University of BRISTOL

Bristol Dental School

Breast Pathology

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ST1 Block Teaching Week - Bristol

bristol.ac.uk

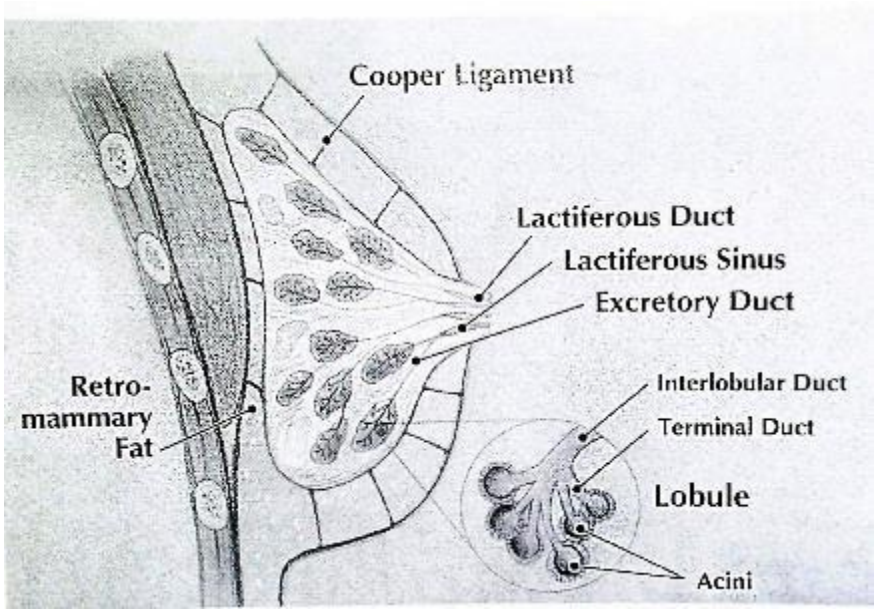
Learning outcomes

- After this lecture you should be able to
  - Classify common diseases of breast
  - Describe risk factors for breast cancers
  - Explain different common types of breast cancers and their prognostic and therapeutic significance including the difference between in-situ and invasive tumours.
  - Understand the different diagnostic tools and treatment modalities for breast cancers.
  - Explain the breast cancer screening program and role of histopathologists in diagnosis and management of breast cancers.

Normal Breast
ANATOMY

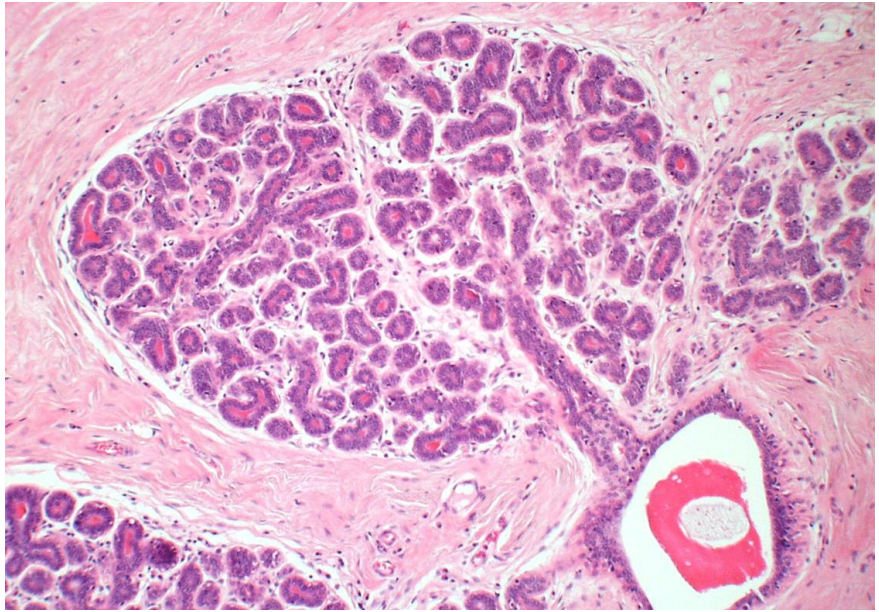
- The breast is a modified sweat gland covered by skin and subcutaneous tissue.
- It rests on the pectoralis muscle from which it is separated by a fascia.

- Dense connective tissue extends from the underlying pectoralis fascia to the skin of the breast called Cooper's ligament. These ligaments hold the breast upward.



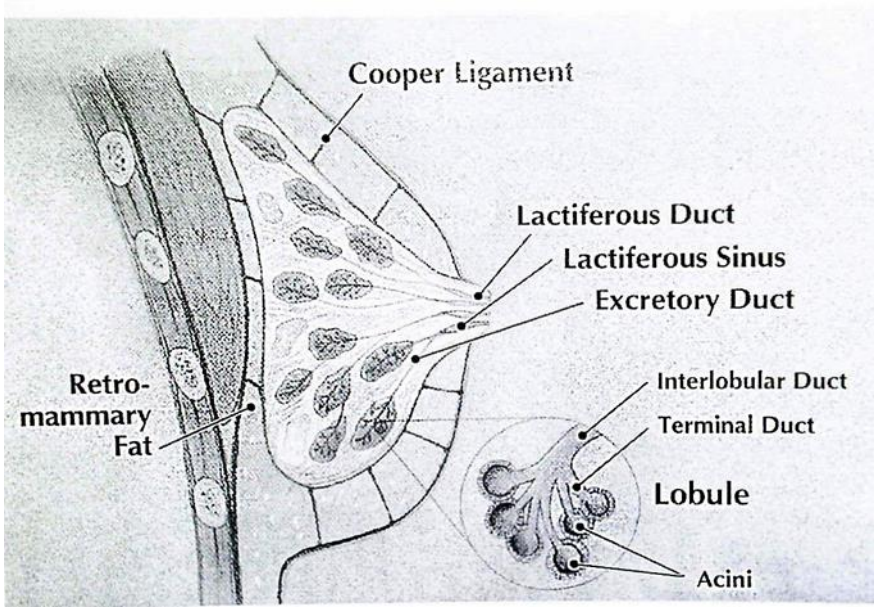
Normal Breast
HISTOLOGY

- Histologically breast consist of glandular (parenchymal) and supporting (connective) tissue.
- Glandular element is divided into branching duct system and terminal duct lobular units (TDLU).
- The TDLU is formed by the lobule and terminal ductule and represents the secretory portion of the gland.



