Breast pathology update

Elizabeth A Mallon

Abstract

The surgeon involved in the management of breast disease must work as part of an effective multidisciplinary team. The surgeon must work with all team members communicating effectively and working together. Histopathology provides diagnostic, prognostic and predictive information. The surgeon must understand the implications of the histopathology report for effective patient management. Improvements in core biopsy techniques have provided additional information resulting in lower open biopsy rates and improved pre-operative diagnostic rates for facilitating surgical planning. Assessment of margin status, lymph node status and prognostication are continually evolving and shaping surgical practice towards less surgical intervention in the field of breast disease.

Keywords B3 lesions; basal cell markers; evolving practice; histopathology core biopsy; prognosis

Introduction

An effective multidisciplinary team (MDT) is essential for the management of breast disease in the clinical setting. The multidisciplinary team pulls the expertise of surgeons, radiologists, radiographers, oncologists and clinical nurse specialists to ensure that all of the necessary skills are utilized to provide the best patient journey.

As we embark on a world of personalized medicine and the greater understanding of the molecular aspects of breast disease, molecular pathologists and clinical scientists will become more involved with our multidisciplinary team. As clinicians we should understand and embrace developments in molecular pathology to improve our knowledge of breast disease and personalized treatment.

Histopathology (cellular pathology) is 'gold standard' in providing an initial diagnosis and providing essential information in patient management. It is essential that the surgeon is familiar with all aspects of the pathology report as accurate interpretation is important for optimal patient management. Although multidisciplinary interaction is essential, the surgeon must always carefully read and understand the full pathology report before embarking on any treatment pathway. This is a clinical reponsibility and necessary for safe and effective practice.

This article will provide insight into some essential pathological diagnostic, prognostic and predictive factors and update in areas of changing practice and evolving practice.

Assessment of breast disease

All breast patients should be managed by an effective multidisciplinary team, both in the screening and symptomatic setting. To allow effective working the team must communicate well and respect the input of all team members in a professional manner.

Video conferencing can be used to allow effective communication; however, it is essential that all team members meet regularly to discuss process, protocols and keep each other updated in advances and emerging technologies within their field.

Diagnostic assessment

Triple assessment is essential for the accurate diagnosis of breast disease. In the past, fine needle aspiration cytology was commonly used for an immediate diagnosis within the clinical setting; however use of this technique has waned over the last 10 years. In the current clinical setting core biopsy and an accurate tissue diagnosis provides the third arm of triple assessment along with imaging and clinical examination.

Through expertise gained through The National Breast Screening Programme there has been a vast improvement in biopsy technique. Ultrasound-guided biopsy, stereotactic biopsy and large-volume core biopsies are now available and often carried out by the radiologist/radiographer rather than the surgeon. This has resulted in improvement of the quality and quantity of tissue available for histological assessment and has significantly contributed to a decrease in open benign diagnostic biopsies as well as an improvement in pre operative diagnostic rates for malignant disease.

When small mammographic lesions or microcalcifications are biopsied the radiologist may insert a marker clip at the time of biopsy. This aids any subsequent surgical localization and pathological localization of an excised abnormality.

Currently I believe there is no role for frozen section as a diagnostic process in differentiating between benign and malignant breast disease. Frozen section diagnosis was popular prior to the improvement in accurate pre operative diagnosis, but in the current setting is rarely utilized and few histopathologists have experience in frozen section breast pathology even within specialist centres.

NHS breast screening programme

The NHS breast screening programme invites all women between the ages of 50 and 70 for screening mammography once every 3 years.

The aim of the programme is to detect breast carcinoma at the earliest stage, if possible before the development of invasive carcinoma and the possibility of metastatic disease.

Breast carcinoma is an ideal malignancy for population screening as the natural history is understood, there is an appropriate and acceptable screening test available, early detection is known to improve outcome and, in terms of population screening, has a suitable health economic profile.

However, the programme has been criticised for over diagnosis, resulting in diagnosis and management of in situ and invasive disease which would not have affected the individual's life span. The MARMOT REPORT of 2012 concluded that breast screening did reduce the number of breast cancer deaths. This report estimated that if 10,000 UK women are invited to screening from the age of 50 for 20 years, 681 cancers will be

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detected of which 129 will represent over-diagnosis and 43 breast cancer deaths will be prevented. The panel concluded that breast screening should continue but clear communication of the harms and benefits should be conveyed to women invited for screening to allow individual choices to be made.

