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Grainger & Allison's DIAGNOSTIC RADIOLOGY

A Textbook of Medical Imaging

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The Breast

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CHAPTER OUTLINE

Breast cancer is the most common malignancy in the UK with over 55,000 diagnoses annually—almost half of cases (48%) occur in those over the age of 65. It accounts for nearly 11,500 deaths per annum. Imaging is essential for the early detection and accurate diagnosis of breast cancer. Population screening with mammography aims to reduce mortality by detecting the disease at an earlier stage, before it has spread beyond the breast.

Mammography and ultrasound are the first-line imaging investigations in women with breast symptoms. Magnetic resonance imaging (MRI) is established as an adjunctive diagnostic tool because of its high sensitivity for invasive breast cancer. Percutaneous image-guided breast biopsy is used for the pathological assessment of breast lesions. The combination of imaging, clinical examination and needle biopsy—known as 'triple assessment'—is the expected standard for breast diagnosis.

MAMMOGRAPHIC TECHNIQUES

Digital mammography, producing a two-dimensional (2D) radiographic view of the breast, remains one of the principal imaging modalities for diagnosis. Advanced mammographic applications also have been developed to produce pseudo 3D imaging of the breast in the form of digital breast tomosynthesis (DBT) and to introduce an element of functional imaging with contrast-enhanced spectral mammography (CESM).

The main indications for mammography are in women over the age of 40 to evaluate breast symptoms and signs, including masses, skin thickening, deformity, nipple retraction, nipple discharge and nipple eczema. It is the primary technique for breast cancer screening and for follow-up of patients with previously treated breast cancer. It can also be used to guide biopsy and preoperative localisation procedures.

Mammography places stringent demands on equipment and image quality. The breast is composed predominantly of fatty tissue and has a relatively narrow range of inherent densities. Consequently, special x-ray tubes are required to produce the low-energy radiation necessary to achieve high tissue contrast, enabling the demonstration of small changes in breast density. High spatial resolution is required to identify tiny structures within the breast, such as microcalcifications measuring in the order of 100 μm; and short exposure times are necessary to limit movement unsharpness. Where the breasts are thicker or are composed of denser glandular tissue, higher energy radiation is required, although the radiation dose must be kept to a minimum.

X-ray tubes produce a spectrum of radiation energies, which are determined by the target and filter combination and the peak kilovoltage (kVp). A molybdenum target is used because it produces a low-energy spectrum with peaks of 17.5 and 19.6 kiloelectron volts (keV), providing high contrast. A tungsten target is less desirable because it produces higher energies (Fig. 63.1). The spectrum is refined further by adding a filter to reduce the proportion of radiation above and below the desired range. Commercially available target/filter combinations include molybdenum/molybdenum, molybdenum/rhodium, rhodium/rhodium, tungsten/molybdenum and tungsten/rhodium. Molybdenum/molybdenum is the most frequently used combination.

To achieve the required spatial resolution, mammography tubes must have an extremely small focal spot, 0.3 mm for routine mammography. For magnification mammography a smaller focal spot of 0.1 mm is required. Tube current should be as high as possible in order to keep exposure times short. Movement unsharpness may occur when exposure times exceed 1 second. Grids are used routinely for all mammographic studies. These reduce scattered radiation and so increase contrast, especially in the dense or thick breast. Mammography machines have a facility for automatic selection of target/filter combination, kVp and tube current according to the breast density and the thickness of the compressed breast. In addition, automatic exposure control devices detect the amount of radiation striking the detector and terminate the exposure at a pre-set level. The detector for digital mammography is a full-field flat-panel device typically utilising amorphous silicon, selenium or silicon dioxide-based technology.

Standard Projections

There are two standard mammographic projections: a mediolateral oblique (MLO) view and a craniocaudal (CC) view (Figs 63.2 and 63.3). Correct positioning is crucial to avoid missing lesions situated at the margins of the breast. The MLO view is taken with the x-ray beam directed from superomedial to inferolateral, usually at an angle of 30 to 60 degrees, with compression applied obliquely across the chest wall, perpendicular to the long axis of the pectoralis major muscle (see

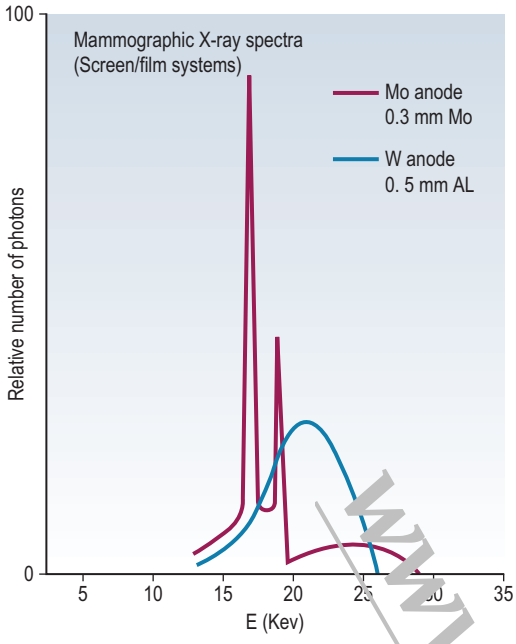

Fig. 63.1 X-ray spectra obtained from a molybdenum *(Mo)* target tube set at 29 kVp and a tungsten *(W)* target tube set at 26 kVp. (With permission from Haus AG, Metz CE, Chiles JT, Rossman K. The effect of X-ray spectra from molybdenum and tungsten target tubes on image quality in mammography. Radiology 1976;118:705–709.)

Fig. 63.3A). The MLO projection is the only projection in which all the breast tissue can be demonstrated on a single image. A well-positioned MLO view should demonstrate the inframammary angle, the nipple in profile, and the nipple positioned at the level of the lower border of the pectoralis major, with the muscle across the posterior border of the film at an angle of 25 to 30 degrees to the vertical (Fig. 63.2A).

For the CC view, the x-ray beam travels from superior to inferior. Positioning is achieved by pulling the breast up and forward away from the chest wall, with compression applied from above (Fig. 63.3B). A well-positioned CC view should demonstrate the nipple in profile. It should demonstrate virtually all of the medial tissue and most of the lateral tissue except the axillary tail of the breast. The pectoralis major is demonstrated at the centre of a CC film in approximately 30% of individuals and the depth of breast tissue demonstrated should be within 1 cm of the distance from the nipple to the pectoralis major on the MLO projection (Fig. 63.2B).

Additional Projections

Supplementary views may be taken to solve specific diagnostic problems. For example, the CC view can be rotated to visualise either more of the lateral or medial aspect of the breast, compared with the standard CC projection. Localised compression or 'paddle views' can be performed. This involves the application of more vigorous compression to a localised area using a compression paddle (Fig. 63.4A and B). These views are used to distinguish real lesions from superimposition of normal tissues and to define the margins of a mass. A true lateral view may be used to provide a third imaging plane in order to distinguish superimposition of normal structures from real lesions or to increase the accuracy

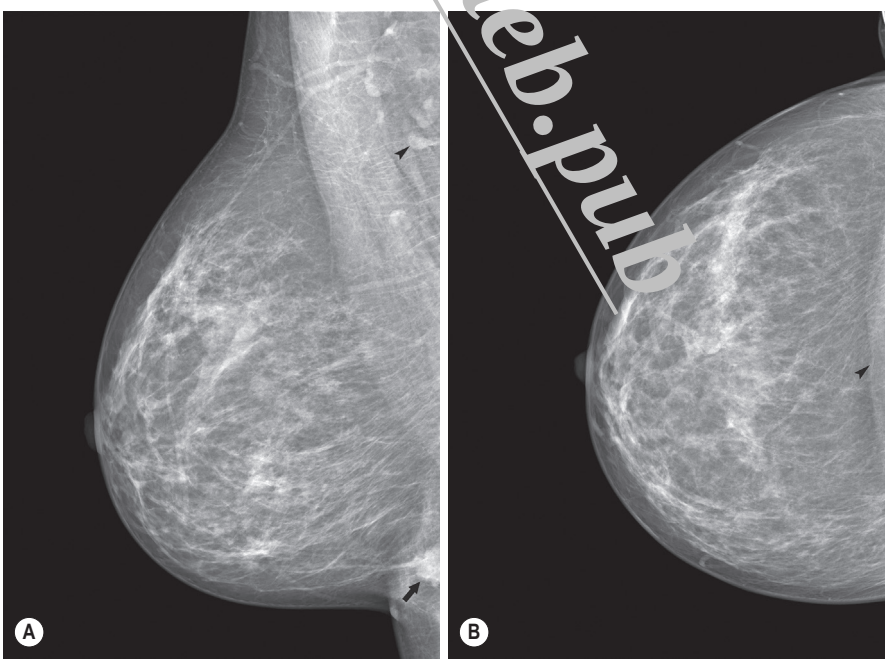

Fig. 63.2 Standard Set of Mammograms. This consists of the mediolateral oblique (MLO) view (A) and the craniocaudal (CC) view (B). (A) A cancer is seen in the inframammary area on the MLO view *(arrow)*, illustrating the importance of correct positioning to avoid missing lesions. Normal lymph nodes *(arrowhead)* are frequently seen on the MLO projection. (B) The cancer is not demonstrated on this correctly positioned CC view, with pectoral muscle visualised at the back of the mammogram *(arrowhead)*.

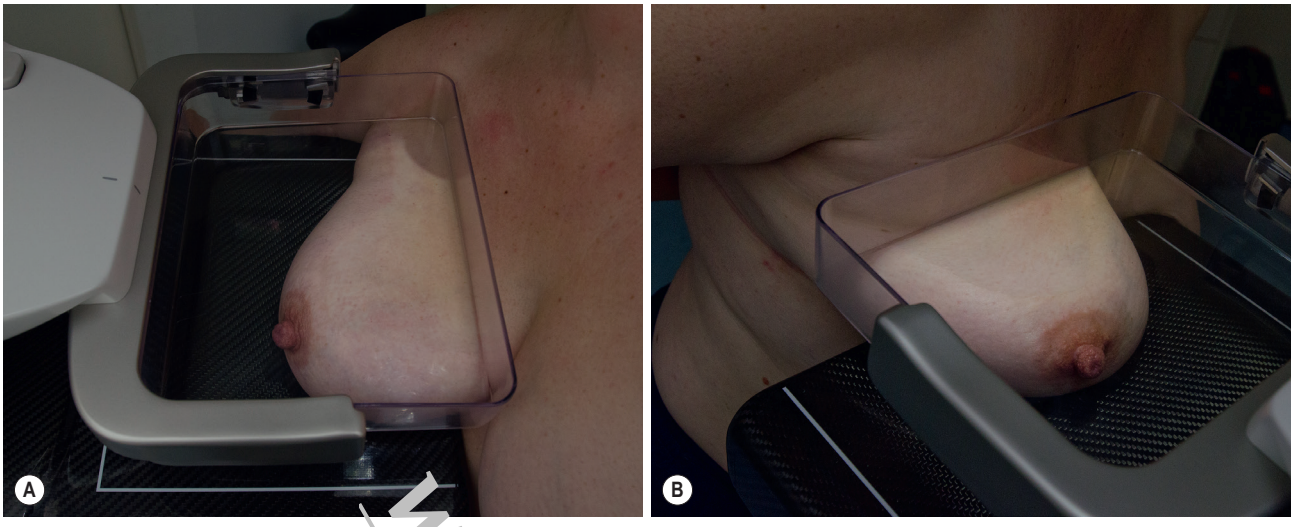

Fig. 63.3 Breast Positioning. Positioning for the (A) mediolateral oblique and (B) craniocaudal views.

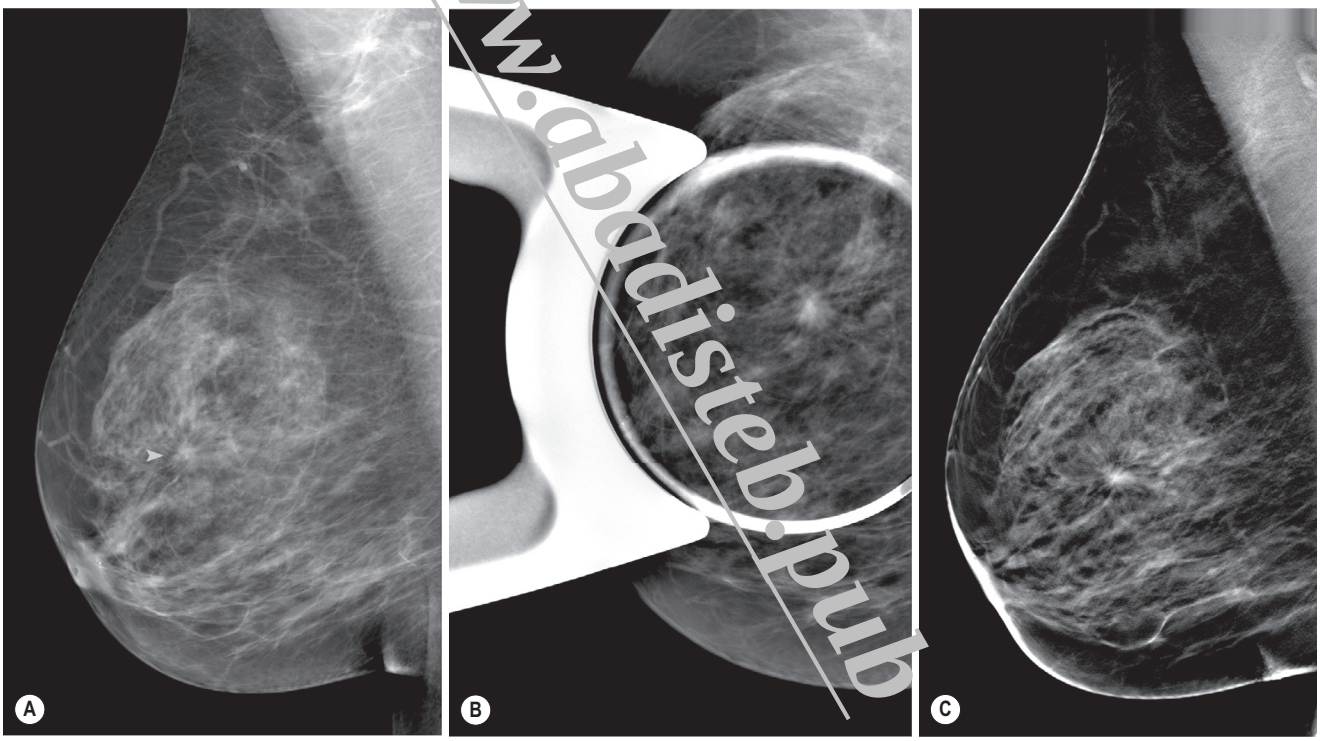

Fig. 63.4 Additional Mammographic Views. An area of concern was identified lying centrally on this mediolateral oblique mammogram (A) *(arrowhead)*. A spiculate mass is more clearly demonstrated on this 'paddle-view' (B), as well as on this single slice from a digital breast tomosynthesis study (C). A ductal carcinoma of intermediate histological grade was diagnosed on biopsy.

of wire localisations of non-palpable lesions. The true lateral view is performed with the mammography unit turned through 90 degrees and a mediolateral or lateromedial x-ray beam. Magnification views are most frequently performed to examine areas of microcalcifications within the breast, to characterise them and to establish their extent. Magnification views are typically performed in the CC and lateral projections. The magnified lateral view will demonstrate 'teacups' typical of benign microcalcifications, described later in the chapter.

Mammographic technique may need to be modified in women with breast implants. Silicon and saline implants are radio-opaque and may obscure much of the breast tissue. Consequently, mammography is of limited diagnostic value in some women. The Eklund technique can be employed to displace the implant posteriorly, behind the compression plate, maximising the volume of breast tissue that is compressed and imaged. Mammography-induced implant rupture has not been reported to date.

Breast Compression

Compression of the breast is essential for good mammography, for the following reasons:

- It reduces geometric unsharpness by bringing the object closer to the film.
- It improves contrast by reducing scatter.
- It diminishes movement unsharpness by permitting shorter exposure times and immobilising the breast.
- It reduces radiation dose, as a lesser thickness of breast tissue needs to be penetrated and scatter is reduced.
- It achieves more uniform image density: a homogeneous breast thickness prevents overexposure of the thinner anterior breast tissues and underexposure of the thicker posterior breast tissues.
- It provides more accurate assessment of the density of masses. As cysts and normal glandular tissue are more easily compressed, the more rigid carcinomas are highlighted.
- It separates superimposed breast tissues so that lesions are better seen.

Radiation Dose

Mammography uses ionising radiation to image the breast. The risks of ionising radiation are well known and any exposure needs to be justified, with doses kept as low as possible. The radiation dose for a standard two-view examination of the breast is approximately 3 mGy. The average effective dose of radiation from mammography is equivalent to 61 days of average natural background radiation. Dose is more of an issue in a population screening programme, where women who may never develop breast cancer are being exposed to radiation. It has been estimated that the risk of inducing a breast cancer in women screened in the United Kingdom National Health Service Breast Screening Programme (NHSBSP) is between 1 in 49,000 and 1 in 98,000 per visit. A risk–benefit calculation has established that the benefits of screening far outweigh the risk of inducing a cancer, with the ratio of lives saved to lives lost calculated as approximately 300:1.

Digital Breast Tomosynthesis

One of the limitations of mammography is that it produces a 2D radiographic view of what is a 3D structure and, as a consequence, cancers may not be detected due to overlapping normal glandular tissue obscuring the presence of a tumour, leading to false negative interpretations. This is a particular issue in women with a denser background glandular pattern, typically younger, pre-menopausal women, where the sensitivity of mammography for detecting malignancy may be below 50%. In addition, lesions may be simulated by the superimposition of normal tissue, leading to false positive interpretations and unnecessary recalls following screening mammography.

Breast tomosynthesis (DBT) is a digital mammographic technique which aims to alleviate these issues. It produces thin slices through the breast, reconstructed from multiple low-dose projections acquired at different angles of the x-ray tube. The resulting thin sections or thicker 'slabs' can be scrolled through or viewed in the form of a movie clip. Structures within a particular plane are more clearly visualised without interference from breast tissue in front or behind the region of interest. This alleviates the effects of tissue superimposition potentially improving the sensitivity and specificity for detecting breast cancer compared with conventional 2D mammography (Fig. 63.5).

Different manufacturers have adopted different technical parameters to produce the DBT image. The range of angles through which the x-ray tube moves ranges from 15 to 50 degrees. The tube may move in a continuous fashion or 'step and shoot' during acquisition with images reconstructed using iterative or filtered back projection techniques. The optimal system geometry is open to debate but can impact on image quality; for instance, a wider tube angle may improve depth resolution (thinner slices), but at the expense of resolution within a particular slice.