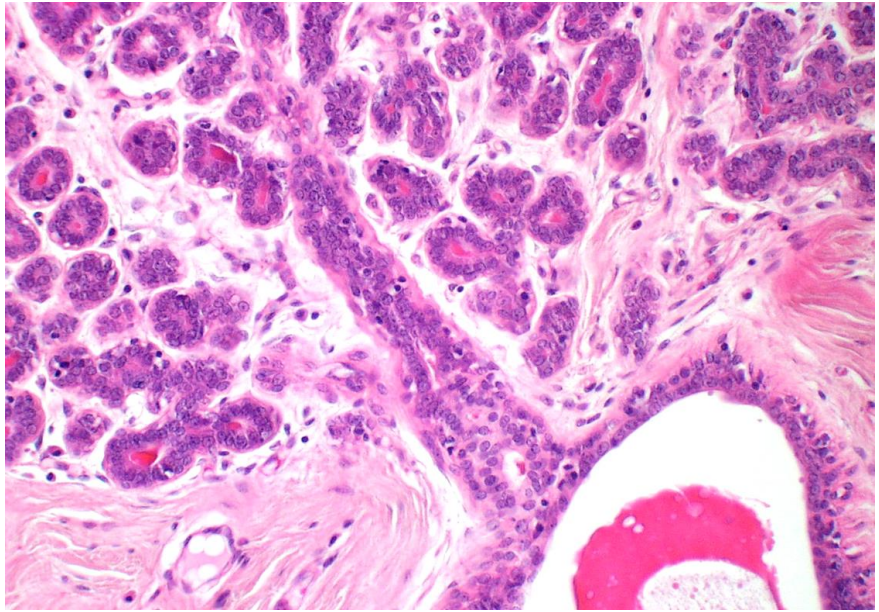
Normal Breast
HISTOLOGY

The TDLU connects with the sub-segmental duct, which in turn leads to a segmental duct and this to a collecting/lactiferous duct which empties into the nipple. The latter are 15-20 in number on each side.



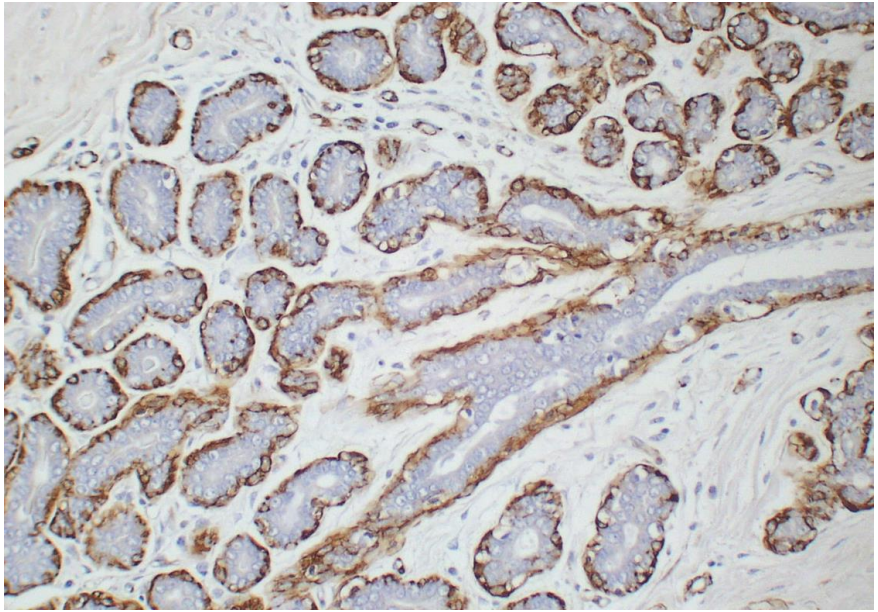
Normal Breast
HISTOLOGY

- The entire ductal-lobular system of the breast is lined by two cell types;
  - the inner epithelial cells
  - the outer myoepithelial cells



Normal Breast
HISTOLOGY

- These two cell types have distinctive ultrastructural and immunohistochemical features that differ considerably from each other.
- Various markers are used to identify myoepithelial cells including SMM, p63 and ck5/6



Diseases of Breast

Classification

- INFLAMMATORY
  - Acute mastitis
  - Chronic mastitis
  - Mammary duct ectasia
  - Fat necrosis
- PROLIFERATIVE
  - Fibrocystic change
  - Radial Scar

