node

Radial Scar

- Mimics invasive carcinoma on mammogram and on physical exam (if large enough to be palpable).
- Bilateral in 45%.
- A frequent finding in women with fibrocystic disease.
- No risk for subsequent development of invasive carcinoma.



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A female presents complaining of nipple pain during breastfeeding with focal erythema and warmth of breast on physical exam.

Mastitis or Breast Abscess

- Usual etiology: Staphylococcus aureus or streptococcus infection.
- Most commonly occurs during breast-feeding.
- Focal tenderness with erythema possibly with a fluctuant mass.
- Ultrasound helpful with diagnosis.
- Antibiotics with or without drainage is usual treatment.
- If abscess needs drainage.

A 30 year old female presents with a painful breast mass several weeks after sustaining significant trauma from a seat belt after an auto accident.

Fat Necrosis

- History of trauma in 50% of patients.
- Often present after breast reconstruction.
- Irregular mass without discrete borders may or may not be tender.
- Often indistinguishable from carcinoma clinically or mammographically.
- Diagnosis by excisional biopsy.



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A 38 year old female enters your office with a history of a large mass in her left breast. She states that it has expanded rapidly over the last month.

Phyllodes Tumor

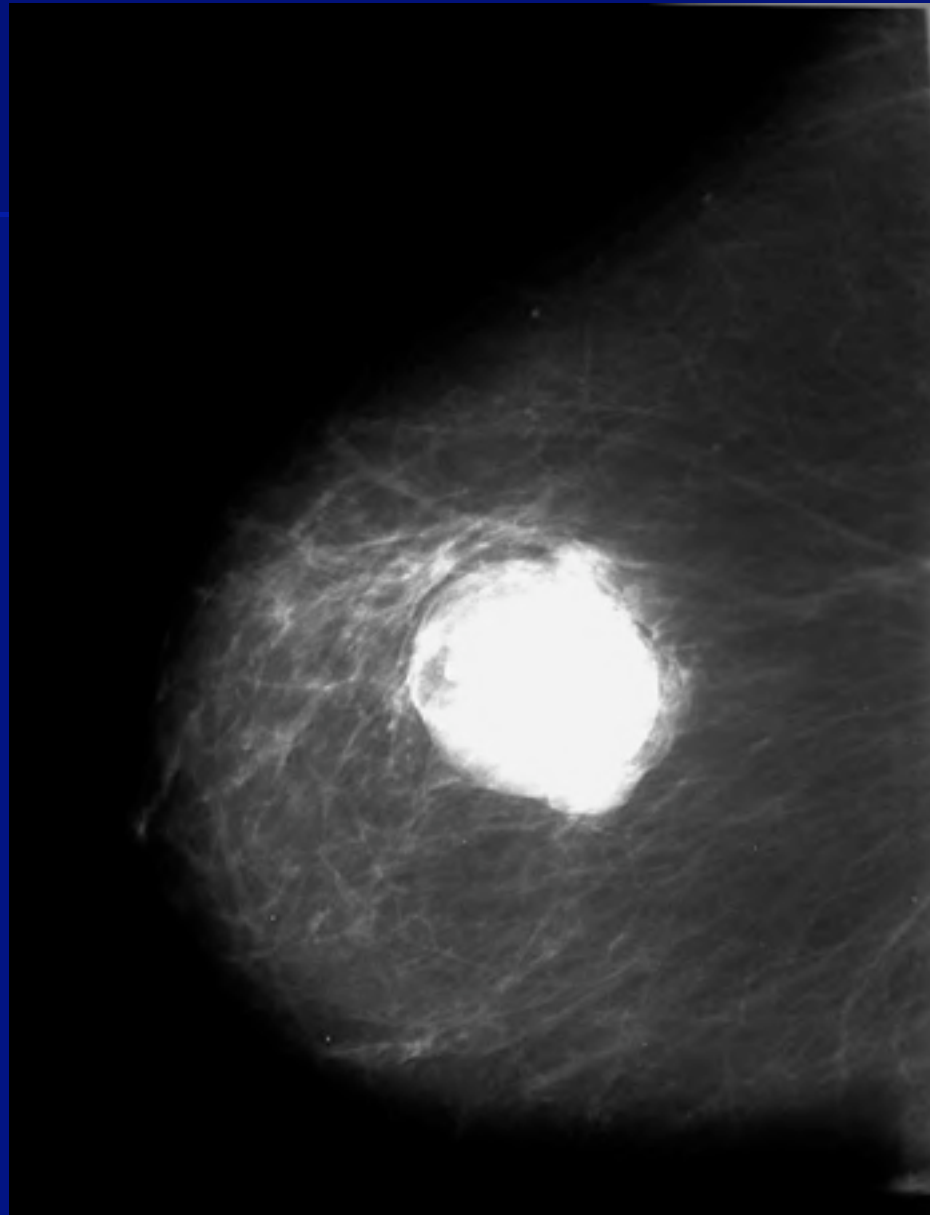
(Crystosarcoma Phyllodes)

