# 2

# Assessment of patient with breast symptoms

Matthew D. Barber
Nisha Sharma

Patients with breast concerns that cannot be adequately managed in primary care should be referred to a specialist breast clinic. Such clinics were traditionally run by surgeons but are now often multidisciplinary. These clinics can perform a combination of clinical, radiological and pathological examinations. Assessment of a breast lump requires triple assessment.

## Triple assessment

Triple assessment is the combination of clinical, radiological and pathological evaluation of a breast lump. Triple assessment should be used in all patients with a confirmed breast lump or asymmetric localised nodularity and may be relevant in women with other symptoms.[1] Imaging assessment consists of mammography in those aged 40 or over and ultrasonography for all palpable lesions and significant radiological findings requiring further study. Histological assessment usually involves core biopsy.[2]

This combination of clinical and imaging assessment with core biopsy increases the reliability of determining the cause of an abnormality.[3–6] It is recommended that all elements of the assessment process are reported on a scale of 1–5 with increasing concern of malignancy[7] (Table 2.1). The availability of clinical and radiological assessment and biopsy at a single clinic visit ('one-stop' clinics) is the standard of care for assessing those referred with breast problems. Immediate reporting of cytology from fine-needle aspirates or touch preparation cytology from core biopsy specimens or frozen section of core biopsy specimens is possible in some centres, but given the inability of cytology to differentiate invasive from in situ cancer has limited utility.

In the USA and European countries the BIRADS scoring system is used for radiology[8] (Table 2.2). The key difference between the UK and USA classifications is that all benign-looking lesions would be biopsied in the UK rather than offered short-term follow-up, as they are in the USA.

It is important to classify the level of concern independently on clinical examination, imaging and histology. This allows the clinician to determine if all the components of triple assessment are concordant or not. Results of all patients undergoing biopsy should be discussed in a multidisciplinary setting to ensure concordance of findings and minimise chances of missing a breast cancer. (See Table 2.3.)

## Clinical evaluation

### Clinical history

A history is taken from the patient of the duration and nature of the presenting symptom. Further specific details can be of value for certain symptoms and are outlined below. The presence and type of past personal or familial breast problems should be elucidated. General factors such as past medical history, drugs and allergies should be recorded. Hormonal risk factors for cancer, such

**Table 2.1** • Scoring system for triple assessment

| | |
|---|---|
| 1 | Normal (or inadequate cytology) |
| 2 | Benign (or normal cytology) |
| 3 | Suspicious but probably benign |
| 4 | Suspicious and probably malignant |
| 5 | Malignant |

The score is preceded by an initial based on the relevant element of assessment (e.g. E, examination; R, mammography; U, ultrasound; M, MRI; C, cytology; B, biopsy).

**Table 2.2** • BIRADS classification

| BIRADS score | Classification |
|---|---|
| 0 | Incomplete imaging – further information required |
| I | Negative |
| II | Benign findings |
| III | Probably benign, short interval follow-up suggested |
| IV | Suspicious abnormality and biopsy recommended. Further subdivided into:<br>IVa: low level of suspicion for malignancy<br>IVb: intermediate suspicion for malignancy<br>IVc: moderate suspicion for malignancy |
| V | Highly suggestive of malignancy |
| VI | Known biopsy-proven malignancy |

as age of menarche and menopause, parity, age of first birth, breastfeeding, oral contraceptive or hormone replacement therapy use, are traditionally documented for epidemiological purposes although they are of no specific value in achieving a diagnosis in an individual case.

The history and examination findings should be recorded legibly and contemporaneously in the medical records, aided by the use of a standard form.

## Clinical examination

Breast examination (see **Fig. 2.1**) should be conducted in a good light with the patient stripped to the waist and in the presence of a chaperone. Examination of the male breast is similar, with particular attention paid to whether an abnormality is present within the breast tissue or whether the problem being complained of is breast tissue.

Initial examination is by inspection, with the patient in the sitting position with hands by her side, paying particular attention to symmetry, nipple inversion, skin changes and any alteration of breast contour. The breast should also be inspected both with arms raised and with the chest wall muscles tensed to show changes in the dynamic setting.

Palpation of the breasts is best performed in the supine position with the head supported and the arms above the head. Putting the hands above the head spreads the breast out over the chest wall and reduces the depth of breast tissue between the examiner's hands and the chest wall and makes abnormal areas much easier to detect and define. All of the breast tissue is examined using the fingertips. If an abnormality is identified, then it should be assessed for size, contour, texture and any deep fixation. All palpable lesions should be measured with callipers[10] and location and size should be clearly recorded.

If there is a history of nipple discharge, the nipple should be gently squeezed to determine whether a pathological discharge is present. Careful note should be taken of whether discharge is emerging from single or multiple ducts, and whether blood is present (either frankly or on dipstick testing).

All women complaining of breast pain or tenderness should be examined for tenderness of the chest wall. With the patient in the sitting position, the hand may be pushed up behind the breast from below with pressure on the chest wall. The patient may also be rolled onto their side, allowing the breast to fall medially, exposing the edge of the pectoral muscle to palpation. With the patient sitting or on their side, pressure can be placed on the breast tissue alone

**Table 2.3** • Accuracy of investigations in symptomatic breast clinic[9]

| | Clinical examination | Mammography | Ultrasonography | Fine-needle aspiration cytology | Core biopsy |
|---|---|---|---|---|---|
| Specificity for cancer | 86% | 86% | 85% | 95% | 90% |
| Specificity for benign disease | 90% | 90% | 88% | 95% | 95% |
| Positive predictive value for cancer | 95% | 95% | 90% | 99.8% | 100% |

Specificity includes assessment as malignant and probably malignant.
Accuracy of mammography varies with age. Accuracy of biopsy techniques is improved by image guidance.

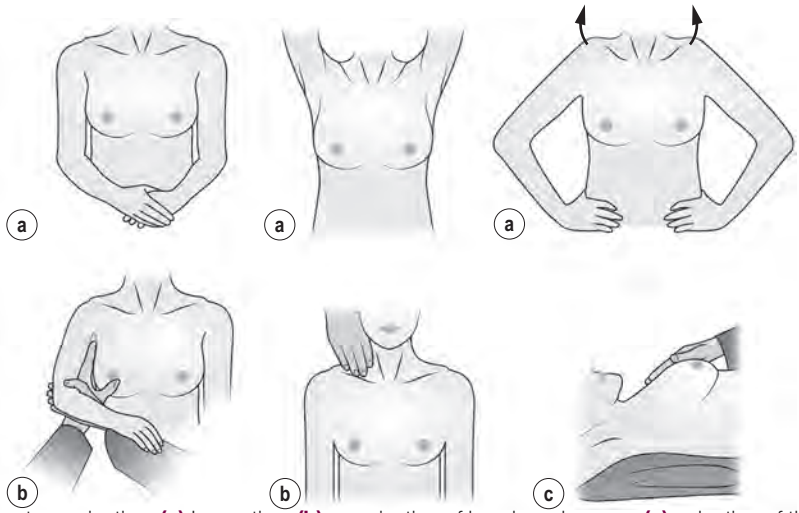



**Figure 2.1** • Breast examination. **(a)** Inspection; **(b)** examination of lymph node areas; **(c)** palpation of the breast tissue.

between the examiner's two hands to provide a contrast with pressure on the chest wall. The patient should be asked to indicate if there is any localised tenderness on palpation of the chest wall and whether any discomfort evident during examination is similar to the pain they normally experience. Allowing the woman herself to confirm that the site of maximal tenderness is in the underlying chest wall rather than the breast is effective in reassuring patients that there is no significant breast problem.