Diseases of Breast

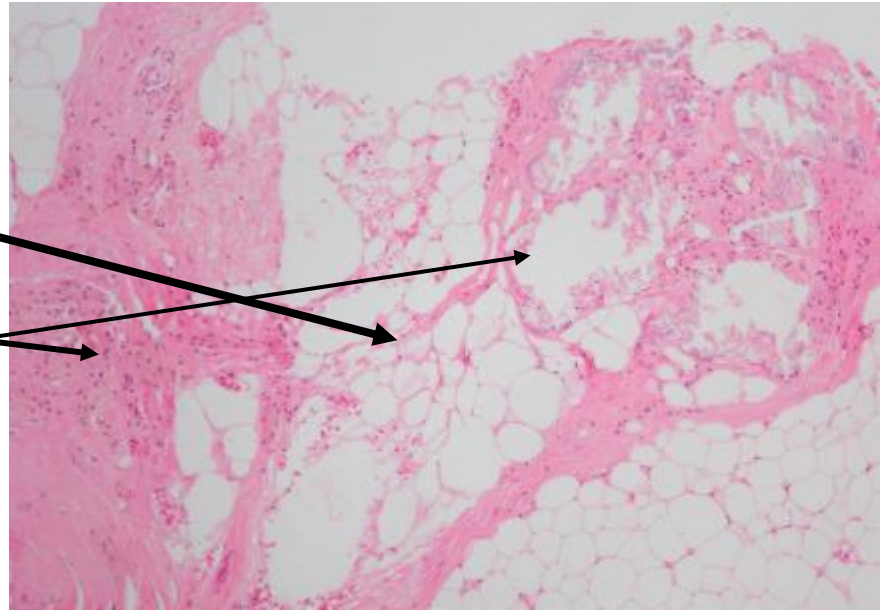
Fat Necrosis:

Variably sized fat cells lacking nuclei.

Macrophages in the stroma

Dystrophic calcification

Significance: Due to irregular border, density and calc on mammogram this lesion can mimic breast cancer.



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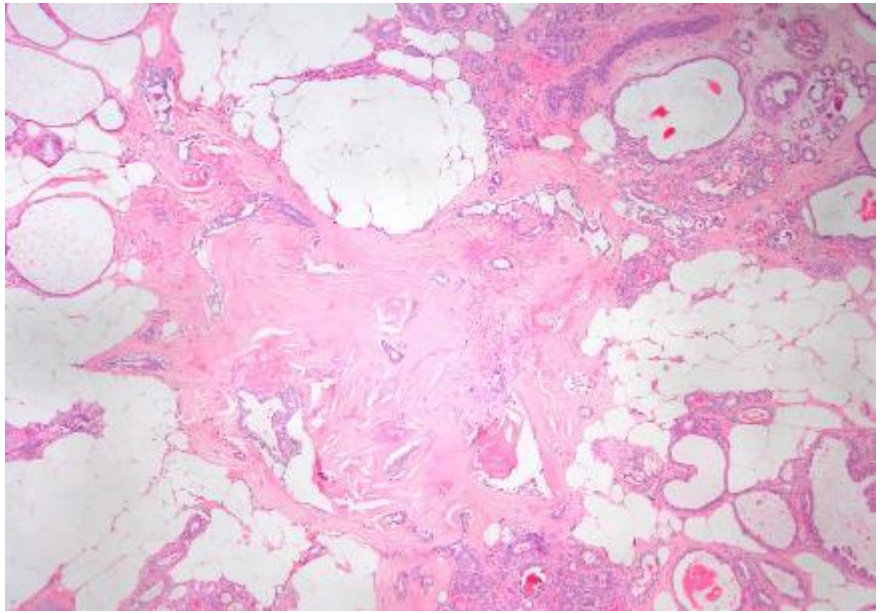
Diseases of Breast

Radial Scar

- Stellate lesion on mammogram therefore can mimic breast cancer.
- Occasionally may be associated with tubular carcinoma, therefore scored as B3 lesion for adequate sampling.

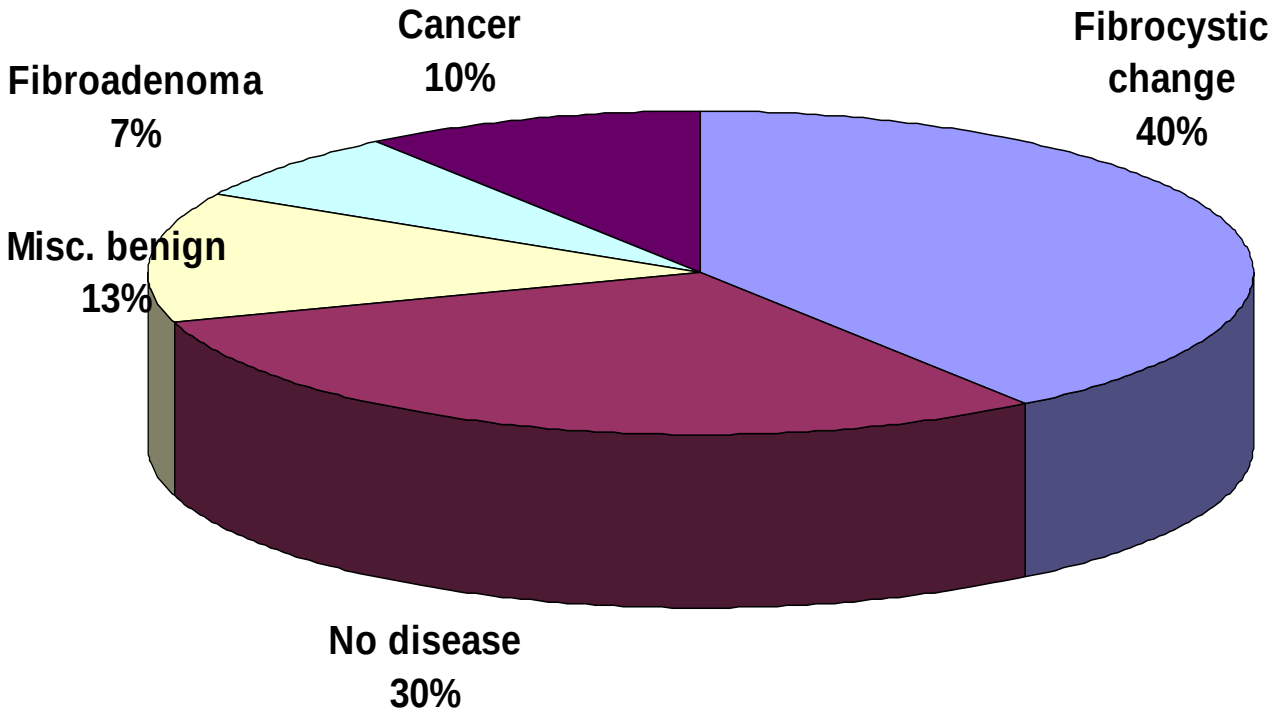


Diseases of Breast

Classification

- NEOPLASTIC
  - Benign
    - Adenoma
    - Fibroadenoma
    - Papilloma
  - Malignant
    - Carcinoma
    - Sarcoma
    - Paget's disease
    - Phylloides tumour