- <.5% of all breast tumors.
- Majority are benign.
- A variant of fibroadenoma
- Most present as a large mass.
- Often present for many years before sudden enlargement.
- Occasionally quite massive and stretch the skin, displace the nipple and distend overlying veins.

Treatment of Phyllodes Tumor

- Excision with at least 1 cm margin.
- Simple Mastectomy or Lumpectomy.
- Axillary dissection usually not indicated (axillary nodes palpable in 20% but positive in <.5%).
- Radiation if chest wall involvement.
- Chemotherapy for metastatic disease (sarcoma protocol).

8-20-04



PC-TMCL

Source Undetermined



A 60 year old male comes to your office complaining of bilateral enlargement of his breasts over the last 6 months.

Gynecomastia

- Development of female like breast tissue in males.
- Most common abnormality of male breast.
- Often associated with other disease conditions, hyperthyroidism, cirrhosis, chronic renal failure, pulmonary malignancy, testicular tumors.
- Secondary to certain drug use: antibiotic steroids, digitalis, cimetidine, spironolactone, marijuana, and tricyclic antidepressants.

A 35 year old lady undergoes a right breast excisional biopsy for a suspected fibroadenoma. Pathology returns diagnosis of fibroadenoma + LCIS or atypical ductal hyperplasia.

High Risk Lesions of the Breast

- Atypical ductal hyperplasia.
- Lobular carcinoma in-situ.
- If found must do wire localization excisional biopsy 15-20% have DCIS.
- Do not need margins for LCIS or ADH.

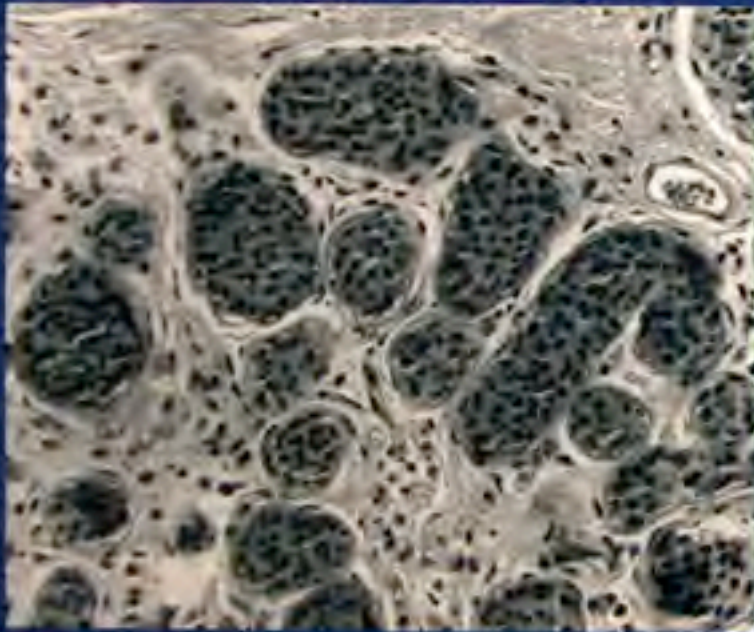
Lobular Carcinoma In-Situ (LCIS)