The dose for each projection from which the DBT data set is derived is very small, so the overall dose of DBT is not much more than a standard 2D mammogram. The mean glandular dose at DBT for average sized breasts is 2.3 mGy per view, which is about 1 to 1.5 times higher than conventional 2D mammography.

The role of DBT is still being defined and there is debate surrounding its use as an adjunct or replacement for conventional 2D digital mammography. It can be used as a replacement for traditional spot compression (paddle) views in the work-up of screen-detected abnormalities and equivocal mammographic findings (Fig. 63.4C), with trials demonstrating equivalent accuracy. Its use as a screening tool is also being explored.

SUMMARY BOX: Digital Breast Tomosynthesis

- DBT is a mammographic technique producing thin slice images through the breast, reducing the effects of tissue superimposition
- DBT can improve the sensitivity and specificity of breast cancer screening by increasing cancer detection rates and reducing recall rates
- DBT is replacing the traditional spot compression view in the work-up of screen detected abnormalities

DBT, Digital breast tomosynthesis.

Digital Breast Tomosynthesis in Breast Cancer Screening

The use of DBT has the potential to improve both the sensitivity and specificity of mammographic screening. Multiple retrospective reading studies of DBT have shown the ability to increase cancer detection and reduce false positives by reducing the recall rate for additional tests following a screening mammogram. The most powerful evidence for its use in a screening setting to date comes from four European prospective studies (Table 63.1). All these studies show an increase in cancer detection, ranging from 31% to 43%. The effect on recall rates

TABLE 63.1 Summary of the Evidence for the Use of Digital Breast Tomosynthesis in Breast Cancer Screening From Four European Prospective Trials

Author	Year	Manufacturer	*N*	Views	Findings
Ciatto (STORM)	2013	Hologic	7,292	2	**CDR ↑ from 5.3 to 8.1 RR ↓ by 17%**
Skaane (Oslo)	2013	Hologic	12,631	2	**CDR ↑ from 6.1 to 8.0 RR ↓ by 13%**
Lang (Malmo)	2016	Siemens	7,500	1	**CDR ↑ from 6.3 to 8.9 RR ↑ by 43%**
Bernardi (STORM2)	2016	Hologic	9,672	2	**CDR ↑ from 6.3 to 8.5 RR ↑**

CDR, Cancer detection rate; *RR*, recall rate.

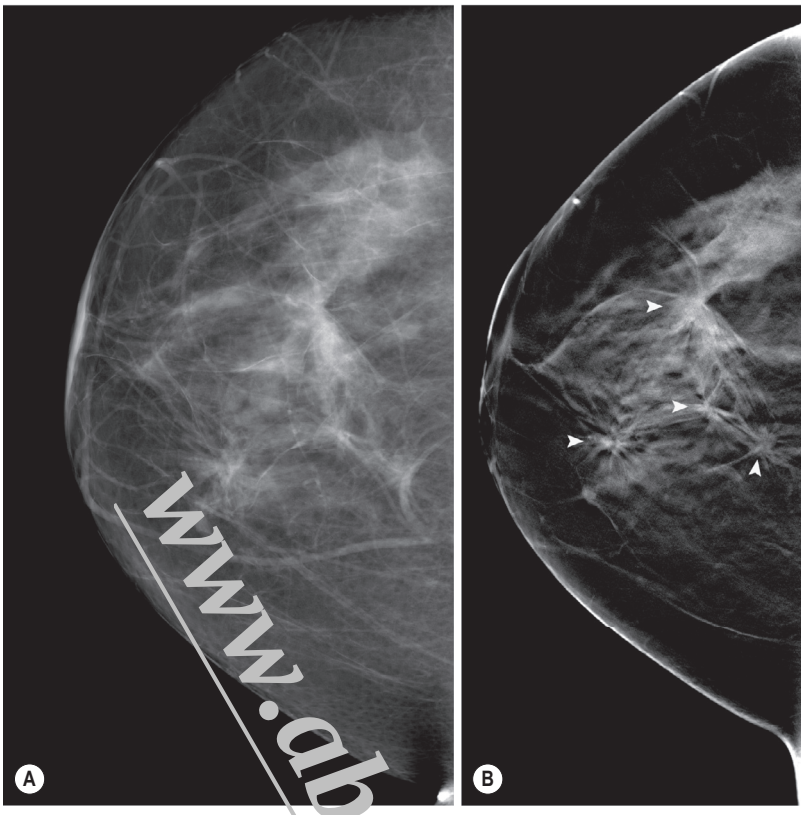

Fig. 63.5 Digital Breast Tomosynthesis. This cranio-caudal projection from a conventional 2D digital screening mammogram (A) shows several possible areas of distortion. This single slice from the digital breast tomosynthesis study (B) more clearly demonstrates four separate spiculated masses *(arrowheads)*. A diagnosis of multifocal carcinoma was made following ultrasound guided biopsies and a mastectomy was performed.

is less clear; two of the studies show a decrease and two an increase in recall rates, although all of them were performed in already very low screening recall environments where screening mammography is read by two readers (double reading). Where screening recall rates are higher, typically when single reading is the norm, recall rates often exceed 10% and the positive effect on recall rates is more dramatic. In North America, DBT screening is already being introduced into routine practice. Friedewald et al (2014) published a time series analysis from nearly half a million screening examinations across 13 centres that had already introduced DBT screening and showed an increase in cancer detection rate from 4.2 to 5.4 per 1000 women screened—a 29% increase. Recall rates fell from 10.7% to 9.1%—a 9.3% reduction.

There is plenty of enthusiasm surrounding DBT screening, but there are other issues that need to be addressed. It is possible that some of the increase in cancer detection may represent a prevalent screening round effect, with this new technology picking up small, slow-growing, less aggressive cancers, which may have been present for many years. DBT is particularly good at picking up spiculate lesions or architectural distortions, which can be associated with lower histological grade tumours. More information is needed on tumour biology to ensure that any additional cancers detected are likely to lead to survival benefits for patients, rather than representing 'over-diagnosis'. Similarly, we would expect to see a fall in cancers detected between screening rounds (interval cancers). The Oslo DBT screening trial published its interval cancer rates in February 2018, demonstrating no change after the introduction of DBT. Consequently, so far, there is insufficient evidence to be able to recommend DBT as a means of decreasing breast cancer mortality.

Even when DBT is performed, a 2D component remains an important part of the examination. It is used to facilitate the assessment of symmetry between the breasts, to aid comparison with previous mammograms and to identify the presence of microcalcifications where the evidence for detection with DBT is less robust. Most equipment has the facility to work in a 'combo' mode where DBT and 2D mammography is acquired using two separate exposures in the same breast compression. This has the effect of at least doubling the radiation dose of the whole examination, which, in an asymptomatic screening population, may not be considered acceptable. Algorithms have been developed to synthesise a 2D image from the DBT data set, producing a 2D image without the need for a separate radiation exposure. Synthetic 2D mammograms have been tested in the Oslo and STORM 2 prospective DBT screening trials demonstrating equivalent performance to conventional 2D mammography when read in conjunction with the DBT examination.

There are issues around the cost effectiveness of DBT screening. Reading times are at least double those of conventional 2D mammography, which has significant work force implications. The size of DBT data files is large. This may impact on storage and image transfer. Conventional 2D mammography equipment would need replacing or upgrading before a widespread roll out of DBT screening was possible. Randomised controlled trials (RCTs) are planned to assess DBT in screening (PROSPECTS in the UK and TMIST in North America), which will provide cost-benefit analysis and feasibility information to determine the future role of DBT screening.

Contrast Enhanced Spectral Mammography

Another approach to improve the sensitivity of conventional 2D mammography, particularly in younger patients with a dense mammographic background pattern, is to introduce iodinated contrast agent to provide an element of functional imaging. The growth of breast cancers is

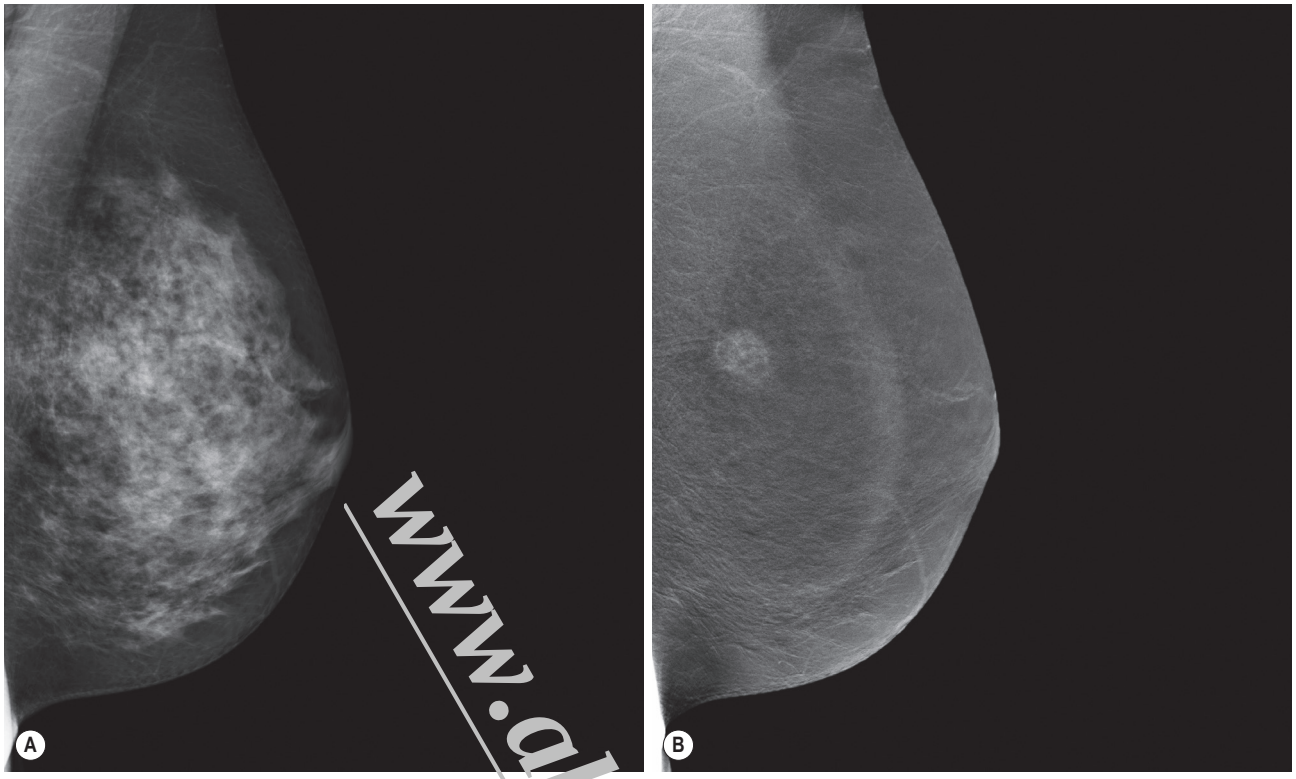

Fig. 63.6 Contrast Enhanced Spectral Mammography. The clinically palpable mass in a woman with a dense parenchymal background pattern is mammographically occult on the low energy image (A), but clearly demonstrated on the recombined image (B). A wide local excision was performed of this solitary 12 mm high-grade ductal carcinoma.

accompanied by angiogenesis, and CESM images the enhancement associated with this neo-vascularisation in a similar fashion to contrast enhanced MRI.

CESM is a mammographic technique utilising a dual-energy exposure undertaken during a single breast compression following the injection of iodinated contrast agent (1.5 mL/kg body weight). Two minutes after injection, standard MLO and CC projections are undertaken of each breast. CESM yields two sets of images, a low energy set, which is equivalent to the standard digital mammogram, and a recombined high energy set, which displays contrast uptake (Fig. 63.6). Retrospective reading studies comparing CESM with standard 2D mammography have all shown a significant improvement in the sensitivity and specificity of CESM for detecting breast carcinomas.

CESM compares favourably with MRI for the local staging of breast cancer. In several studies of women with known carcinomas, CESM approaches the sensitivity of MRI with superior specificity. It is potentially more available, cheaper and more acceptable to patients. However, there are disadvantages, with a radiation dose between 1.2 and 1.8 times that of a standard 2D mammogram, but these are well within UK and European quality assurance guidelines. In addition the administration of iodinated contrast agent carries a low risk of allergic reactions. Physiological/benign background parenchymal enhancement can be seen with CESM in a similar manner to that observed in breast MRI. As with MRI, it is significantly associated with menopausal status, radiation therapy, hormonal treatment and breast density.

CESM has been shown to be a useful first-line imaging test in patients presenting with clinically palpable abnormalities, resulting in more accurate tumour sizing and the identification of unsuspected multifocal disease at the first clinic visit. It has been used successfully in assessing women recalled to assessment clinics following conventional 2D screening mammography, improving diagnostic accuracy and acting as a useful problem-solving tool for screening recalls. There is also interest in CESM as a potential screening tool, particularly in women who are at increased risk for breast cancer who do not meet the criteria for MRI screening.

ULTRASOUND

Ultrasound is widely used for breast imaging and is the primary technique for the assessment of breast problems in women under the age of 40. It is used to characterise palpable mass lesions in all age groups and for the further assessment of abnormalities detected on a mammogram. It is the preferred method for image-guided breast biopsy and preoperative localisations.

Breast ultrasound requires high-quality, high-resolution grey-scale imaging, using linear probes with high frequencies up to 15 MHz. Higher frequencies result in greater resolution, but as the frequency increases, the ability of the ultrasound beam to penetrate to deeper breast tissue decreases. Consequently, the frequency selected has to be appropriate for the size of the breast to be examined. Parameters, such as harmonics and compounding, are available on modern ultrasound machines and can be applied to enhance the displayed image. Their use is subject to operator preference. Techniques such as colour flow imaging (Doppler) and elastography also may have a role in lesion characterisation.

Elastography is an ultrasound technique that can provide additional information based on tissue stiffness or hardness. The concept that malignant lesions feel firmer or stiffer than the surrounding breast tissue is well recognised from clinical palpation. There are two methods of producing an elastography image or elastogram: strain elastography, where the operator gently manually compresses the breast tissue, and shear wave elastography (SWE), where pulses are generated by the

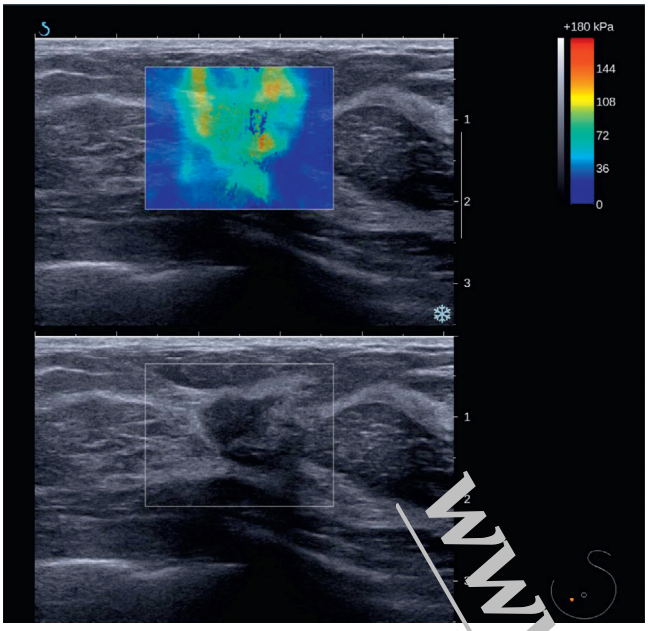

Fig. 63.7 Elastography. A hypoechoic mass is demonstrated in the left breast. Shear wave elastography is displayed simultaneously as a colour overlay. The colour scale is seen to the right and set to a maximum of 180 kPa. The zone of stiffness is larger, irregular and heterogeneous, with elasticity values in the yellow to red end of the spectrum (108–180 kPa). All these features are suspicious of malignancy, with biopsy confirming an invasive ductal carcinoma.

transducer producing transverse shear wave propagation through the breast tissue. The main advantage of SWE is that the technique is quantitative and highly reproducible. Information regarding stiffness can be displayed as a black and white or colour overlay onto the grey-scale image (Fig. 63.7). Features on the elastogram that can be measured include quantitative elasticity (stiffness) in kPa and size ratios relative to conventional grey-scale imaging. In general, breast cancers tend to be stiff, with benign lesions or normal tissue appearing softer (elasticity <80 kPa). Invasive breast cancers often produce areas of stiffness that are larger than the grey-scale abnormality, likely due to changes in the tumour-associated stroma. Elastography has the potential to improve the specificity of breast ultrasound for differentiating benign from malignant masses, reducing the number of benign biopsies. In the BE1 multinational study, the use of SWE resulted in a significant improvement in the specificity of breast mass assessment from 61.1% to 78.5%. The stiffness of cancers has been shown to be related to their aggressiveness. High stiffness has been shown to be associated with high histological grade, nodal metastases and resistance to neo-adjuvant chemotherapy.

Ultrasound Technique

The patient is examined in the supine position with the ipsilateral arm placed behind the patient's head. When imaging the outer portion of the breast it helps to turn the patient into a more oblique position. The aim is to flatten the breast tissue against the chest wall, reducing the thickness of breast tissue to be imaged. It is best to image the breast tissue in two planes perpendicular to each other. A transverse plane and a sagittal plane are a common combination, but some authors advocate examining the breast in a radial and anti-radial direction. The theory behind this method is that the ducts of the breast are positioned in a radial direction, running towards the nipple rather like the spokes of a bicycle wheel. Most breast cancers begin in the ducts and so tumours extending along the ductal system may be better visualised in this plane.

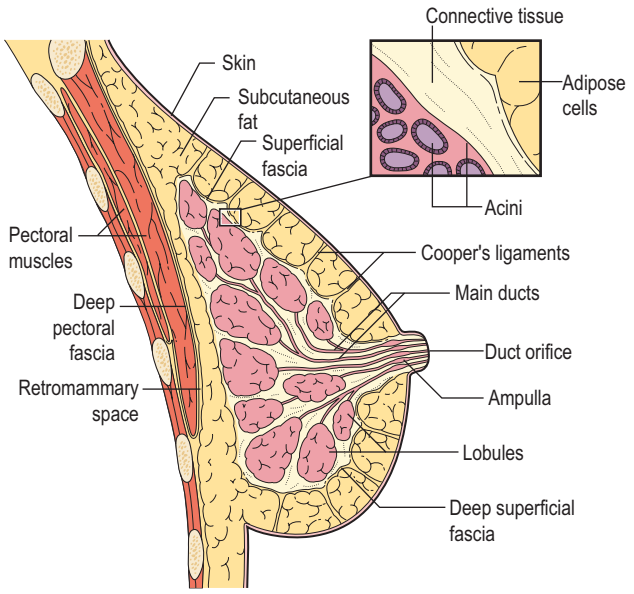

Fig. 63.8 Gross Anatomy of the Breast.