Result of the survey of 1000 consecutive patients attended a breast clinic with a breast lump



Diseases of Breast

Signs and Symptoms

- NIPPLE
  - Discharge
    - Milky — Pregnancy
    - Bloody — duct papilloma / carcinoma
  - Retraction — Invasive carcinoma
  - Erythema & scaling — Paget's disease or eczema

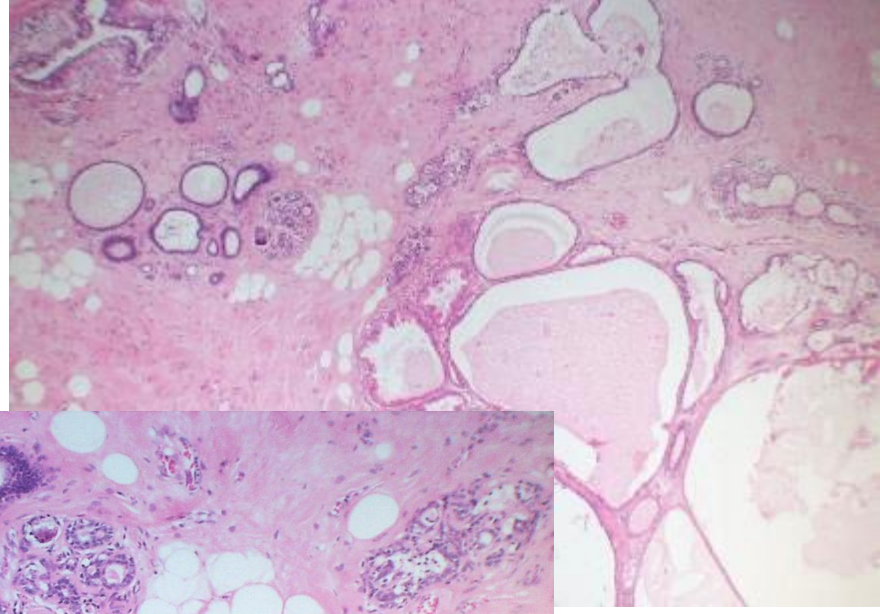
Diseases of Breast
Signs and Symptoms

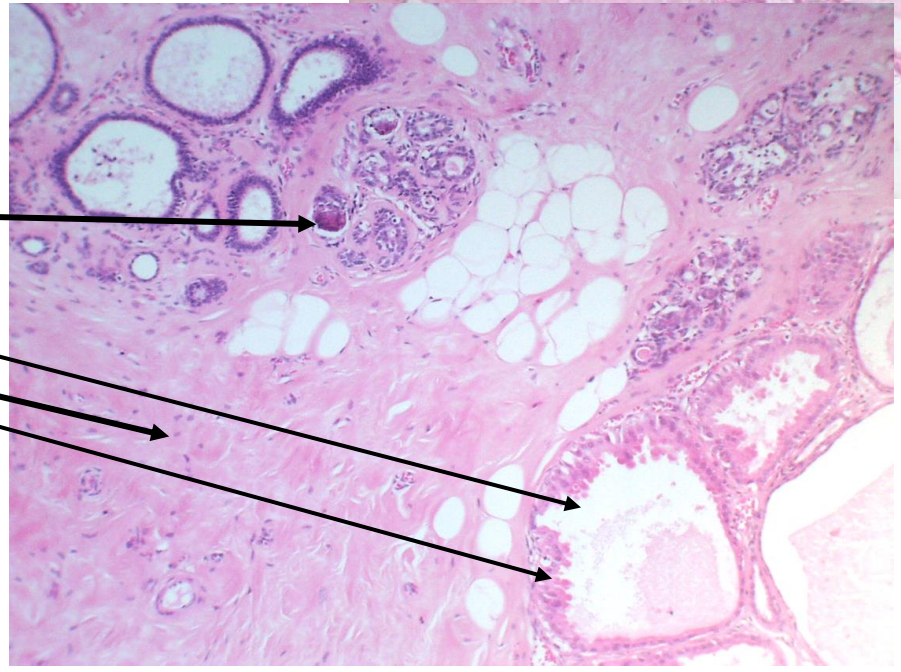
- BREAST PAIN
  - Cyclical Benign breast diseases
  - On palpation Inflammatory
- SKIN FEATURES
  - oedema peau d'orange - carcinoma
- MICROCALCIFICATION
  - DCIS or fat necrosis

Proliferative Diseases of Breast

Fibrocystic change

- Different terminology
- Common in 25 - 45 yrs age group
- Pathogenisis - Hormones
- Microscopic picture
  - TDLU
  - Calcification
  - cysts
  - fibrosis
  - Apocrine metaplasia
  - epithelial hyperplasia