- A predictor of increased risk of subsequent invasive carcinoma.
- If invasive carcinoma develops most are ductal.
- Risk of 20 to 30% bilateral.
- Almost always found incidentally.
- No mammographic finding.
- 20-25% of women will develop invasive cancer.

Treatment of LCIS

- Careful follow-up (physical exam every 6 months and mammogram yearly).
- Prophylactic bilateral simple mastectomies with or without reconstruction.
- Chemoprevention with Tamoxifen or other agent.

Lobular Carcinoma In-situ (LCIS)



A proliferation within the lobule of a uniform population of loosely cohesive, round epithelial cells with little cytoplasm and indistinct cell borders. Usually the entire lobule is enlarged.



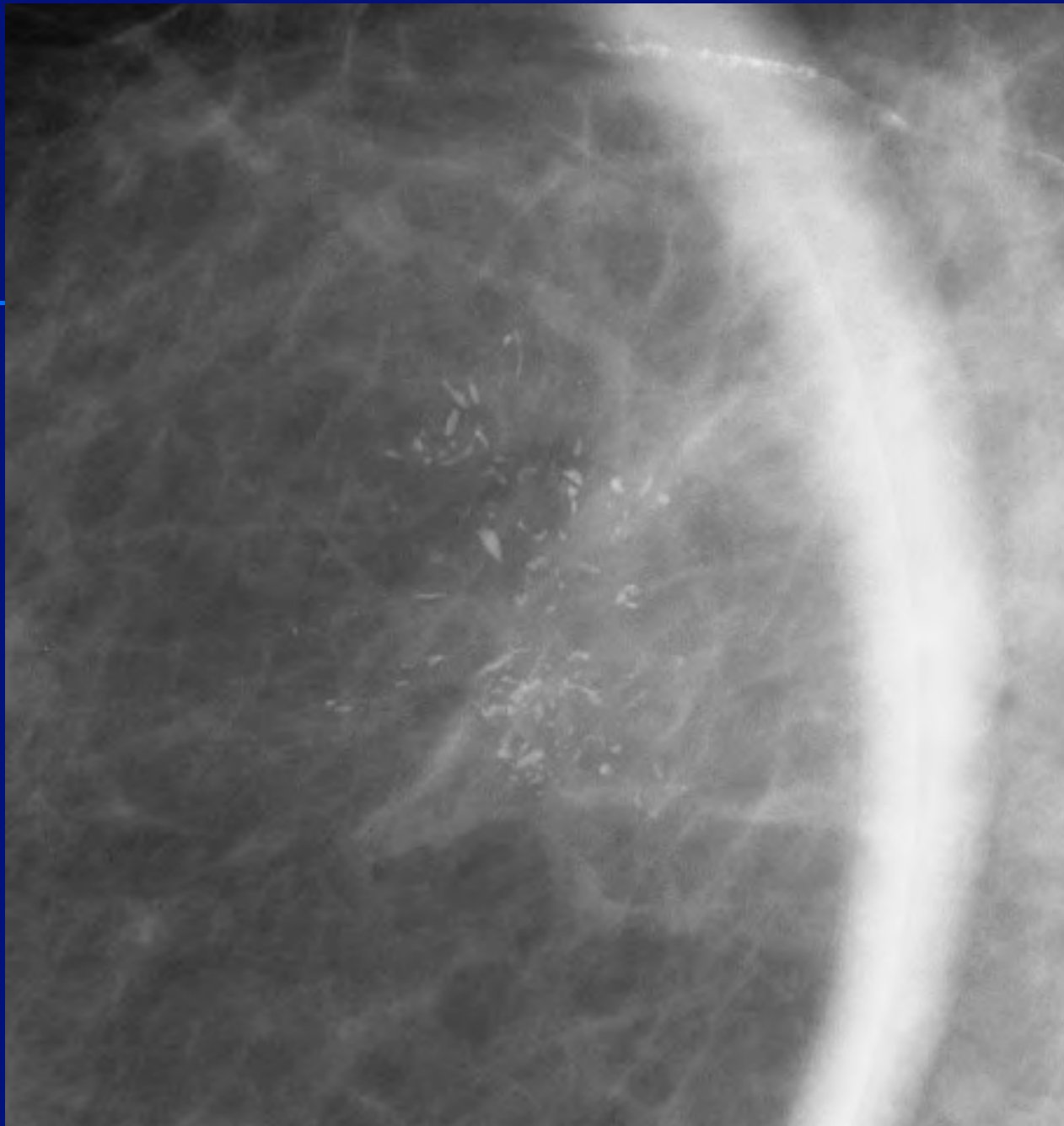
A 45 year old female comes to your office with a mammogram containing microcalcifications.