NORMAL BREAST ANATOMY

The breast lies on the chest wall on the deep pectoral fascia, with the superficial pectoral fascia enveloping the breast. Suspensory ligaments—Cooper's ligaments—connect the two layers, providing a degree of support to the breast and giving the breast its shape (Fig. 63.8). Centrally, there is the nipple-areolar complex. Collecting ducts open onto the tip of the nipple. There are sebaceous glands within the nipple-areolar complex called Montgomery's glands. Small raised nodular structures called Morgagni's tubercles are distributed over the areola, representing the openings of the ducts of Montgomery's glands onto the skin surface. Deep to the nipple-areolar complex, the breast is divided into 15 to 25 lobes, each consisting of a branching duct system leading from the collecting ducts to the terminal duct lobular units (TDLUs), the site of milk production in the lactating breast. The number of TDLUs per lobe varies according to age, lactation, parity and hormonal status. At the end of reproductive life there is an increase in the amount of adipose tissue and, although the main duct system is preserved, there is considerable loss of lobular units. These changes in breast composition are manifested by changes in the breast density on mammography. Younger women will typically have denser background patterns, with density decreasing in older women as the denser glandular tissue is replaced by fat.

Breast density is an independent risk factor for breast cancer with a dense background pattern associated with a higher risk of developing breast cancer and more aggressive tumour characteristics. The mechanism through which increased density contributes to breast cancer risk remains unclear, but is likely to reflect increased cellular populations and turnover, resulting in a higher mutational load. Stromal cells, which have a key role in promoting carcinogenesis, have been shown to be activated in women with dense breasts but not in women with fatty breasts. In addition, dense breast tissue may hide abnormalities in the breast, making cancer detection more difficult. There is increasing awareness of the risk associated with denser glandular background patterns. Most states in the USA now mandate the reporting of breast density in women attending for screening mammography. Most radiologists make a subjective visual assessment of breast density on a mammogram, although automated computerised systems have been developed to try and quantify

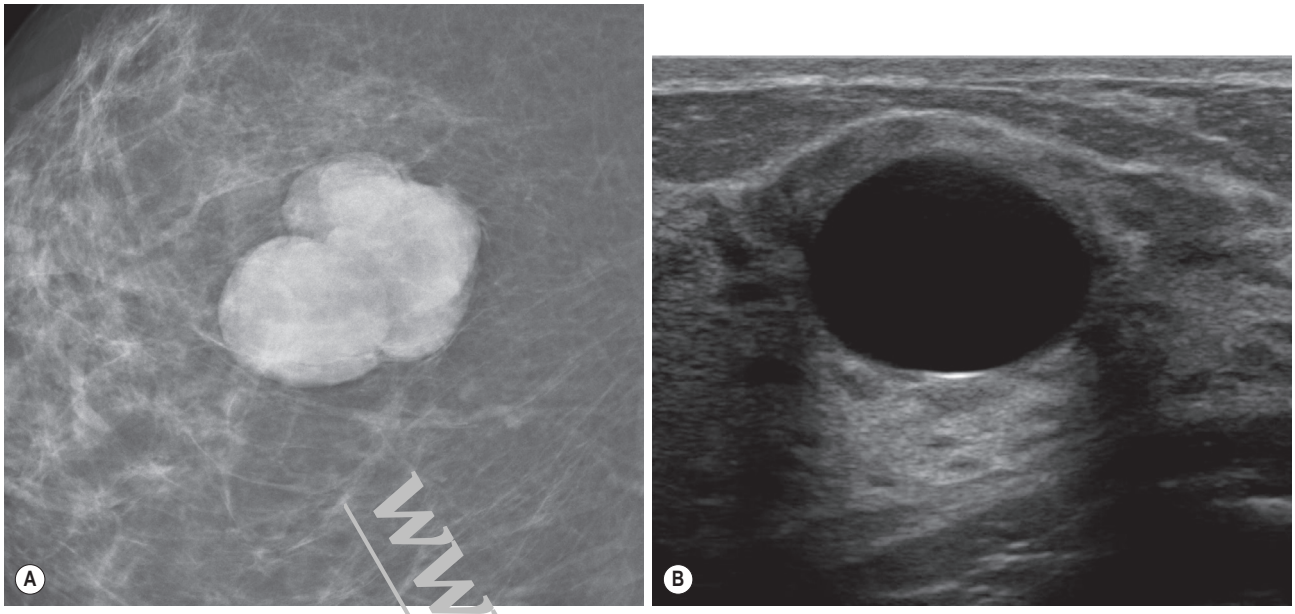

Fig. 63.9 Cyst. (A) A well-defined rounded mass, with an associated lucent halo typical of a cyst. (B) The absence of internal echoes and the posterior enhancement of the ultrasound beam are diagnostic of a cyst.

density in a more objective and reproducible way. The American College of Radiology (ACR) breast imaging reporting and data system (BI-RADS) lexicon defines four patterns of increasing density, where 1 is almost entirely fatty and 4 is extremely dense. Typically, 10% of women will fall into the entirely fatty group and 10% into the extremely dense group. Women with the densest background pattern have a 4- to 6-times increased risk of breast cancer compared with those with the almost entirely fatty background pattern. In the future, breast density could be combined with family history, reproductive history and information from blood tests (single nuclear polymorphisms) to enable a more individualised stratification of risk. There is controversy around the role of supplementary screening for women at increased risk and uncertainty as to the imaging technique to offer. Whole breast ultrasound, MRI, tomosynthesis and contrast-enhanced mammography are all being considered and investigated, potentially leading to a more personalised approach to screening.

BREAST PATHOLOGY

Benign Lesions With Mass Effect

Cysts

Cysts are the most common cause of a discrete breast mass, although they are often multiple and bilateral. They are common between the ages of 20 and 50 years, with a peak incidence between 40 and 50 years. Simple cysts are not associated with an increased risk of malignancy and have no malignant potential. On mammography they are seen as well-defined, round or oval masses (Fig. 63.9A). Sometimes a characteristic halo is visible on mammography. Ultrasound also demonstrates well-defined margins, with an oval or round shape. There is an absence of internal echoes indicating the presence of fluid. The area of breast tissue behind a cyst appears bright on ultrasound (posterior enhancement) due to improved transmission of the ultrasound beam through the cyst fluid (Fig. 63.9B). When these features are present, a cyst can be diagnosed with certainty. Aspiration is easily performed under ultrasound guidance to alleviate symptoms or when there is diagnostic uncertainty. Cytology on cyst fluid is not routinely performed unless there are atypical imaging features or the aspirate is bloodstained.

Fibroadenomas and Related Conditions

Fibroadenomas are the most common cause of a benign solid mass in the breast. They present clinically as smooth, well-demarcated, mobile lumps. They are most frequently encountered in younger women with a peak incidence in the third decade. With the advent of screening, many previously asymptomatic lesions are detected. On mammography, fibroadenomas are seen as well-defined, rounded or oval masses (Fig. 63.10A). Coarse calcifications may develop within fibroadenomas, particularly in older women.

Ultrasound features have been described that are characteristic of benign masses. These include hyper-echogenicity compared with fat, an oval well-circumscribed lobulated or gently curving shape and the presence of a thin echogenic pseudocapsule. If these features are present with no features suggestive of malignancy, then a mass can be confidently classified as benign. Many of these features are demonstrated by fibroadenomas (Fig. 63.10B). Most fibroadenomas are isoechoic or mildly hypoechoic relative to fat, with an oval shape and lobulated contour. A thin echogenic pseudocapsule may be seen. Percutaneous biopsy may be avoided in women under the age of 30, where the risks of any mass being malignant are very small; however, in other cases, even though the mass appears benign, percutaneous biopsy is undertaken to confirm the diagnosis.

Fibroadenomas must be distinguished from well-circumscribed carcinomas; this is done by percutaneous biopsy. Phyllodes tumour can also have a similar appearance to fibroadenoma, leading to diagnostic difficulties (Fig. 63.11). The pathological characteristics can also be similar to those of large fibroadenomas. Most phyllodes tumours are benign, but some (<25%) are locally aggressive and may even metastasise. When a diagnosis of phyllodes tumour is made, surgical excision must be complete with clear margins to prevent the possibility of recurrence. Many larger fibroadenomas (over 3 cm) and those that show a rapid increase in size are excised in order to avoid missing a phyllodes tumour.

Papilloma

Papillomas are benign neoplasms, arising in a duct, either centrally or peripherally within the breast. Many papillomas secrete watery material, leading to a nipple discharge. They are often friable and bleed easily,

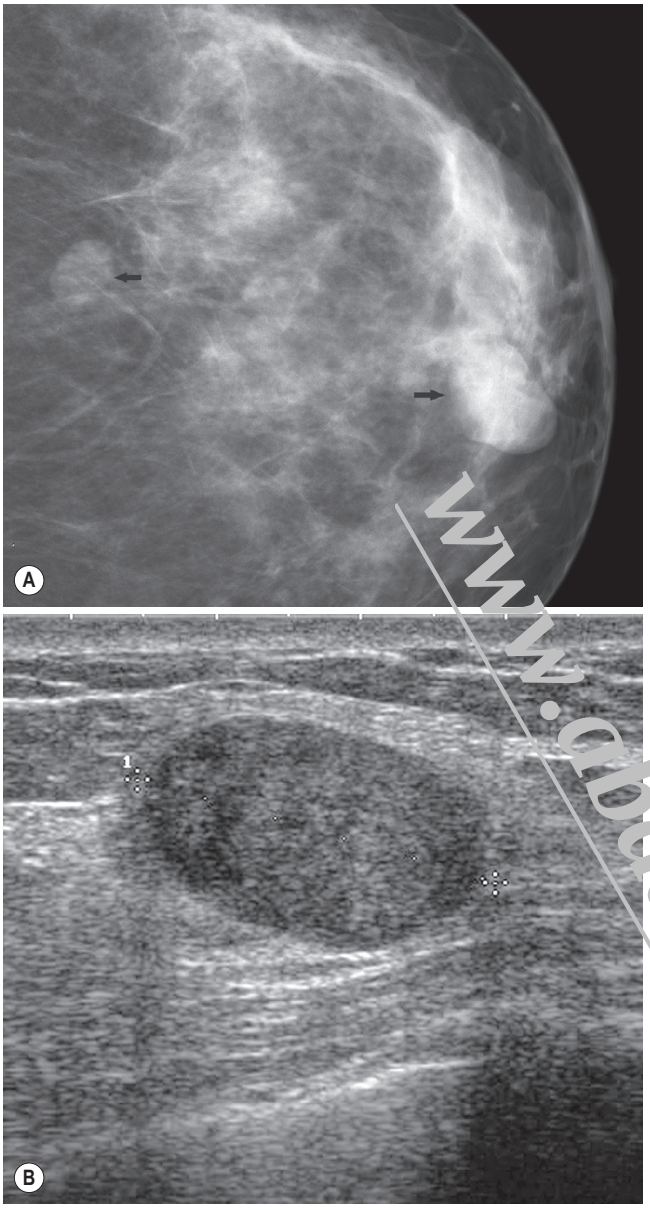

Fig. 63.10 Fibroadenoma. (A) Two well-defined masses on mammography *(arrows)*. (B) Ultrasound of the lesion nearer the nipple showed a well-defined oval mass. Both lesions were confirmed as fibroadenomas on ultrasound-guided core biopsy.

so the discharge may become bloodstained. On mammography, they are most commonly seen as a well-defined mass, in a retroareolar location, and may be multiple in number (Fig. 63.12A). Sometimes the mass is associated with microcalcifications. On ultrasound, they typically appear as a filling defect within a dilated duct or cyst (Fig. 63.12B). On aspiration, any cystic component may be bloodstained. Papillomas may be associated with cellular atypia in which case they carry an increased risk of malignancy, particularly if they are multiple or occur in a more peripheral location within the breast. As it is impossible to differentiate papillomas from papillary carcinomas on imaging criteria, percutaneous biopsy is required. Excision of papillary lesions may be therapeutic in cases of nipple discharge and desirable when associated with atypia. In situations where percutaneous biopsy shows no evidence of cellular atypia, an alternative to surgical excision is piecemeal percutaneous excision using a vacuum-assisted biopsy (VAB) device.

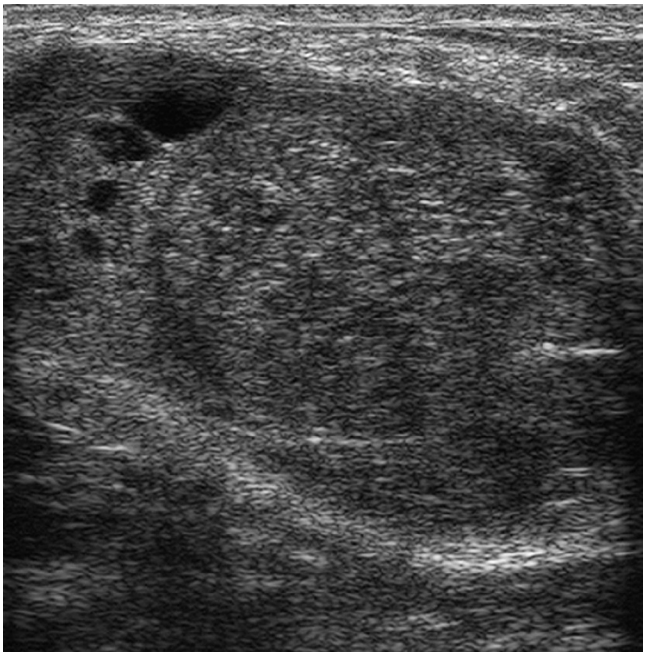

Fig. 63.11 Phyllodes Tumour. The presence of several cystic spaces within this large, well-defined mass suggested the possibility of a phyllodes tumour. This was confirmed on core biopsy and surgical excision.

Lipoma

Lipomas are benign tumours composed of fat. They present clinically as soft, lobulated masses. Large lipomas may be visible on mammography as a radiolucent mass (Fig. 63.13A). On ultrasound their characteristic appearance is that of a well-defined lesion, hyperechoic compared with the adjacent fat (see Fig. 63.13B).

Hamartoma

Hamartomas are benign breast masses composed of lobular structures, stroma and adipose tissue—the components that make up normal breast tissue. They occur at any age. On imaging they may be indistinguishable from other benign masses, such as fibroadenomas. Sometimes large hamartomas are detected on screening mammograms and are impalpable. On mammography they classically appear as large, well-circumscribed masses containing a mixture of dense and lucent areas, reflecting the different tissue components present (Fig. 63.14). Diagnostic difficulty may be encountered because percutaneous biopsy specimens may be reported as normal breast tissue.

Invasive Carcinoma

Breast carcinomas originate in the epithelial cells that line the TDLU. When malignant cells have extended across the basement membrane of the TDLU into the surrounding normal breast tissue, the carcinoma is invasive. Malignant cells contained by the basement membrane are termed non-invasive or in situ.

Classification of Invasive Breast Cancer

There is much confusion regarding the classification of breast cancer. Some tumours show distinct patterns of growth, allowing certain subtypes of breast cancer to be identified. Those with specific features are called invasive carcinoma of special type, while the remainder are considered to be of no special type (NST or ductal NST). Special-type tumours include lobular, medullary, tubular, tubular mixed, mucinous, cribriform and papillary. Different types of tumour have different clinical patterns

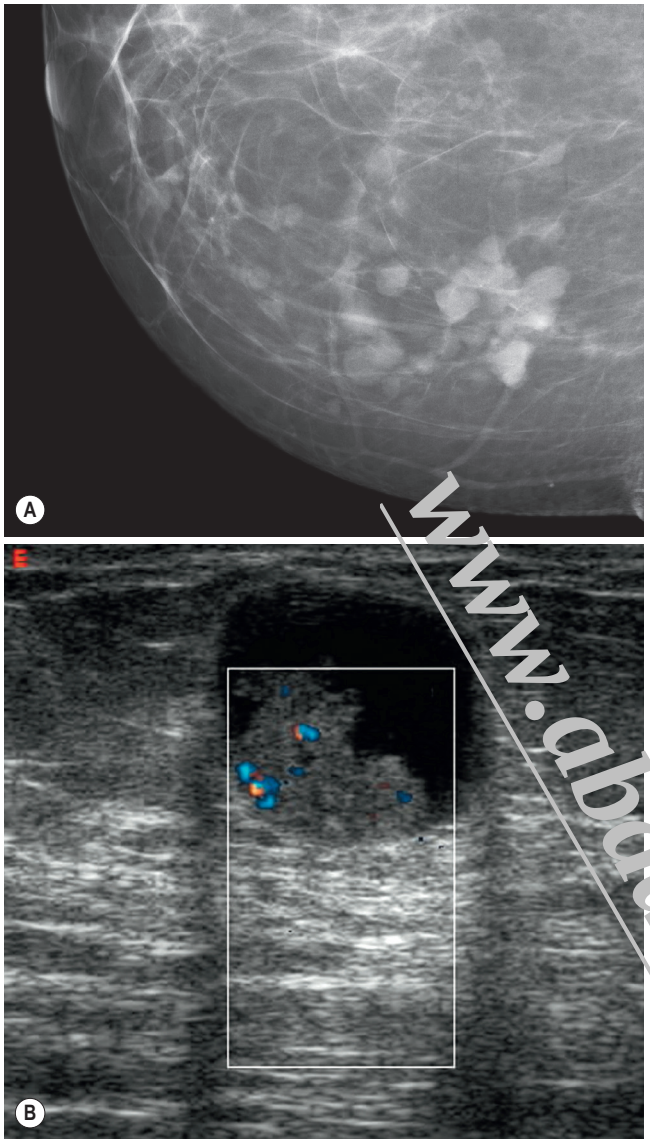

Fig. 63.12 Multiple Small Papillomas. (A) Papillomas are frequently well defined on mammography, although part of the mass may have an irregular or ill-defined contour. (B) On ultrasound, the presence of a filling defect within a cystic structure suggests the diagnosis. Colour Doppler can be useful for distinguishing debris within a cyst from a soft-tissue mass.