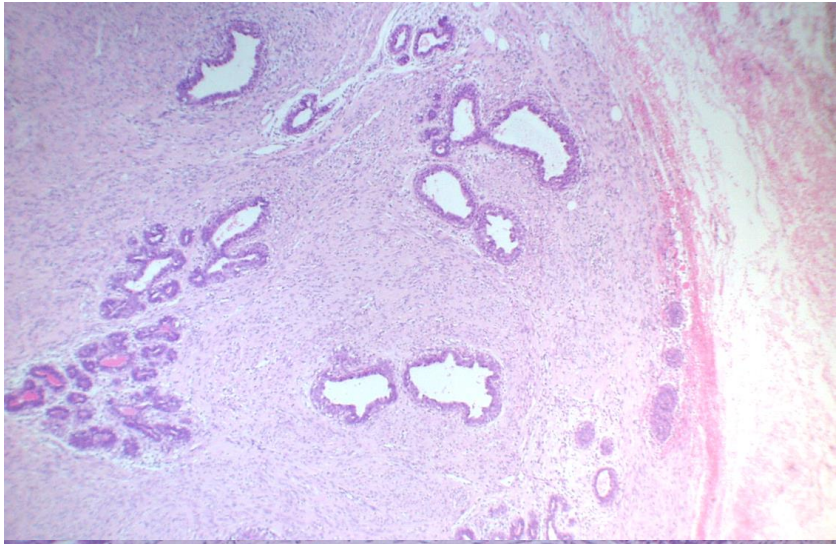


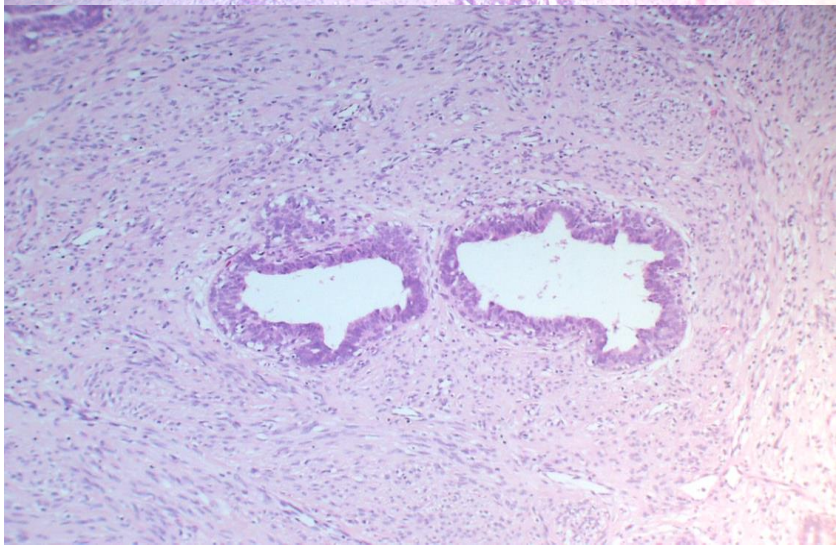


Neoplastic Diseases of Breast

Fibroadenoma

- Commonest benign breast tumour
- B/W the ages of 20-35yrs
- Increases in size during pregnancy
- Decrease in size with age
- M/s composed of both proliferating ducts and connective tissue stroma.





Malignant Diseases of Breast

Carcinoma

- 20% of all cancers in women
- In UK 1 in 8 women develop breast cancer.
- Commonest cause of death in women in 35-55 years age group.

Carcinoma

RISK FACTORS

- Female sex and age
- reproductive history
    - early menarche
    - late menopause
    - nulliparous women
    - 1st pregnancy after 30yrs of age
- obesity
- family history in 1st degree relative
    - 1.5-2x if 1 relative
    - 4-6x if two affected relatives
- geography
- atypical hyperplasia

Carcinoma

Aetiological mechanisms

- Hormonal Factors
- Genetic factors
  - BRCA 1, ch 17, ovary and breast
  - BRCA 2, ch 13
- Environmental influences

Carcinoma
Classification

- Carcinoma of breast are broadly classified on the basis of two criteria.

  - Invasion of basement membrane
    - In-situ
    - Invasive

  - Morphology
    - ductal
    - lobular

Significance of diagnosis of carcinoma in-situ

In-situ carcinoma cannot metastasize, therefore,

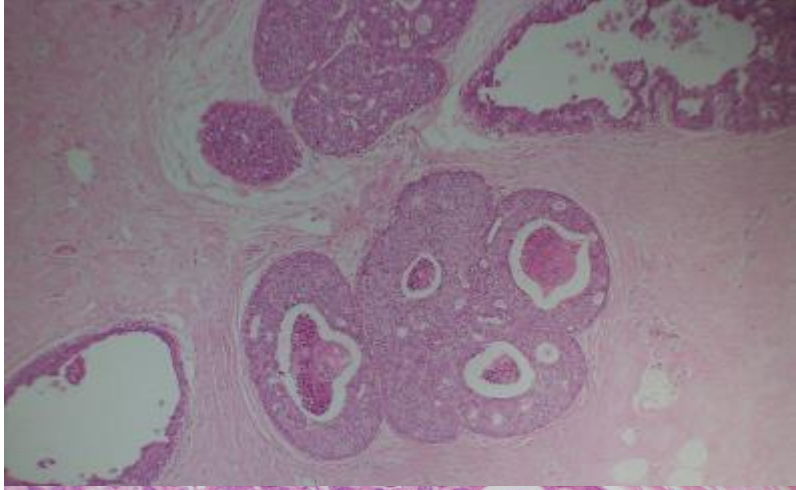
- you can potentially cure the patient by complete local excision.
- lymph node excision is not required.
- better prognosis.