The axilla is best examined with the patient sitting. The examiner's ipsilateral arm supports the patient's arm while the examiner's contralateral hand is placed high in the axilla on the chest wall and run carefully downwards.

The supraclavicular fossa is examined from behind, with the patient in a sitting position.

A general examination of the cardiovascular and respiratory systems is useful in those in whom surgery is being contemplated. If metastatic disease is suspected then examination for bony tenderness, hepatomegaly and pleural effusion may be valuable.

The association between symptoms and cancer risk is indicated in Table 2.4.

**Table 2.4** • Symptoms and cancer risk in those attending a symptomatic clinic (South-east Scotland figures)

| | % of referrals | % with cancer | % of cancers |
|---|---|---|---|
| Lump | 63.8 | 16.6 | 80.5 |
| Pain | 17.1 | 4.2 | 5.1 |
| Nipple discharge | 4.4 | 5.4 | 1.7 |
| Change in shape | 2.5 | 38.1 | 6.8 |

## Lump

Concern over a possible breast lump is the commonest reason for referral to a symptomatic breast clinic. More than 90% of all patients who attend such clinics and more than 80% of those referred with a lump will not have cancer.

All patients with a localised abnormality (lump or localised nodularity) require triple assessment.[2] As outlined previously, distinguishing an area of normal breast nodularity from a pathological lump clinically can be difficult. This is particularly important in young women with breast cancer who may present with localised nodularity rather than a discrete mass.

The likely cause of a lump varies markedly with age. Fibroadenomas are typically found in the teens and twenties, cysts in the mid- to late forties, with cancer becoming the most common cause of a lump in women over 50.

**Figure 2.2** summarises procedure for the investigation of a lump.

### Axillary lump

Common causes of an axillary lump include lymph nodes, skin lesions and accessory breast tissue. Ultrasound will characterise nodes in the majority of cases. A history of skin problems or recent systemic illness will often explain innocent-looking nodes. If nodes are suspicious, imaging of the breast, survey of the skin in the draining area for lesions such as melanoma and examination of other lymph node areas should be performed. Biopsy of concerning nodes is required. A suspicion of lymphoma may require surgical excision to allow full histological analysis. Prominent nodes are increasingly a cause of recall from breast screening.

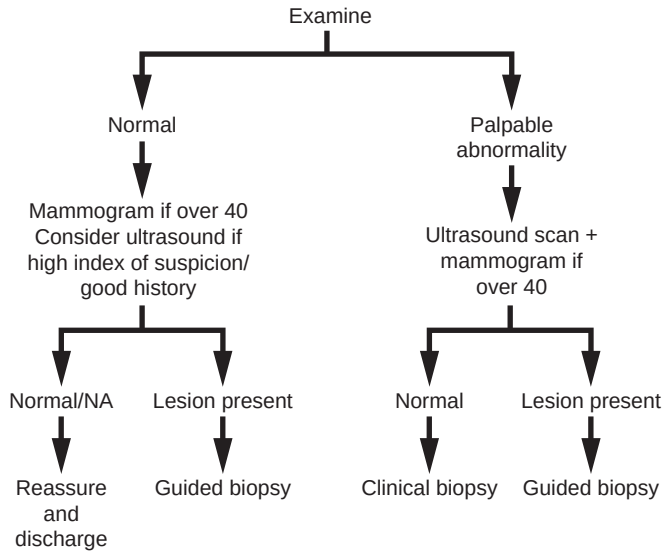



**Figure 2.2** • Flowchart for the investigation of a breast lump.

## Pain

Pain related to the breast is a common cause of referral but an uncommon sign of cancer. If cancer is diagnosed it is usually an incidental finding and not the cause of the pain. The most common causes of pain in the breast are musculoskeletal chest wall pain and cyclical breast pain. These are usually easily distinguished by the history and careful examination (**Fig. 2.3**). Treatment is often unsatisfactory and largely symptomatic but explanation of the symptoms and reassurance are helpful.

## Discharge (Figs 2.4–2.6)

Nipple discharge accounts for 5% of all symptomatic breast clinic referrals and is usually innocent. Important elements of the history are the nature of the discharge, whether the discharge is spontaneous or provoked, whether it is troublesome and any medications being taken. Examination and appropriate imaging are required. Palpable or radiographic abnormalities must be addressed on their own merits.

The majority of patients with multiple duct discharge have so-called physiological nipple discharge or duct ectasia (a normal ageing change).

True galactorrhoea, a copious bilateral milky discharge not associated with pregnancy or breastfeeding, is rare and usually drug-induced. In galactorrhoea with no obvious cause, prolactin levels should be checked and if pathologically raised, scanning of the pituitary for a prolactin-secreting tumour should be considered.

Features of nipple discharge which raise suspicion of an underlying malignancy include discharge that is copious in amount (regularly stains clothes), is persistent, bloodstained or contains moderate or large amounts of blood on dipstick testing and emerges from a single duct. The older the age of the patient, the more the concern but malignant changes can be seen in all ages of women with discharge. The majority of patients with troublesome, single duct, bloodstained nipple discharge have benign causes, the most common being intraduct papillomas and duct ectasia.[11] Nipple cytology has a low sensitivity and has no role in routine management. Visual examination of the ducts is possible using a fibreoptic endoscope around 1 mm in diameter with a working channel to allow biopsy or washings for cytology. This technique has its enthusiasts but is time-consuming, requires specific equipment and expertise and often does not preclude the requirement for surgery for treatment.[12]

Duct excision is recommended for definitive diagnosis in all women with significant discharge.[13] This involves a short incision at the areolar margin, division of the ducts just behind the skin at the back of the nipple and excision of the underlying ducts for 2–3 cm into the breast. Note should be taken of any serous or bloodstained discharge into the cavity on division of the proximal ducts. Any such concerning discharge from the divided proximal ducts should be pursued by further excision of the affected area to ensure more proximal lesions are not missed. In women wishing to breastfeed further children, excision of the affected duct alone (microdochectomy) can be considered. The affected duct can often be identified by cannulation with a probe prior to the incision. This technique

