

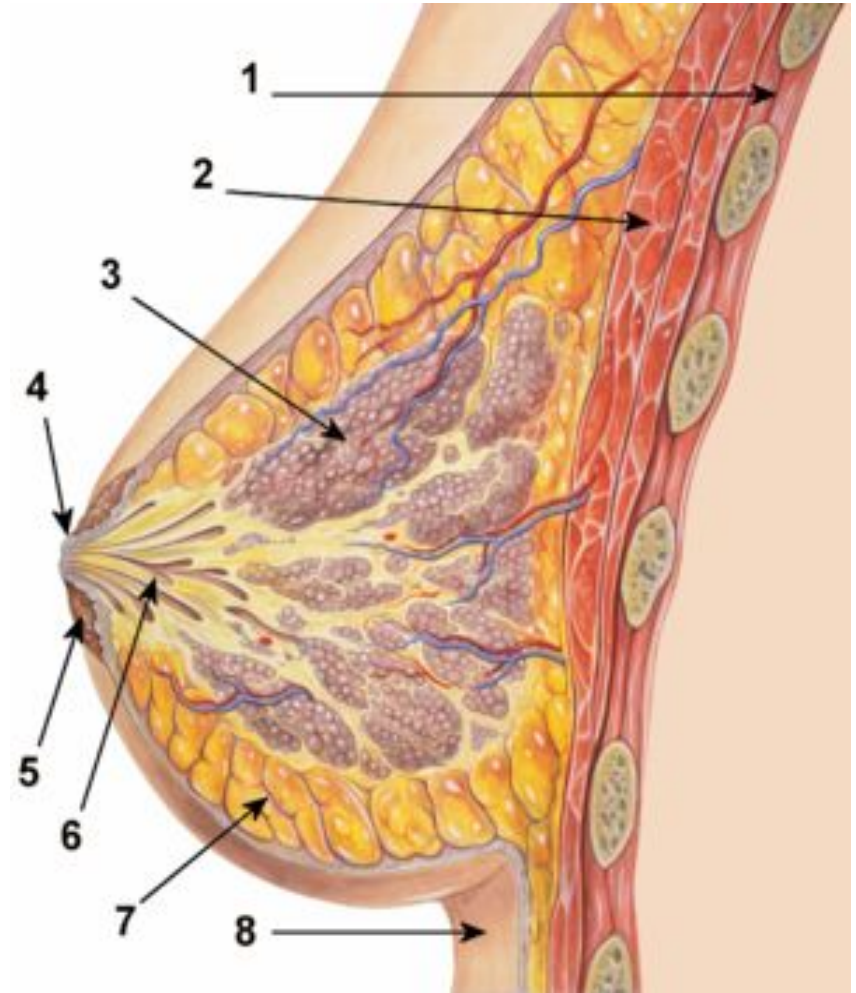
# THE BREAST

**DR. NAHEDH RAOOF ALAMAAR**

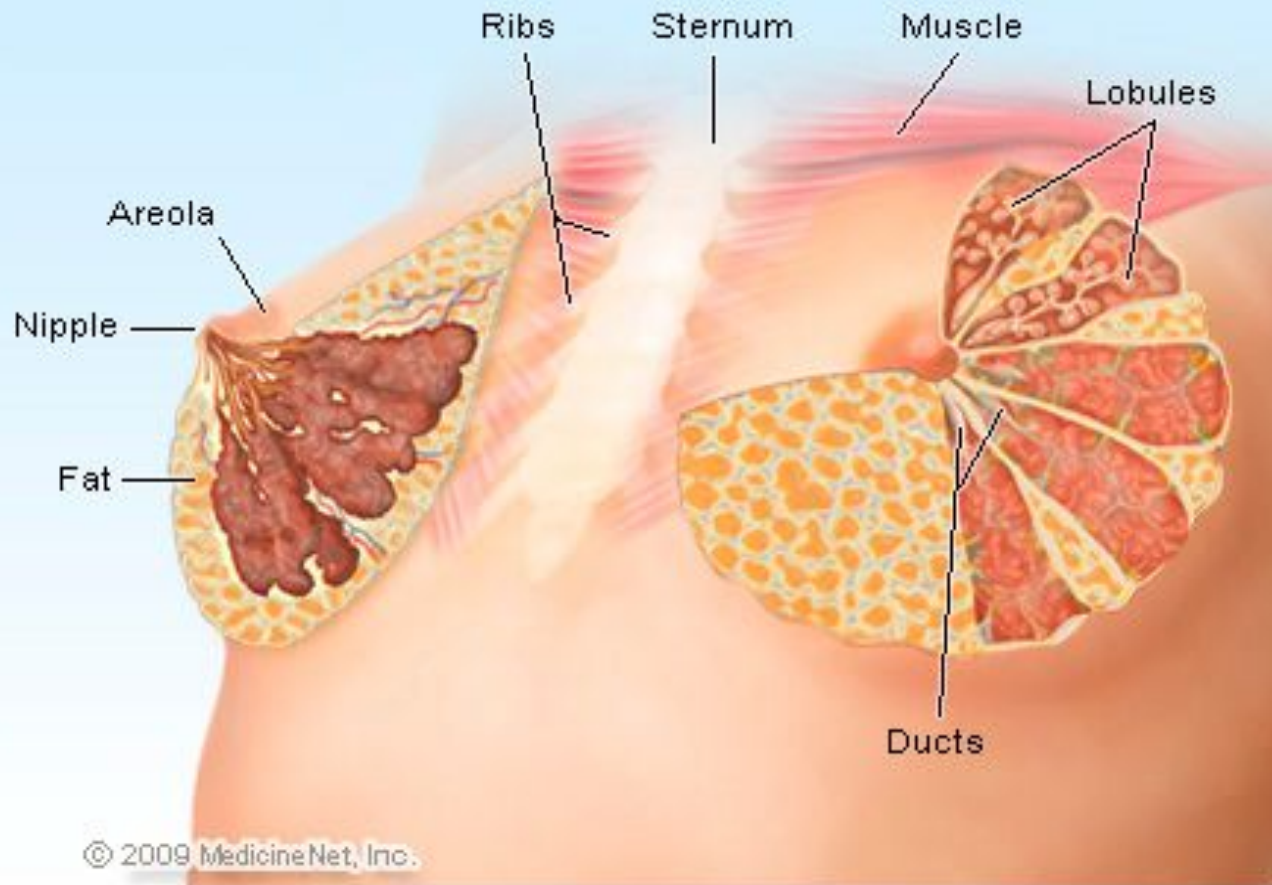
# Anatomy

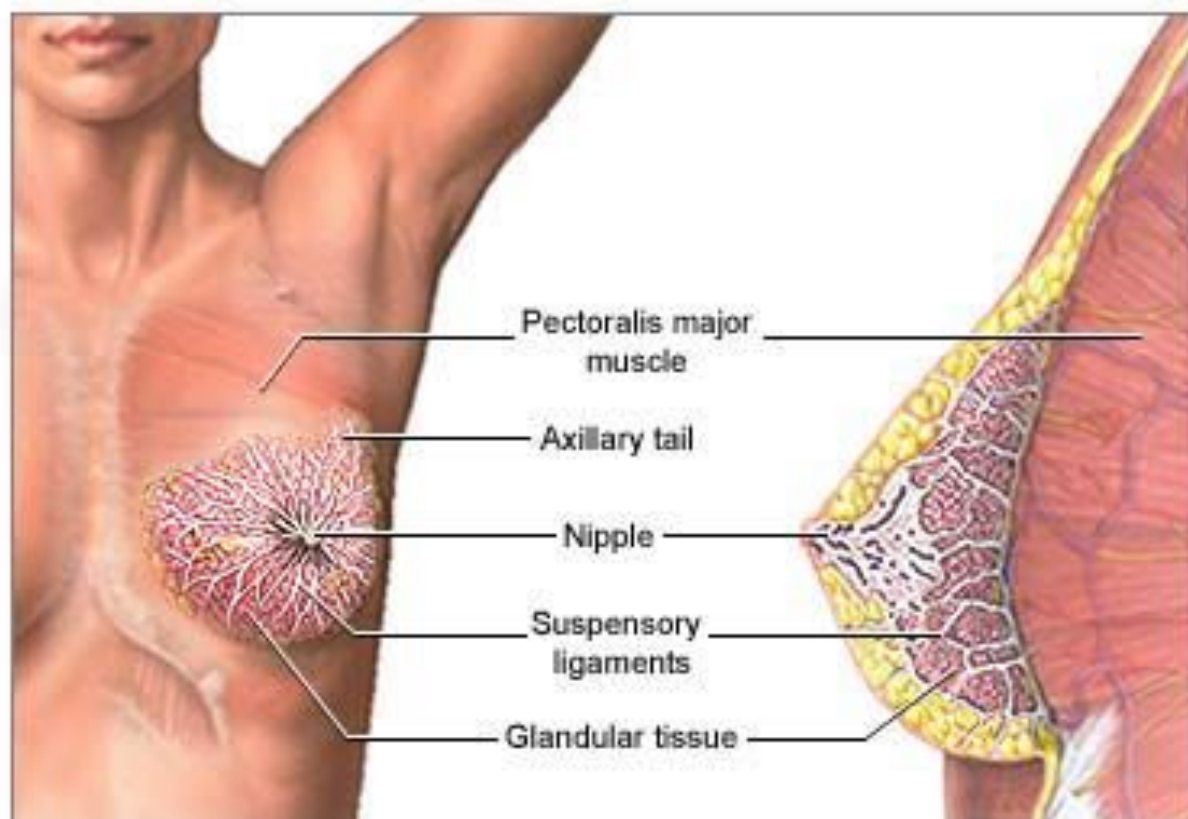
The Breast: cross-section scheme of the [mammary gland](#).