Differential Diagnosis of Microcalcifications

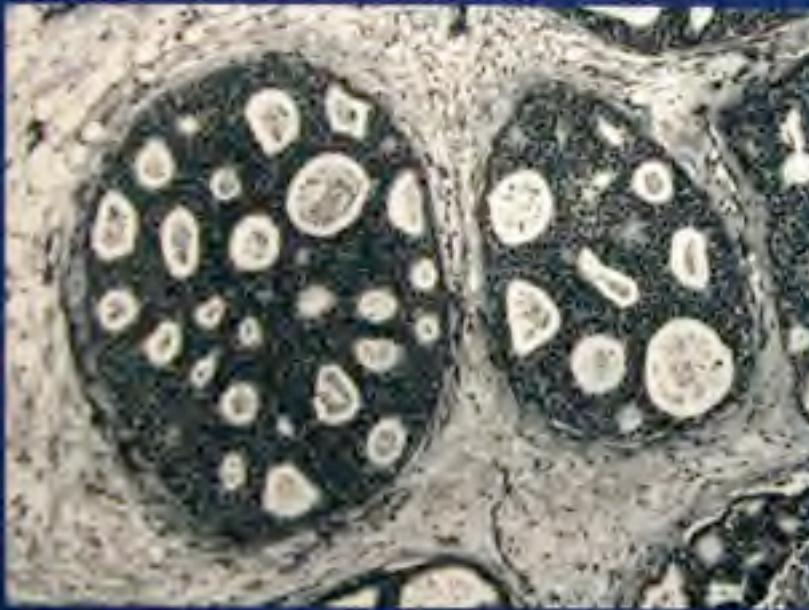
- 15% will be malignant.
- Invasive carcinoma of breast.
- Ductal carcinoma in-situ
- Benign causes
 - Fibroadenoma
 - Sclerosing adenosis
 - Fibrocystic disease

Ductal Carcinoma In-Situ

- Usually heralded by microcalcifications on mammography.
- Sometimes associated with a mass.
- Must excise with 3 mm margin.
- Treat with radiation post-op.
- Sentinel lymph node biopsy usually not necessary.
- If recurs 50% are invasive.
- Most recur within 1 cm of previous excision.
- If ER+, PR+ treat with SERM.



Intraductal Carcinoma (DCIS)



A proliferation of epithelial cells with morphologic features of malignancy that are confined to the ductal system and do not demonstrate stromal invasion. Myoepithelial cell layer may be present.



PD-IMCL

Source Undetermined

A 45 year old female presents to your office with a mass in her right breast which she identified 1 month ago while showering.