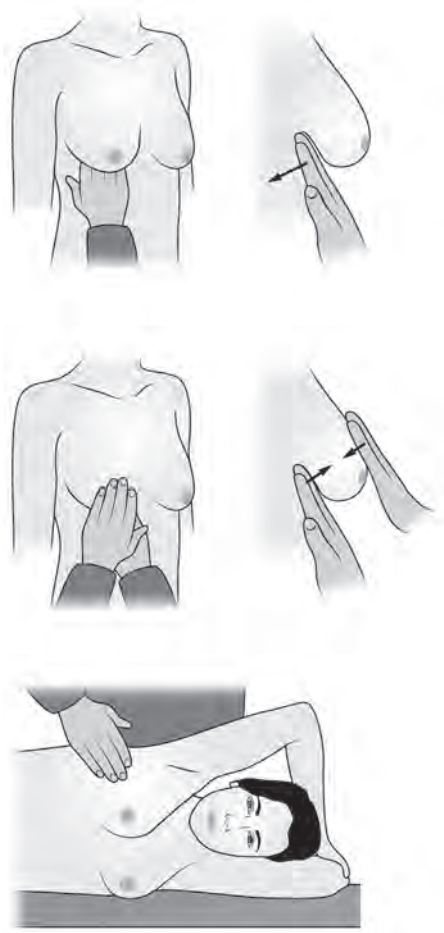


**Figure 2.3** • Examination for chest wall pain. The chest wall is examined for tenderness by pressing up under the breast or by examining the patient on their side to allow the breast to fall away medially. Breast tenderness can be assessed by compressing the breast tissue between the hands.

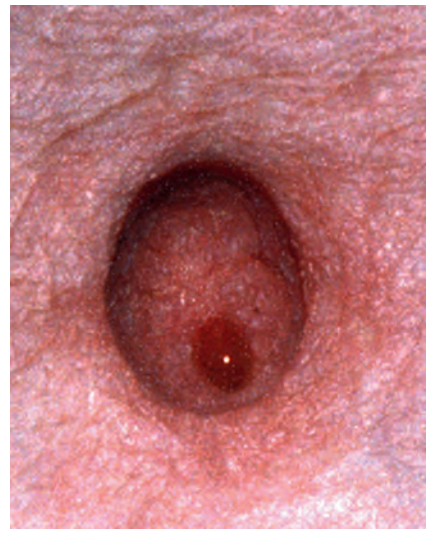


**Figure 2.4** • Single duct serous/bloody discharge.

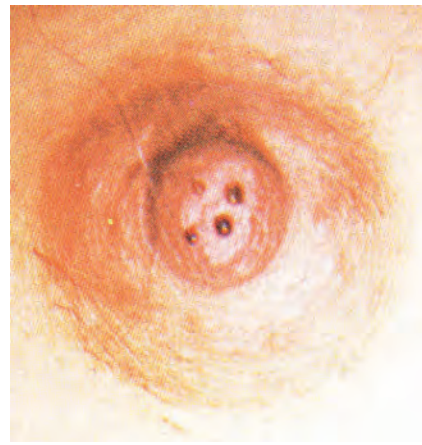


**Figure 2.5** • Physiological multiple duct discharge.

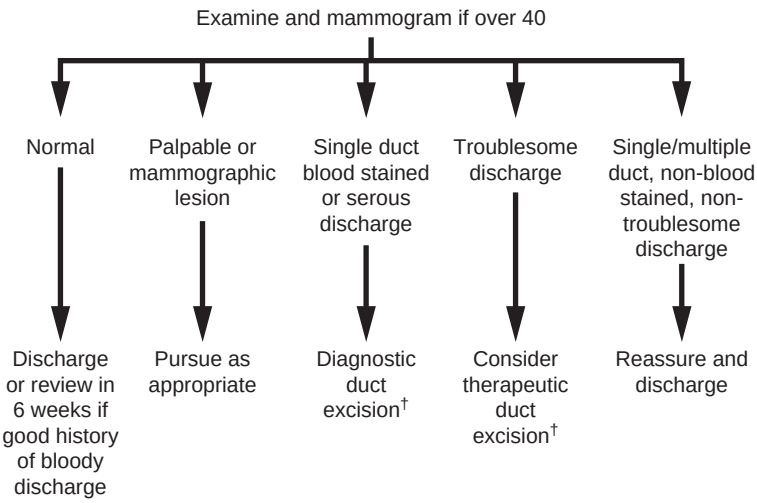



**Figure 2.6** • Flowchart for the investigation and management of nipple discharge. †Total duct excision in older women who have completed their family.

minimises damage to other ducts but as duct ectasia is a common cause and affects all ducts, repeat surgery may be required, which has a higher rate of wound problems.

## Nipple retraction

Benign nipple retraction (**Fig. 2.7**) is common and has a characteristic symmetrical appearance with a central horizontal slit. In such patients the nipple can usually be manipulated by tension on the areolar margin to evert it. Malignant nipple inversion (**Fig. 2.8**) is often eccentric rather than central, the nipple cannot be manually everted and is usually seen in association with other signs of malignancy.

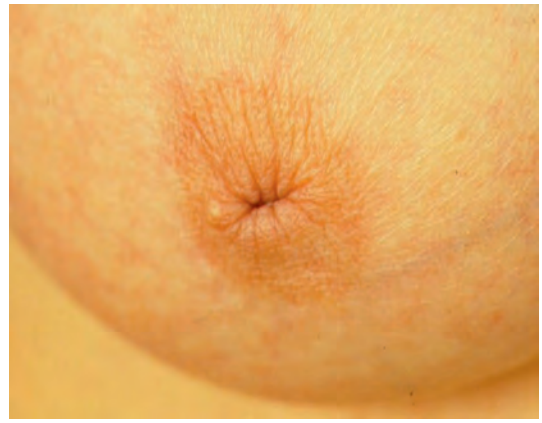


**Figure 2.7** • Benign nipple retraction.

## Change in breast shape

A degree of breast asymmetry is normal but a significant asymmetry following breast development may require plastic surgical techniques to correct. Changes in breast contour are uncommon but are not infrequently associated with underlying malignancy due to distortion of the connective tissue framework of the breast by the cancer. Fat necrosis following trauma (including surgical trauma) may give rise to skin dimpling (**Fig. 2.9**) and lumps. Mondor's disease (**Fig. 2.10**), due to thrombosis of dermal vessels, can result in linear dimpling and may be palpable.[14] Atrophy of the breast with age can also lead to irregularities of breast contour. Careful clinical assessment and imaging with a high degree of underlying suspicion is recommended.