Core biopsy

Due to the improvement in core biopsy techniques, the number of open diagnostic biopsies for benign disease has decreased significantly.

I will now discuss the categorization of core biopsy with some description of the pathology encountered.

By convention breast core biopsies are categorized by the B Coding System (B1-5).

- B1: normal – insufficient material for diagnosis
- B2: benign lesion
- B3: lesion of uncertain malignant potential
- B4: suspicious
- B5a: in situ malignancy
- B5b: invasive malignancy.

Multidisciplinary interaction begins at this stage. It is essential that the radiologist/clinician provides an appropriate clinical history to the reporting pathologist, and if the biopsy is for microcalcification, the reporting pathologist must have access to specimen X-ray images.

All biopsies should be discussed by the multidisciplinary team to ensure that the pathological findings correlate with the imaging and clinical findings.

Pathological features in core biopsy (Figure 1)

B1 – normal is a biopsy containing normal breast tissue with no specific abnormality. If the biopsy is for microcalcification and there are benign changes with no calcification this will be classified as B1. In all B1 biopsies MDT discussion is essential to assess the adequacy of the biopsy in relation to the mammographic/clinical abnormality.

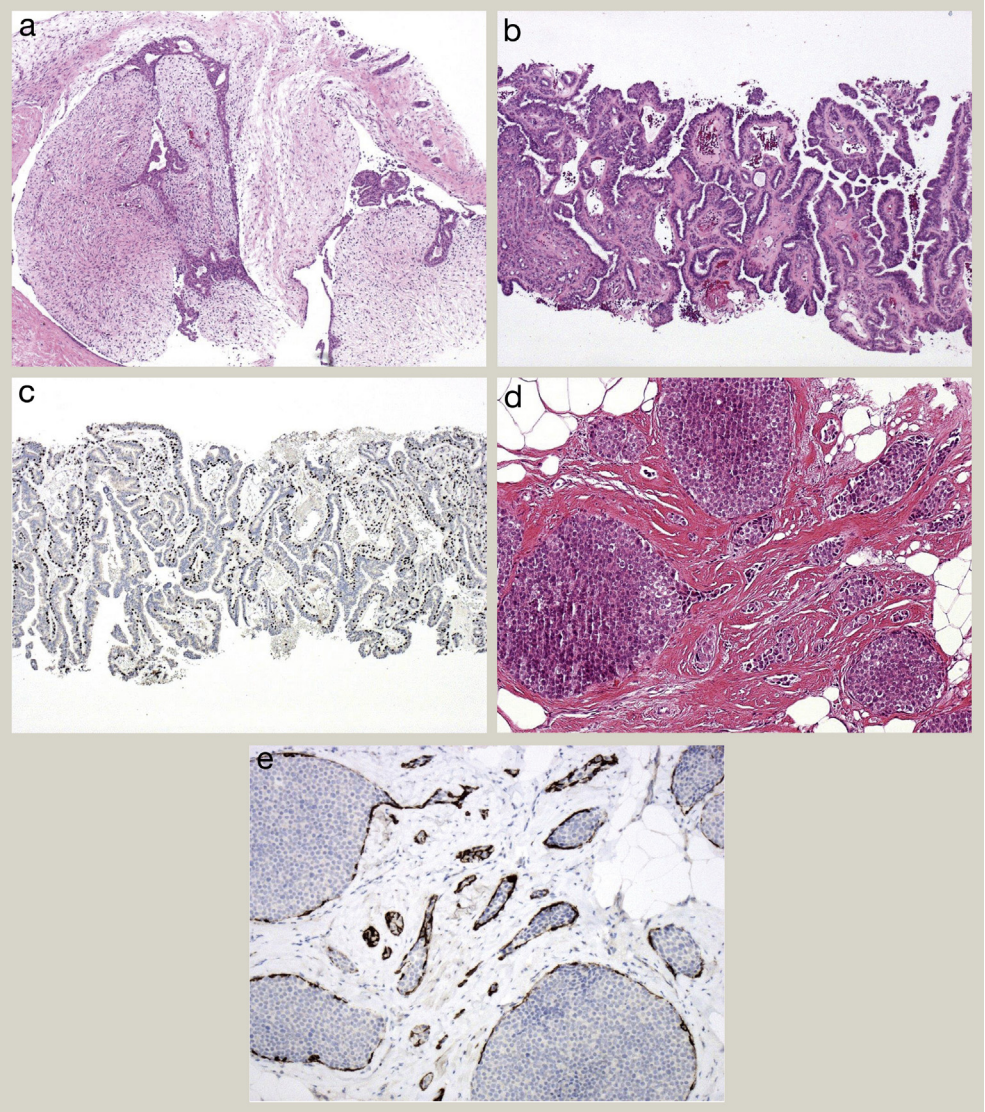


Figure 1 (a) Cellular fibroadenomatoid lesion (B3) H&E ×100. **(b)** Papilloma (B3) H&E ×100. **(c)** Papilloma (B3) P63 for myoepithelial cells ×100. **(d)** Classical LCIS and sclerosing adenosis (B3) H&E ×200. **(e)** Classical LCIS (B3) CK14 for myoepithelial cells ×200.

The MDT will decide if repeat biopsy is required on a case by case basis.

B2 – benign breast change: This will include lesions such as a fibroadenoma, fibrocystic change, columnar cell change, sclerosing adenosis and epithelial hyperplasia of usual type.

Inflammatory change such as duct ectasia, fat necrosis and abscess formation will be included in the B2 category. If the biopsy is for microcalcification the pathology report will include a comment on the presence or absence of calcification and structures in which calcification are noted.

Calcification is often seen in relation to fibrocystic change and columnar cell change.

Calcification may be of conventional type, easily visualized on H&E examination, or may be Wedelite type calcification. This is calcium oxalate dihydrate calcification which is only apparent if the pathologist polarizes the section to view this process.