Important Historical Questions

- When was last mammogram.
- Family history of breast cancer.
- Age at menarche.
- Age at menopause (if appropriate).
- Age at first pregnancy.
- History of ionizing radiation exposure.
- Postmenopausal hormone replacement therapy.
- Use of oral contraceptives.
- Did the patient breast feed children.

Increased Risk

- Prior personal history of breast cancer.
- History of atypical ductal hyperplasia or LCIS.
- Early menarche < 13 years.
- Late menopause \geq 55 years.
- Nulliparity.
- Exposure to radiation.
- First degree relative with breast cancer, prostate cancer or ovarian cancer.
- Postmenopausal hormone replacement.
- Genetic predisposition (BRCA 1 or 2, P53, mutation).

Diagnostic Options

- Mammography.
- Ultrasound.
- Core biopsy (percutaneous or image guided).
- Fine needle aspiration (FNA).
- Wire localization excisional biopsy.
- Excisional biopsy.
- Sentinel lymph node biopsy.
- FNA of lymph nodes.

Mammography

- Sensitivity 80-90%.
- Identifies about 5 cancers/1000 women.
- If detected by mammography 80% have negative nodes vs. 45% if detected clinically.
- Much less effective in < 35 age group and in patients who have taken endogenous hormones.

Ultrasound

- No ionizing radiation
- Cheap.
- Good for identifying cystic disease.
- Can aid in biopsying a mass or calcifications.
- May be helpful in patients with dense breast tissue.

Fine Needle Aspiration (FNA)

- Low morbidity.
- Cheap.
- False positive 1-2%.
- False negative up to 10%.
- Requires a skilled pathologist.
- More difficult to determine receptor status.

Stereotactic Core Biopsy

- Fewer complications compared to wire localization.
- Less chance of a sampling error than core biopsy alone.
- Does not require OR.
- Receptor status easily determined.
- Used for non-palpable lesions.

Wire Localization Biopsy

- Requires the OR.
- May cause deformity of the breast.
- Requires a surgeon.
- Must coordinate surgeon and radiologist times.
- Non-palpable lesions.
- May be necessary depending on location of the lesion.

Breast Cancer Epidemiology

- One in 8 women will contract.
- Approximately 215,000 new cases in United States this year.
- 15% of all cancer deaths in women in U.S.
- Incidence increases with age.
- More common in Caucasians except in the under 40 age group.
- <1% occur in men.

Invasive Ductal Carcinoma

- Most common type of invasive carcinoma of the breast 75-80%.
- Most common sites of metastasis are axilla, lungs, liver, bone, and brain.
- Usually diagnosed after finding a mass on mammography or by palpation.

Treatment Options

- Lumpectomy and sentinel lymph node (SLNB) biopsy.
- Mastectomy and sentinel lymph node (SLNB) biopsy.
- Lumpectomy or mastectomy and axillary lymph node dissection (ALND).
- Neoadjuvant chemotherapy.
- Hormonal therapy.
- Adjuvant chemotherapy.
- Radiation therapy.