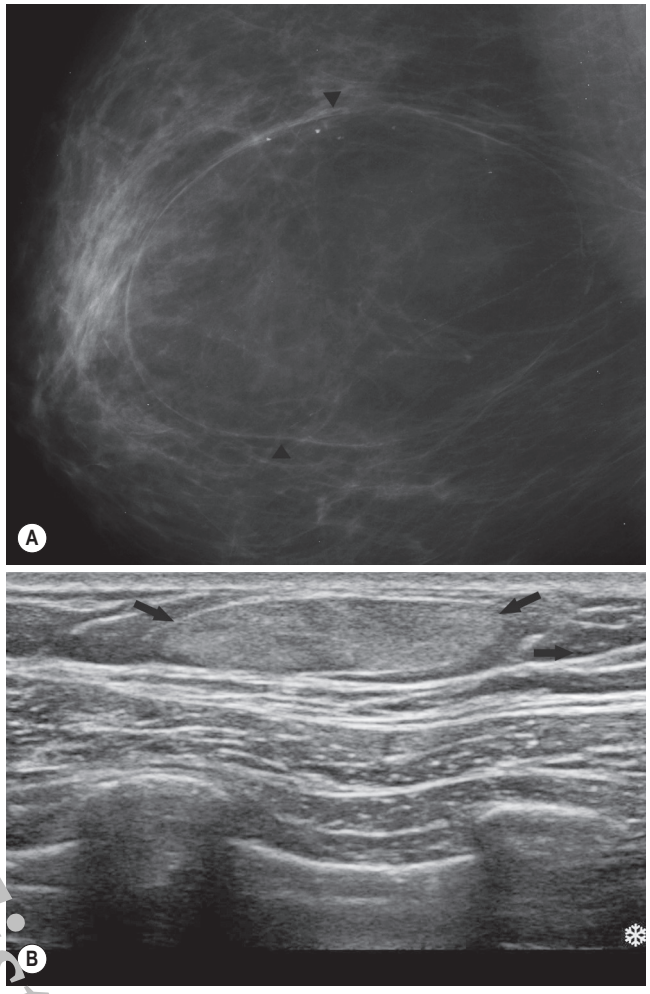

Fig. 63.13 Lipoma. (A) On mammography, a lipoma may be seen as a well-defined mass of fat density, contained within a thin capsule *(arrowheads)*. (B) On ultrasound, a well-defined hyperechoic lesion characteristic of a lipoma is seen *(arrows)*.

of behaviour and prognosis. It should be understood that when a tumour is classified as of a special type this does not imply a specific cell of origin, but rather a recognisable morphological pattern.

Histological grade has implications for tumour behaviour, imaging appearances and prognosis. The morphological features on which histological grade is based are tubule formation, nuclear pleomorphism and frequency of mitoses. Low-grade tumours that are well differentiated grow slowly and are less likely to metastasise.

More recently breast cancer has been increasingly classified according to its immunophenotype. Luminal cancers are positive for oestrogen (ER) and progesterone receptors (PR) while being negative for human epidermal growth factor-2 (HER-2). The luminal group is often split into A and B sub-groups depending on the cellular proliferation rate measured by the presence of the Ki67. The presence of the Ki67 protein identifies a high proliferative subset of women who derive greater benefit from chemotherapy. HER-2 positive cancers are a separate group often treated with anti HER-2 agents such as Herceptin, while triple negative tumours (ER, PR and HER-2 receptor negative) are a particularly aggressive subgroup.

Imaging Appearance of Invasive Breast Cancer

Mammography. Carcinomas typically appear as ill-defined or spiculated masses on mammography (Fig. 63.15A and B). Lower-grade cancers tend to be seen as spiculated masses, due to the presence of an associated desmoplastic reaction in the adjacent stroma. Higher-grade tumours are usually seen as an ill-defined mass, but sometimes a rapidly growing triple negative tumour may appear relatively well defined, with similar appearances to a benign lesion such as a fibroadenoma (Fig. 63.15C). Many breast cancers arise from areas of ductal carcinoma in situ (DCIS) and are associated with microcalcifications on mammography (Fig. 63.15A). This is particularly true for high-grade HER-2 positive invasive ductal carcinomas that are often associated with high-grade DCIS.

Special-type tumours can have particular mammographic characteristics. Lobular carcinomas can be difficult to perceive on a mammogram due to their tendency to diffusely infiltrate fatty tissue. Compared with ductal NST tumours, lobular cancers are more likely to be seen on

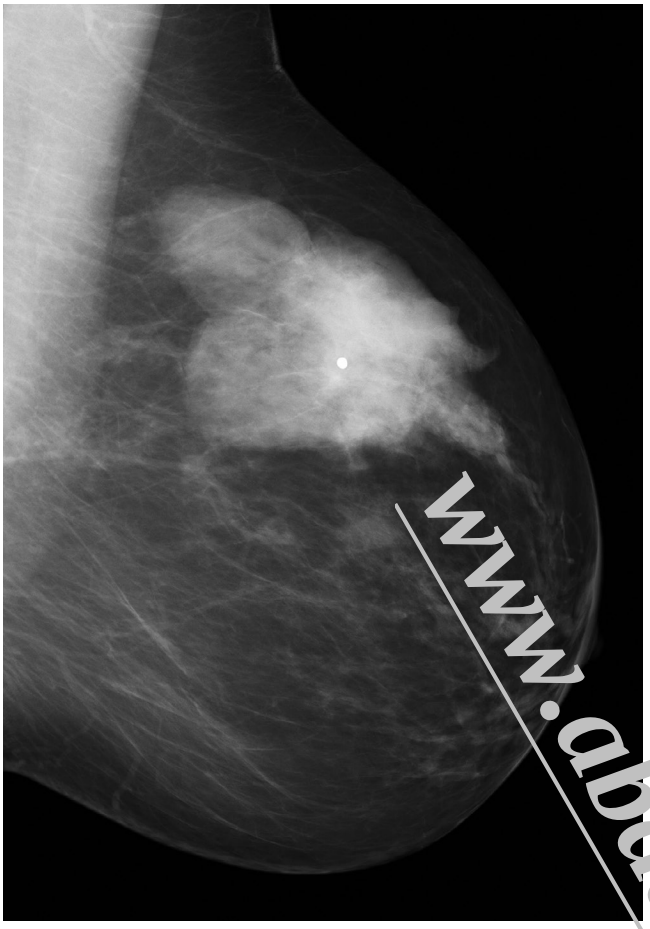

Fig. 63.14 Hamartoma. Hamartomas are frequently encountered on screening mammograms as large, lobulated masses with areas of varying density reflecting the presence of elements that are of fat and soft-tissue density.

only one mammographic view, are less likely to be associated with microcalcifications and are more often seen as an ill-defined mass or an area of asymmetrically dense breast tissue. Tubular and cribriform cancers often present as architectural distortions or small spiculated masses. Papillary, mucinous and medullary neoplasms may appear as new or enlarging multi-lobulated masses and may be well defined, simulating an apparently benign lesion. Inflammatory breast cancer is a particularly aggressive form of cancer, which presents clinically with breast enlargement, redness, pain and peau d'orange. On mammography, skin and trabecular thickening is seen with or without an underlying mass.

Sometimes the only clue to the presence of an invasive tumour may be abnormal trabecular markings, known as an architectural distortion, or the presence of microcalcifications, which tend to be visible even when the breast parenchyma is dense. The ability to perceive small or subtle cancers on a mammogram is improved by having the two standard mammographic views available and seeking out previous studies for comparison. An increase in the size of a mass or the presence of a new mass is suspicious of malignancy, whereas a lesion that remains unchanged over many years is invariably benign. Multiple masses in both breasts would favour a benign disease such as cysts or fibroadenomas.

Ultrasound. There are characteristic malignant features on ultrasound:

- Carcinomas are seen as ill-defined masses and are markedly hypoechoic compared with the surrounding fat (Fig. 63.16A).
- Carcinomas tend to be taller than they are wide (the anterior to posterior dimension is greater than the transverse diameter).
- There may be an ill-defined echogenic halo around the lesion, particularly around the lateral margins, and distortion of the adjacent breast tissue may be apparent, analogous to spiculation on the mammogram.
- Posterior acoustic shadowing is frequently observed, due to a reduction in the through transmission of the ultrasound beam in dense tumour tissue.
- Poorly differentiated, high-grade tumours are more likely to be well defined, without acoustic shadowing (Fig. 63.16B); hence, the importance

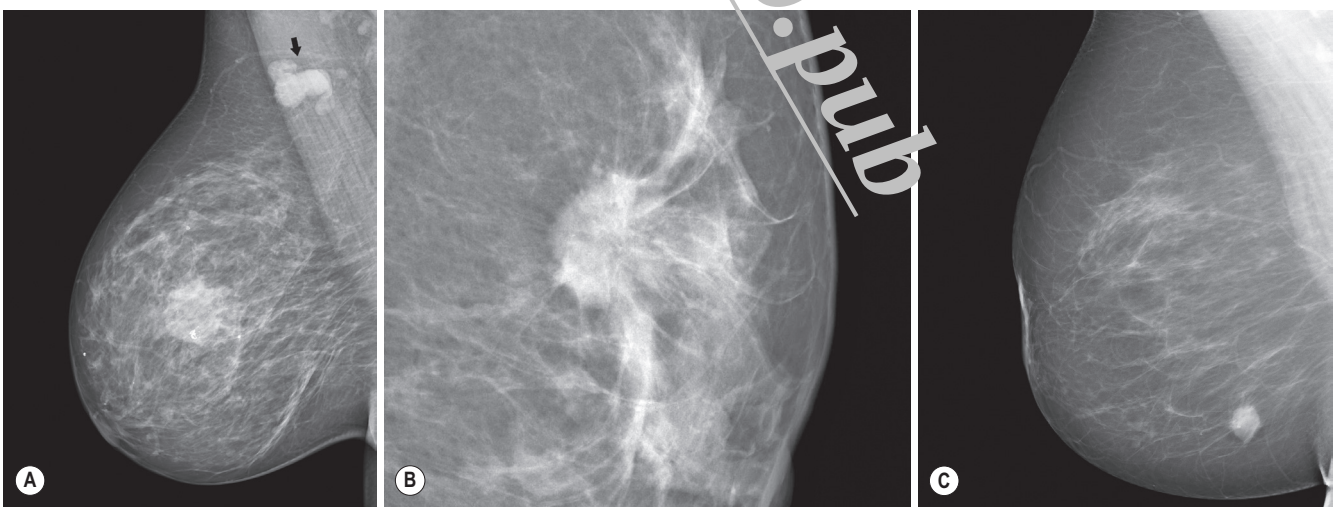

Fig. 63.15 Mammographic Appearances of Invasive Carcinoma. Ill-defined and spiculate masses are typical of malignancy. (A) There is an ill-defined mass lying centrally in the right breast, containing some microcalcifications. Calcifications, representing DCIS, may be found in association with invasive carcinoma. There are also several enlarged lymph nodes in the axilla *(arrows)* which were proven to contain tumour on ultrasound-guided biopsy. (B) A spiculate mass that proved to be a ductal NST tumour of intermediate histological grade on ultrasound-guided biopsy. (C) Sometimes high-grade tumours that exhibit rapid growth may appear well defined.

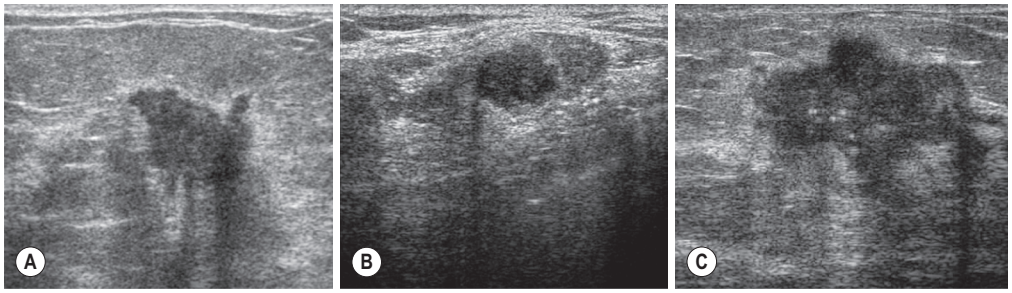

Fig. 63.16 Ultrasound Appearances of Invasive Carcinoma. (A) This irregular hypoechoic mass with acoustic shadowing and an echogenic halo is typical of a carcinoma. (B) Occasionally, high-grade tumours may appear well defined, mimicking benign lesions. This shows the importance of performing a core biopsy even on apparently benign-appearing lesions with mass effect. (C) Small echogenic foci of microcalcification associated with malignant lesions may be identified.

of carrying out a biopsy of solid masses even when the ultrasound appearances are benign. Microcalcifications are sometimes observed, and are associated with high-grade tumours arising in areas of DCIS, although this is less frequently encountered than with mammography (Fig. 63.16C). Lobular carcinomas can be difficult to demonstrate on ultrasound. They may produce vague abnormalities, such as subtle alterations in echotexture, or the ultrasound findings may even be normal. Doppler imaging and elastography can help differentiate benign from malignant masses. Doppler may show abnormal vessels that are irregular and centrally penetrating in a malignant mass. Conversely, benign lesions, such as fibroadenomas, tend to show displacement of normal vessels around the edge of a lesion. Elastography of malignant lesions tends to demonstrate areas of increased elasticity, with the area of increased tissue stiffness larger than the grey-scale abnormality (Fig. 63.7).

Ultrasound is a useful tool in the local staging of breast cancer within the breast and the axilla. It tends to be a better predictor of tumour size compared with mammography and may detect intraductal tumour extension or unsuspected multifocal disease not visible on a mammogram. It has long been recognised that involvement of axillary lymph nodes is one of the most important prognostic factors for women with breast cancer. Traditionally, the axilla has been staged at the time of surgery by lymph node sampling procedures, sentinel node biopsy or clearance of the axillary lymph nodes. Surgical clearance of axillary lymph nodes carries the risk of significant postoperative morbidity, with some women developing disabling lymphoedema in the arm. Ultrasound can identify abnormal nodes preoperatively that can then be biopsied percutaneously under ultrasound guidance (Fig. 63.17A,B), allowing a preoperative diagnosis of lymph node involvement to be made in just over 40% of patients who are lymph node positive. Accurate preoperative staging of the axilla with ultrasound enables axillary clearance to be targeted to those patients with a preoperative diagnosis of axillary disease, with the sampling or sentinel node procedures reserved for those patients with a much lower risk of axillary involvement. In recent years, the need for performing an axillary clearance on all node positive axilla has been challenged and is being investigated by the UK POSNOC trial. Consequently, the need for aggressive preoperative diagnosis of all node positive axillae has been called into question.

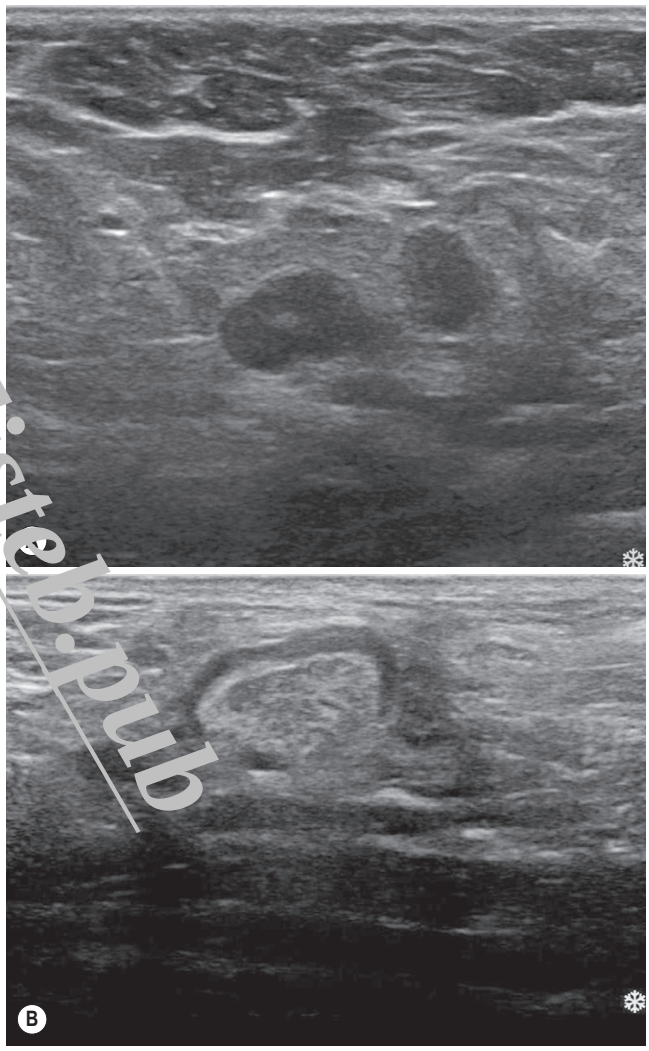

Fig. 63.17 Axillary Lymph Nodes. Axillary lymph nodes can be assessed on the basis of shape and the morphology of the cortex. (A) Nodes are likely to contain tumour if their longitudinal-to-transverse diameter ratio is less than 2 (the node appears round rather than oval). Nodes are more likely to contain tumour if the cortex is thickened to more than 2 mm. (B) This node has a normal shape, but the cortex has a thickness of 3 mm. Ultrasound-guided biopsy showed a tumour containing lymph nodes in both cases.

The Differential Diagnosis of Malignancy

Many apparently suspicious findings seen on mammography or ultrasound can be caused by benign disease or even normal breast tissue. Superimposition of normal breast tissue may produce apparent masses, distortions or worrying asymmetric densities on mammography. Whether a lesion is real or just a summation shadow can be determined by the use of localised compression views or DBT (Fig. 63.4). Ultrasound

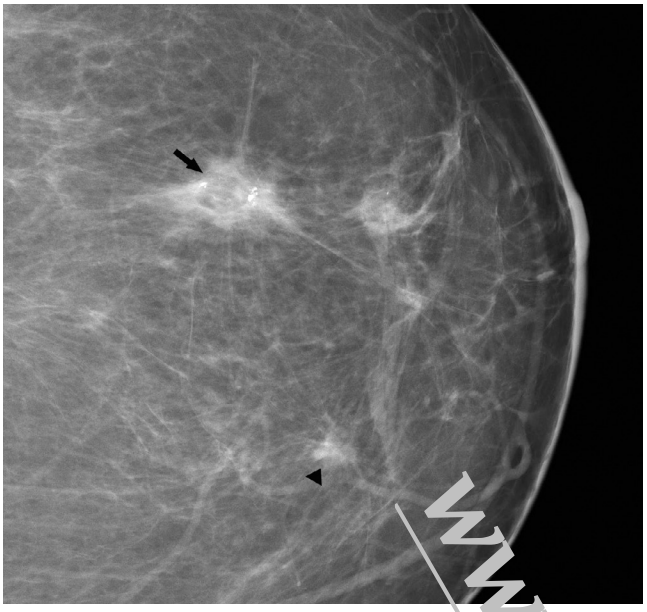

Fig. 63.18 Postoperative Scar. A surveillance mammogram on a patient who has undergone a previous wide excision for a screen-detected cancer. The surgical scar *(arrow)* contains an area of lucency and coarse calcifications indicating associated fat necrosis. A small spiculate mass is demonstrated adjacent to the surgical scar *(arrowhead)*; this was found to be a recurrent tumour on ultrasound-guided biopsy.