1. [Chest wall](#)
2. [Pectoralis muscles](#)
3. [Lobules](#)
4. [Nipple](#)
5. [Areola](#)
6. [Milk duct](#)
7. [Fatty tissue](#)
8. [Skin](#)



# Anatomy of the Breast





## COMPARATIVE AND SURGICAL ANATOMY

The protuberant part of the human breast is generally described as overlying the second to the sixth ribs and extending from the lateral border of the sternum to the anterior axillary line. Actually, a thin layer of mammary tissue extends considerably further, from the clavicle above to the seventh or eighth rib below and from the midline to the edge of the latissimus dorsi posteriorly. This fact is important when performing a mastectomy, the aim of which is to remove the whole breast.

The *axillary tail of the breast is of surgical importance*. In some normal subjects it is palpable and, in a few, it can be seen premenstrually or during lactation. A well-developed axillary tail is sometimes mistaken for a mass of enlarged lymph nodes or a lipoma.

The *lobule is the basic structural unit of the mammary gland*. The number and size of the lobules vary enormously: they are most numerous in young women. From 10 to over 100 lobules empty via ductules into a lactiferous duct, of which there are 15–20. Each lactiferous duct is lined with a spiral arrangement of contractile myoepithelial cells and is provided with a terminal ampulla, a reservoir for milk or abnormal discharges.

The internal mammary nodes are fewer in number. They lie along the internal mammary vessels deep to the plane of the costal cartilages, drain the posterior third of the breast and are .not routinely dissected although they were at one time biopsied for staging

The *ligaments of Cooper* are hollow conical projections of fibrous tissue filled with breast tissue; the apices of the cones are attached firmly to the superficial fascia and thereby to the skin overlying the breast. These ligaments account for the dimpling of the skin overlying a carcinoma.

The *areola* contains involuntary muscle arranged in concentric rings as well as radially in the subcutaneous tissue. The areolar epithelium contains numerous sweat glands and sebaceous glands, the latter of which enlarge during pregnancy and serve to lubricate the nipple during lactation (Montgomery's tubercles).

The *nipple* is covered by thick skin with corrugations. Near its apex lie the orifices of the lactiferous ducts. The nipple contains smooth muscle fibres arranged concentrically and longitudinally; thus, it is an erectile structure, which points outwards.

The *lymphatics of the breast* drain predominantly into the axillary and internal mammary lymph nodes. The axillary nodes receive approximately 85% of the drainage and are arranged in the following groups:

- *lateral, along the axillary vein;*
- *anterior, along the lateral thoracic vessels;*
- *posterior, along the subscapular vessels;*
- *central, embedded in fat in the centre of the axilla;*
- *interpectoral, a few nodes lying between the pectoralis major*

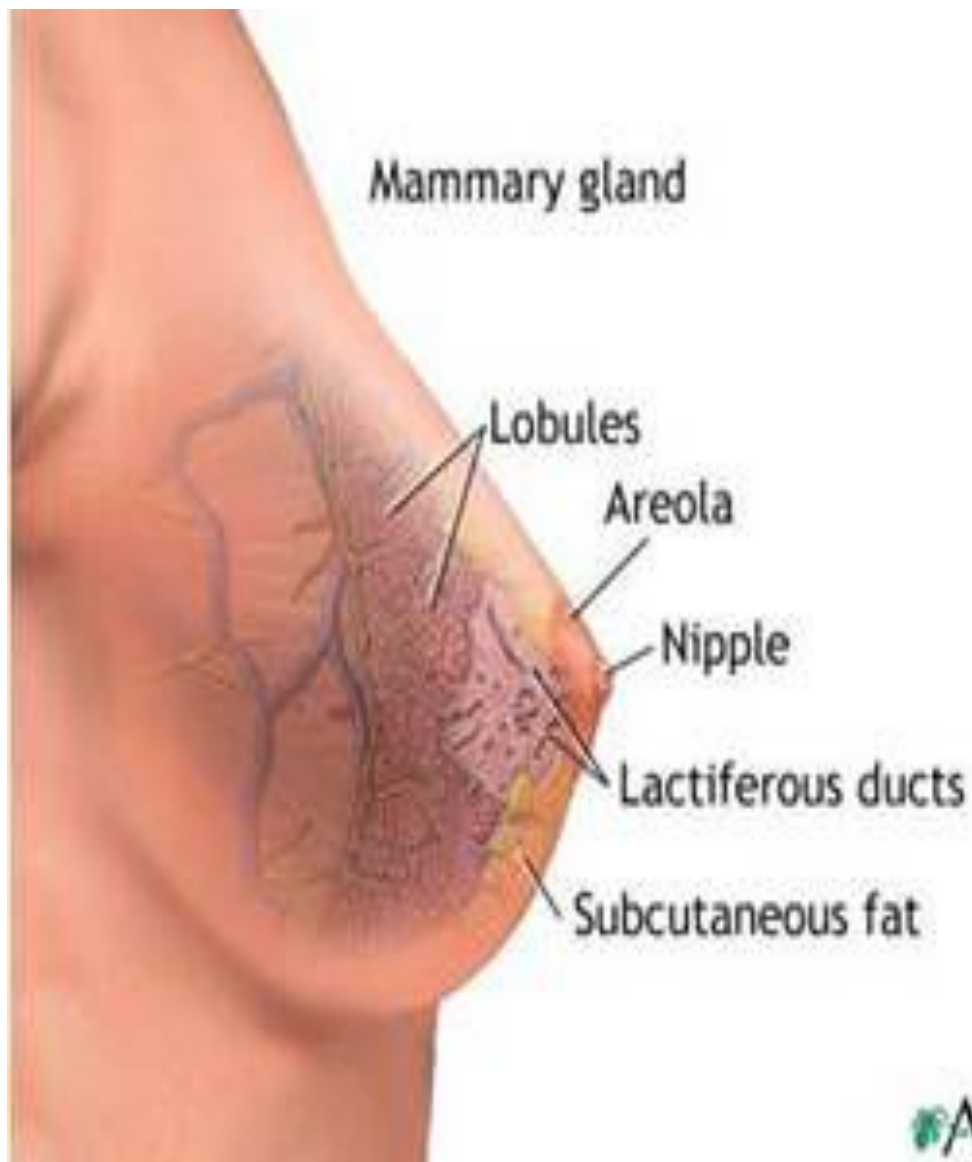
and minor muscles;

- *apical, which lie above the level of the pectoralis minor tendon*

in continuity with the lateral nodes and which receive the efferents of all the other groups.

The apical nodes are also in continuity with the supraclavicular nodes and drain into the subclavian lymph trunk, which enters the great veins directly or via the thoracic duct or jugular trunk.

.The *sentinel node* is defined as the first lymph node draining the tumour-bearing area of the breast



# INVESTIGATION OF BREAST SYMPTOMS

## Mammography

Soft tissue radiographs are taken by placing the breast in direct contact with ultrasensitive film and exposing it to low-voltage, high amperage X-rays . The dose of radiation is approximately 0.1 cGy and, therefore, mammography is a very safe investigation. The sensitivity of this investigation increases with age as the breast becomes less dense. In total, 5% of breast cancers are missed by population-based mammographic screening programmes; even in retrospect, such carcinomas are not apparent. Thus, a normal mammogram does not exclude the presence of carcinoma. Digital mammography is being introduced, which allows manipulation of the images and computer-aided diagnosis.