Receptor Status of Tumor

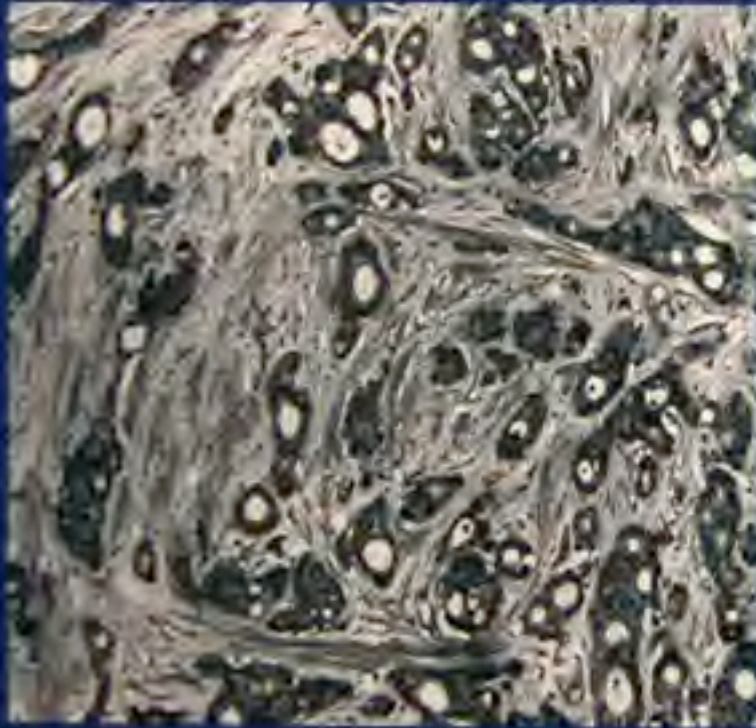
- Estrogen receptor + better prognosis. Can use SERMS (Selective estrogen receptor modulators).
- Estrogen receptor (-). Worse prognosis SERMS not effective.
- HER-2-NEU receptor overexpressed worse prognosis.
- Current controversy over use of SERMS in ER –PR+ patients.
- ER+ tumors have poorer response to chemotherapy.

Invasive Ductal Carcinoma

Mammogram



Invasive Ductal Carcinoma



Irregular or rounded solid aggregates of cells admixed with single cells and cords that usually appear as poorly formed tubules and have glandular lumens. **Tubules and aggregates lack a basal lamina and surrounding myoepithelial cells.**



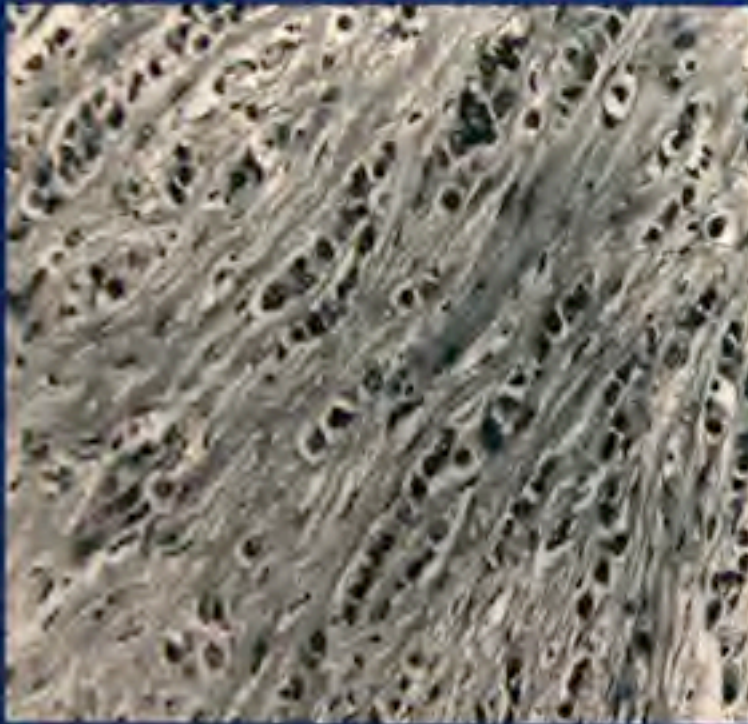
PD-EMCL

Source Undetermined

Invasive Lobular Carcinoma

- 5-15% of all invasive carcinomas of the female breast.
- Usually presents as ill-defined, painless mass or a vague thickening or nodularity.
- Tends to be more extensive than mammography suggest.
- 15-30% multicentric.
- Contralateral carcinoma develops in 10% to 15%.
- Treatment is same as invasive ductal carcinoma.

Invasive Lobular Carcinoma



Cords of uniform, loosely cohesive, small cells with a thin rim of cytoplasm that invade stroma. Tumor cell nuclei tend to be round or notched and have inconspicuous nucleoli. Some cells have intracytoplasmic lumina.