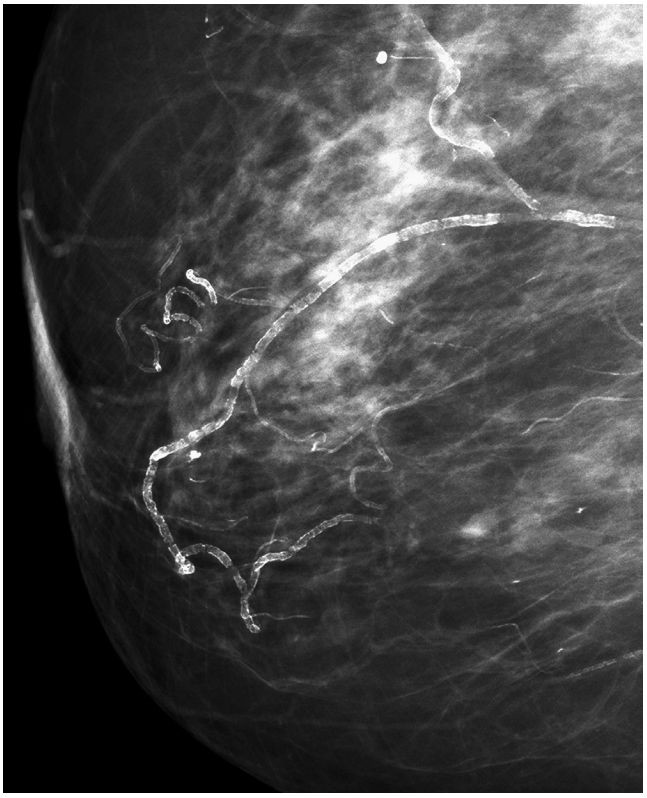

Fig. 63.19 Vascular Calcifications.

of the area of mammographic concern also can help to determine whether a lesion is truly present.

A surgical scar may result in a spiculated mass or an architectural distortion (Fig. 63.18). Radiographers should be encouraged to record the presence and position of any scars when performing a mammogram to aid image interpretation.

Radial scars, also called complex sclerosing lesions, can produce a spiculated lesion, indistinguishable from malignancy on both mammography and ultrasound. Many of these lesions are asymptomatic and are encountered on screening mammography. Epithelial atypia, DCIS and invasive carcinoma may be found in association with radial scars and so excision or wider sampling is recommended.

Infection and inflammatory processes in the breast can be mistaken for malignancy on mammography and ultrasound. Breast abscesses are typically encountered in young lactating women. Treatment is with antibiotics and aspiration of the pus, frequently under ultrasound guidance. Inflammation in a non-lactating breast is a more worrying feature, although infections and more unusual inflammatory conditions, such as granulomatous mastitis, can occur. In any case of unexplained inflammation, or when infection fails to resolve, percutaneous biopsy is required to make the diagnosis or to exclude malignancy.

Microcalcifications

Microcalcifications are frequently encountered on routine screening mammograms. In many cases these microcalcifications turn out to be benign, but occasionally are a feature of DCIS. Some calcifications have a characteristic benign appearance and require no further action. There is a considerable overlap between the appearance of benign and malignant microcalcifications, necessitating percutaneous biopsy in many cases.

Benign Microcalcifications

Many benign processes in the breast can cause microcalcifications, including fibrocystic change, duct ectasia, fat necrosis and fibroadenomatoid hyperplasia. Fibroadenomas and papillomas can also become calcified. Sometimes normal structures, such as the skin or small blood vessels, calcify. Calcifications can also develop in atrophic breast lobules or normal stroma.

Vascular calcifications have a characteristic 'tramline' appearance caused by calcification in both walls of the vessel (Fig. 63.19). Similarly, duct ectasia has a classical appearance that rarely causes diagnostic difficulty. In this condition, coarse rod and branching calcifications are recognised due to calcification of debris within dilated ducts. These calcifications have been described as having a 'broken needle' appearance and are usually bilateral (Fig. 63.20A). Sometimes the debris may extrude from the duct into the adjacent parenchyma, leading to an inflammatory-type reaction. Fat necrosis may then occur and the calcifications take on a characteristic 'lead-pipe' appearance (see Fig. 63.20B). In many cases the diagnosis is obvious, but sometimes biopsy may be required, particularly if the calcifications are unilateral or focal.

Fibrocystic change is a common cause of microcalcifications (Fig. 63.21). On a lateral magnification view, layering of calcific fluid contained within microcysts can be appreciated, producing a characteristic 'teacup' appearance. In many cases the diagnosis is less clear and percutaneous biopsy is required to exclude DCIS.

Fat necrosis is a frequently encountered cause of benign calcifications, particularly when there is a history of trauma or previous surgery (Fig. 63.22). It may present as 'egg shell' calcifications within the wall of an oil cyst or as coarse dystrophic calcifications associated with areas of scarring (Fig. 63.18). Fibroadenomas may become calcified, particularly after the menopause. Classically, the calcifications have a coarse, 'popcorn' appearance (Fig. 63.23). However, they can be small and punctate, necessitating a biopsy to establish the diagnosis. Fibroadenomatoid hyperplasia is an increasingly common cause of microcalcifications detected during screening. Histologically, there are features of a fibroadenoma and fibrocystic change. There is usually no associated lesion with mass effect, and in many cases biopsy is required to exclude DCIS (Fig. 63.24).

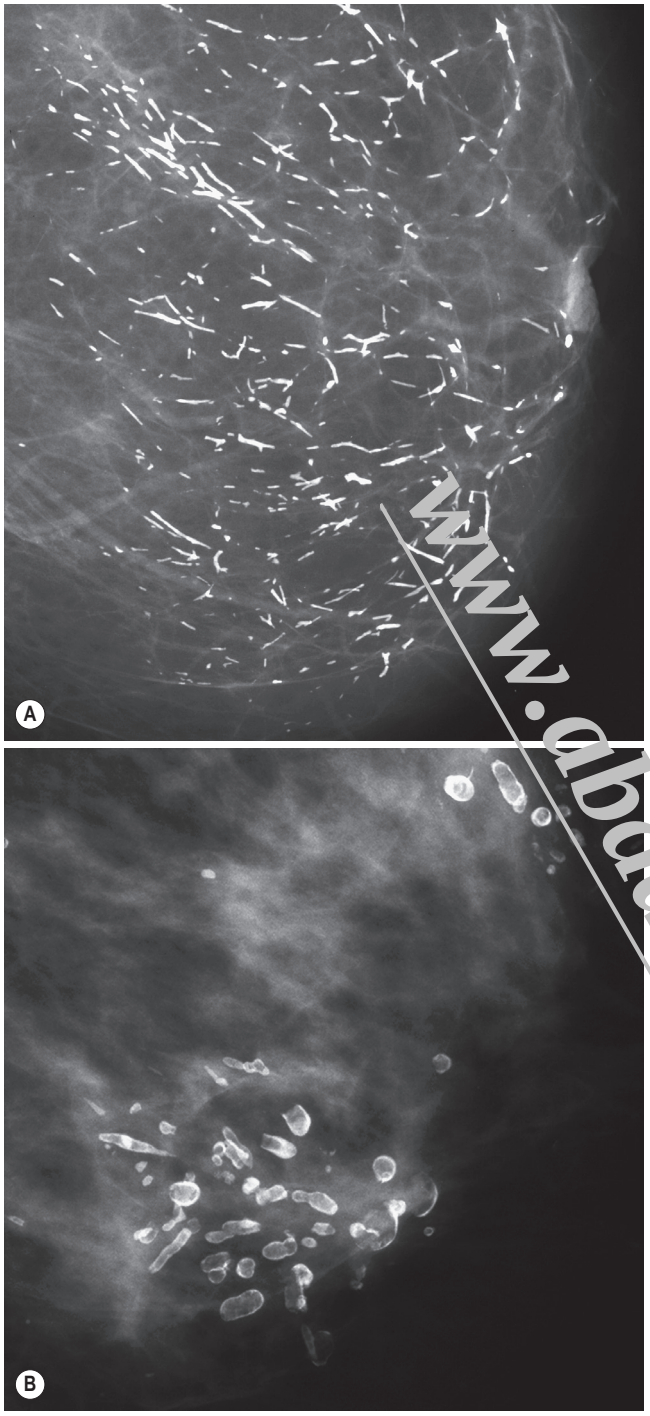

Fig. 63.20 Duct Ectasia. (A) Broken-needle appearance, typical of duct ectasia. (B) Sometimes thicker, more localised calcifications can be seen, giving a 'lead-pipe' appearance.

Skin calcifications are characteristically round, well defined, have a lucent centre and are very often bilateral and symmetrical. Talcum powder or deodorants on the skin, as well as tattoo pigments, can mimic microcalcifications.

Malignant Microcalcifications

Microcalcifications are found associated with invasive breast cancer and DCIS. Calcifications are more likely to be malignant if they are

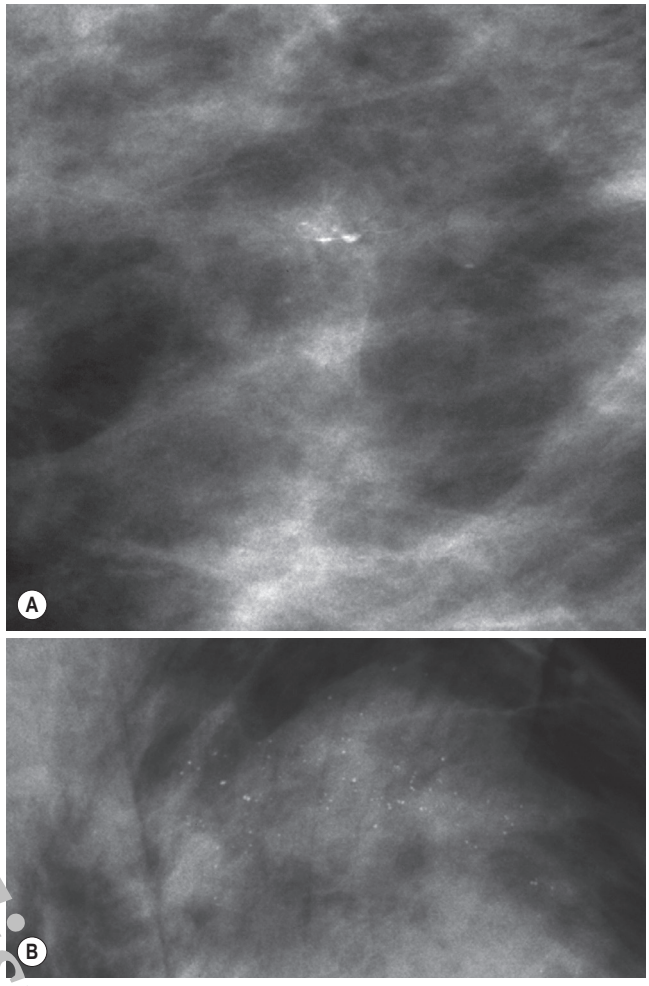

Fig. 63.21 Fibrocystic Change. (A) 'Teacups' representing the layering out of calcific material in the dependent portion of microcysts on a lateral magnification view. (B) Calcifications associated with areas of fibrocystic change may not exhibit this characteristic appearance so x-ray guided biopsy may be required.

clustered rather than scattered throughout the breast, if they vary in size and shape (pleomorphic), and if they are found in a ductal or linear distribution. Malignant microcalcifications associated with high histological grade DCIS are classically rod-shaped and branched. These calcifications are known as casting or comedo microcalcifications and represent necrotic debris within the ducts; hence, their linear, branching structure (Fig. 63.25).

Approximately one-third of malignant microcalcification clusters have an invasive focus within them at surgical excision. The greater the number of flecks of microcalcification associated with an area of DCIS, the greater the risk of invasive disease. In the screening setting, it is often the presence of mammographically visible calcifications associated with high-grade DCIS that leads to the diagnosis of small, high-grade cancers. Calcifications are much less frequently found in low-grade DCIS, as there is usually no intraductal necrosis. When they do occur, they are clustered, but otherwise have a non-specific appearance.

The sensitivity of ultrasound for detecting DCIS is significantly lower than that of mammography, which is one of the reasons why ultrasound is not a useful screening test for breast cancer. However, ultrasound may be able to identify areas of microcalcifications seen on a mammogram, aiding percutaneous biopsy.

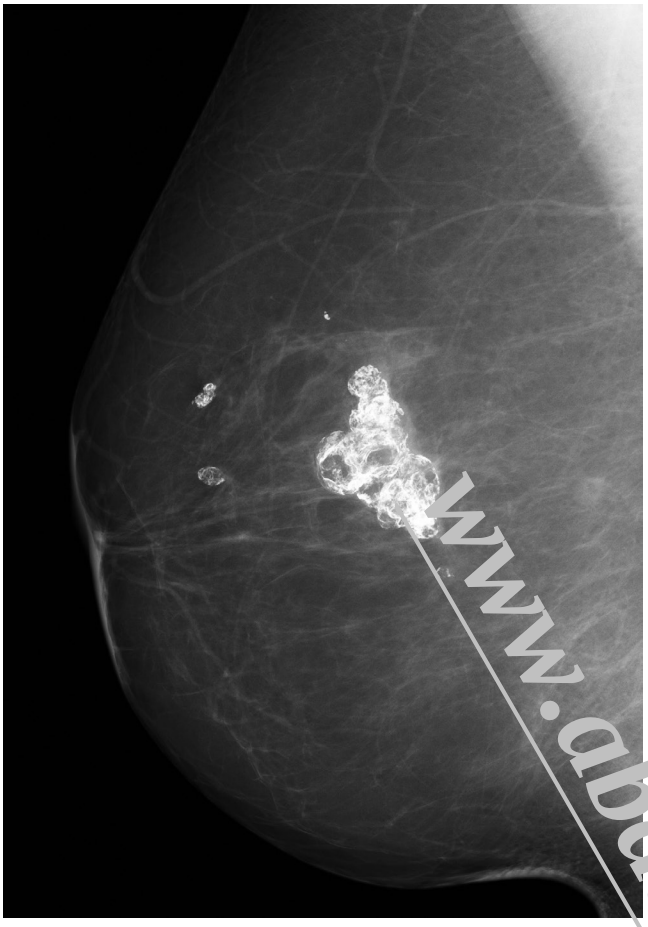

Fig. 63.22 Egg-Shell Calcifications of Fat Necrosis.

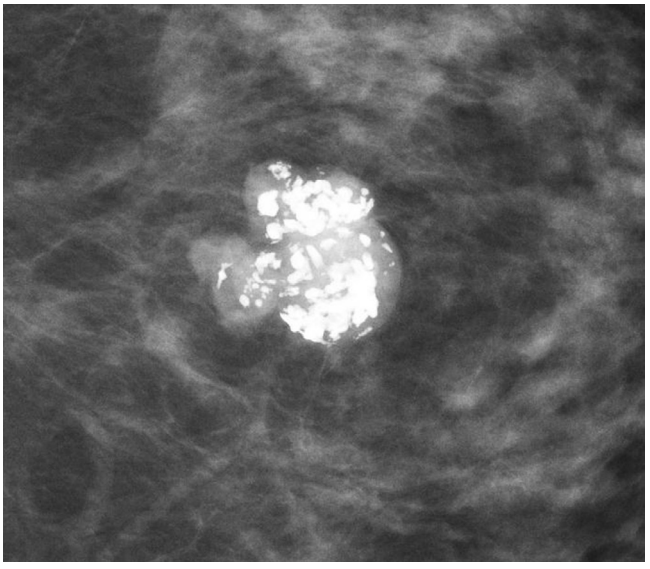

Fig. 63.23 Fibroadenomas. Fibroadenomas may develop coarse 'popcorn'-type calcifications.

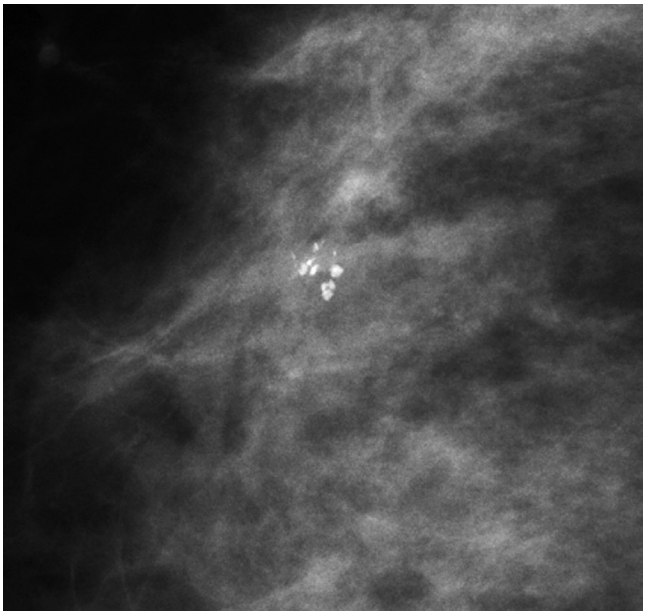

Fig. 63.24 Small Cluster of Indeterminate Microcalcifications. Stereotactic biopsy revealed fibroadenomatoid change.

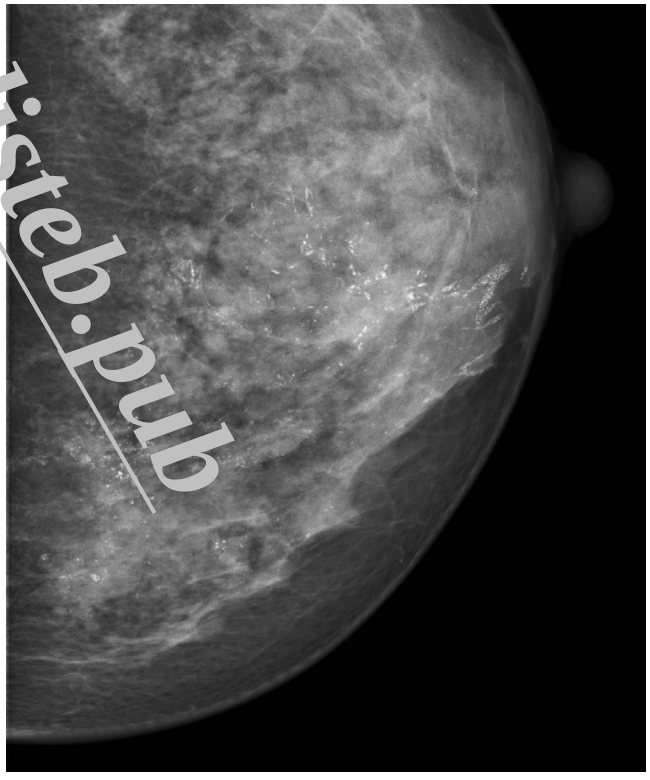

Fig. 63.25 Ductal Carcinoma In Situ. Mammography shows the segmental distribution of pleomorphic microcalcifications. Granular, rod-shaped and branching calcifications can be identified. The appearances are typical of high-grade ductal carcinoma in situ.