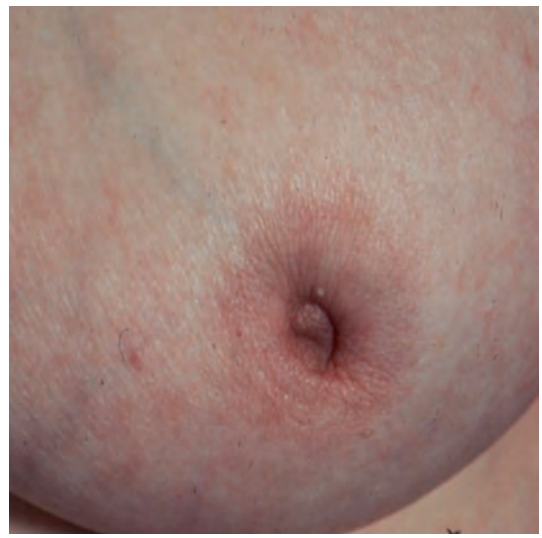
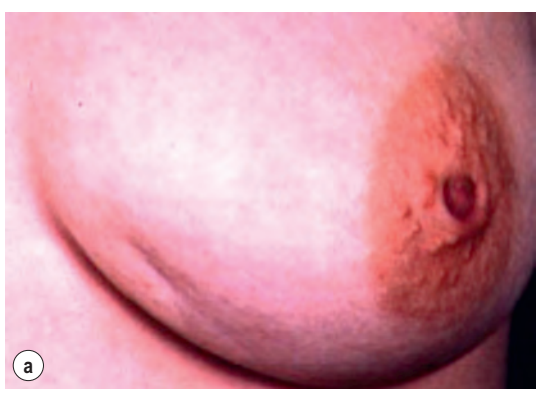


**Figure 2.8** • Malignant nipple retraction.



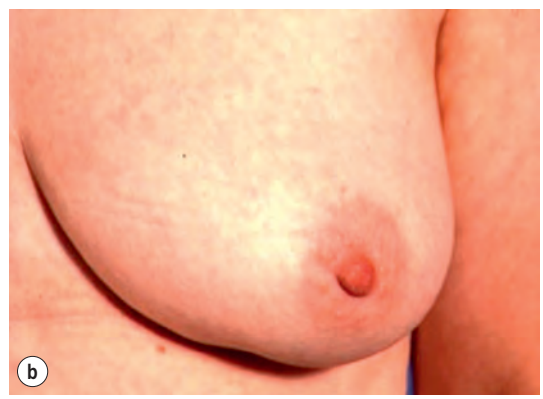




**Figure 2.9** • **(a,b)** Malignant skin dimpling.

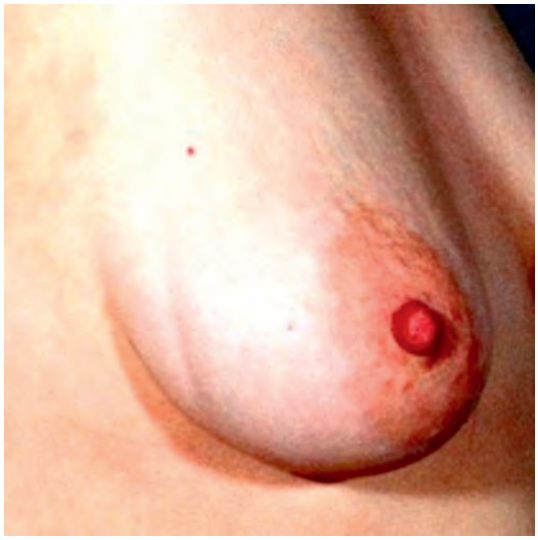


**Figure 2.10** • Mondor's disease.

## Skin changes

The skin of the breast is susceptible to the full range of dermatological conditions, including eczema, naevi and epidermal inclusion cysts. Skin cancers may also occur on the breast.

Paget's disease of the nipple arises when malignant cells spread to involve the epithelium of the nipple skin resulting in a red, scaling appearance that can sometimes be difficult to differentiate from eczema. Paget's disease always involves the nipple but may also spread beyond the nipple to involve the surrounding areolar area. Eczema starts on the areola and usually spares the nipple itself. If there is concern that Paget's disease is present, a punch biopsy or a core biopsy including nipple skin should be performed under local anaesthetic in the outpatient clinic. If Paget's disease is confirmed, further investigation is required to determine whether underlying ductal carcinoma in situ (DCIS) or invasive malignancy is present.

Breast cancer can directly invade the skin of the breast or nipple resulting in a hard pink lump or ulceration. Metastatic tumour nodules within the skin but distant from the primary breast cancer may also be seen. Blockage of skin lymphatics by breast cancer cells results in breast oedema producing a peau d'orange appearance. Erythema is a feature of so-called inflammatory cancer.

## Gynaecomastia

Gynaecomastia is due to hyperplasia of the glandular tissue of the male breast.[15] It is common, particularly in newborns, teenage boys and old men, when it is due to physiological hormonal changes. It can be a source of embarrassment. Care should be taken to differentiate it from pseudogynaecomastia due to accumulation of fat in the breast area without glandular development.

Gynaecomastia is due to a relative imbalance of androgen and oestrogen (Table 2.5) and is thus a manifestation of a systemic issue rather than a specific breast problem. Assessment must therefore address potential systemic causes as well as ensuring that there is no local problem with the breast tissue. Breast lumps must be investigated as such. Lumps not involving the breast tissue such as lipomas are also not uncommon in men.

The aetiology of gynaecomastia can often be determined from the history. Enquiries should focus on factors associated with the condition, such as liver disease, testicular problems and drugs (including recreational drugs such as alcohol, cannabis, opiates and anabolics) (Table 2.6). The impact of the gynaecomastia on the patient is worth exploring.

**Table 2.5** • Pathological causes of gynaecomastia

| |
|---|
| Decreased androgens |
| Chromosomal abnormalities – e.g. Klinefelter's syndrome |
| Testicular failure – cryptorchism, torsion, orchitis |
| Renal failure |
| Androgen resistance – testicular feminisation |
| Increased oestrogens |
| Increased secretion – testicular tumours, lung cancer |
| Increased aromatisation – liver disease, obesity, adrenal disease, hyperthyroidism |

**Table 2.6** • Drugs commonly associated with gynaecomastia*

| |
|---|
| Hormones – anabolics, androgens, antiandrogens, oestrogenic agents |
| Recreational drugs – alcohol, cannabis, heroin, methadone, amphetamines |
| Cardiovascular drugs – digoxin, spironolactone, ACE inhibitors, amiodarone, calcium channel blockers |
| Antiulcer drugs – $H_2$ receptor blockers, proton pump inhibitors |
| Antibiotics – ketoconazole, metronidazole, minocycline, antiretrovirals |
| Psychoactive agents – tricyclics, diazepam, phenothiazines |
| Others – domperidone, metoclopramide, penicillamine, phenytoin, theophylline, allopurinol |

*Not exhaustive. There are other drugs but these are common ones.

Some men are not concerned and therefore may require no intervention, others become haunted by it and are desperate for treatment.

Examination should include a general examination (for signs of liver/hormonal problems), examination of breast tissue, axillary lymph nodes and testes (**Fig. 2.11**). Feeling testicular tumours is rare but atrophic or even an absent testicle may be noted, limiting the need for further investigation. The extent of gynaecomastia can be classified according to the extent of breast tissue and redundant skin (Table 2.7).