Other Types of Breast Cancer

- Papillary
- Tubular
- Medullary
- Inflammatory
- Paget's Disease
- Male Breast Cancer

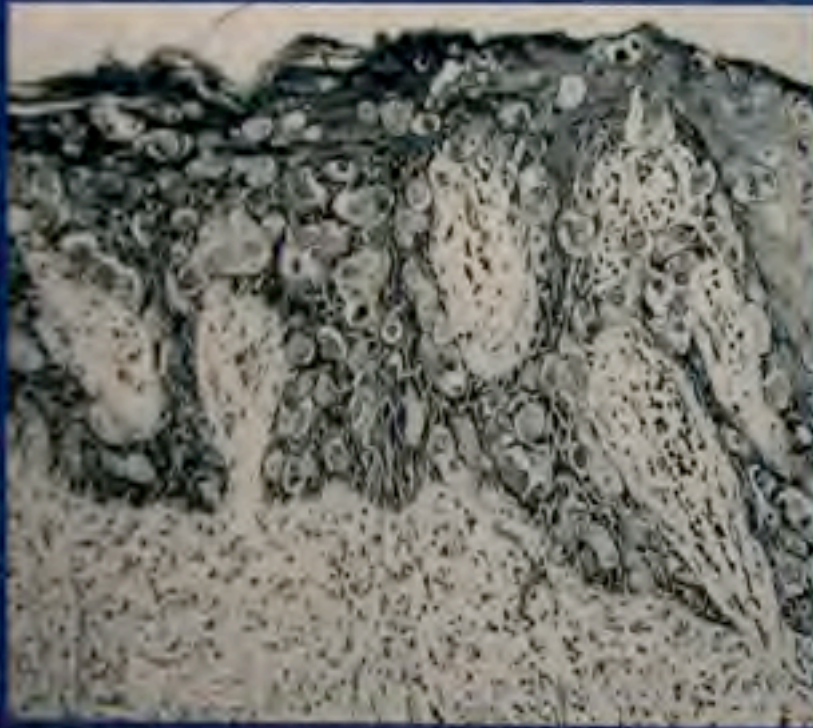
Inflammatory Breast Cancer

- One to 2% of all invasive breast cancers.
- Most lethal breast cancer.
- Vascular and lymphatic invasion commonly seen at pathologic evaluation.
- Frequently presents with erythema, “peau d’orange”, and nipple retraction.
- Treatment is neoadjuvant chemotherapy followed by surgery and radiation.
- Surgical treatment is a Modified Radical Mastectomy.

Paget's Disease of the Breast

- About 2% of all invasive breast cancers.
- Usually associated with underlying ductal carcinoma extending within the epithelium of the main excretory ducts to the skin of the nipple and areola.
- Presentation: Tender, itchy nipple with or without bloody discharge with or without subareolar palpable mass.
- Treatment is either central segmentectomy or mastectomy with SLN or ALND.
- Chemotherapy and/or radiation as indicated.

Paget's Disease



Large, round to oval cells with abundant, pale eosinophilic or amphophilic cytoplasm with prominent round nuclei and distinct nucleoli are scattered singly or in clusters in the surface epithelium of the nipple. **An underlying carcinoma present in 95%.**

Breast Cancer In Males

- Less than 1% of all breast cancers.
- Predisposing factors: Klinefelter's Syndrome, estrogen therapy, elevated endogenous estrogen, previous irradiation and trauma.
- Infiltrating ductal carcinoma most common.
- Diagnosis tends to be late often with mass, nipple retraction and skin changes.
- Stage by stage survival is same as women.
- Treatment involves mastectomy and SLNB/or ALND.

Breast Cancer in Pregnant and Lactating Women

- Three breast cancers per 10,000 pregnancies.
- Biopsy should be done if there is a suspicious mass.
- Mammography can be done if there is proper shielding.
- Radiation is not advised for pregnant women therefore MRM is advised.
- Delay chemotherapy to the second trimester.
- Suppress lactation after delivery.