BREAST MAGNETIC RESONANCE IMAGING

Although mammographic techniques and ultrasound remain the most frequently used imaging investigations for the breast, contrast-enhanced MRI is increasingly important, largely because of its high sensitivity for detecting invasive breast cancer, which approaches 100% in many studies. The main indications are local staging of breast cancer, screening of high-risk women and monitoring the response to neoadjuvant chemotherapy. MRI is also used to assess the integrity of breast implants.

SUMMARY BOX: Breast Magnetic Resonance Imaging

- MRI has a very high sensitivity for detecting invasive breast cancer
- A combination of lesion morphology and enhancement kinetics following gadolinium injection is key to successful diagnosis
- MRI is used for local staging of primary breast cancer, monitoring response to neoadjuvant chemotherapy and high-risk screening
- The routine use of MRI for preoperative staging remains a controversial area as there is little evidence for improved patient outcomes
- Non-contrast MRI is the most accurate technique for assessing the integrity of breast implants

MRI, Magnetic resonance imaging.

Technique

Successful breast MR studies require at least a 1.5-Tesla system and the use of a dedicated breast coil. Some breast coils have inbuilt compression devices to stabilise the breast and reduce the number of slices required to cover the whole of the breast. Patients are examined in the prone position, with the breast hanging down into the coil. The intravenous injection of gadolinium-based contrast agent is required (dose of 0.1 mmol/kg body weight); it is the presence of abnormal vasculature within the lesion that enables detection.

Some method of eliminating the signal from fat is needed as an enhancing lesion and fat display a similar high signal on a T_1 weighted image. Fat suppression may be active or passive: active fat suppression is typically achieved by the use of spectrally selective pulse sequences to suppress the signal from fat; passive fat suppression involves subtraction of the unenhanced images from the enhanced images. A combination of both active suppression and subtraction is typically used to identify and evaluate areas of true enhancement. Parallel imaging techniques, allow fat suppression to be achieved with shorter examination times while maintaining good spatial and temporal resolution.

Fast 3D gradient-echo pulse sequences provide the optimum method for imaging small lesions. Temporal resolution is important because the maximum contrast between malignancy and normal breast tissue is often achieved in the first 2 minutes following the injection of gadolinium. Later, normal breast tissue may start to show non-specific enhancement, masking the presence of disease. Other signs of malignancy, such as a rapid uptake of contrast agent followed by a 'washout' phase, may only be apparent if images are acquired dynamically every minute over a period of 6 to 7 minutes after the gadolinium injection. A higher temporal resolution allows rapid dynamic imaging but at the expense of spatial resolution or the volume of the breast imaged. Good spatial resolution can only be achieved at the expense of an increased examination time. With modern equipment it should be possible to achieve a slice thickness of less than 3 mm while maintaining a temporal resolution of 60 to 90 seconds, covering the whole of both breasts. At 3 Tesla there is an increase in the signal-to-noise ratio, leading to potential improvements in image quality. There are issues with field inhomogeneity at 3 Tesla that can lead to problems, particularly with fat suppression.

Techniques, such as diffusion-weighted imaging (DWI) and spectroscopy, have been developed to try and improve specificity and provide additional functional tumour information. DWI is an unenhanced echoplanar sequence that measures the mobility of water molecules within the breast tissue. Cancers generally have a higher cellular density, and extracellular water is less able to diffuse; thus values of apparent diffusion coefficient (ADC) are lower (typically $<1.5 \times 10^{-3}$ mm^2/s) compared with benign lesions or normal breast tissues (typically $>1.6 \times 10^{-3}$ mm^2/s). There is overlap between the ADC values of benign and malignant lesions, but the use of DWI has the potential to increase the specificity of breast MRI. DWI has potential as a non-invasive biomarker for the assessment of tumour subtypes, hormone receptor status and histological grade. It may also have a role in patients undergoing neoadjuvant chemotherapy as changes in the ADC value may be apparent before changes in size and neovascularisation are apparent.

Spectroscopy provides metabolic information about a tumour. Choline is an important component of phospholipid synthesis and so is a marker of membrane biosynthesis. Consequently, choline levels are elevated in rapidly proliferating breast cancer cells. The presence or absence of a choline peak on the MR spectra has been used as a way of differentiating malignant from benign lesions, although sometimes choline can be detected in benign or normal tissue. Changes in choline levels may also occur before tumour shrinkage in patients undergoing neoadjuvant chemotherapy, acting as a biomarker for treatment response. MRI spectroscopy can be performed as a single-voxel or multi-voxel technique enabling information to be gathered from a large volume of tissue. Multi-voxel techniques, also referred to as spectroscopic or chemical shift imaging, have the ability to provide quantitative information of choline concentration.

Lesion Characterisation

There are two main approaches to image interpretation: the first relates to lesion morphology and the second to assessment of enhancement kinetics. The architectural features that indicate benign and malignant disease are similar to those already described for mammography and ultrasound. Benign lesions tend to be well defined with smooth margins, whereas malignant lesions are poorly defined and may show spiculation or parenchymal deformity.

Malignant lesions tend to enhance rapidly following the injection of contrast agent and may show characteristic ring enhancement. Dynamic contrast-enhanced MRI enables more detailed enhancement curves to be calculated to aid characterisation. Malignant lesions usually show a rapid uptake of contrast agent in the initial phase of the examination, followed by a washout or plateau in the intermediate and late periods after injection, whereas benign lesions exhibit a steady increase in signal intensity throughout the time course of the examination. There is some overlap in the enhancement characteristics of benign and malignant lesions. One of the strengths of breast MRI is that invasive cancer can be effectively excluded with a high degree of certainty if no enhancement is seen.

A combination of architectural features and enhancement kinetics is used to differentiate benign from malignant lesions. The use of the BI-RADS lexicon aids reporting. Using this system, lesions can be characterised into one of three morphological groups: (1) a focus (a lesion <5 mm, rarely worthy of further investigation); (2) a mass (>5 mm); and (3) non-mass enhancement (an area of enhancement without a morphological correlate). Further descriptors can then be used to describe the shape, margin and enhancement characteristics of lesions with mass effect and the distribution and internal enhancement characteristics of lesions with no mass effect. Enhancement kinetics are

helpful in the assessment of lesions with mass effect, but are not useful in the assessment of non-mass enhancement where DCIS and lobular carcinoma are part of the differential diagnosis.

Normal breast tissue may enhance and this enhancement is in part dependent on the phase of the menstrual cycle. The optimum time for performing a breast MRI is during the second week of the menstrual cycle (between days 7 and 13) when background glandular enhancement should be least intense. Timing the MRI examination with the second week of the menstrual cycle may not be possible for patients undergoing cancer staging, but should be undertaken for screening and follow-up studies. Recent surgery or radiotherapy can interfere with image interpretation. Enhancement patterns return to normal between 3 and 6 months after radiotherapy. Percutaneous breast biopsy (fine-needle aspiration cytology [FNAC], core or VAB) rarely interferes with MRI interpretation.

Indications for Breast Magnetic Resonance Imaging

Local Staging

Contrast-enhanced breast MRI is used for local staging of primary breast cancer. MRI is the most accurate technique for sizing invasive breast carcinomas and will sometimes show unsuspected multifocal disease in the same breast or even additional tumour foci in the contralateral breast. MRI can be expected to show additional tumour foci in the affected breast away from the primary tumour site in around 16% of cases, and additional disease in the contralateral breast in around 4% of cases. This may lead to a change in the therapeutic approach, potentially avoiding inappropriate breast-conserving surgery or unnecessary mastectomies. MRI is usually reserved for patients where estimating tumour size is proving difficult by conventional methods, including mammographically occult lesions, patients with dense breast parenchyma, and where there is significant discrepancy between size estimations at mammography, ultrasound and clinical examination.

Another group of patients who benefit from preoperative staging with MRI are those whose carcinomas have lobular features. Lobular carcinomas are more likely to be multifocal compared with ductal NST tumours. They are more difficult to detect and size with mammography and ultrasound because of their infiltrating growth pattern due to the loss of a cell adhesion molecule called E-cadherin. In approximately 50% of such patients MRI will show more extensive tumour (Fig. 63.26).

Another important role of MRI is identifying an occult primary tumour in women presenting with malignant axillary lymphadenopathy with a normal mammogram and breast ultrasound. In this situation, MRI is highly sensitive for identifying an occult primary.

Monitoring Response to Neoadjuvant Chemotherapy

Neoadjuvant chemotherapy, once the preserve of inoperable locally advanced breast cancer, is increasingly used as the primary treatment for patients with newly diagnosed breast cancer, particularly for tumours that are of high histological grade, hormone and HER2 receptor negative (triple negative breast cancer) or have axillary nodal metastases at the time of diagnosis. Most of these patients would traditionally undergo chemotherapy post-surgery (adjuvant treatment). Administering chemotherapy upfront allows the efficacy of the treatment to be determined by observing tumour response; when chemotherapy is given in the adjuvant setting there is no measurable disease to follow. MRI is the gold standard to assess response to treatment in women receiving neoadjuvant chemotherapy (Fig. 63.27). It can recognise responders to treatment earlier than other imaging methods by demonstrating a reduction in lesion size, or a change in the enhancement pattern, with the level of enhancement reducing or taking on a more benign appearance.

Neoadjuvant chemotherapy also can be used to downstage large breast cancers to enable breast conserving surgery to become a treatment option. MRI can be used to plan the extent of surgical resection in positive responders, with successful breast conservation possible in around 59% of women where mastectomy would have been necessary.

High-Risk Screening

Genetic abnormalities account for up to 10% of breast cancer cases; mutations involving the BRCA1 and BRCA2 genes are the best known. These women have a lifetime risk of developing breast cancer of around 85%. Breast cancer is also a leading cause of death in lymphoma survivors who received mantle radiotherapy treatment in the second and third decades of life. Breast cancers begin to emerge around 10 years post-irradiation and by 40 to 45 years of age 13% to 20% of these women will have been diagnosed with breast cancer, with a risk broadly similar to gene mutation carriers. The sensitivity of mammography for detecting malignancy is low in both these groups of women, so MRI has an important role in screening. In the UK, MRI screening of gene mutation carriers and those with a history of chest irradiation is undertaken by the NHSBSP.

Managing Magnetic Resonance Imaging-Detected Lesions

Abnormalities detected at MRI require proper work-up, including histological diagnosis where appropriate. Surgical management should not be changed unless any additional enhancing lesions are histologically proven to represent malignancy. Findings should be correlated with mammography, but probably the most useful is a targeted, second-look ultrasound of the area. In many cases, ultrasound will identify any additional lesions and facilitate image-guided biopsy. Lack of an ultrasound correlate makes the chances of malignancy much less likely. In one study, carcinoma was found in 43% of MRI lesions that had an ultrasound correlate compared with 14% of MRI lesions that lacked an ultrasound correlate. An ultrasound correlate is more likely for invasive carcinoma compared with DCIS. However, where MRI lesions are suspicious or indeterminate, the absence of a corresponding ultrasound abnormality does not negate the need to pursue a histological diagnosis and MRI-guided biopsy should be considered. For lesions that are considered low risk, follow-up MRI after a suitable period of time, typically 1 year, is acceptable.

Controversies Surrounding the Use of Breast Magnetic Resonance Imaging

It would seem reasonable to assume that the identification of additional tumour foci in the breast at the time of diagnosis should improve surgical planning and long-term patient outcomes with a decrease in both tumour recurrence rates and the incidence of contralateral disease in the years following treatment. No robust evidence is available to support these assumptions. If the use of MRI for surgical planning is effective, a reduction in surgical re-excision rates would be expected in women who underwent preoperative MRI. Two RCTs have been performed to examine this issue; neither found any benefit in women undergoing preoperative MRI. The COMICE trial (Comparative Effectiveness of MRI in Breast Cancer) found re-excision rates of 19% in both groups. The MONET trial (MR Mammography of Non-palpable Breast Tumours) found in an increase in re-excisions in the group undergoing pre-operative breast MRI. Also there is very little evidence that MRI improves long-term outcomes for patients. In one study by Solin and colleagues (2008), local recurrence rates and the incidence of contralateral disease were assessed over an 8-year period in women who had undergone breast-conserving surgery: no significant difference

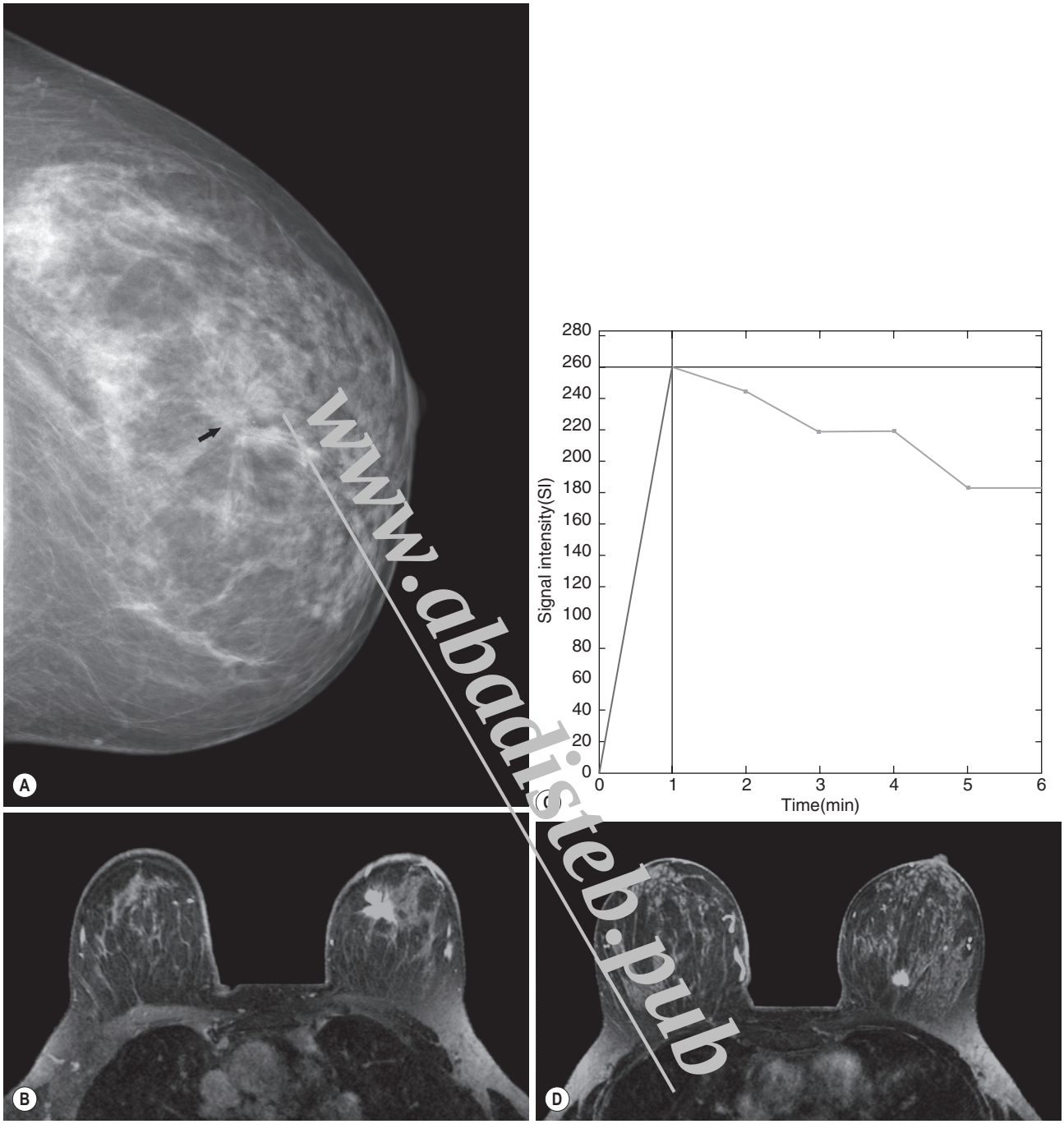

Fig. 63.26 Magnetic Resonance Imaging for Local Tumour Staging. This patient presented with a mass in the left breast. Mammography showed a spiculate lesion *(arrow)* lying centrally within the breast, best appreciated on the craniocaudal view (A). Biopsy indicated a carcinoma with lobular features. Magnetic resonance imaging confirmed the presence of a malignant spiculate lesion (B) with a typically malignant enhancement curve (rapid uptake of contrast agent followed by a washout phase) (C). An additional tumour focus was identified away from the primary tumour site (D). This was confirmed at biopsy.

was observed in women who underwent preoperative MRI compared with those who did not. There is evidence that pre-operative MRI can lead to changes in the surgical approach with a tendency for women to undergo more extensive surgery than was initially planned, which could include a change from breast conservation to mastectomy.