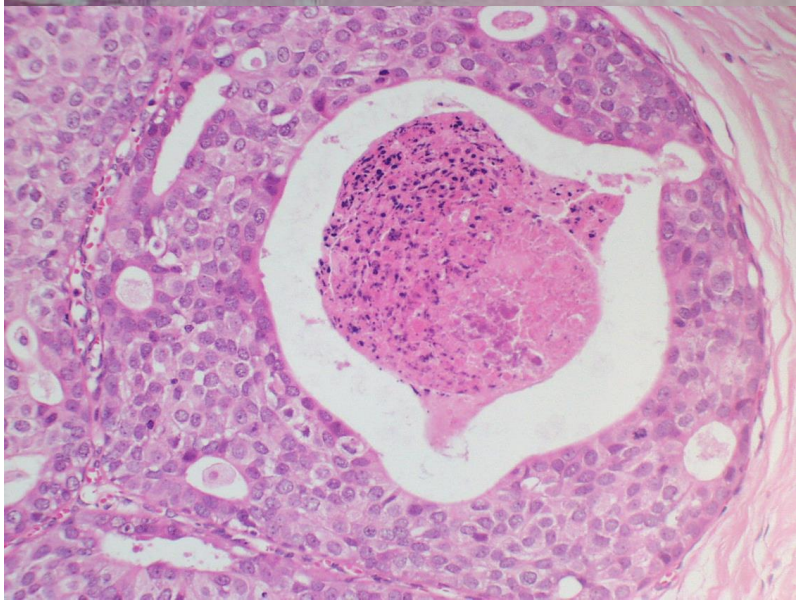
Carcinoma
Classification

- Insitu carcinoma
  - –Ductal carcinoma in situ
  - –Lobular carcinoma in situ
- Invasive carcinoma
  - –Invasive ductal carcinoma NST (75-85%)
  - –Invasive lobular carcinoma (10%)
  - –Others (5%)

Ductal Carcinoma in-situ (DCIS)

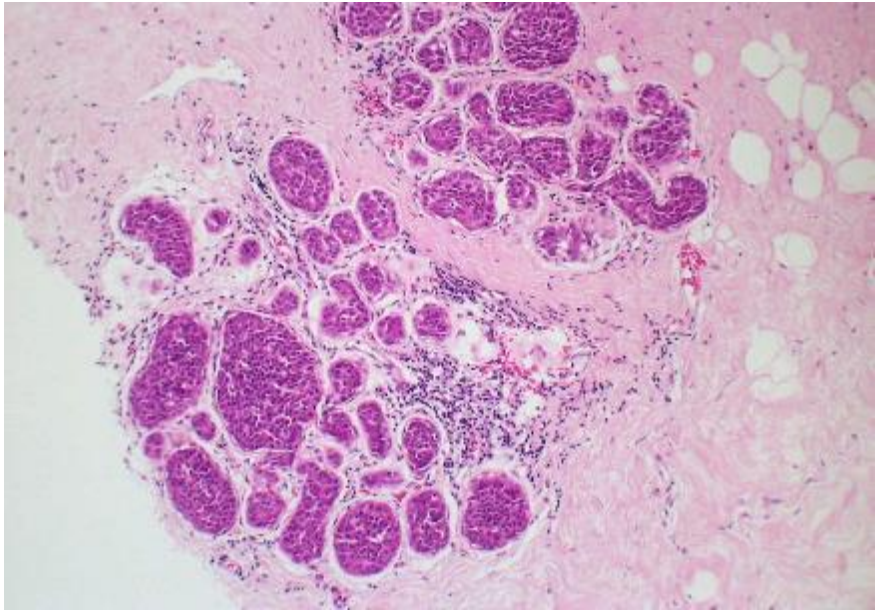
- Dilated ducts filled with neoplastic epithelial cells.
- Myo-epithelial cell layer is intact, meaning no invasion of basement membrane.
- Sometimes show central necrosis and calcification, a marker for diagnosis on mammogram.
- Classified into high, intermediate and low nuclear grades





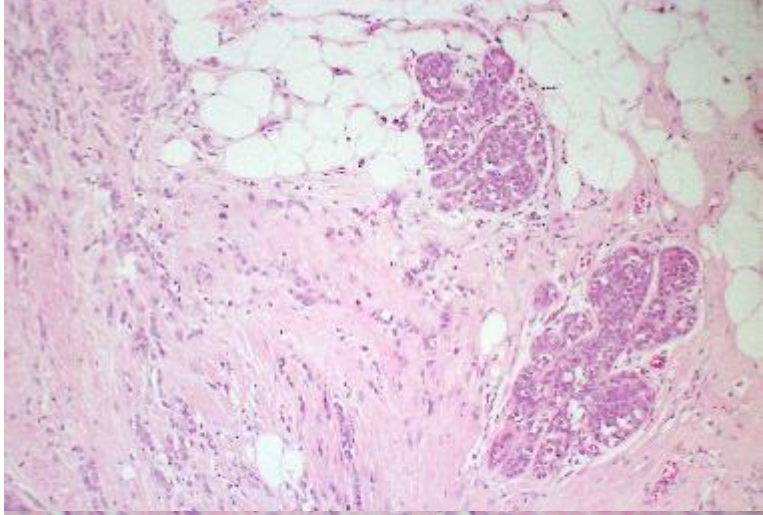
Lobular carcinoma in situ (LCIS)

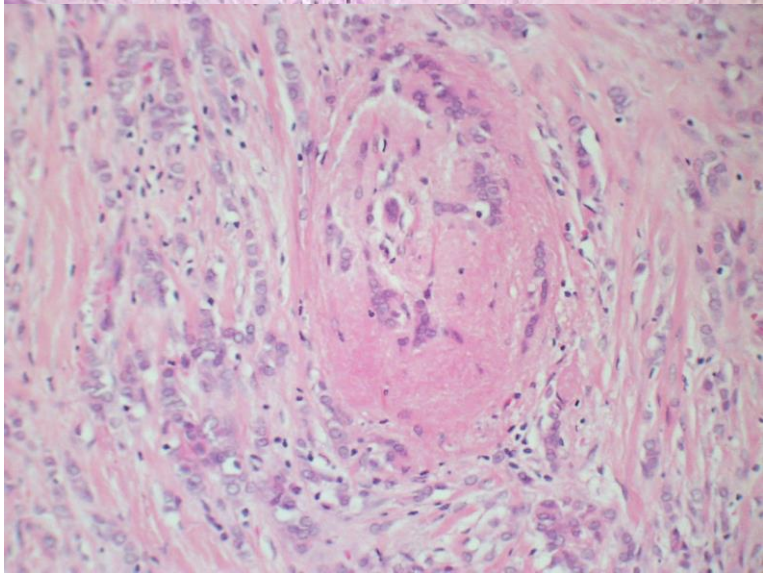
- Lobules with distended acini filled with neoplastic epithelial cells
- The cells are round and regular.
- Myo-epithelial cell layer is intact.
- Immunostaining for e-cadherin is negative (a feature which helps in differentiation of LG DCIS from LCIS)