**Table 2.7** • Classification of extent of gynaecomastia[16]

| Grade | Appearance |
|---|---|
| I | Small development of breast but no excess skin |
| IIa | Moderate breast development with no excess skin |
| IIb | Moderate breast development with excess skin (nipple at or above inframammary fold) |
| III | Marked breast development with excess skin (nipple below inframammary fold) |

In those aged between 18 and 60 without an obvious cause from the history and examination *and* significant enlargement of breast tissue (not just fat) the following blood tests are recommended: urea and electrolytes, liver function tests, luteinising hormone, follicle-stimulating hormone, testosterone, prolactin, alphafetoprotein and beta-human chorionic gonadotrophin.

Mammograms are recommended in those aged 40 or over. Ultrasound is recommended if a discrete lesion is present and imaging may help distinguish fatty swelling from glandular breast tissue.

Discrete lesions should undergo core biopsy. Fine-needle aspiration cytology is not recommended as cytological appearance can be overcalled in gynaecomastia.

If abnormalities are identified from the history or examination, further investigation such as testicular ultrasound or chest X-ray may be warranted.

Management is directed at any underlying cause if identified. The patient should be reassured of the innocent nature of the condition and the fact that it often resolves spontaneously although this may take many months. If an endocrine abnormality is identified the involvement of an endocrinologist may be useful.

If treatment is justified, danazol, tamoxifen, aromatise inhibitors and clomiphene have been used as medical therapy although none is specifically licensed for this purpose. For convenience and side-effect profile, tamoxifen 10–20 mg daily for up to 6 months may be considered as initial treatment.

Surgery is rarely required and the results of open surgery are often disappointing, with a significant risk of a poor cosmetic result. Excision of the breast tissue through a periareolar incision may be worthwhile if only a small amount of breast tissue is present. Some breast tissue behind the nipple and thick skin flaps should be left to minimise the risk of a saucer-shaped deformity corresponding with the excised area. If the underlying cause is still present, breast tissue may regrow. Seroma after such surgery

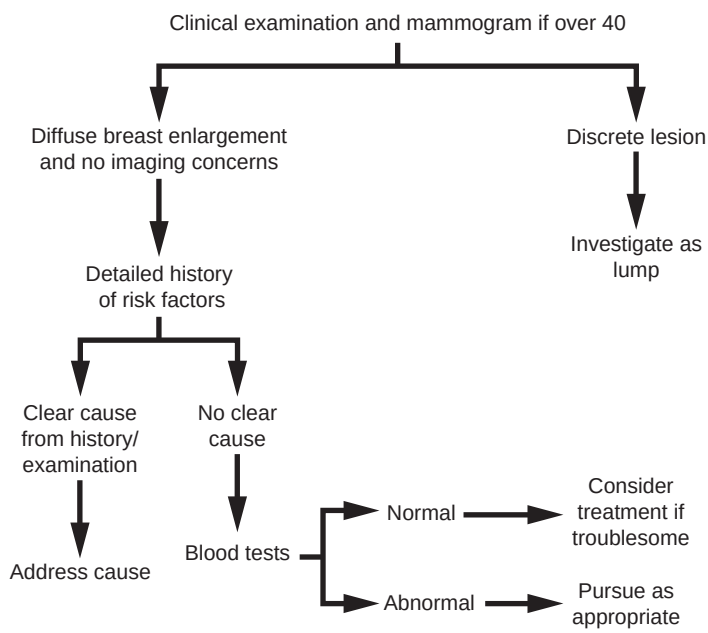



**Figure 2.11** • Flowchart for the investigation and management of gynaecomastia.

is not uncommon. The nipple is likely to be numb after surgery and there is a small risk of nipple necrosis. A small amount of excess skin will often remodel but in those with more, excision of skin may be required, possibly requiring repositioning of the nipple with a breast reduction-type approach.

Liposuction, sometimes in association with limited surgical excision, is increasingly being used to sculpt the tissue over the chest wall in an attempt to improve the cosmetic outcome from surgery for gynaecomastia. The involvement of a plastic surgeon in the surgical management of gynaecomastia is encouraged.

# Radiological assessment

## Mammography

X-ray mammography (see **Fig. 2.12**) has been the basis of breast imaging for more than 30 years. Initially this was with film-screen mammography but now all mammograms are performed with full-field digital mammography (FFDM) within the UK. This allows the images to be viewed on monitors and allows for electronic transfer of images between hospitals. Internationally there are some countries still using film-screen mammography. The transition to FFDM followed the DMIST study,[17] which showed the overall diagnostic accuracy was similar for digital and film mammography but the accuracy of digital mammography exceeded that of film mammography in women younger than 50 years, women with heterogeneously or extremely dense breasts, and premenopausal and perimenopausal women.

The sensitivity of mammography for breast cancer is age-dependent. The denser the breast, the less effective this method is for detecting early signs of breast cancer. Breast density tends to be higher in younger women and increased density obscures early signs of breast cancer. The sensitivity of mammography for breast cancer in women over 60 years of age approaches 95%, while mammography can be expected to detect less than 50% of breast cancers in women under 40 years of age.[18] Mammography uses ionising radiation to obtain an image and therefore should only be used where there is likely to be a clinical benefit. The consensus is that the benefits of mammography in women over the age of 40 years are likely to far outweigh any oncogenic effects of repeated exposure. Imaging of symptomatic women over the age of 40 by mammography is accepted practice and the NHSBSP imaging guidelines for higher-risk surveillance recommend mammographic screening from the age of 40.[19] In symptomatic practice, there is rarely an indication for performing mammography in women under the age of 40[2] unless there is a strong clinical suspicion of malignancy. Mammography is routine in all women in the screening age group attending symptomatic clinics that have not had a screening mammogram in the past year.

Mammography is the basis of stereotactic breast biopsy, which can be carried out using a dedicated prone biopsy table or by using an add-on device to a conventional upright mammography unit. Stereotaxis is used to biopsy impalpable lesions that are not clearly visible on ultrasound (e.g. microcalcifications).


**Figure 2.12** • Digital mammogram being performed. Courtesy of HOLOGIC, Inc. and affiliates.

## Additional mammographic techniques

### Tomosynthesis

The primary limitation of mammography is that overlapping dense fibroglandular tissue within the breast can decrease visibility or even obscure malignant lesions, which then present later as interval breast cancers. It has been shown that 15–30% of cancers are not detected by standard screening.[20] This percentage is higher in women under 50 years[21] and in women with dense breasts.[18,22] Conversely, superimposition of normal fibroglandular tissue may mimic the appearance of malignancy leading to an increase in the number of false-positive recalls.[23]

Digital breast tomosynthesis (DBT) is an X-ray mammography technique in which tomographic images of the breast are reconstructed from multiple low-dose projection images acquired by moving the X-ray tube in an arc over a limited angular range. The range of angles employed varies by manufacturer from 15 to 50 degrees. The exposure used for each projection is relatively small and the overall mean glandular dose for DBT is comparable with that of standard FFDM. The tomosynthesis projection images are processed by reconstruction algorithms to produce a set of parallel image planes through the whole breast, typically with 1-mm spacing. Readers view images on a workstation (see **Fig. 2.13**) and are able to scroll vertically through the tomographic images and compare them with corresponding FFDM images.