At MDT discussion the team must assess if the pathological findings correlate with the imaging/clinical findings and, if for calcification, that calcification present in the specimen X-ray is representative of that on the mammogram as microscopy can detect foci of calcification smaller than the resolution of digital mammography.

B3 – lesions of uncertain malignant potential: This category encompasses a diverse group of lesions which are benign on core biopsy but are known to be associated with increased risk of malignancy. Large-volume techniques have allowed the pathologist to assess larger volumes of tissue, allowing for upgrade of some of these lesions in relation to previous 14 gauge core biopsy.

Previously all B3 lesions required open diagnostic surgical biopsy, however, it has been recognized that the level of risk associated with entities classified as B3 varies, and is increased in the presence of atypia (Table 1). New guidelines allow for vacuum assisted biopsy/vacuum assisted excision (Figure 2). This has decreased the need for open surgical biopsy in many benign cases. A comprehensive guide to the management of these lesions is available on the NHSBSP website.

Lesions categorized as B3 include:

Phyllodes tumours – these are biphasic fibroepithelial lesions. The differential diagnosis between fibroadenoma and phyllodes tumour depends on stromal features present in the biopsy. These include stromal cellularity, stromal mitoses, stromal atypia, stromal necrosis and stromal overgrowth. In a core biopsy it is not posible to asses the margins of the lesion, a feature used in the diagnosis of phyllodes tumour in open diagnostic biopsy.

Due to the small amount of tissue present in a core biopsy it may be difficult to differentiate between a cellular fibroadenoma and a phyllodes tumour and assess the grade of the phyllodes tumour (benign, borderline, and malignant).

Atypical intraductal epithelial proliferation (AIDEP) – this category encompasses a group of atypical intraductal epithelial proliferations associated with cytological or architectural atypia. These abnormalities show some atypical features in relation to architectural pattern and cytological appearance but are insufficient for the diagnosis of ductal carcinoma in situ (DCIS). This includes proliferations such as those classified as atypical ductal hyperplasia (ADH) on surgical excision biopsies.

In excision biopsies atypical hyperplasia is a lesion extending over less than 2 mm. As it is not possible to assess the size of the lesion on core biopsy, the term AIDEP is preferred.

Other lesions falling into the category of AIDEP include atypical columnar cell change, where there is a columnar proliferation associated with architectural complexity or flat epithelial atypia where ducts and lobules are lined by cells showing some similarity to those seen in tubular carcinoma.