There are two factors to consider when explaining why routine preoperative staging MRI has not been shown to affect outcomes in breast cancer patients. The first relates to the specificity of MRI and the second to a form of over diagnosis. Although MRI is very sensitive for detecting malignancy, reported specificities are lower, varying between 81% and 97%. Consequently, it is very important that any additional lesions identified at MRI are proven to be malignant before management changes are made, avoiding potential unnecessary mastectomies. Obtaining a tissue diagnosis can increase the number of percutaneous biopsies

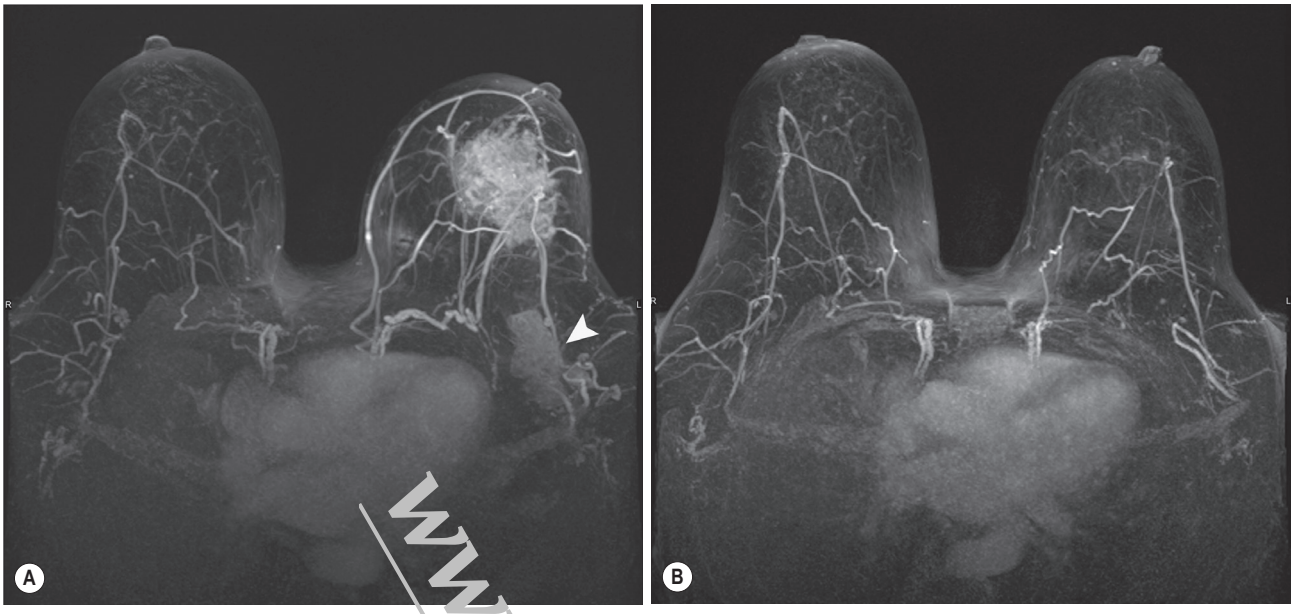

Fig. 63.27 Monitoring Response to Neoadjuvant Chemotherapy. This woman presented with a locally advanced carcinoma in the left breast (A), biopsy-proven malignant axillary lymph nodes are also demonstrated in the axilla *(arrowhead)*. She had a complete response to neoadjuvant chemotherapy with no tumour visible on the post-treatment magnetic resonance imaging (B) and underwent successful breast conserving surgery.

performed and the diagnostic uncertainty may precipitate some women choosing more radical surgery. The second factor is the clinical significance of any additional disease identified. There is no doubt that breast MRI does find additional disease, but some of this may not be clinically relevant in patients undergoing breast-conserving surgery followed by radiotherapy, chemotherapy and hormone treatments. It is well established that these adjuvant treatments are effective at reducing local recurrence rates by controlling foci of residual disease not excised at the time of breast-conserving surgery.

Magnetic Resonance Imaging for Imaging Breast Implants

MRI is more accurate than mammography, ultrasound and clinical examination for assessing the integrity of breast implants, with a sensitivity and specificity of over 90%. When imaging breast implants, no contrast agent is required unless malignancy is suspected. Imaging should be performed in the prone position using a dedicated breast coil. The main goal is to determine whether the implant has ruptured and, if so, to establish the location of the leaked filler (usually silicon). When implants fail, the rupture may be either intracapsular or extracapsular: intracapsular rupture occurs when silicon has escaped from the plastic shell of the implant, but is contained within the fibrous implant capsule (Fig. 63.28); signs of intracapsular rupture include the 'wavy line', 'linguini', 'key-hole' and 'salad oil' signs. False-positive interpretations can be made when normal implant folds are mistaken for signs of rupture. Extracapsular rupture is diagnosed when silicon is demonstrated outside the fibrous capsule. In this situation, ultrasound can be diagnostic, demonstrating free silicon, silicon granulomas or silicon-containing axillary lymph nodes (Fig. 63.29).

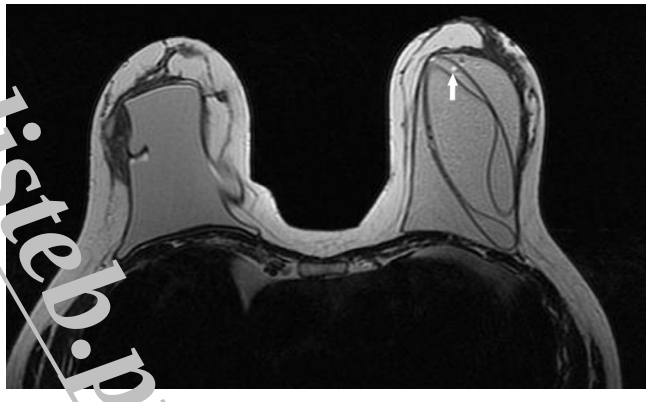

Fig. 63.28 Intracapsular Implant Rupture. On these T_2 weighted fast spin-echo images the plastic shell of the left breast implant can be seen floating within the silicon, producing a 'wavy line' or 'linguini' sign. Note the presence of a bright dot of water-like material *(arrow)*, the 'salad oil' sign.

NUCLEAR MEDICINE TECHNIQUES

Sestamibi imaging using ^{99m}Tc-MIBI and positron emission tomography (PET) imaging techniques using ^{18}F-FDG have been developed following the observation that many breast cancers show uptake of these isotopes. Breast-specific gamma imaging (sometimes referred to as scintimammography) and FDG positron emission mammography (PEM) have significantly improved in recent years with the development of high-resolution mini-camera detectors designed specifically for imaging the breast. The indications for its use overlap with those for MRI and include local staging, searching for a mammographically occult primary particularly where there is dense mammographic background pattern, and detecting recurrence in the postsurgical breast. Research is continuing, but so far these techniques have failed to establish a place in routine practice.

INTERVENTIONAL BREAST RADIOLOGY

Breast radiology requires skills in interventional techniques, particularly ultrasound and x-ray guided needle sampling, percutaneous excision

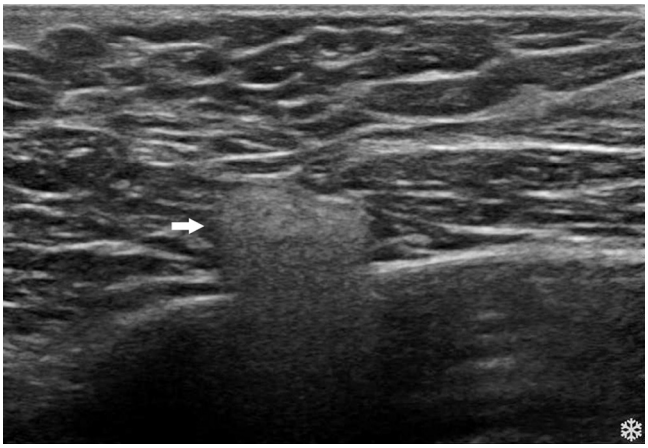

Fig. 63.29 Extracapsular Implant Rupture. A small silicon granuloma is visible, lying adjacent to a breast implant *(arrow)*. The silicon granuloma has a characteristic 'snow storm' appearance.

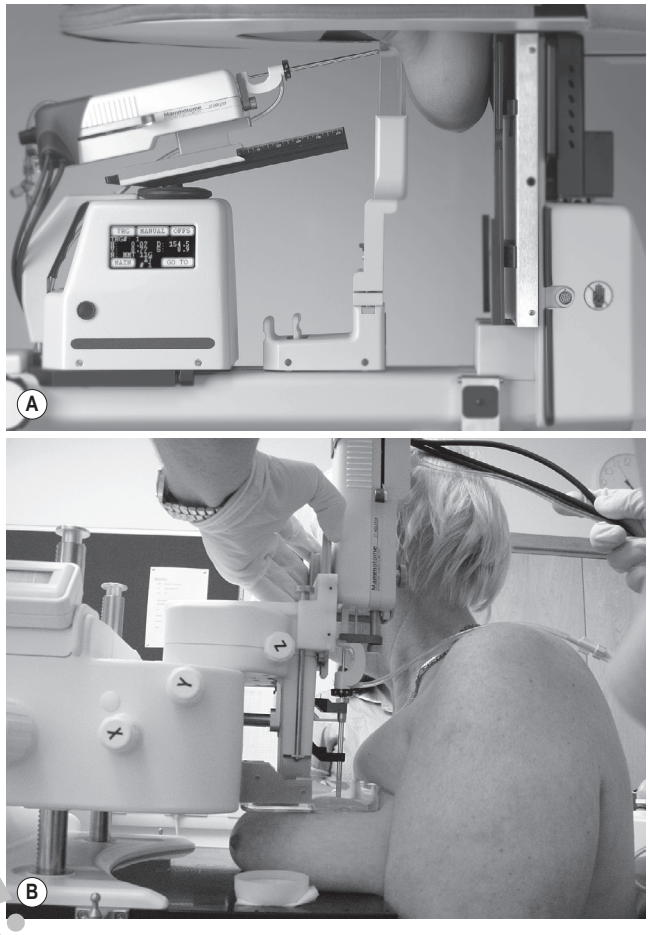

Fig. 63.30 Stereotactic Breast Biopsy. (A) A prone stereotactic x-ray breast biopsy table. (B) An upright add-on breast biopsy device showing vacuum-assisted biopsy being performed with vertical positioning of the biopsy needle.

of benign and borderline lesions and localisation of abnormalities for surgical excision. Eighty per cent of abnormalities detected by screening mammography are impalpable and need to be biopsied and localised using image-guided techniques.

Needle biopsy is highly accurate in determining the nature of most breast lesions and is now used in place of open surgical biopsy. For patients with breast cancer, needle biopsy provides accurate information on the nature of malignant disease, such as histological type and grade, and allows the assessment of tumour biology, cell markers and genetics. The methods most frequently used for percutaneous breast diagnosis are needle core biopsy and VAB. FNAC is now rarely outside of the axilla.

Core Needle Biopsy

Core biopsy of breast tissue is carried out using a 14G diameter needle with a 20-mm sample notch attached to an automated spring-loaded device. Smaller-gauge needles give less reliable results. The needle retrieves a core of tissue, approximately 15 to 20 mg in weight, which is suitable for histological assessment. FNAC is still favoured by some operators for sampling axillary lymph nodes, although most abnormal nodes lie low in the axilla, away from vascular structures, and are amenable to a 14G core biopsy.

Vacuum-Assisted Biopsy (VAB)

The predominant reasons for failure to achieve accurate diagnosis by needle biopsy are sampling error and failure to retrieve sufficient representative material. VAB addresses these issues. Systems typically use 7 to 11G needles to obtain multiple cores, each weighing up to 300 mg. VAB can be used under ultrasound, stereotactic or MRI guidance. After needle placement in the breast, suction is applied pulling tissue into a sampling chamber. A rotating or cutting inner cannula automatically advances. In most systems, suction is then used to retrieve the specimen so that multiple cores can be obtained without the need to remove the needle from the breast. Contiguous core biopsies can be obtained by rotating the probe through 360 degrees.

VAB significantly improves the diagnostic accuracy for borderline breast lesions. The use of VAB to biopsy microcalcifications halves the risk of missing a coexisting invasive cancer in an area of DCIS compared with 14G core biopsy. Lesions categorised as B3 (of uncertain malignant potential) may be associated with co-existing adjacent malignancy and some are also associated with a longer-term increased risk of developing cancer. These lesions include radial scars and papillary lesions, areas of atypical intraductal epithelial proliferation, lobular neoplasia mucocele like lesions and flat epithelial atypia. A review of current literature on upgrade rates to malignancy for each type of B3 lesion shows that most warrant further histological examination, traditionally necessitating open surgical biopsy. An alternative approach is to perform a percutaneous vacuum assisted excision using a VAB device, with the aim of removing 4g of tissue (the equivalent of 12 × 7G cores), potentially avoiding a surgical procedure.

Guidance Methods for Breast Needle Biopsy

Ultrasound guidance is the method of choice for biopsy of both palpable and impalpable breast lesions, as it provides real-time visualisation of the biopsy procedure and visual confirmation of adequate sampling. Between 80% and 90% of breast abnormalities that need to be biopsied are visible on ultrasound. For impalpable abnormalities not visible on ultrasound, stereotactic or DBT x-ray-guided biopsy is required. A few lesions are visible only on MRI and require MR-guided biopsy.

X-ray guided biopsy is used for impalpable lesions that are not visible on ultrasound, typically microcalcifications and mammographic architectural distortions. There are two types of equipment: add-on devices that attach to a conventional upright mammography machine and dedicated prone table devices (Fig. 63.30). Prone table devices are expensive and can only be used for breast biopsy; they require a room

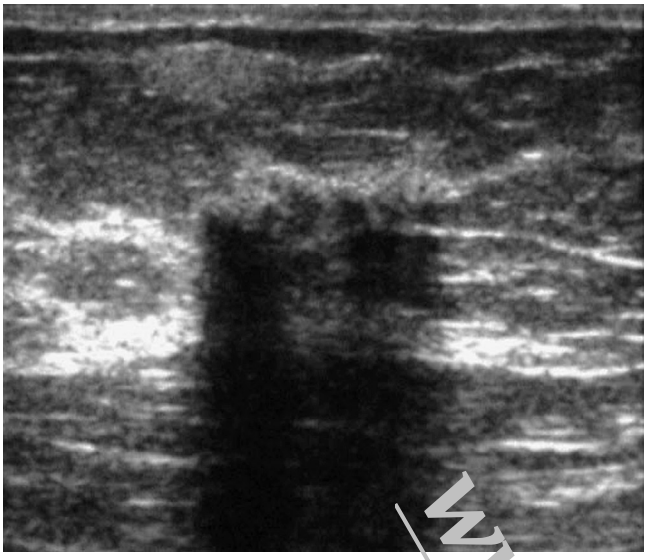

Fig. 63.31 Ultrasound Visible Biopsy Marker. An ultrasound image of breast tissue containing gel pellets placed at the site of a stereotactic biopsy showing how the mass effect with distal shadowing allows the biopsy site to be easily identified on ultrasound.

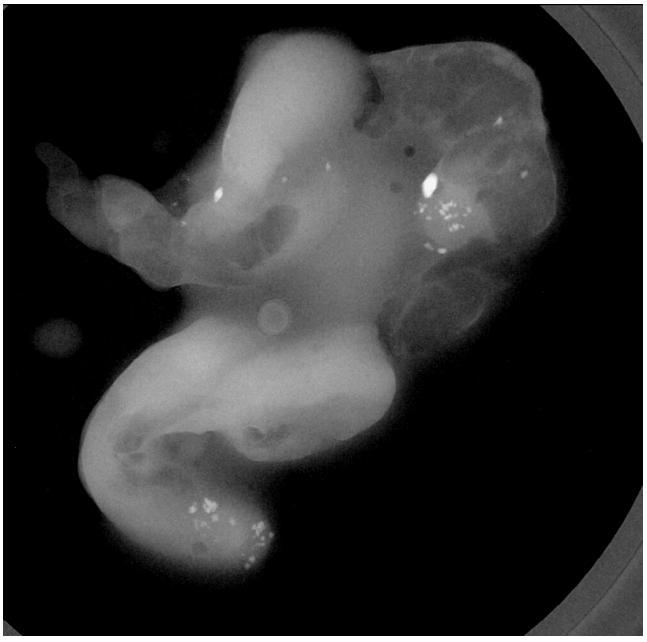

Fig. 63.32 Core Specimen Radiography. A specimen radiograph showing a good yield of microcalcifications in several vacuum-assisted biopsy samples.

in the breast imaging department dedicated for this purpose. The main advantage of this type of device is that the patient cannot see the biopsy procedure while it is being done and vasovagal episodes are said to be less frequent. Add-on devices can be attached to a mammography machine that is otherwise available for routine mammography. These are less expensive and do not require dedicated space. The two methods have equally high levels of accuracy (95% retrieval of representative material) and both are associated with low levels of morbidity and few complications. Vasovagal episodes can be minimised by giving the patient an anxiolytic agent such as sublingual lorazepam 30 minutes before the procedure. Upright add-on systems also can be used with the patient lying in the lateral decubitus position. X-ray-guided biopsy devices typically use stereotactic methods to allow precise localisation of the lesion by acquiring two images, 15 degrees on either side of the central axis of the x-ray gantry. The *x*, *y* and *z* coordinates of the lesion are calculated from the relative positions of the target lesion on the two stereotactic images compared with a fixed reference point. Alternatively, DBT-guided biopsy is now available with coordinates calculated directly from a single tomosynthesis image, potentially speeding up the biopsy process. Once the lesion is localised and local anaesthetic injected, the biopsy needle is advanced into the breast via a small skin incision through a needle holder that guides it to the correct location and depth.

It is possible, particularly after VAB, that the whole of the mammographic abnormality may be removed, so a marker should be placed at the biopsy site. A variety of metal clip and gel pellet markers are available for this purpose; combined gel and metal markers are ideal as these render the biopsy site ultrasound-visible, allowing subsequent localisation procedures to be carried out under ultrasound rather than stereotactic guidance (Fig. 63.31).

Number of Samples

Sufficient material must be obtained but it is unnecessary to take multiple cores as a matter of routine. For ultrasound-guided biopsy, a minimum of two core specimens is recommended. Stereotactic biopsy is typically used for abnormalities that are more difficult to define or sample, so a minimum of five core specimens should be obtained. Core specimen radiography is performed when sampling microcalcifications to prove that representative material has been obtained (Fig. 63.32). The identification of microcalcifications in at least three separate cores and/or a total of five separate flecks of calcification in the biopsy specimen should allow an accurate diagnosis to be made. When diagnostic uncertainty remains, larger-gauge VAB can be used to obtain greater tissue volumes.

Magnetic Resonance Imaging-Guided Biopsy

A few breast lesions are only visible with MRI and therefore have to be biopsied under MRI guidance. A number of different approaches have been developed for this procedure, but one of the most widely used systems involves the patient lying prone within the breast coil with the breast immobilised between compression plates, one of which is in the form of a grid (Fig. 63.33A). VAB is the preferred method of tissue sampling under MRI guidance. Compression is important to stabilise the breast and to keep a lesion's location fixed once initially localised. It is important to avoid over-compression, as this can interfere with lesion conspicuity. A vitamin E capsule is placed over the expected lesion position and sagittal imaging is performed following an intravenous gadolinium injection. The position of the lesion within the breast relative to the skin can then be determined by reference to the skin marker and the gridlines; depth is calculated on the basis of the slice thickness and the number of slices between the skin and the lesion. Following the injection of local anaesthetic, an introducing cannula is inserted through a needle guide into the breast with the correct position confirmed by further imaging (see Fig. 63.33B). The biopsy device is inserted through the introducing cannula and the biopsy samples obtained (see Fig. 63.33A). The patient is re-imaged to ensure that the correct area has been sampled and a biopsy marker deployed.