Digital breast tomosynthesis reduces the problems arising from tissue overlap. A prospective screening trial – the Oslo trial[24] – has shown an increase in cancer detection rate of 27%, a significant (40%) increase in the detection of invasive cancers, and an estimated 15% decrease in false-positive recall rate using tomosynthesis in combination with FFDM compared with FFDM alone.

Tomosynthesis is currently FDA approved as an adjunct to standard mammography, and does not replace it. It has also been approved for use in the second stage of screening by the UK national screening programme.[25]

**Figure 2.13** • Reading tomosynthesis images on a workstation.
Courtesy of HOLOGIC, Inc. and affiliates.

### Contrast-enhanced spectral mammography (CESM)

This is a new technology that combines mammography with intravenous contrast. This technique requires an injection of an iodinated contrast agent, 2 minutes after which CESM acquires a set of low and high-energy images in quick succession while the breast remains compressed. Recent studies show that the accuracy of CESM for detecting breast cancer is superior to conventional mammography and might even be similar to breast MRI, though breast MRI might be better in describing the extent of multifocal breast cancers. Interestingly, the number of false-positive findings appeared much lower for CESM when compared to breast MRI.[26] Recent literature has demonstrated that the addition of contrast-enhanced mammography to standard mammography and ultrasound in a diagnostic setting improves reader sensitivity from 71% to 78% and improved overall reader performance when compared with mammography and ultrasound alone.[27] In 2011, the FDA approved contrast-enhanced digital mammography in the USA as an adjunct to standard mammographic views. This technology is currently under review in Europe and the UK.

## Ultrasound

High-frequency (≥10 MHz) ultrasound is a very effective diagnostic tool for the investigation of focal breast symptoms.[28] It does not involve ionising radiation, is safe and quick to perform.

Ultrasound is the technique of choice for the further investigation of focal symptomatic breast problems at all ages. Under 40 years of age, when the risk of breast cancer is very low, it is usually the only imaging technique required. Over 40, when the risk of breast cancer begins to increase, it is often used in conjunction with mammography. Ultrasound is the technique of first choice for guiding biopsy of both palpable and impalpable breast lesions visible on scanning. Ultrasound is also used routinely to assess the axilla in women with breast cancer. Axillary nodes that show abnormal morphology can be sampled accurately by fine-needle aspiration (FNA) or needle core biopsy.[29]

Ultrasound is less sensitive than mammography for the early signs of breast cancer and is therefore not used for population screening. However, ultrasound does increase the detection of small breast cancers in women who have a dense background pattern on mammography.[30]

In the screening setting there is clear evidence that the addition of ultrasound improves small cancer detection rates, particularly in women with dense breasts. Adding ultrasound to mammography or magnetic resonance imaging (MRI) screening does increase cancer detection but also significantly increases the false-positive rate.

The rate of biopsy following screening ultrasound in the American College of Radiology Imaging Network (ACRIN) 6666 trial[31] was 5%, with a positive predictive value of 11%. Generalisation of these results is limited because all study participants were at elevated risk, with over half having a personal history of breast cancer.

In the USA the enactment of Connecticut Bill 458 in October 2009 mandated that women were to be informed of their breast density and the possible benefit of ultrasound as an additional screening modality.[30]

### Additional ultrasound techniques

#### Automated whole breast ultrasound (ABUS)

ABUS is a promising technology that aims to standardise the way that screening ultrasound examination is performed and produces a high-quality examination to improve the conspicuity of cancers. Typically, the study is performed with robotic guidance of a standard ultrasound probe over the entirety of both breasts followed by cine presentation of closely spaced images in the axial plane or reconstruction of the images to present a series of images in the coronal plane.[32]

A large multi-institutional trial[33] evaluating more than 15 000 asymptomatic women with dense breasts using mammography and supplemental ABUS found that mammography detected 5.4 cancers per 1000 women but mammography with supplemental ABUS detected 7.3 cancers per 1000 women. They concluded that the addition of ABUS to screening mammography in a generalisable cohort of women with dense breasts increased the cancer detection yield of clinically important cancers, but it also increased the number of false-positive results.

## Magnetic resonance imaging

Breast MRI is now widely available. It is used as a screening tool in women with a significant family history of breast cancer and is also used as a problem-solving tool in women diagnosed with breast cancer. In order to image the breast the patient is scanned prone and injection of intravenous contrast is required. Breast MRI requires high temporal and spatial resolution, and that both morphologic and kinetic enhancement characteristics should be considered when evaluating breast MRI lesions. MRI is the most sensitive technique for detection of breast cancer, approaching 100% for invasive cancer and up to 92% for ductal carcinoma in situ (DCIS), but it has a high false-positive rate.[34–36]

Rapid acquisition of images facilitates assessment of signal enhancement curves that can be helpful in distinguishing benign from malignant disease. The significant overlap in the enhancement patterns seen means that needle sampling of the lesions detected is still usually required.

The quality standards of the UK National Institute for Health and Care Excellence (NICE) have stated that breast MRI should be performed very selectively in those with breast cancer. It is indicated in invasive lobular cancer where breast conservation is planned, where breast density prevents accurate sizing of the tumour on mammography and where there is discordance regarding clinical and radiological size.[1] Magnetic resonance-guided breast biopsy is available in a few centres but most breast lesions seen on MRI that are larger than 5 mm can be seen on a second-look ultrasound if they are clinically significant. MRI is the best technique for imaging women with breast implants. It is also of benefit in identifying recurrent disease where conventional imaging and biopsy have failed to exclude recurrence. Provided it is carried out more than 18 months after surgery, MRI can accurately distinguish between scarring and tumour recurrence. Breast MRI is of value in assessing the response of large or locally advanced breast cancers to neoadjuvant chemotherapy. MRI of the axilla can demonstrate axillary metastatic disease but its sensitivity is not sufficient to replace surgical staging of the axilla. For advanced breast cancer, MRI is the technique of choice for assessing spinal metastatic disease.

### MRI as a screening tool

Several studies have evaluated the use of breast MRI for screening of women at high risk for breast cancer. The patient populations have varied, but the majority of investigations included women at risk because of a known genetic mutation or those with a greater than 25% lifetime risk based primarily on family history. The results of these studies showed MRI consistently demonstrated higher sensitivity (reported range of 71–100%) for detecting breast cancer in this clinical setting than mammography (13%–59%) or ultrasound (13%–65%). The average positive predictive value, defined as the number of malignancies found at biopsy divided by the total number of biopsies performed, is

45%, close to the 25–40% desirable positive biopsy rate range recommended by the American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS).[37]

The American Cancer Society now recommends annual screening breast MRI in addition to mammography in women who are at high risk because of a known genetic mutation, who have not been tested but who have a first-degree relative with a known mutation, who have a greater than 20–25% lifetime risk of breast cancer as determined by currently available risk assessment tools, and women who received chest irradiation between the ages of 10 and 30 (usually for lymphoma). The NHS Breast Screening Programme in the UK has incorporated high-risk surveillance into the breast screening programme which offers annual MRI screening (from 30 years of age [20 years of age for TP53 mutation]) and annual mammography screening from 40 years of age.[19]

An abbreviated breast MRI protocol has been developed where only one pre- and one post-contrast acquisition was obtained and from these sequences a first post-contrast subtracted and maximum-intensity projection images were obtained. Kuhl et al.[38] showed that the total MRI acquisition time was 3 minutes and reading time was <30 seconds with a negative predictive value of 99.8% and resulted in an additional cancer yield of 18.2 per 1000. This is currently being evaluated by screening programmes across the world.