Invasive Lobular Carcinoma with LCIS

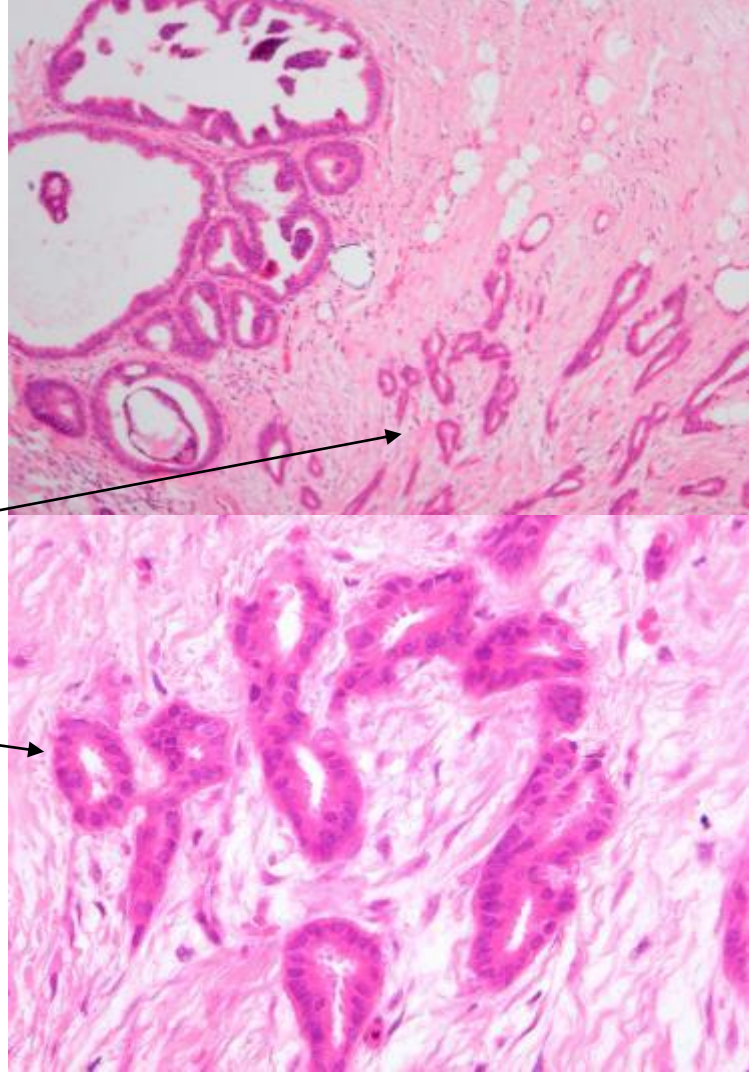
- Cells are arranged in single file pattern and infiltrating the stroma.
- No myoepithelial cell layer in invasive component.
- These tumour can be very deceptive clinically, radiologically and on histology.
- Can be multifocal/multicentric





Invasive Ductal Carcinoma
with DCIS

The invasive tumour consist of small tubular structures lacking myoepithelial cell layer meaning these cells have invaded the basement membrane.



Carcinoma

Treatment

- Surgery
- Chemotherapy
- Radiotherapy
- Hormonal treatment

Treatment

Surgery

- Breast
  - Breast Conserving
    - Wire-guided wide local excision
    - Lumpectomy
    - Segmentectomy
    - Quadrantectomy
    - Central wedge excision
  - Mastectomy
    - Simple mastectomy
    - Skin sparing mastectomy
    - Sub-cutaneous mastectomy
- Axillary Lymph nodes
  - Sentinel lymph node
  - Axillary node sampling
  - Axillary lymph node clearance level 1,2 and 3

Treatment

Chemotherapy

- Selected cases
  - Large Grade 3 tumours with nodal metastasis
  - Triple negative or Her2 positive tumours
  - Borderline cases have further genetic tests like Oncotype DX to decide chemotherapy
  - Adjuvant v/s Neo-adjuvant chemotherapy

Treatment

Radiotherapy

- Radiotherapy to breast – after conservative surgery in all except:
  - >65yrs,
  - <2cm,
  - Grade 1 tumour,
  - ER+ve, Her2 -ve
- Radiotherapy to chest wall:
  - >5cm tumour
  - Grade 3, T2 with LVI
  - +ve margin
  - 4 or more LN
- Radiotherapy to axilla
  - If SLN positive but no axillary clearance
- Radiotherapy to SCF
  - If 4 or more LNs positive
- Neoadjuvant Radiotherapy
  - In fungating tumour - rare

Treatment

Hormone therapy

- All patients with oestrogen receptor (ER) positive breast cancers
- 80% of breast cancers are positive for ER
- For 5 yrs
- Premenopausal – Tamoxifen
- Post-menopausal – Aromatase inhibitors (AI)

Carcinoma
Prognosis

- Size of the tumour
- Grade of the tumour
- Histological type of tumour
- Vascular invasion
- Stage of the tumour
  - nodal status
- Receptor status of the tumour

Breast Cancer Screening Programme

CRITERIA

- All women aged between 48 - 69 years whose names are in the Family Practitioner Committee Register are invited for mammographic examination.