Tomo-mammography is also being assessed as a more sensitive diagnostic .modality



# Mammogram showing a carcinoma

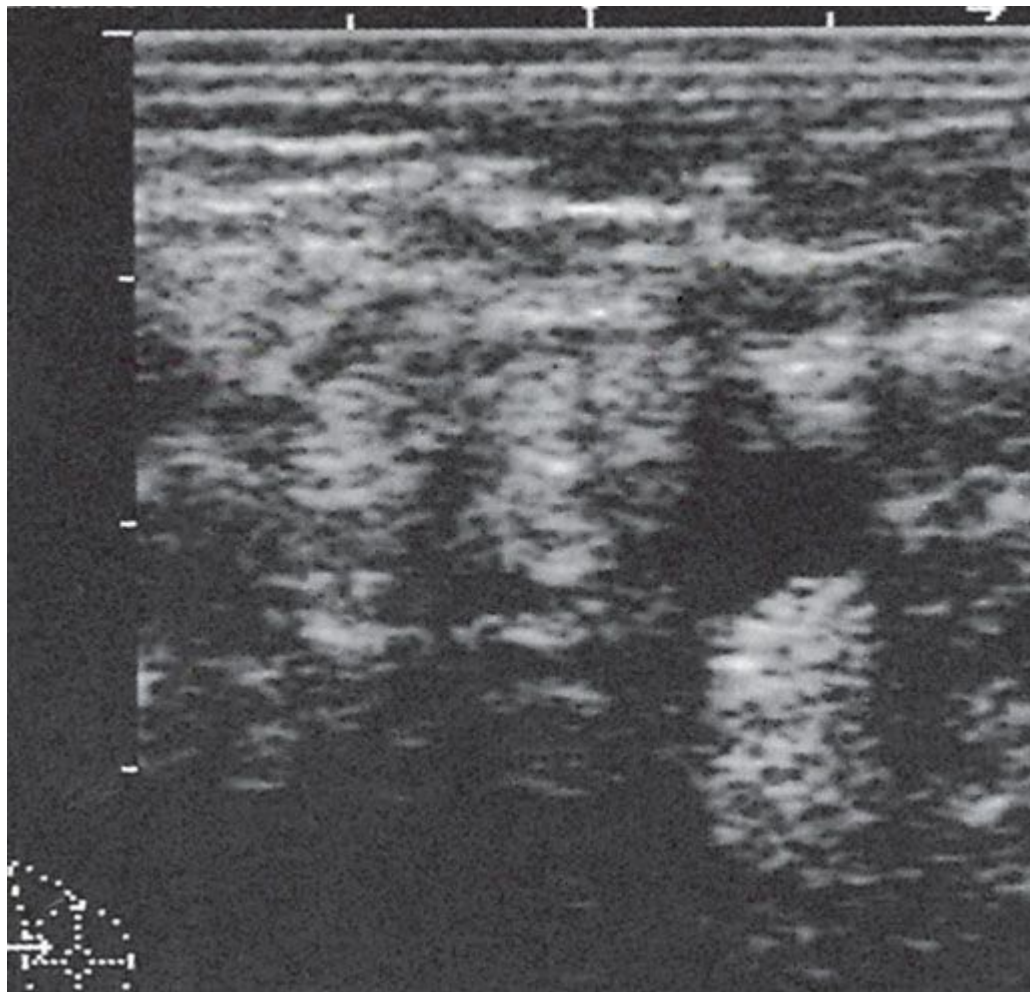


## Ultrasound

Ultrasound is particularly useful in young women with dense breasts in whom mammograms are difficult to interpret, and in distinguishing cysts from solid lesions. It can also be used to localise impalpable areas of breast pathology. It is not useful as a screening tool and remains operator dependent.

Increasingly, ultrasound of the axillary tissue is performed when a cancer is diagnosed and guided percutaneous biopsy of .any suspicious glands may be performed

Ultrasound of the breast showing a cyst



Ultrasound of the breast showing a carcinoma



## **Magnetic resonance imaging**

Magnetic resonance imaging (MRI) is of increasing interest to breast surgeons in a number of settings:

- It can be useful to distinguish scar from recurrence in women who have had previous breast conservation therapy for cancer (although it is not accurate within 9 months of radiotherapy because of abnormal enhancement).
- It is the best imaging modality for the breasts of women with implants
- It has proven to be useful as a screening tool in high-risk women (because of family history).
- It is less useful than ultrasound in the management of the axilla in both primary breast cancer and recurrent disease .

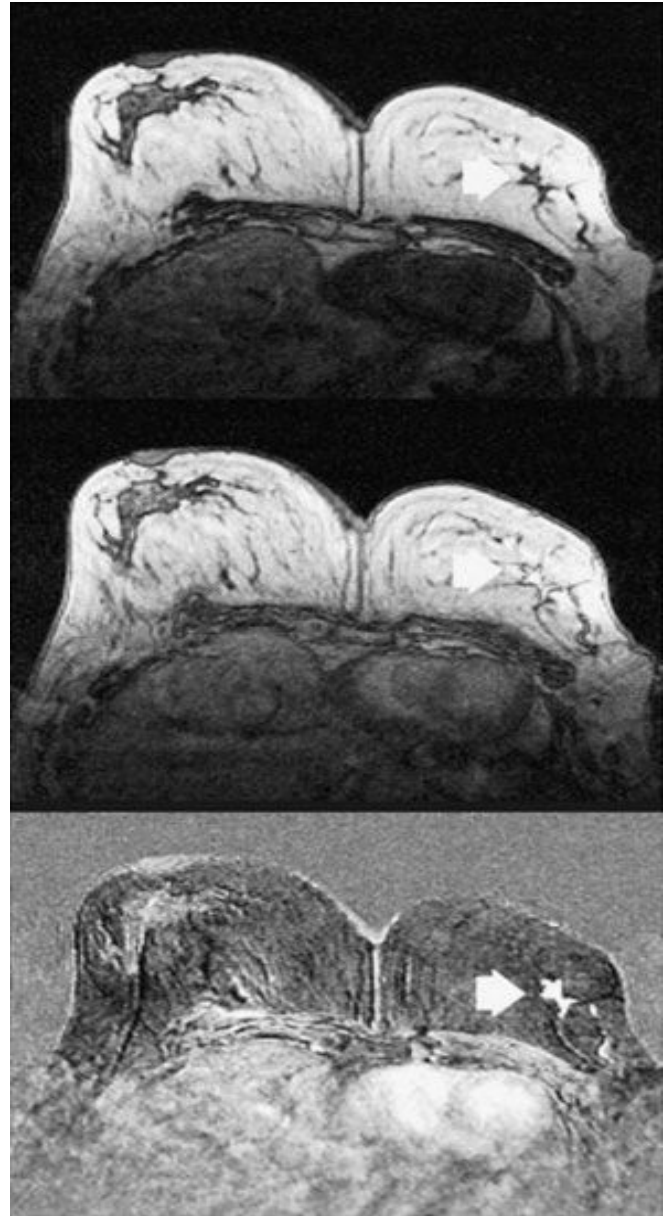
Although biopsies can be performed with MRI guidance this is complicated because of the configuration of the imaging system. With improved ultrasound equipment, an MRI-detected lesion can often be found on a .second-look ultrasound and biopsied using this modality

Magnetic resonance imaging scan of the breasts showing carcinoma of the left breast (arrows)

(a) Pre-contrast;

(b) postgadolinium contrast;

(c) subtraction image



## Needle biopsy/cytology

Histology can be obtained under local anaesthesia using a springloaded core needle biopsy device . Cytology is obtained using a 21G or 23G needle and 10-ml syringe with multiple passes through the lump with negative pressure in the syringe.

The aspirate is then smeared on to a slide, which is air dried or fixed .

Fine-needle aspiration cytology (FNAC) is the least invasive technique of obtaining a cell diagnosis and is rapid and very accurate if both operator and cytologist are experienced.

However, false negatives do occur, mainly through sampling error, and invasive cancer cannot be distinguished from *in situ disease*. A histological specimen taken by core biopsy allows a definitive preoperative diagnosis, differentiates between duct carcinoma *in situ (DCIS)* and *invasive disease* and also allows the tumour to be

stained for receptor status. This is important before commencing .neoadjuvant therapy

# Corecut biopsy of breast





## **Large-needle biopsy with vacuum systems**

The sampling error decreases as the biopsy volume increases and using 8G or 11G needles allows more extensive biopsies to be taken. This is useful in the management of microcalcifications or in the complete excision of benign lesions such as fibroadenomas.

## **Triple assessment**

In any patient who presents with a breast lump or other symptoms suspicious of carcinoma, the diagnosis should be made by a combination of clinical assessment, radiological imaging and a tissue sample taken for either cytological or histological analysis, the so called triple assessment. The positive predictive value (PPV) of this combination should exceed 99.9%

# THE NIPPLE

Absence of the nipple is rare and is usually associated with amazia (congenital absence of the breast). Supernumerary nipples not uncommonly occur along a line extending from the anterior fold of the axilla to the fold of the groin

## **Nipple retraction**

This may occur at puberty or later in life. Retraction occurring at puberty, also known as *simple nipple inversion*, is of unknown aetiology (benign horizontal inversion). In about 25% of cases it is bilateral. It may cause problems with breast-feeding and infection can occur, especially during lactation, because of retention of secretions. Recent retraction of the nipple may be of considerable pathological significance. A slit-like retraction of the nipple may be caused by duct ectasia and chronic periductal mastitis, but circumferential retraction, with or without an underlying lump, may well indicate an underlying carcinoma.