## CT scanning

Computed tomography (CT) has no current proven role in primary imaging of the breast but dedicated low-dose breast CT is being introduced; its clinical efficacy has yet to be determined. The limitations are related to microcalcifications.[39]

CT is used to assess and stage those with a significant risk of systemic spread of breast cancer at diagnosis or with suspicious symptoms following treatment and to assess response of metastatic disease to treatment, particularly lung, pleural and liver metastases. Some patients with breast cancer have their cancers picked up incidentally during CT scanning for another indication.

In most centres, where there is high risk or symptoms suggestive of metastatic disease, CT scanning is performed in conjunction with isotope bone scanning. Increasingly, some units are relying on just CT scanning to detect bone metastases.[40]

## Isotope bone scan

An isotope bone scan (BS) provides a relatively sensitive and inexpensive evaluation of the entire skeleton in a single imaging examination using radionuclide imaging[41] and is recommended for evaluation of patients with multiple sites of bone pain or for staging of patients at high risk of having metastases.[42] BS images osteoblastic lesions, sclerotic/mixed bone lesions and reparative bone formed around lytic lesions.[43] One of the limitations of BS is that it lacks anatomic resolution, which increases the difficulty in distinguishing tumour from non-tumour uptake (traumatic or degenerate changes in the bone) and may lead to false-positive BS.

SPECT (single photon-emission computed tomography) allows for 3D imaging and can be combined with CT to produce hybrid images that can be displayed in the axial, sagittal, or coronal plane (SPECT-CT). SPECT has been reported to identify more metastases than planar BS because of its cross-sectional nature,[44] and its accuracy is enhanced by the fused CT.[45,46] SPECT imaging is not as widely available and is more expensive than a conventional bone scan.

## Molecular imaging

Positron emission mammography (PEM)[47] and breast-specific gamma imaging (BSGI) use molecular imaging to increase specificity in cancer detection by demonstrating increased metabolic activity. Both these techniques have high positive predictive values and low negative predictive values. They are currently being evaluated in clinical trials.

18 F-FDG (fluorodeoxyglucose) PET (positron emission tomography)/CT is not routinely used in those with breast cancer but is sometimes employed to answer specific questions. It can evaluate response to therapy and detect post-treatment recurrence. Evidence is emerging that shows that PET/CT offers prognostic stratification when used as an initial staging test for patients with locally advanced breast cancer or inflammatory breast cancer.[48]

## Radiation-induced cancers

Ionising radiation can increase the risk of cancer. Mammography involves ionising radiation and therefore women are exposed to radiation during mammographic examination. This amounts about 0.4 mSv (range 0.1–0.6 mSv) per 2-view mammographic examination.

A single chest X-ray amounts to 0.014 mSV and is equivalent to 3 days' natural background radiation and a CT scan of the whole spine is about 10 mSv.

The NHSBSP Report 54 concluded that the risk of radiation-induced cancer for a woman attending mammographic screening is about 1 in 20 000 visits and that screening within the NHSBSP (every 3 years, 50–70 years of age) saved 80 lives for every

life lost due to radiation-induced cancer.[49] The risk of radiation-induced breast cancer is dependent on the screening round (annually versus 3-yearly), breast size (larger breasts receive higher dose) and additional mammographic investigations at time of recall from breast screening.[50] A study from the USA[51] reported in 2011 that in a cohort of 100 000 women, mammographic screening conducted annually from ages 40 to 55years and biennially until 74 years of age would induce 86 breast cancers, in which 11 deaths would be attributable to radiation-induced breast cancer. They concluded that for a screening cohort of 100 000, 10 670 woman-years would be saved by breast screening compared to 136 woman-years lost due to radiation-induced cancer.

# Image-guided breast intervention

Image-guided percutaneous breast intervention plays an important role in the management of breast lesions. It has evolved over the last two decades such that the use of breast imaging has expanded from a diagnostic role to a treatment role and has played a significant part in changing the way breast disease is currently managed. It is safe, accurate and minimally invasive. It is well tolerated by patients, with minimal breast deformation or scarring when compared with surgical biopsy.

## Techniques

### Fine-needle aspiration

Fine-needle aspiration (FNA) has largely been superseded by core biopsy.

FNA is mostly confined to aspiration of cysts, lymph node assessment or sampling an area where a core biopsy is technically not possible. It requires a skilled cytologist and gives limited information. Malignant cytology is unable to distinguish between non-invasive or invasive cancer. Molecular markers are difficult to obtain and there are a higher number of false-positive and false-negative cases.[52,53]

### Core biopsy

In 1994, Parker published data on the outcomes of 6152 core biopsies from 20 institutions, using long-throw spring-loaded 14-gauge (G) needles and showed an overall 1.5% false-negative rate for percutaneous breast biopsy.[54] This resulted in conventional core biopsy being considered the method of choice over FNA.[55]

Currently there is a wide range of automated needles available commercially. These are spring-loaded devices where tissue is obtained by firing a stylet at high speed into the area of concern, rapidly followed by a cutting cannula. A 14G core needle has a 2.2 cm throw and is routinely used for conventional core biopsy. The needles are single-use, either for use with a reusable biopsy device, or a fully disposable needle biopsy device. All require multiple insertions to retrieve multiple samples.

### Vacuum-assisted diagnostic biopsy (VAB)

Although 14G core biopsy is routinely used there are limitations related to under-sampling as the tissue samples retrieved are small and there is potential for sampling error related to missing the target lesion.

The vacuum-assisted biopsy technique was developed at the end of 1995.[56] A needle device is placed percutaneously into the breast through a small incision in the skin. A rotating cutter within the needle takes a sample of breast tissue which is drawn by vacuum into the hilt of the device outside the breast. The samples can either be collected manually or are collected from a chamber at the end of the procedure. The needle gauge varies from 7G to 14G and the smaller the gauge the larger the volume of tissue removed per core biopsy (**Fig. 2.14**).[57]

The main advantages of vacuum-assisted biopsy are a decrease in the likelihood of histological underestimation, a decrease in imaging-histological discordance and a decrease in the re-biopsy rate. Complete lesion removal may be possible. The main drawback is that it is significantly more costly than conventional core biopsy. Because of this, VAB has often been used when the initial core biopsy has failed to give a definitive diagnosis. Many screening units are moving towards using VAB, instead of core biopsy for X-ray- guided procedures.