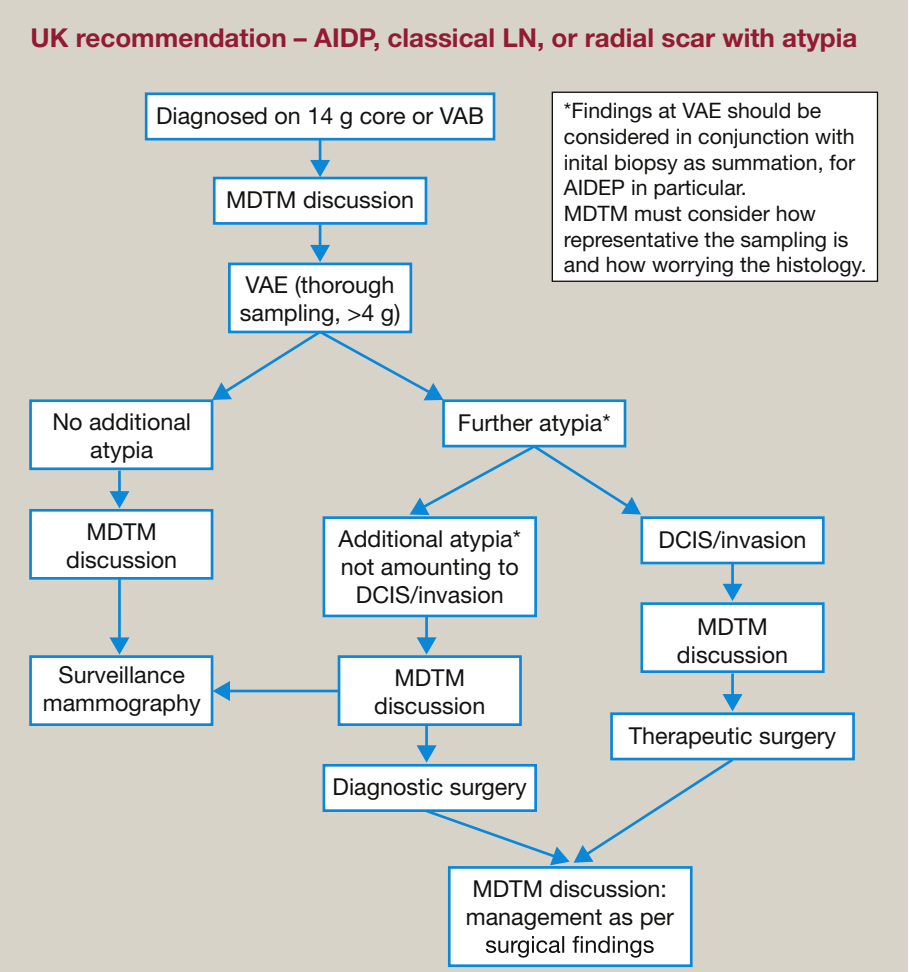
Immunohistochemistry (IHC) can be helpful to the pathologist when assessing the heterogeneity of intraductal proliferations.

Positive predictive values (PPV) of the different groups of B3 lesions reported on NCB in this study (1025 cases) combined with the previous study (523 cases) from the East Midlands region (Total 1548 B3 NCB)

Reason for B3 diagnosis on NCB	Current study		Previous study		Total	
	No (%)	PPV%	No (%)	PPV%	No(%)	PPV%
Epithelial atypia	432 (42)	42.5	188 (36)	32.4	620 (40)	39.5
Lobular neoplasia	79 (8)	29.1	33 (6)	33.3	112 (7)	30.3
No atypia (other B3 lesions)	514 (50)	10.7	302 (58)	7.9	816 (53)	9.9
Papillary lesion	185 (18)	16.7	124 (24)	10.5	309 (20)	14.2
With atypia	30	36.7	25	36	55	36.4
Without atypia	155	12.9	99	4	254	9.4
RS/CSL	329 (32)	13.6	156 (26)	12	485 (31)	13.2
With atypia	51	39.2	24	29	75	36.0
Without atypia	278	8.9	132	9	410	9.0
FE lesions	52 (5)	1.9	32 (6)	0	84 (5)	1.2
B3 miscellaneous	52 (5)	15.4	21 (4)	23.8	83 (5)	21.7
Total	1,025	25.6	523	20	1,548	23.7

From Rakha EA, Lee AHS, Jenkins JA, Murphy AE et al. Characterisation and outcome of breast needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening. **Int J Cancer** 2011; **129:** 1417-1424. (Reproduced with kind permission from John Wiley.)