### ***Treatment***

Treatment is usually unnecessary and the condition may spontaneously resolve during pregnancy or lactation. Simple cosmetic surgery can produce an adequate correction but has the drawback of dividing the underlying ducts. Mechanical suction devices have been used to evert the nipple, with some effect.

## **Cracked nipple**

This may occur during lactation and be the forerunner of acute infective mastitis. If the nipple becomes cracked during lactation, it should be rested for 24–48 hours and the breast should be emptied with a breast pump. Feeding should be resumed as soon as possible

Recent nipple  
retraction.

(a) Slit-like retraction of  
duct ectasia with  
mammary duct fistula.



(b) Circumferential  
retraction with  
underlying carcinoma



## **Papilloma of the nipple**

Papilloma of the nipple has the same features as any cutaneous papilloma and should be excised with a tiny disc of skin. Alternatively, the base may be tied with a ligature and the papilloma will spontaneously fall off.

## **Retention cyst of a gland of Montgomery**

These glands, situated in the areola, secrete sebum and if they become blocked a sebaceous cyst forms.

## **Eczema**

Eczema of the nipples is a rare condition and is often bilateral; it is usually associated with eczema elsewhere on the body. It is treated with 0.5% hydrocortisone (not a stronger steroid preparation).

## **Paget's disease**

Paget's disease of the nipple must be distinguished from eczema. The former is caused by malignant cells in the subdermal layer. Eczema tends to occur in younger people who have signs of eczema elsewhere (look at the antecubital fossae).

## **Discharges from the nipple**

Discharge can occur from one or more lactiferous ducts. Management depends on the presence of a lump (which should always be given priority in diagnosis and treatment) and the presence of blood in the discharge or discharge from a single duct. Mammography is rarely useful except to exclude an underlying impalpable mass. Cytology may reveal malignant cells but a negative result does not exclude a carcinoma

## ***Treatment***

Treatment must firstly be to exclude a carcinoma by occult blood test and cytology. Simple reassurance may then be sufficient but, if the discharge is proving intolerable, an operation to remove the affected duct or ducts can be performed (microdochectomy).

## ***Microdochectomy***

It is important not to express the blood before the operation as it may then be difficult to identify the duct in theatre. A lacrimal probe or length of stiff nylon suture is inserted into the duct from which the discharge is emerging. A tennis racquet incision can be made to encompass the entire duct or a periareolar incision used and the nipple flap dissected to reach the duct. The duct is then excised. A papilloma is nearly always situated within 4–5 cm of the nipple orifice.

Ductoscopy (inspection of the internal structure of the duct system) using microendoscopes is technically feasible but generally disappointing. The affected duct may not be visualised and biopsy systems are currently rudimentary.

## ***Cone excision of the major ducts (after Hadfield)***

When the duct of origin of nipple bleeding is uncertain or when there is bleeding or discharge from multiple ducts, the entire major duct system can be excised for histological examination without sacrifice of the breast form. A periareolar incision is made and a cone of tissue is removed with its apex just deep to the surface of the nipple and its base on the pectoral fascia. The resulting defect may be obliterated by a series of purse-string sutures although a temporary suction drain will reduce the chance of long-term deformity. It is vital to warn the patient that she will be unable to breast-feed after this and may experience altered nipple sensation

*A clear, serous discharge may be 'physiological' in a* •  
*parous* woman or may be associated with a duct papilloma or mammary dysplasia. Multiduct, multicoloured discharge is physiological and the patient may be reassured.

- *A blood-stained discharge may be caused by duct ectasia, a duct papilloma or carcinoma. A duct papilloma is usually single and situated in one of the larger lactiferous ducts; it is sometimes associated with a cystic swelling beneath the areola.*

- *A black or green discharge is usually the result of duct ectasia and its complications*

# **BENIGN BREAST DISEASE**

This is the most common cause of breast problems; up to 30% of women will suffer from a benign breast disorder requiring treatment at some time in their lives. The most common symptoms are pain, lumpiness or a lump. The aim of treatment is to exclude cancer and, once this has been done, to treat any remaining symptoms.

## **Congenital abnormalities**

### ***Amazia***

Congenital absence of the breast may occur on one or both sides. It is sometimes associated with absence of the sternal portion of the pectoralis major (Poland's syndrome). It is more common in males.

### ***Polymazia***

Accessory breasts have been recorded in the axilla (the most frequent site), groin, buttock and thigh. They have been known to function during lactation.

### ***Mastitis of infants***

Mastitis of infants is at least as common in boys as in girls. On the third or fourth day of life, if the breast of an infant is pressed

lightly, a drop of colourless fluid can be expressed; a few days later there is often a slight milky secretion, which disappears during the third week. This is popularly known as 'witch's milk' and is seen only in full-term infants. It is caused by stimulation of the fetal breast by prolactin in response to the drop in maternal oestrogens and is essentially physiological. True mastitis is uncommon and is predominately caused by *Staphylococcus aureus*.

### ***Diffuse hypertrophy***

Diffuse hypertrophy of the breasts occurs sporadically in otherwise healthy girls at puberty (benign virginal hypertrophy) and, much less often, during the first pregnancy. The breasts attain enormous dimensions and may reach the knees when the patient is sitting. The condition is rarely unilateral. This tremendous overgrowth is apparently caused by an alteration in the normal sensitivity of the breast to oestrogenic hormones and some success in treating it with anti-oestrogens has been reported. Treatment is otherwise by reduction mammoplasty



# Injuries of the breast

## *Haematoma*

Haematoma, particularly a resolving haematoma, gives rise to a lump, which, in the absence of overlying bruising, is difficult to diagnose correctly unless it is biopsied.

## *Traumatic fat necrosis*

Traumatic fat necrosis may be acute or chronic and usually occurs in stout, middle-aged women. Following a blow, or even indirect violence (e.g. contraction of the pectoralis major), a lump, often painless, appears. This may mimic a carcinoma, even displaying skin tethering and nipple retraction, and biopsy is required for diagnosis. A history of trauma is not diagnostic as this may merely have drawn the patient's attention to a pre-existing lump. A seatbelt may transect the breast with a sudden deceleration injury, as in a road traffic accident

# Acute and subacute inflammations of the breast

## ***Bacterial mastitis***

Bacterial mastitis is the most common variety of mastitis and is associated with lactation in the majority of cases.

### **Aetiology**

Lactational mastitis is seen far less frequently than in former years. Most cases are caused by *Staphylococcus aureus* and, if hospital acquired, are likely to be penicillin resistant. The intermediary is usually the infant; after the second day of life, 50% of infants harbour staphylococci in the nasopharynx. Although ascending infection from a sore and cracked nipple may initiate the mastitis, in many cases the lactiferous ducts will first become blocked by epithelial debris leading to stasis; this theory is supported by the relatively high incidence of mastitis in women with a retracted nipple. Once within the ampulla of the duct, staphylococci cause clotting of milk and, within this clot, organisms multiply.

### **Clinical features**

The affected breast, or more usually a segment of it, presents the classical signs of acute inflammation. Early on this is a generalised cellulitis but later an abscess will form

## **Treatment**

During the cellulitic stage the patient should be treated with an appropriate antibiotic, for example flucloxacillin or co-amoxiclav. Feeding from the affected side may continue if the patient can manage. Support of the breast, local heat and analgesia will help to relieve pain. If an antibiotic is used in the presence of undrained pus, an 'antibioma' may form. This is a large, sterile, brawny oedematous swelling that takes many weeks to resolve. It used to be recommended that the breast should be incised and drained if the infection did not resolve within 48 hours or if after being emptied of milk there was an area of tense induration or other evidence of an underlying abscess. This advice has been replaced with the recommendation that repeated aspirations under antibiotic cover (if necessary using ultrasound) be performed. This often allows resolution without the need for an incision scar and will also allow the patient to carry on breast-feeding. The presence of pus can be confirmed with needle aspiration and the pus sent for bacteriological culture . In contrast to the majority of localised infections, fluctuation is a late sign. Usually, the area of induration is sector shaped and, in early cases, about one-quarter of the breast is involved; in many late cases the area is more extensive . When in doubt an ultrasound scan may .clearly define an area suitable for drainage

## ***Operative drainage of a breast abscess***

This is less commonly needed as prompt commencement of antibiotics and repeated aspiration is usually successful. Incision of a lactational abscess is necessary if there is marked skin thinning and can usually be performed under local anaesthesia if an analgesic cream such as EMLA (lidocaine) is applied 30 min before surgery.

The usual incision is sited in a radial direction over the affected segment, although if a circumareolar incision will allow adequate access to the affected area this is preferred because it gives a better cosmetic result. The incision passes through the skin and the superficial fascia. A long artery forceps is then inserted into the abscess cavity. Every part of the abscess is palpated against the point of the artery forceps and its jaws are opened. All loculi that can be felt are entered. Finally, the artery forceps having been withdrawn, a finger is introduced and any remaining septa are disrupted. The wound may then be lightly packed with ribbon gauze or a drain inserted .to allow dependent drainage

# Large breast abscess



## ***Chronic intramammary abscess***

A chronic intramammary abscess, which may follow inadequate drainage or injudicious antibiotic treatment, is often a very difficult condition to diagnose. When encapsulated within a thick wall of fibrous tissue the condition cannot be distinguished from a carcinoma without the histological evidence from a biopsy.