MRI-guided biopsies are more challenging than other breast biopsies, due to lesion access and visibility. Modern breast coils enable the breast to be accessed from medial, lateral and even superior directions, but problems can be encountered with posterior lesions that cannot be captured within the compression grid. Lesion visibility tends to decrease

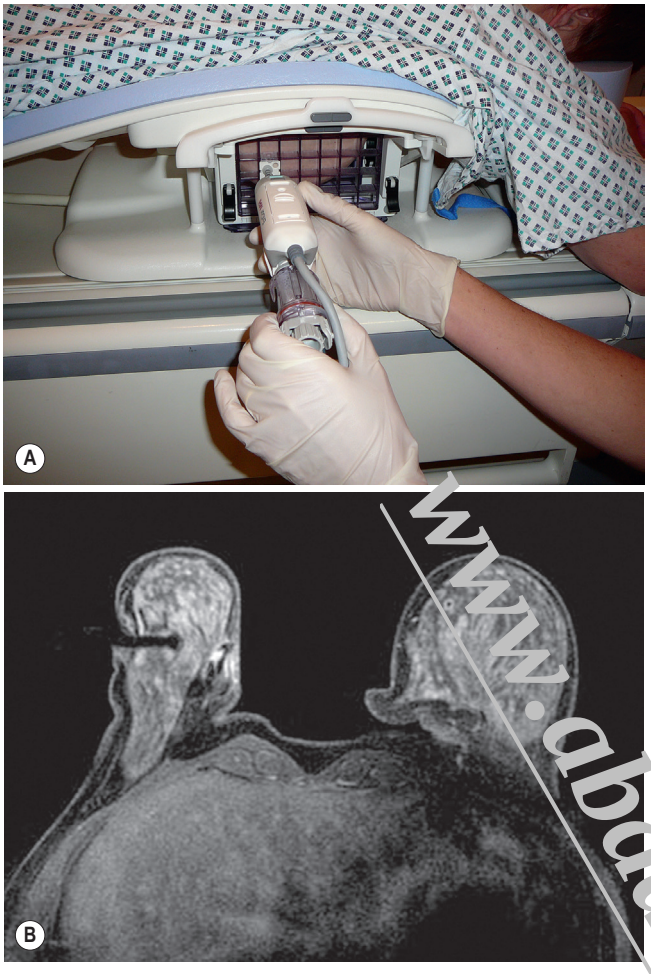

Fig. 63.33 Magnetic Resonance Imaging-Guided Breast Biopsy. (A) The breast being biopsied is immobilised by the grid compression plate and the vacuum biopsy device inserted via the introducing cannula. (B) The introducing cannula is visible on this axial magnetic resonance imaging image, enabling the position to be checked before the biopsy.

with time following the injection of gadolinium due to a combination of contrast washout from the lesion and increased background enhancement. Despite these limitations, vacuum-assisted MRI-guided biopsy offers a safe and accurate way of obtaining a tissue diagnosis from MRI-only-visible breast lesions.

Managing the Result of Needle Biopsy

It is important that the result of needle breast biopsy is correlated with the imaging and clinical findings. This is best achieved by reviewing each case at a multidisciplinary meeting at which the imaging, clinical and pathological findings are reviewed, and management decisions and choices to be offered are discussed and agreed before the patient is seen with the results.

Preoperative Localisation of Impalpable Lesions

The purpose of preoperative localisation is to ensure that an impalpable lesion is accurately marked, facilitating complete surgical excision. For malignant lesions, the aim is to remove a minimum of 5 mm (and preferably 10 mm) of surrounding normal tissue at all margins. Without localisation, much larger volumes of tissue may be removed, with the potential to cause unnecessary deformity of the breast. Specimen radiography is used to confirm that the lesion has been removed and

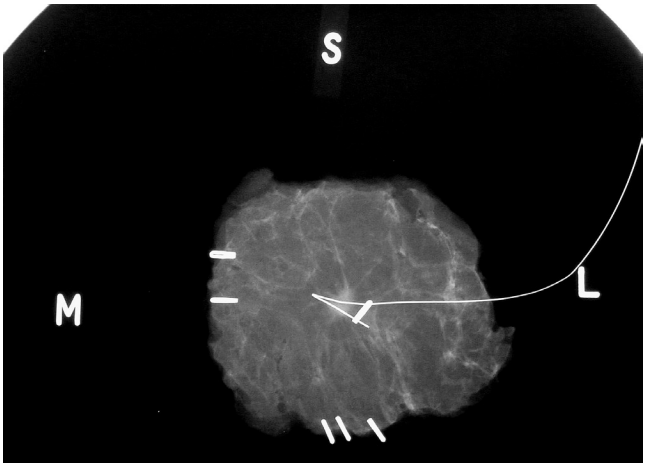

Fig. 63.34 Surgical Specimen Radiograph. A specimen radiograph of a marker localisation surgical biopsy showing the hook wire through the small lesion with mass effect. The specimen is orientated by surgical clips showing the superior *(S)*, lateral *(L)* and medial *(M)* margins. The radiograph shows clear margins of excision.

that adequate margins have been achieved (Fig. 63.34). The specimen is orientated using radio-opaque markers to identify the margins. If excision appears inadequate, further margin excision can be carried out during the same operation.

There are a number of methods available for preoperative localisation. These include simple skin marking over the lesion or the insertion of a wire, or seed. In all cases ultrasound is the preferred method of image guidance. The ideal wire is easy to deploy, maintains a stable position in the breast and is flexible enough to allow check mammography to take place following insertion. Several types of hook wire systems are available, all of which use an introducing needle through which the wire is advanced into the breast. For lesions with mass effect and small clusters of microcalcification, the wire should be placed directly through the lesion or area, with the tip of the wire just beyond it. For a larger area of microcalcifications, several wires may be used to 'bracket' the area to be removed. Check mammograms should be performed to confirm that the correct area has been localised; these should be available to the surgeon. Wires are placed on the day of surgery due to the risk of displacement so this has the potential to interfere with surgical scheduling. There are several non-wire localisation techniques that can be inserted up to 30 days in advance of surgery. Radioactive seeds consisting of a 5 mm I^{125} pellet (half-life 60 days) in a titanium shell can be inserted into the lesion under image guidance. The surgeon uses an intra-operative gamma probe to identify and excise the seed and the tumour. Alternatively, the MAGSEED is a 5 mm metallic marker containing iron particles. Once placed in the lesion the surgeon uses an intra-operative probe that transiently magnetises the iron particles so a signal from the seed can be detected.

BREAST CANCER SCREENING PROGRAMMES

Introduction

Breast cancer mortality in the UK is amongst the highest in the world. The causes of breast cancer are not well understood and, in the absence of any effective preventative measures, much effort and healthcare resources have been focused on the quest to reduce breast cancer mortality by early detection through screening. A number of RCTs and case control studies carried out since the mid-1960s have shown that screening by mammography can reduce breast cancer mortality.

SUMMARY BOX: Breast Cancer Screening in the United Kingdom

- The UK breast programme was the first population-based screening programme in the world and has been running for over 30 years
- Evidence for screening comes from a number of randomised controlled trials
- Women are routinely invited every 3 years from the age of 50 to 70 years for a two-view mammography with double reading
- Cancer detection rates are around 8 per 1000 women screened with a recall rate of around 4%
- Routine breast cancer remains a controversial area, but a recent UK review (Marmot 2012) concluded that the mortality reduction outweighed the risk of over-diagnosis and over-treatment

The NHSBSP was set up in 1988 following the publication of the Forrest Report. This document, commissioned by the UK Department of Health under the chairmanship of Professor Sir Patrick Forrest, reviewed the scientific evidence for population breast cancer screening. It recommended the immediate introduction of screening by mammography in the UK.

Within a year of publication, population breast cancer screening—free at the point of delivery—was introduced into the UK National Health Service. This was the first population-based breast screening programme in the world. Currently in the UK, breast cancer screening by mammography is provided for all women over the age of 50. Women between the ages of 50 and 70 are invited every 3 years. Two-view mammography is used for all screens and the mammograms are double read. Women over 70 are not invited but are encouraged to attend by self-referral. There is an ongoing trial to assess the possible mortality benefits of extending the screening invitation from 47 to 73. Some of the recent performance figures are shown in Table 63.2.

TABLE 63.2 UK National Health Service Breast Screening Programme: Performance in England 2015–2017

	2015/2016	2016/2017
Number of women invited	2,853,297	2,959,954
Acceptance rate (% of invited)	72.1%	71.1%
Number of women screened (invited)	2,040,709	2,086,612
Number of women screened (self-referred)	120,559	112,730
Total number of women screened	2,161,268	2,199,342
Number of women recalled for assessment	88,654	89,104
Women recalled for assessment (%)	4.1%	4.1%
Women undergoing core biopsy/cytology	40,747 (46%)	40,255 (45.2%)
Women undergoing open surgical biopsy	1,616 (1.8%)	1,443 (1.6%)
Number of cancers detected	18,320	18,402
Cancer detected per 1000 women screened	8.5	8.4
Number of in situ cancers detected	3,830 (20.9%)	3,827 (20.8%)
Number of invasive cancers less than 15 mm	7,543 (41.2%)	7,635 (41.5%)

NHSBSP Annual Review 2015/2016, NHSBSP Annual Review 2016/2017, NHSBSP Publications, Sheffield, UK.

The Evidence for Population Screening

Data from RCTs provide the strongest evidence of the efficacy of screening in reducing breast cancer mortality. The design of RCTs enables the elimination of lead-time bias. Most of the RCTs of screening were carried out in Sweden. An overview of some of these trials was published in 2017 and included data from Malmo, Gothenburg and Stockholm. Almost a quarter of a million women were included in these studies, with approximately half being invited for screening and the other half making up the control group. The median trial time was 6.5 years and the median follow-up was over 20 years. The overall results indicated a 15% reduction in breast cancer mortality. The mortality reduction was largest in women aged 40 to 49 and lowest in women aged 50 to 59. The precise mortality reduction attributable to screening is controversial as RCTs may underestimate the benefit of screening due to non-attendance and contamination (mammography occurring within the control group). It has been suggested that regular attendance for mammographic screening may result in a 63% reduction in breast cancer deaths.

Which Age Groups Should Be Screened?

There is definite evidence from RCTs of a reduction in mortality in women aged 40 to 69, but there is no evidence from RCTs to support the screening of women over the age of 70. Although the mammograms of older women are easy to read and the incidence of cancer is high, there would be a significant risk of over diagnosis and consequently overtreatment in this age group. Over diagnosis is the detection and treatment of cancers that would not become clinically apparent or threaten life. Pathological lesions that might be considered an over diagnosis and treatment are low-grade DCIS and invasive tubular cancers. A number of studies are now addressing this issue by suggesting either less invasive treatment or a watch and wait policy for such lesions.

A meta-analysis of RCTs screening women aged 39 to 49 has shown a statistically significant mortality reduction of 17%. The Malmo and Gothenburg studies have both shown statistically significant mortality reductions in this age group. Breast cancer is only half as common in women in their 40s compared with women in their 50s, but preventing breast cancer deaths in younger women will result in a larger number of life-years gained, and it has been shown that breast cancers arising in women in their 40s account for 34% of life-years lost due to the disease.

There are other issues to consider when screening women in their 40s. The lower cancer incidence results in the specificity of both recall and biopsy being lower than that in older women. The sensitivity of mammography for detecting malignancy is also lower for women in their 40s. The interval at which a screening mammogram needs to be repeated is determined by lead-time, which is age related. The lead-time of screening is that time between mammographic detection of breast cancer and clinical presentation. The lead-time of screening in women under the age of 50 in the Gothenburg screening trial was 2.2 years.

This suggests the ideal screening interval for women under the age of 50 is either every 18 or 12 months. The high frequency of screening required in younger women and the lower incidence of breast cancer have led to questions being raised regarding the cost effectiveness of screening in this age group. These disadvantages may be partly negated by the large number of life-years gained per life saved. In contrast, the lead-time of screening for older women aged over 50 is 3 to 4 years, so the 3-year screening interval in the UK would seem appropriate. However, reducing the screening interval to 2 years for the over-50s would be beneficial as a high rate of interval cancers are seen in the UK in the third year after screening.

The Screening Process and Assessment

Screening mammograms are carried out by female radiographers, either at static sites or using mobile vans. In the UK, interpretation of screening mammograms is limited to practitioners who read a high volume of cases (>5000 examinations per year). Evidence suggests that high-volume readers have a significantly increased sensitivity for detection of breast cancer compared with medium- and low-volume readers. In the UK there has been a national shortage of breast screening radiologists. This has led to the introduction of radiographer readers. Radiographers have been shown to have identical sensitivity and specificity when compared with screening radiologists for the equivalent years of experience.

Double reading is standard practice in the UK screening programme, with consensus or arbitration adopted to deal with discordant double-reading opinions. For consensus double reading, disparate opinions are discussed by the two film readers and a consensus achieved. Arbitration involves a third reader independently reviewing the mammograms and deciding whether recall is necessary. Data from the UK screening programme have shown that double reading with arbitration results in the best small invasive cancer detection rate whilst maintaining acceptable recall rates.

Approximately 5% of women are called back for assessment. Fig. 63.35 outlines the assessment process; typically, it involves a combination of extra mammographic views, ultrasound and physical examination. Approximately one in seven of those recalled have breast cancer.

Interval Cancers

Interval cancers are cancers that arise symptomatically in women who have had a normal screening mammogram result before their next screening invitation and are an inevitable part of any screening programme. Interval cancers occur in approximately 3 in every 1000 women

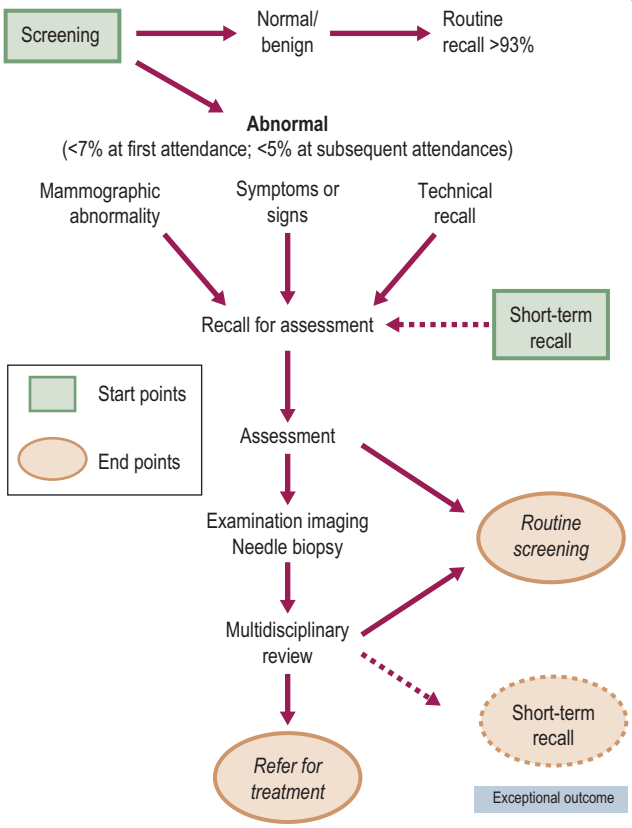

Fig. 63.35 The Screening Assessment Process.

screened, with the vast majority (80%) having no signs on mammography at the previous screen. Interval cancer analysis helps assess the effectiveness of a screening programme and enables radiologists to learn by reviewing the screening mammograms of women who later present with symptomatic cancers. Interval cancers have a prognosis similar to symptomatic cancers in the non-screening population, which is worse than that of cancers detected at screening. The mammographic features most frequently missed or misinterpreted on screening mammograms are calcification and architectural distortion.

Interval cancers in the NHSBSP are divided into three subtypes:

- ***1—Satisfactory***: An interval cancer where the interpretation of the previous screening mammograms was satisfactory, with normal or benign mammographic findings and no reason to recall even in retrospect. This is the largest group accounting for 80% of cases.
- ***2—Satisfactory with learning points***: An interval cancer where the previous screening mammograms show radiological features only seen with hindsight that are difficult to perceive and not obviously malignant, which not all readers would recall. Review of these cases may provide valuable education and learning opportunities. This group makes up 13% of interval cancer cases.
- ***3—Unsatisfactory***: An interval cancer where the previous screening mammogram shows obviously malignant features, which should have been recalled. All readers reviewing the case agree that they would recall. This tiny minority of cases (around 7% of interval cancers) are classified as notifiable safety incidents under UK Duty of Candour Legislation.

The Benefits and Harms of Breast Cancer Screening

Most of the benefit of mammographic screening is due to the detection of small lymph node-negative invasive cancers. Finding high-grade invasive breast cancer less than 10 mm in size is particularly useful as the prognosis of such tumours is excellent, whereas grade 3 invasive breast cancers presenting symptomatically have a very poor prognosis. However, some of the low-grade tubular cancers detected at screening are so indolent that a number of these lesions may never threaten life and mammographic screening in these instances may lead to over diagnosis and overtreatment.

Approximately 25% of cancers detected by mammographic screening are DCIS. High-grade DCIS is accepted by most authorities to be a precursor of high-grade invasive disease. Most DCIS diagnosed through screening is high-grade, so detection is beneficial. The merit of detecting low-grade DCIS is more controversial, with only approximately 40% of cases eventually developing low-grade invasive breast cancer.

In 2012 an independent panel, jointly commissioned by Cancer Research UK and the UK Department of Health under the chairmanship of Professor Sir Michael Marmot, published a report on the benefits and harms of breast cancer screening. They concluded that breast screening extends lives, with women invited to participate in a 20-year screening programme benefiting from a 20% mortality reduction. On the negative side, there is a 1% chance of a woman having a cancer diagnosed and treated that would never have caused a problem if she had not been screened. The panel estimated that for 10,000 UK women invited for screening from the age of 50 over a 20-year period, 681 cancers will be detected of which 129 will represent over diagnosis, and 43 deaths from breast cancer will be prevented. The panel concluded that the UK breast cancer screening programme conferred benefit and should continue.

CONCLUSION

Mammography and ultrasound continue to be the primary imaging tools for the assessment and diagnosis of breast disease. The development

of digital mammographic techniques such as DBT and CESM and high-resolution ultrasound has led to further improvements in image quality and breast cancer detection. MRI is an important additional tool for screening high-risk women, monitoring the response to neo-adjuvant chemotherapy and local staging in carefully selected cases.

The modern breast radiologist requires interventional skills, with biopsies performed under ultrasound, x-ray and MRI guidance. Accurate preoperative diagnosis is crucial in the management of breast disease, with surgery reserved for treatment rather than diagnosis. Increasingly sophisticated VAB devices are available to improve the yield of representative tissue during biopsy, further improving preoperative diagnosis rates.

The past 20 years have seen a reduction in breast cancer mortality despite increasing incidence of the disease. Population-based breast cancer screening with mammography aims to reduce mortality by early detection. This remains a controversial area, but the benefits of screening in reducing mortality continue to outweigh the risks of over-diagnosis and over-treatment.

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