Table 1



Sagittal slicing specimen examination method with coloured inks used to indicate specimen orientated margins based on conventional block size.
Reproduced by kind permission of Professor Sarah Pinder, Consultant Pathologist, King's College, London

Figure 2

Basal cell markers such has high molecular rate cytokeratins, P63 and smooth muscle myosin show heterogeneity of expression in epithelial hyperplasia of usual type and the lack of such a pattern raises the possibility of an atypical proliferation or in-situ malignancy.

Oestrogen receptor staining is also helpful in this setting with heterogeneous staining in usual type proliferation and monotonous staining in atypical or malignant proliferations.

Lobular neoplasia is a process where lobules and ducts are expanded by a monotonous proliferation of globoid discohesive epithelial cells which tend to be smaller than those seen in atypical ductal proliferation.

Distinction between atypical lobular hyperplasia and lobular carcinoma in situ depends on the extent of the process. An assessment of extent cannot always be made on core biopsy and as such it is recommended that these lesions be categorized as lobular neoplasia (B3).

Immunohistochemical staining with E cadherin may be helpful in such cases.

E cadherin staining is negative in neoplastic lobular processes but positive in ductal processes.

Papillary lesions – are biphasic proliferations with a complex architecture associated with fibroepithelial cores/fronds lined by epithelial cells. Myoepithelial cells may also be present.

This again is a heterogeneous group of lesions ranging from a benign papillary lesion, papilloma, papilloma with atypia, papillary DCIS and papillary carcinoma.

Papilloma and papilloma with atypia will be categorized as B3.

The pathologist may sub-categorize the lesions using immunohistochemistry (basal cell markers). There will be positive staining with basal cell markers in benign/atypical papillary proliferations and lack of staining in malignant papillary proliferation.

Radial scar – complex sclerosing lesion is another group of abnormalities categorized as B3.

These abnormalities will be detected as parenchymal distortion or stellate lesions on imaging. On histology there is fibro-elastotic stroma surrounding entrapped benign structures which may show epithelial hyperplasia. In a sclerosing lesion the pathologist will

comment on the presence or absence of atypia in relation to the hyperplastic process. Again immunohistochemical assessment for basal marker expression is helpful in differentiating between benign sclerosing lesions and tubular carcinoma or usual type hyperplasia and atypia. Myoepithelial cells will be detected in benign sclerosing lesions and absent in tubular carcinoma.

Mucocele-like lesions – are unusual and invariably associated with microcalcification. There are spaces lined by columnar epithelium with mucin and extravassation of mucin into the surrounding connective tissue. There may be associated epithelial atypia.

Other B3 lesions – other unusual lesions categorized as B3 abnormalities include spindle cell lesions such as fibromatosis, neural or smooth muscle lesions, adenomyoepithelial lesions, microglandular adenosis, cysts and vascular lesions.

In such instances it is likely that the pathologist will perform a wide panel of immunohistochemical staining to aid a definitive diagnosis.

B4: lesions – suspicious: this categorization is invariably used in lesions with a very small focus of a lesion which is suspicious but not diagnostic of invasive malignancy. This may be due to the volume of tissue present or due to technical problems resulting in biopsy trauma.

In many instances where a B4 diagnosis is reached on core biopsy a larger volume/repeat biopsy may result in a definitive diagnosis prior to open surgical biopsy. If repeat core biopsy is not possible open surgical biopsy should be performed in these cases.

B5 – malignant:

B5a: in situ proliferation

- **Ductal carcinoma in situ:** the pathology report will comment on nuclear grade of the DCIS (low, intermediate and high), the presence or absence of necrosis and the presence or absence of calcification. The report may also include a comment if calcification is also associated with a benign process in the biopsy.

  If there is extensive calcification on imaging and mastectomy is the treatment of choice, it may be prudent to biopsy 2 sites (distant extents of the imaging abnormality) to prove that all of the calcification is associated with a malignant process.
- **Pleomorphic lobular carcinoma in situ** is categorized as B5a. This is a lobular proliferation (stains negatively with E cadherin) but is composed of pleomorphic cells and may be associated with necrosis and microcalcification.
- **Malignant papillary lesions** include papillary ductal carcinoma in situ and encapsulated/encysted papillary carcinoma. Again the pathologist will use basal markers to assess these lesions.