## ***Tuberculosis of the breast***

Tuberculosis of the breast, which is comparatively rare, is usually associated with active pulmonary tuberculosis or tuberculous cervical adenitis.

Tuberculosis of the breast occurs more often in parous women and usually presents with multiple chronic abscesses and sinuses and a typical bluish, attenuated appearance of the surrounding skin. The diagnosis rests on bacteriological and histological examination. Treatment is with anti-tuberculous chemotherapy. Healing is usual, although often delayed, and mastectomy should be restricted to patients with persistent residual infection.

## ***Actinomycosis***

Actinomycosis of the breast is rarer still. The lesions present the essential characteristics of faciocervical actinomycosis

## ***Mondor's disease***

Mondor's disease is thrombophlebitis of the superficial veins of the breast and anterior chest wall , although it has also been encountered in the arm.

In the absence of injury or infection, the cause of thrombophlebitis (like that of spontaneous thrombophlebitis in other sites) is obscure. The pathognomonic feature is a thrombosed subcutaneous cord, usually attached to the skin. When the skin over the breast is stretched by raising the arm, a narrow, shallow subcutaneous groove alongside the cord becomes apparent. The differential diagnosis is lymphatic permeation from an occult carcinoma of the breast. The only treatment required is restricted arm movements and, in any case, the condition subsides within a few months without recurrence, complications or deformity.

There are case reports of Mondor's disease being associated with subsequent development of malignancy although this has been .unsubstantiated by others and is thought to be coincidental

Mondor's disease under the right  
.breast (arrow)





## ***Duct ectasia/periductal mastitis***

### *Pathology*

This is a dilatation of the breast ducts, which is often associated with periductal inflammation. The pathogenesis is obscure and almost certainly not uniform in all cases, although the disease is much more common in smokers. The classical description of the pathogenesis of duct ectasia asserts that the first stage in the disorder is a dilatation in one or more of the larger lactiferous ducts, which fill with a stagnant brown or green secretion. This may discharge. These fluids then set up an irritant reaction in surrounding tissue leading to periductal mastitis or even abscess and fistula formation . In some cases, a chronic indurated mass forms beneath the areola, which mimics a carcinoma. Fibrosis eventually develops, which may cause slit-like nipple retraction. An alternative theory suggests that periductal inflammation is the primary condition and, indeed, anaerobic bacterial infection is found in some cases. A marked association between recurrent periductal inflammation and smoking has been demonstrated. This was thought by some to indicate that arteriopathy is a contributing factor in its aetiology although others believe that smoking increases the virulence of the commensal bacteria. It is certainly .clear that cessation of smoking increases the chance of a long-term cure

## ***Clinical features***

Nipple discharge (of any colour), a subareolar mass, abscess, mammary duct fistula and/or nipple retraction are the most common symptoms.

## ***Treatment***

In the case of a mass or nipple retraction, a carcinoma must be excluded by obtaining a mammogram and negative cytology or histology. If any suspicion remains the mass should be excised. Antibiotic therapy may be tried, the most appropriate agents being co-amoxiclav or flucloxacillin and metronidazole.

However, surgery is often the only option likely to bring about cure of this notoriously difficult condition; this consists of excision of all of the major ducts (Hadfield's operation). It is particularly important to shave the back of the nipple to ensure that all terminal ducts are removed. Failure to do so will lead to .recurrence

# **involution Aberrations of normal development and**

## ***Aetiology***

The breast is a dynamic structure that undergoes changes throughout a woman's reproductive life and, superimposed upon this, cyclical changes throughout the menstrual cycle . The pathogenesis of ANDI involves disturbances in the breast physiology extending from a perturbation of normality to well-defined disease processes. There is often little correlation between the histological appearance of the breast tissue and the symptoms.

## ***Pathology***

The disease consists essentially of four features that may vary in extent and degree in any one breast.

- *Cyst formation. Cysts are almost inevitable and very variable in size.*
- *Fibrosis. Fat and elastic tissues disappear and are replaced with dense white fibrous trabeculae. The interstitial tissue is infiltrated with chronic inflammatory cells.*
- *Hyperplasia of epithelium in the lining of the ducts and acini may occur, with or without atypia.*
- *Papillomatosis. The epithelial hyperplasia may be so extensive .that it results in papillomatous overgrowth within the ducts*

## ***Clinical features***

The symptoms of ANDI are many as the term is used to encompass a wide range of benign conditions, but often include an area of lumpiness (seldom discrete) and/or breast pain (mastalgia).

- A benign discrete lump in the breast is commonly a cyst or fibroadenoma. True lipomas occur rarely.
  - Lumpiness may be bilateral, commonly in the upper outer quadrant or, less commonly, confined to one quadrant of one breast. The changes may be cyclical, with an increase in both lumpiness and often tenderness before a menstrual period.
  - Non-cyclical mastalgia is more common in peri-menopausal than post-menopausal women. It may be associated with ANDI or with periductal mastitis. It should be distinguished from referred pain, for example a musculoskeletal disorder.
- ‘Breast’ pain in post-menopausal women not taking hormone replacement therapy (HRT) is usually derived from the chest wall

## ***Treatment of lumpy breasts***

If the clinician is confident that he or she is not dealing with a discrete abnormality (and clinical confidence is supported by mammography and/or ultrasound scanning if appropriate), then initially the woman can be offered firm reassurance. It is perhaps worthwhile reviewing the patient at a different point in the menstrual cycle, for example 6 weeks after the initial visit, and often the clinical signs will have resolved by that time. There is a tendency for women with lumpy breasts to be rendered unnecessarily anxious and to be submitted to multiple random biopsies because the clinician lacks the courage of his or her convictions

## **Treatment of breast pain**

*Exclude cancer*

*Reassure*

Use pain chart if unsure if cyclical or non-cyclical. Also allows time for reassurance to become active!

*Adequate support*

Firm bra during the day and a softer bra at night

*Exclude caffeine*

Works for some although not very efficacious in author's practice

*Consider medication*

Evening primrose oil (GLA) Better effect in women over 40 years old than in younger women

Danazol, 100 mg t.d.s. Start at 100 mg per day and increase (seldom used these days)

Tamoxifen Not licensed for this indication but occasionally very helpful

## **Breast cysts**

These occur most commonly in the last decade of reproductive life as a result of a non-integrated involution of stroma and epithelium. They are often multiple, may be bilateral and can mimic malignancy. Diagnosis can be confirmed by aspiration and/or ultrasound. They typically present suddenly and cause great alarm; prompt diagnosis and drainage provides immediate relief.

### ***Treatment***

A solitary cyst or small collection of cysts can be aspirated. If they resolve completely, and if the fluid is not blood-stained, no further treatment is required. However, 30% will recur and require reaspiration. Cytological examination of cyst fluid is no longer practised routinely. If there is a residual lump or if the fluid is blood-stained, a core biopsy or local excision for histological diagnosis is advisable, which is also the case if the cyst reforms repeatedly. This will exclude .cystadenocarcinoma, which is more common in elderly women

## **Fibroadenoma**

These usually arise in the fully developed breast between the ages of 15 and 25 years, although occasionally they occur in much older women. They arise from hyperplasia of a single lobule and usually grow up to 2–3 cm in size. They are surrounded by a wellmarked capsule and can thus be enucleated through a cosmetically appropriate incision. A fibroadenoma does not require excision unless associated with suspicious cytology, it becomes very large or the patient expressly desires the lump to be removed.

Giant fibroadenomas occasionally occur during puberty. They are over 5 cm in diameter and are often rapidly growing but, in other respects, are similar to smaller fibroadenomas and can be enucleated through a submammary incision. They are more common in the Afro-Caribbean population



## **Phyllodes tumour**

These benign tumours, previously sometimes known as serocystic disease of Brodie or cystosarcoma phyllodes, usually occur in women over the age of 40 years but can appear in younger women. They present as a large, sometimes massive, tumour with an unevenly bosselated surface.

Occasionally, ulceration of overlying skin occurs because of pressure necrosis. Despite their size they remain mobile on the chest wall. Histologically, there is a wide variation in their appearance, with some of low malignant potential resembling a fibroadenoma and others having a higher mitotic index, which are histologically worrying. The latter may recur locally but, despite the name of cystosarcoma phyllodes, they are rarely cystic and only very rarely develop features of a sarcomatous tumour. These may metastasise via the bloodstream.