Common Chemotherapeutic Drugs

- Anthracyclines (Adriamycin)
- Cyclophosphamide (Cytosan)
- 5-fluorouracil
- Taxanes (Paclitaxel, Taxotere)
- Trastusumab (Herceptin)

Other Agents

- Monoclonal antibodies
 - Transtuzumab (Herceptin)
 - Bevacizumab (Avastin)
 - Impedes neovascularization
 - Interferes with VEGF
 - Bisphosphonates – inhibits Osteoclastic activity
 - Zometa

Hormone Manipulation

- Tamoxifen (receptor blocker)
- Aromatase inhibitor
 - Arimidex (anastrozole)
 - Femara (letrozole)
 - Exemestane (aromasin)
- Faslodex (fulvestrant)

Radiation

- Give when breast sparing procedure
- Give when tumor involves the chest wall or skin.
- Give when four or more nodes positive.
- Decrease local recurrence by 40-50%.

Oncotype DX

- Gene – based assay of tumor tissue
- Helps determine the risk of recurrence
- Helps guide chemotherapy decisions
- Applies to ER⁺ HER2NEU⁻ patients
- Patients must be node negative or have micrometastasis .2-2mm
- Tumors 6 mm – 1 cm with moderately to poorly differentiated features or unfavorable features
- Tumors > 1 cm with favorable features
- TAILOR X trial

Referral for Genetics Evaluation

An affected individual with 1 or more of:

- Early age onset breast cancer
- Triple negative disease
- Two primary breast cancers
- Breast cancer at any age, plus
 - ≥ 1 Close relative with breast cancer under age 50
 - ≥ 1 Close relative with ovarian, fallopian tube or primary peritoneal cancer at any age
 - ≥ 2 Close relatives with breast cancer or pancreatic cancer at any age

Referral for Genetics Evaluation

An affected individual with one or more of:

- Combination of breast cancer with one or more of:
 - Thyroid cancer, sarcoma, adrenocortical carcinoma, endometrial cancer, pancreatic cancer, brain cancer, diffuse gastric cancer, mucocutaneous lesions or leukemia/lymphoma on the same side of the family
- Ovarian, fallopian tube or primary peritoneal CA
- Male breast cancer

Referral for Genetics Evaluation

An unaffected individual with a FHx of 1 or more of:

- ≥ 2 Breast cancer primaries from same side
- ≥ 1 Ovarian cancer primaries from same side
- Combination of breast cancer with 1 or more of:
 - Thyroid cancer, sarcoma, adrenocortical carcinoma, endometrial cancer, pancreatic cancer, brain cancer, diffuse gastric cancer, mucocutaneous lesions or leukemia/lymphoma from same side of family
- Known mutation in breast cancer gene
- Male breast cancer
- From a population at risk

Genetics

- Malone et al conducted a population based case control study on data from 1983-1992
 - The likelihood that a women with breast cancer under age 35 has a detectable BRCA1/2 mutation is 9.4%

Malone et al. Frequency of BRCA1/BRCA2 mutations in a population-based sample of young breast carcinoma cases. *Cancer*. 2000; 88:1393-1402.



Genetics

- Li-Fraumeni Syndrome
 - Autosomal dominant
 - Highly penetrant
 - Young age at onset of malignancies
 - Identifiable germline mutation in TP53

Genetics

- Li-Fraumeni syndrome diagnostic criteria
 - A proband diagnosed with sarcoma when younger than 45 years of age
 - A first-degree relative with any cancer diagnosed when younger than 45 years of age
 - Another first-degree or second-degree relative of the same genetic lineage with any cancer diagnosed when younger than 45 years or sarcoma at any age

Genetics

- Cowden's syndrome
 - Autosomal dominant
 - Variable expression, high penetrance
 - Prevalence of 1 in 200,000
 - Mutation in PTEN
 - Breast cancer in 20-35%