  Encysted/encapsulated papillary lesions lack basal markers, a feature usually associated with invasive processes, but these lesions behave like in situ carcinoma, thus currently these lesions should be categorized as in situ proliferations (B5a).
- **Micro-invasive carcinoma** is a focus of invasive carcinoma measuring less than 1 mm associated with ductal carcinoma in situ and not extending outwith specialized peri-lobular stroma.

  This will be mentioned in the pathology report but categorized as B5a and such cases should be managed as in situ carcinoma.

Low-risk lesions – the breast screening programme has been criticised for detecting and over-diagnosing lesions which would not have affected the individual life span. It can be questioned whether the issue is over-diagnosis or over-treatment.

To address these issues trials are in place examining low-risk lesions and the possibility of less surgical intervention.

One category which is being studied is low risk ductal carcinoma in situ.

In the UK the LORIS Trial is studying low risk ductal carcinoma in situ (Low or Intermediate Grade without Necrosis). Individuals with such abnormalities diagnosed on large volume biopsy who agree to participate in the Trial will be randomized to conventional surgery or active monitoring. All cases are subject to central pathology review prior to randomization.

The trial will assess if surgical intervention is needed in such cases.

B5b: invasive carcinoma – (Figure 3 a–f): This diagnosis allows the team to proceed to definitive cancer surgery with axillary surgery.

The pathology report will include a comment on the type of carcinoma, grade and biomarker assessment for hormone receptors and HER2.

If the diagnosis is of an invasive lobular carcinoma then MRI may be considered prior to surgery due to the association of multifocal/bilateral disease.

While a provisional grade will be provided on core biopsy, it must be understood that definitive grading should be carried out on the surgical excision as core biopsy grade can underestimate the grade of the lesion in a significant number of cases.

Concordance is achieved in approximately 70% of cases.

If there is insufficient material for assessment of biomarkers (hormone receptor status and HER2), this should be performed on the definitive surgical specimen. The surgeon should be familiar with the scoring system used to evaluate hormone receptor status within their institution (e.g. Allred scoring system, Quick score, etc.).

Some unusual lesions may be categorized as B5 abnormalities, including spindle cell carcinoma, sarcoma, lymphoma and metastatic carcinoma within the breast. An unusual spindle cell malignancy/sarcoma encountered in breast is angiosarcoma, which is often associated with a previous history of radiotherapy to the breast.

Prior to issuing such a report the pathologist will have performed a panel of immunohistochemical markers to provide the most specific diagnosis possible on the material available.

Currently in the assessment of breast disease **axillary ultrasound** may be performed. If there is an abnormality, fine needle aspiration cytology or core biopsy may be performed.

Previously the diagnosis of metastatic disease in the axilla on histology or cytological assessment would lead to axillary clearance. As this is an area of evolving practice discussion and assessment on an individual case by case basis is advised.

As discussed previously, the use of core/large-volume biopsy has significantly reduced the number of benign open biopsies. Open surgical biopsy will still be required in some cases where there is discordance between clinical, imaging,