### ***Treatment***

Treatment for the benign type is enucleation in young women or wide local excision. Massive tumours, recurrent tumours and those of the malignant type will require mastectomy

# CARCINOMA OF THE BREAST

Breast cancer is the most common cause of death in middle-aged women in western countries. In 2004 approximately one and a half million new cases were diagnosed worldwide. In England and Wales, 1 in 12 women will develop the disease during their lifetime.

## **Aetiological factors**

### ***Geographical***

Carcinoma of the breast occurs commonly in the western world, accounting for 3–5% of all deaths in women. In developing countries it accounts for 1–3% of deaths.

### ***Age***

Carcinoma of the breast is extremely rare below the age of 20 years but, thereafter, the incidence steadily rises so that by the age of 90 years nearly 20% of women are affected.

### ***Gender***

Less than 0.5% of patients with breast cancer are male.

### ***Genetic***

It occurs more commonly in women with a family history of breast cancer than in the general population. Breast cancer

related to a specific mutation accounts for about 5% of breast cancers yet has far-reaching repercussions in terms of counselling and tumour prevention in these women.

### ***Diet***

Because breast cancer so commonly affects women in the 'developed' world, dietary factors may play a part in its causation. There is some evidence that there is a link with diets low in phytoestrogens. A high intake of alcohol is associated with an increased risk of developing breast cancer.

### ***Endocrine***

Breast cancer is more common in nulliparous women and breastfeeding in particular appears to be protective. Also protective is having a first child at an early age, especially if associated with late menarche and early menopause. It is known that in postmenopausal women, breast cancer is more common in the obese.

This is thought to be because of an increased conversion of steroid hormones to oestradiol in the body fat. Recent studies have clarified the role of exogenous hormones, in particular the oral contraceptive pill and HRT, in the development of breast cancer. For most women the benefits of these treatments will far outweigh the small putative risk; however, long-term exposure to the combined preparation of HRT does significantly increase the risk of developing breast cancer

## ***Previous radiation***

This was considered to be of historical interest, with the majority of women exposed to the atomic bombs at Hiroshima and Nagasaki having died. It is, however, a real problem in women who have been treated with mantle radiotherapy as part of the management of Hodgkin's disease, in which significant doses of radiation to the breast are received. The risk appears about a decade after treatment and is higher if radiotherapy occurred during breast development. A surveillance programme has been organised in the UK with MRI and mammographic screening.

## **Pathology**

Breast cancer may arise from the epithelium of the duct system anywhere from the nipple end of the major lactiferous ducts to the terminal duct unit, which is in the breast lobule. The disease may be entirely *in situ*, an *increasingly common finding* with the advent of breast cancer screening, or may be invasive cancer. The degree of differentiation of the tumour is usually described using three grades: well differentiated, moderately differentiated or poorly differentiated. Commonly, a numerical grading system based on the scoring of three individual factors (nuclear pleomorphism, tubule formation and mitotic rate) is used, with grade III cancers roughly equating to the poorly differentiated group

## TYPES OF BREAST CANCER

### **Ductal carcinoma in situ:**

The most common type of noninvasive breast cancer is ductal carcinoma in situ (DCIS). This type of cancer has not spread and therefore usually has a very high cure rate.

### **Invasive ductal carcinoma:**

This cancer starts in a duct of the breast and grows into the surrounding tissue. It is the most common form of breast cancer. About 80% of invasive breast cancers are invasive ductal carcinoma.

### **Invasive lobular carcinoma:**

This breast cancer starts in the glands of the breast that produce milk.

Approximately 10% of invasive breast cancers are invasive lobular carcinoma.

The remaining breast cancers types are much less common and include the following:

**Mucinous carcinomas** are formed from mucus-producing cancer cells.

**Mixed tumors** contain a variety of cell types.

### **Medullary carcinoma**

is an infiltrating breast cancer that presents with well-defined boundaries between the cancerous and noncancerous tissue.

### **Inflammatory carcinoma:**

This cancer makes the skin of the breast appear red and feel warm (giving it the appearance of an infection). These changes are due to the blockage of lymph vessels .by cancer cells

### **Triple-negative breast cancers:**

This is a subtype of invasive cancer with cells that lack estrogen and progesterone receptors and have no excess of a specific protein (HER2) on their surface. It tends to appear more often in younger women and African-American women.

### **Paget's disease of the nipple**

This cancer starts in the ducts of the breast and spreads to the nipple and the area surrounding the nipple. It usually presents with crusting and redness around the nipple.

### **Adenoid cystic carcinoma:**

These cancers have both glandular and cystic features. They tend not to spread aggressively and have a good prognosis.

The following are other uncommon types of breast cancer:

*Papillary carcinoma*

*Phyllodes tumor*

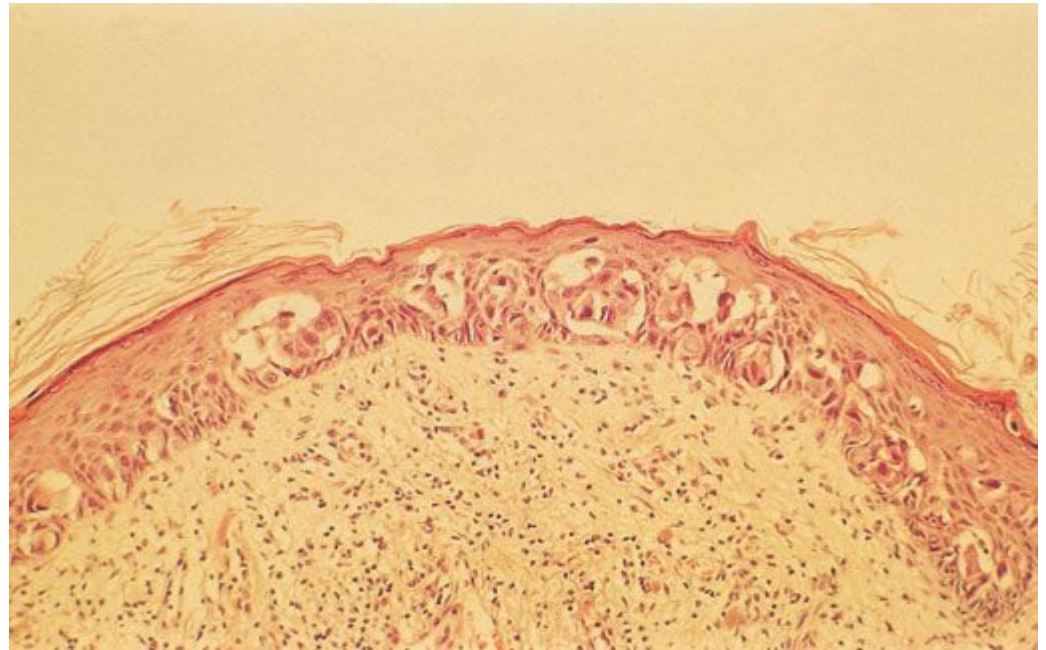
*Angiosarcoma*

*Tubular carcinoma*

Paget's disease of (a)  
the nipple.



(b) Histological  
appearance of Paget's  
.disease



# The spread of breast cancer

## ***Local spread***

The tumour increases in size and invades other portions of the breast. It tends to involve the skin and to penetrate the pectoral muscles and even the chest wall if diagnosed late.

## ***Lymphatic metastasis***

Lymphatic metastasis occurs primarily to the axillary and the internal mammary lymph nodes. Tumours in the posterior onethird of the breast are more likely to drain to the internal mammary nodes. The involvement of lymph nodes has both biological and chronological significance. It represents not only an evolutionary event in the spread of the carcinoma but is also a marker for the metastatic potential of that tumour. Involvement of supraclavicular nodes and of any contralateral lymph nodes represents advanced disease.

## ***Spread by the bloodstream***

It is by this route that skeletal metastases occur, although the initial spread may be via the lymphatic system. In order of frequency the lumbar vertebrae, femur, thoracic vertebrae, rib and skull are affected and these deposits are generally osteolytic. Metastases may also commonly occur in the liver, lungs and brain and, occasionally, the adrenal glands and ovaries; they have, in fact, been described in most body sites



## Clinical presentation

Although any portion of the breast, including the axillary tail, may be involved, breast cancer is found most frequently in the upper outer quadrant. Most breast cancers will present as a hard lump, which may be associated with indrawing of the nipple. As the disease advances locally there may be skin involvement with peau d'orange or frank ulceration and fixation to the chest wall. This is described as cancer-en-cuirasse when the disease progresses around the chest wall. About 5% of breast cancers in the UK will present with either locally advanced disease or symptoms of metastatic disease. This figure is much higher in the developing world. These patients must then undergo a staging evaluation so that the full extent of their disease can be ascertained. This will

include a careful clinical examination, chest radiograph, computerised tomography (CT) of the chest and abdomen and an isotope bone scan. This is important for both prognosis and treatment; a patient with widespread visceral metastases may obtain an increased length and quality of survival from systemic hormone therapy or chemotherapy but is unlikely to benefit from surgery as she will die from her metastases before local disease becomes a problem. In contrast, patients with relatively small tumours (< 5 cm in diameter) confined to the breast and ipsilateral lymph nodes rarely need staging beyond a good clinical examination as the pick-up rate for distant metastases is so low.