- Every three years

- Two views, CC and oblique

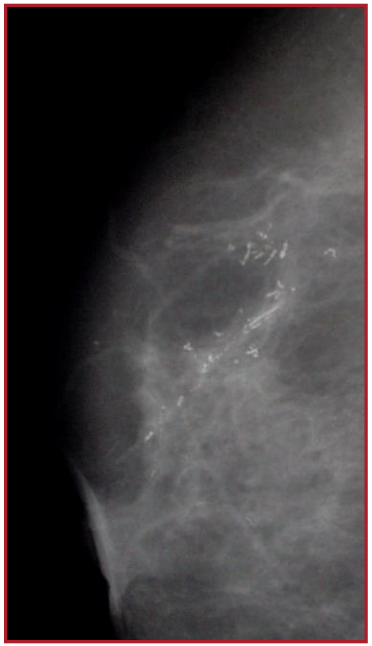
Breast Cancer Screening Programme

WHY DO WE NEED A BREAST CANCER SCREENING PROGRAMME?

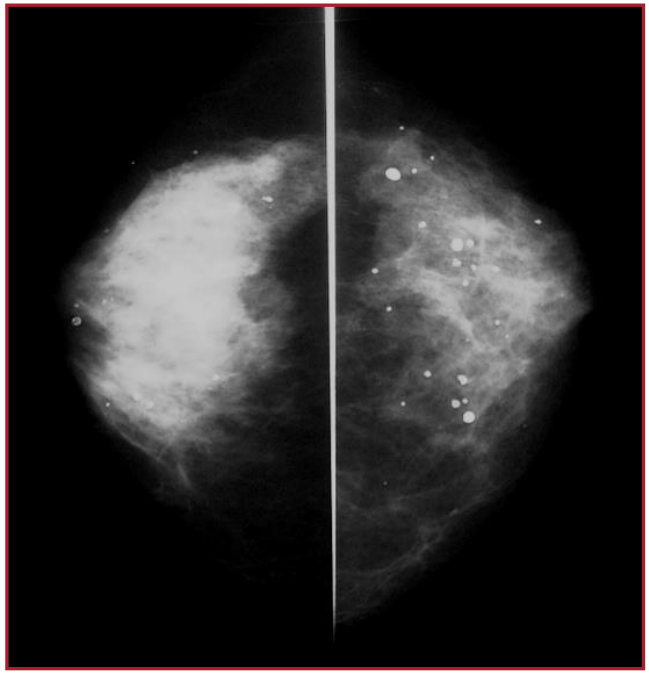
- There is increased incidence of breast cancer in the western world.
- It is estimated that in the high-risk areas that any individual women have a 1 in 8 chance of developing the disease in her lifetime.
- The rationale of the breast screening programme was the 5 year survival related to stage of the disease.
  - Stage I (< 2 cm lesion): 84%, Stage IV (> 5 cm lesion): 18%

Breast Cancer Screening Programme

What is the marker for breast cancer?



MICROCALCIFICATION



Breast Cancer Screening Programme

Where do we see this microcalcification histologically?

It is usually associated with DCIS mostly high grade with central necrosis.

Breast Cancer Screening Programme

Is it always malignant?

No, microcalcification can be associated with benign fibrocystic change.

Breast Cancer Screening Programme

Do all breast cancers have microcalcification?

NO

Breast Cancer Screening Programme

What other mammographic appearances can one have with breast cancers?

- Stellate lesion
- Circumscribed soft tissue density/mass lesion

Breast Cancer Screening Programme

Are these appearances specific for breast cancer?

No

Breast Cancer Screening Programme

What other lesions can mimic breast cancer radiologically?

Microcalcification

Fibrocystic change

Fat necrosis

Calcified fibroadenoma

Calcified eggs of parasites (rarely)

Stellate Lesion

Radial scar

Circumscribed soft tissue density

Fibroadenoma & Phylloides tumour

Breast Cancer Screening Programme
The Role of Pathologist

- Make a histological/cytological diagnosis.

  Specimens:
  a. FNAC
  b. Core biopsy

Breast Cancer Screening Programme

The Role of Pathologist

CATEGORIES OF CYTOLOGICAL DIAGNOSIS

- C1 Inadequate
- C2 Benign
- C3 Atypia, probably benign
- C4 Suspicious of malignancy
- C5 Malignant

Breast Cancer Screening Programme

The Role of Pathologist

CATEGORIES OF HISTOLOGICAL DIAGNOSIS

- B1 Normal
- B2 Benign
- B3 Benign but of uncertain malignant potential
- B4 Suspicious of malignancy
- B5 Malignant

a - in situ

b - invasive

Breast Cancer Screening Programme

The Role of Pathologist

2. To help clinicians in the management of a patient.
   By assessing the extent of the lesion and completeness of excision.
   By evaluating the oestrogen receptor status.

3. Help in predicting the prognosis.
   Type of the tumour
   Grade of the tumour
   Stage of the tumour
   Size of the tumour

Any Questions?

Definitions

- **Cyst**
  a cavity lined by epithelium. This cavity contains secretion released by the epithelium.
- **Abscess**
  – Cavity containing pus. This is lined by granulation (repair) tissue, consist of newly formed blood vessels and fibroblasts.
- **Granuloma**
  – A type of chronic inflammation characterised by localised collection of epithelioid histiocytes (macrophages).
- **Hamartoma**
  Developmental malformation i.e. dis-organised laying down of tissue (which is normally present at the site) resulting in formation of lump.
- **Carcinoma**
  Malignant tumour of epithelial differentiation
- **Sarcoma**
  Malignant tumour of mesenchymal differentiation