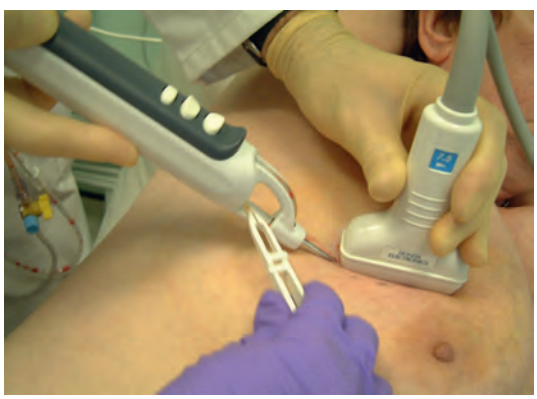


**Figure 2.14** • Vacuum biopsy in progress. The needle is placed within the lesion under ultrasound guidance. A sample of breast tissue is cut out just behind the needle tip and drawn to the hub of the device by suction where it can be removed. Multiple samples can therefore be taken without removing the device.

### Vacuum-assisted excision (VAE)

This uses the same vacuum biopsy device as would be used for diagnostic biopsy but with the aim of removing the entire lesion if small and so replaces the need for surgical excision. It has had approval from NICE and FDA for removal of benign lesions.[58–60]

It is important in individual cases to define whether the vacuum biopsy is being done for diagnosis or excision, as the pathological approach to assessment is different.

VAB and VAE have been useful in the diagnosis and management of indeterminate lesions within the breast, reducing the underestimation rate of malignancy.[61,62] It has been shown to be better than conventional core biopsy with regards to understaging of non-invasive and invasive cancer by approximately half (typically 10% vs 20%).[63,64]

VAE is being used in some units for the management of indeterminate lesions such as papillomas and radial scars,[65] and removal of fibroadenomas.

### INTACT device

The INTACT breast lesion excision system is an automated, vacuum-assisted single-pass biopsy device that encircles the lesion using stereotactic or ultrasound guidance and dissects it free using radiofrequency ablation. This allows percutaneous excision of some breast lesions in one piece.[66] It has NICE approval for benign lesions. It is a relatively new technology that is currently being evaluated clinically.

## Guidance techniques for image-guided intervention

Ultrasound-guided intervention is preferred to X-ray or MRI. Ultrasound provides real-time visualisation of the biopsy procedure and images can be taken showing the needle within the lesion being targeted.

Ultrasound is quick, low cost and does not involve ionising radiation. It is readily accessible. It can be used for both palpable and impalpable lesions. The majority of breast lesions are visible on ultrasound. For impalpable lesions that are not visible on ultrasound, then X-ray-guided biopsy is required. This is predominantly necessary for calcifications or small densities only seen on mammography. If a lesion has been seen on MRI of the breast, then review of the mammogram and ultrasound of the area seen on MRI is advised. If both are normal then an MRI-guided biopsy is required. MRI-guided biopsy is performed using VAB. If there is a clinical palpable abnormality and mammography and ultrasound are normal, the negative predictive value for malignancy is extremely high, with the likelihood of cancer being <1%. In this instance, however, clinical biopsy of the palpable abnormality freehand is necessary to rule out invasive lobular cancer or non-invasive cancer, which may be occult on imaging.

## Marker clip placements

Marker clips are being increasingly used following breast biopsy to mark the area sampled. A mammogram (lateral and cranio-caudal view) is routinely performed following placement of the marker to demonstrate the position of the marker and confirm its relation to the site of the lesion. This needs to be documented in the report. There are many different commercially available markers. Gel pellets or cellulose combined with a metallic marker are preferred as these have the advantage of being visible on ultrasound so that a repeat biopsy or localisation can be ultrasound-guided rather than X-ray guided. It is particularly important that markers are placed following biopsies if the lesion is small (when the lesion may not be visible following biopsy); if the patient is to receive neoadjuvant chemotherapy (when the lesion may disappear); and if there is doubt that a lesion visible on ultrasound is the same as a mammographic abnormality. All MRI-guided biopsies should have a marker placed post VAB.

## Number of samples

There are no set rules, but the aim would be to take enough samples to be able to make a definitive diagnosis.[67,68] For X-ray-guided biopsies of calcifications, at least five flecks of calcification should be seen, or flecks in three separate cores to ensure that the sample is representative.[69] On average, 6–12 cores are taken if using 14G core biopsy and with VAB the cores can vary from 6 to 24 cores depending on the needle gauge. Regarding ultrasound, the more samples taken, the more likely a diagnosis will be reached, but 3–4 14G cores will usually be sufficient if biopsies appear to be on target. (See **Fig. 2.15**.)

## Biopsy results

It is important that the results of the FNA or core biopsy are correlated with the clinical and imaging findings to ensure there is concordance. This should be done in the setting of the multidisciplinary team.

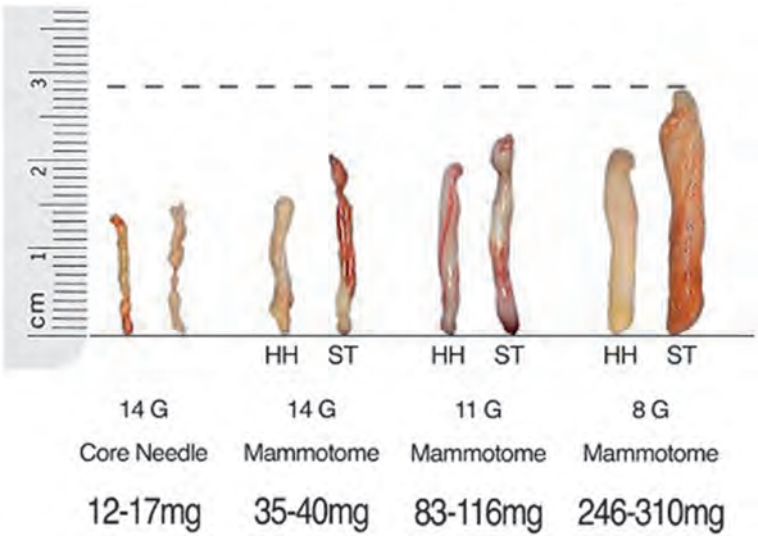



**Figure 2.15** • Core samples showing the difference in the amount of tissue taken from a conventional spring-loaded core device to a vacuum-assisted biopsy with different needle gauges. HH, Hand-held; ST, stereotactic guidance. Courtesy of Johnson & Johnson.

## Key points

- Triple assessment – examination, imaging and needling – is the cornerstone of assessment of breast lesions.
- Mammography and ultrasound scanning are the workhorses of routine breast imaging.
- Image guidance is increasingly being used to guide biopsies in the diagnosis of breast lesions and to guide surgery for impalpable breast lesions.

Recommended videos:
- Breast examination – https://tinyurl.com/ul7k7nk
- Mammography – https://tinyurl.com/yb6jxx9z
- Breast MRI – https://tinyurl.com/reupxfh

Full references available at **http://expertconsult.inkling.com**

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