Currently, a chest radiograph, full blood count and liver function tests are all that are recommended for screening of patients with early-stage breast cancer



Ulcerated carcinoma of the right breast



Peau d'orange of the breast

## **Staging of breast cancer**

Classical staging of breast cancer by means of the TNM (tumour–node–metastasis) or UICC (Union Internationale Contre le Cancer) criteria is used less often as we gain more knowledge of the biological variables that affect prognosis. It is becoming increasingly clear that it is these factors rather than anatomical mapping that influence outcome and treatment. Perhaps a more pragmatic approach would be to classify patients according to .the treatment that they require

## Combination of Manchester and TNM classification

Tis	Tis N0 M0
I	T1 N0 M0
II	T2 N1 M0
IIIa	T3 N2 M0
IIIb	T4 N3 M0
IV	M1

## **Treatment of cancer of the breast**

The two basic principles of treatment are to reduce the chance of local recurrence and the risk of metastatic spread. Treatment of early breast cancer will usually involve surgery with or without

radiotherapy. Systemic therapy such as chemotherapy or hormone therapy is added if there are adverse prognostic factors such as lymph node involvement, indicating a high likelihood of metastatic relapse. At the other end of the spectrum, locally advanced or metastatic disease is usually treated by systemic therapy to palliate symptoms, with surgery playing a much smaller role

### **Algorithm for management of operable breast cancer**

#### ***Achieve local control***

##### ***Appropriate surgery***

- **Wide local excision (clear margins) and radiotherapy, or**
- **Mastectomy ± radiotherapy (offer reconstruction – immediate or delayed)**
- **Combined with axillary procedure (see text)**
- **Await pathology and receptor measurements**
- **Use risk assessment tool; stage if appropriate**

##### ***Treat risk of systemic disease***

- **Offer chemotherapy if prognostic factors poor; include Herceptin if Her-2 positive**
- **Radiotherapy as decided above**
- **Hormone therapy if oestrogen receptor or progesterone receptor positive**

## ***The multidisciplinary team approach***

As in all branches of medicine, good doctor–patient communication plays a vital role in helping to alleviate patient anxiety. Participation of the patient in treatment decisions is of particular importance in breast cancer when there may be uncertainty as to the best therapeutic option and the desire to treat the patient within the protocol of a controlled clinical trial. As part of the preoperative and postoperative management of the patient it is often useful to employ the skills of a trained breast counsellor and also to have available advice on breast prostheses, psychological support and physiotherapy, when appropriate.

In many specialist centres the care of breast cancer patients is undertaken as a joint venture between the surgeon, medical oncologist, radiotherapist and allied health professionals such as .the clinical nurse specialist

## ***Local treatment of early breast cancer***

Local control is achieved through surgery and/or radiotherapy.

### **Surgery**

Surgery still has a central role to play in the management of breast cancer but there has been a gradual shift towards more conservative techniques, backed up by clinical trials that have shown equal efficacy between mastectomy and local excision followed by radiotherapy.

It was initially hoped that avoiding mastectomy would help to alleviate the considerable psychological morbidity associated with breast cancer but recent studies have shown that over 30% of women develop significant anxiety and depression following both radical and conservative surgery. After mastectomy women tend

to worry about the effect of the operation on their appearance and relationships, whereas after conservative surgery they may remain fearful of a recurrence.

*Mastectomy is indicated for large tumours (in relation to the size of the breast), central tumours beneath or involving the nipple, multifocal disease, local recurrence or patient preference.* The radical Halsted mastectomy, which included excision of the breast, axillary lymph nodes and pectoralis major and minor muscles, is no longer indicated as it causes excessive morbidity with no survival benefit. The modified radical (Patey) mastectomy is more commonly performed and is thus described below.

Simple mastectomy involves removal of only the breast with no dissection of the axilla, except for the region of the axillary tail of the breast, which usually has attached to it a few nodes low in the .anterior group



## ***Patey mastectomy***

***The breast and associated structures are dissected en bloc and the excised mass is composed of:***

- the whole breast;
- a large portion of skin, the centre of which overlies the tumour but which always includes the nipple;
- all of the fat, fascia and lymph nodes of the axilla.

The pectoralis minor muscle is either divided or retracted to gain access to the upper two-thirds of the axilla. The axillary vein and nerves to the serratus anterior and latissimus dorsi (the thoraco-dorsal trunk) should be preserved. The intercostal brachial nerves are usually divided in this operation and the

## ***Sentinel node biopsy***

This technique is currently becoming the standard of care in the management of the axilla in patients with clinically node-negative disease. The sentinel node is localised peroperatively by the injection of patent blue dye and radioisotope-labelled albumin in the breast. The recommended site of injection is in the subdermal plexus around the nipple although some still inject on the axillary side of the cancer. The marker passes to the primary node draining the area and is detected visually and with a hand-held gamma camera. The excised node can be sent for frozen-section histological analysis or touch imprint there are only subcapsular micrometastases that are missed at frozen section. In patients in whom there is no tumour involvement of the sentinel node, further axillary dissection can be avoided. A nomogram outlining the chances of further axillary node positivity has been developed by the group at Memorial Sloan Kettering Hospital, New York, and is available on their website .cytology (TIC) if preoperative diagnosis is sought

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patient should be warned about sensation changes postoperatively. The wound is drained using a wide-bore suction tube. Early mobilisation of the arm is encouraged and physiotherapy helps normal function to return very quickly; most patients are able to resume light work or housework within a few weeks.

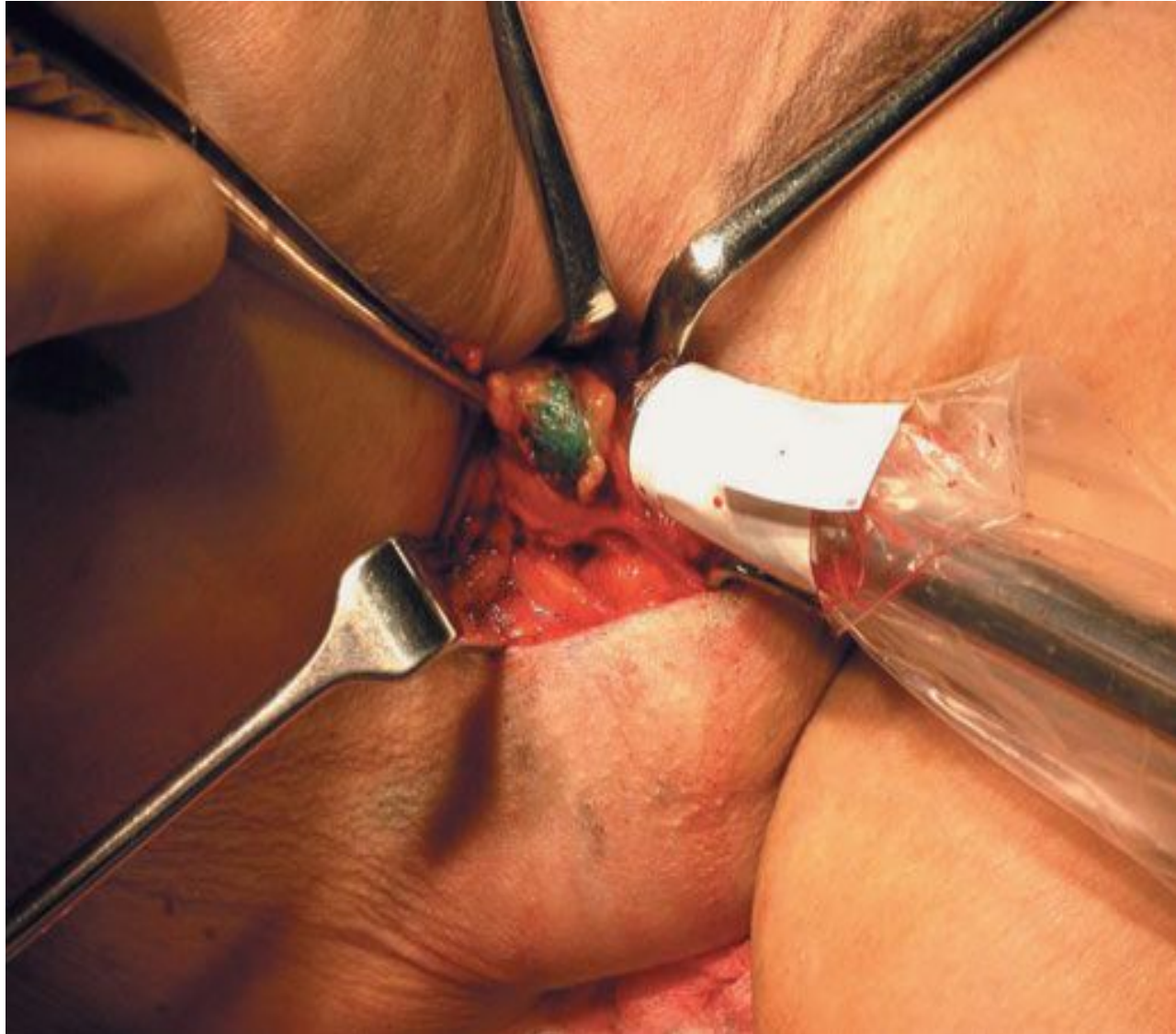
***Conservative breast cancer surgery*** ***This is aimed at removing the*** tumour plus a rim of at least 1 cm of normal breast tissue. This is commonly referred to as a wide local excision. The term lumpectomy should be reserved for an operation in which a benign tumour is excised and in which a large amount of normal breast tissue is not resected. A quadrantectomy involves removing the entire segment of the breast that contains the tumour. Both of these operations are usually combined with axillary surgery, usually via a separate incision in the axilla. There are various options that can be used to deal with the axilla, including sentinel node biopsy, sampling, removal of the nodes behind and lateral to the pectoralis minor (level II) or a full axillary dissection (level .III)

There is a somewhat higher rate of local recurrence following conservative surgery, even if combined with radiotherapy, but the long-term outlook in terms of survival is unchanged. Local recurrence is more common in younger women and in those with highgrade tumours and involved resection margins. Patients whose margins are involved should have a further local excision (or a mastectomy) before going on to radiotherapy. Excision of a breast cancer without radiotherapy leads to an unacceptable local recurrence rate.

The role of axillary surgery is to stage the patient and to treat the axilla. The presence of metastatic disease within the axillary lymph nodes remains the best single marker for prognosis; however, treatment of the axilla does not affect long-term survival, suggesting that the axillary nodes act not as a 'reservoir' for disease but as a marker for metastatic potential. It used to be accepted that only pre-menopausal women should have their axilla staged by operation as there was a good case for giving chemotherapy to lymph node-positive patients; however, it is now clear that post-menopausal women also benefit from chemotherapy and so all patients require axillary surgery. In postmenopausal patients, tamoxifen was once given regardless of axillary lymph node status, but it is now known that all hormone receptor-positive patients, irrespective of age, benefit from this. If mastectomy is performed it is reasonable to clear the axilla as part of the operation, but if a wide local excision is planned the surgeon should dissect the axilla through a separate incision.

Axillary surgery should not be combined with radiotherapy to the axilla because of excess morbidity. Removal of the internal .mammary lymph nodes is unnecessary

# Sentinel node biopsy



# Radiotherapy

Radiotherapy to the chest wall after mastectomy is indicated in selected patients in whom the risks of local recurrence are high.

This includes patients with large tumours and those with large numbers of positive nodes or extensive lymphovascular invasion.

There is some evidence that postoperative chest wall radiotherapy improves survival in women with node-positive breast cancer.

It is conventional to combine conservative surgery with radiotherapy to the remaining breast tissue. Recurrence rates are too high for treatment by local excision alone except in special cases (small node-negative tumours of a special type). Trials are under way to investigate whether radiotherapy can be given intraoperatively at one sitting or as an accelerated postoperative course.

This would have considerable advantages in making conservative surgery available in areas where radiotherapy is not currently used. It would also relieve the burden of the current demand for radiotherapy, which accounts for up to 40% of activity in some departments.

Extrapolation from the Oxford overviews of systemic therapy (carried out every 5 years) suggests that for every four local recurrences one additional life will be spared at 15 years. This means that it is important to get the first treatments right and avoid .local recurrence

## ***Adjuvant systemic therapy***

Over the last 25 years there has been a revolution in our understanding of the biological nature of carcinoma of the breast. It is now widely accepted that the outcomes of treatment are predetermined by the extent of micrometastatic disease at the time of diagnosis. Variations in the radical extent of local therapy might influence local relapse but probably do not alter long-term mortality from the disease. However, systemic therapy targeted at these putative micrometastases might be expected to delay relapse and prolong survival. As a result of many international clinical trials and recent world overview analyses it can be stated with statistical confidence that the appropriate use of adjuvant chemotherapy or hormone therapy will improve relapse-free survival by approximately 30%, which ultimately translates into an absolute improvement in survival of the order of 10% at 15 years. Bearing in mind how common the disease is in northern Europe and the USA, these figures are of major public health importance.

Who to treat and with what are still questions for which absolute answers have yet to be found, but the data from the overviews of recent trials show that lymph node-positive and many higher risk node-negative women should be recommended adjuvant combined chemotherapy. Women with hormone receptor-positive tumours will obtain a worthwhile benefit from about 5 years of endocrine therapy, either 20 mg daily of tamoxifen if pre-menopausal or the newer aromatase inhibitors (anastrozole, letrozole and exemestane) if post-menopausal. It is no longer appropriate to give hormone therapy to women who do not have oestrogen or progesterone receptor-positive disease



## **Hormone therapy**

Tamoxifen has been the most widely used 'hormonal' treatment in breast cancer. Its efficacy as an adjuvant therapy was first reported in 1983 and it has now been shown to reduce the annual rate of recurrence by 25%, with a 17% reduction in the annual rate of death. The beneficial effects of tamoxifen in reducing the risk of tumours in the contralateral breast have also been observed, as has its role as a preventative agent (IBIS-I and NSABP-P1 trials). Trials studying the optimal duration of treatment suggest that 5 years of treatment is preferable to 2 years.

Other hormonal agents that are also beneficial as adjuvant therapy have been developed. These include the LHRH agonists, which induce a reversible ovarian suppression and thus have the same beneficial effects as surgical or radiation-induced ovarian ablation in pre-menopausal receptor-positive women, and the oral aromatase inhibitors for post-menopausal women. The latter group of compounds are now licensed for treatment of recurrent disease, in which they have been shown to be superior to tamoxifen.

A large trial comparing anastrozole to tamoxifen in the adjuvant setting has shown a beneficial effect for the aromatase inhibitor in terms of relapse-free survival, although the data are still immature for overall survival. There is an additional reduction in contralateral disease, which makes this drug suitable for a study of prevention, and the side-effect profile is different from that of tamoxifen. However, it is currently considerably more .expensive

# Chemotherapy

Chemotherapy using a first-generation regimen such as a 6-monthly cycle of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) will achieve a 25% reduction in the risk of relapse over a 10- to 15-year period. It is important to understand that this 25% reduction refers to the likelihood of an event happening. For example, a woman with a 96% chance of survival at, say, 5 years only has a 4% chance of death over this time and the absolute benefit from chemotherapy would be an increase in survival rate of 1%, to 97%. This would not be a sufficient gain to offset the side-effects of this potentially toxic therapy. However, for a woman with a 60% chance of dying (40% survival rate) a 25% reduction in risk would increase her likelihood of survival to 55% and thus treatment would be worthwhile. CMF is no longer considered adequate adjuvant chemotherapy and modern regimens include an anthracycline (doxorubicin or epirubicin) and the newer agents such as the taxanes.

Chemotherapy was once confined to pre-menopausal women with a poor prognosis (in whom its effects are likely to be the result, in part, of a chemical castration effect) but is being increasingly offered to post-menopausal women with poor prognosis disease as well. Chemotherapy may be considered in node-negative patients if other prognostic factors, such as tumour grade, imply a high risk of recurrence. The effect of combining hormone and chemotherapy is additive although hormone therapy is started after completion of chemotherapy to reduce side-effects

High-dose chemotherapy with stem cell rescue for patients with heavy lymph node involvement has now been shown in controlled trials to offer no advantage and has been abandoned. Primary chemotherapy (neoadjuvant) is being used in many centres for large but operable tumours that would traditionally require a mastectomy (and almost certainly postoperative adjuvant chemotherapy). The aim of this treatment is to shrink the tumour to enable breast-conserving surgery to be performed. This approach is successful in up to 80% of cases but is not associated with improvements in survival compared with conventionally timed chemotherapy. For older patients with breast cancers strongly positive for hormone receptors a similar effect can be seen with 3 months of endocrine treatment.

Newer 'biological' agents will be used more frequently as molecular targets are identified – the first of these, trastuzumab (Herceptin), is active against tumours containing the growth factor receptor c-erbB2. Other agents currently available include bevacizumab, a vascular growth factor receptor inhibitor, and lapatinib, a combined growth factor receptor inhibitor. It is unclear how and when these agents will be used, whether in combination or instead of standard chemotherapy agents

## **Follow-up of breast cancer**

Patients with breast cancer used to be followed for life to detect recurrence and dissemination. This led to large clinics with little value for either patient or doctor. It is current practice to arrange yearly or 2-yearly mammography of the treated and contralateral breast. There is a move to return the patient early to the care of the general practitioner with fast-track access back to the breast clinic if suspicious symptoms appear. There is currently no routine role for repeated measurements of tumour markers or imaging other than mammography



***Thank you***