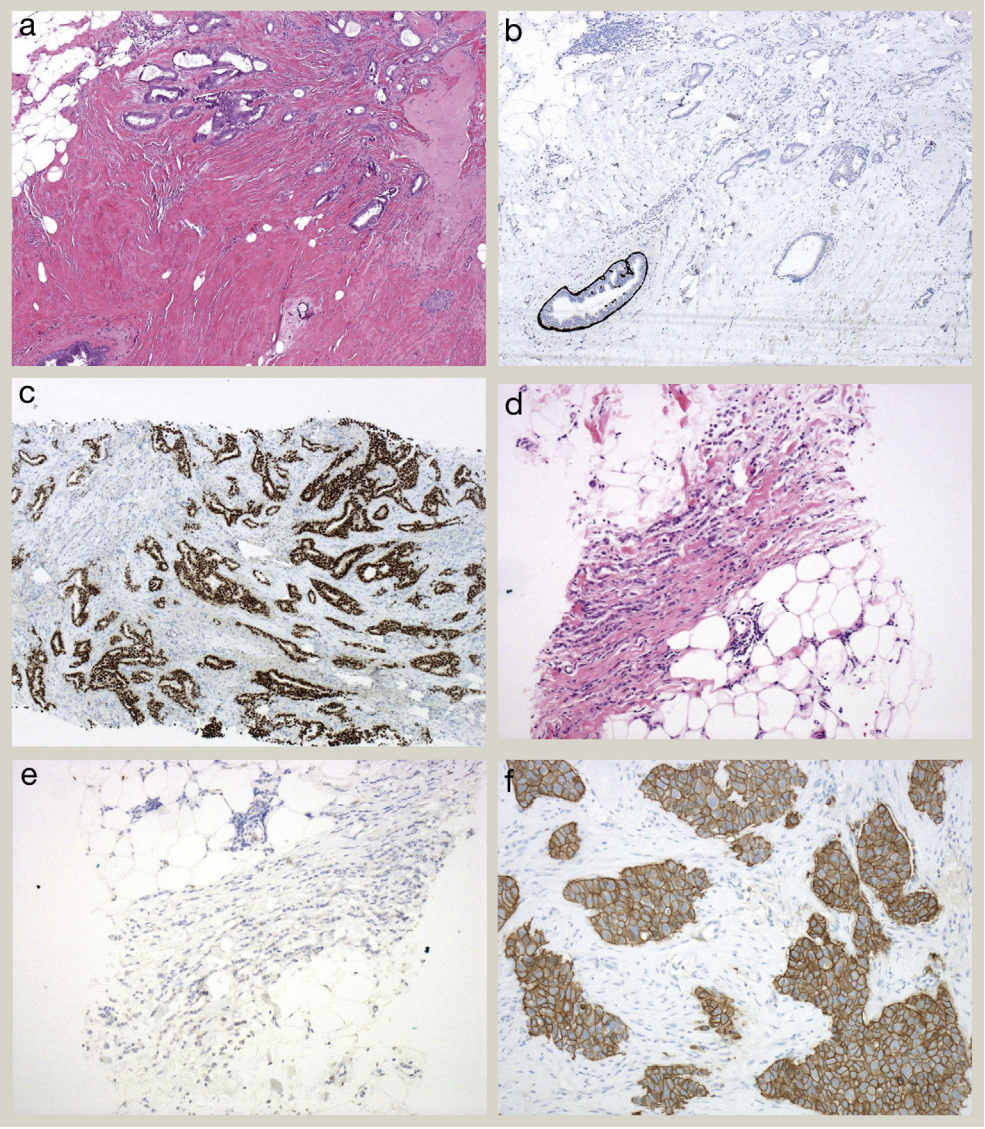


Figure 3 (a) Grade 1 ductal carcinoma (B5b) H&E ×10,000. **(b)** Grade 1 ductal carcinoma CK14 lacking myoepithelial cells with normal duct for control ×100. **(c)** Grade 1 ductal carcinoma strong positive ER ×100. **(d)** Lobular carcinoma (B5b) H&E ×100. **(e)** Lobular carcinoma negative E cadherin ×100. **(f)** HER2-positive ductal carcinoma ×200.

pathological findings, if there is a large abnormality distorting the breast or if the patient requests removal of a lump such as a fibroadenoma.

Breast cancer therapeutic surgery

I would like to concentrate on pathological prognostic factors in relation to breast cancer.

In any surgical excision it is essential that the surgeon provides appropriate clinical and imaging information to the reporting pathologist. If this is an image guided (localised) surgical specimen a specimen X-ray must be available to view. Good communication between all members of the team is essential to ensure opitimal clinical management.

Most surgical specimens will be orientated (Figure 4). It is important that a local protocol is followed and that all team members are aware of the protocol.

The definitive pathology report will include important data items required for assessment for adequacy of surgery, prognosis and prediction. The pathology report will give an indication of size (invasive and whole tumour size), the type of tumour, grade of tumour, lymphovascular channel involvement, margin assessment and lymph node status.

Tumour type and grade

The most common type of invasive breast carcinoma is invasive ductal carcinoma of no special type (NST). This accounts for over 70% of all invasive carcinomas and shows a wide variety of morphological features. As with all types of invasive carcinoma, grading will be performed.

The next most common type of invasive breast carcinoma is invasive lobular carcinoma. As stated previously this is often multifocal and bilateral and therefore, MRI is often indictated prior to definitive surgery.

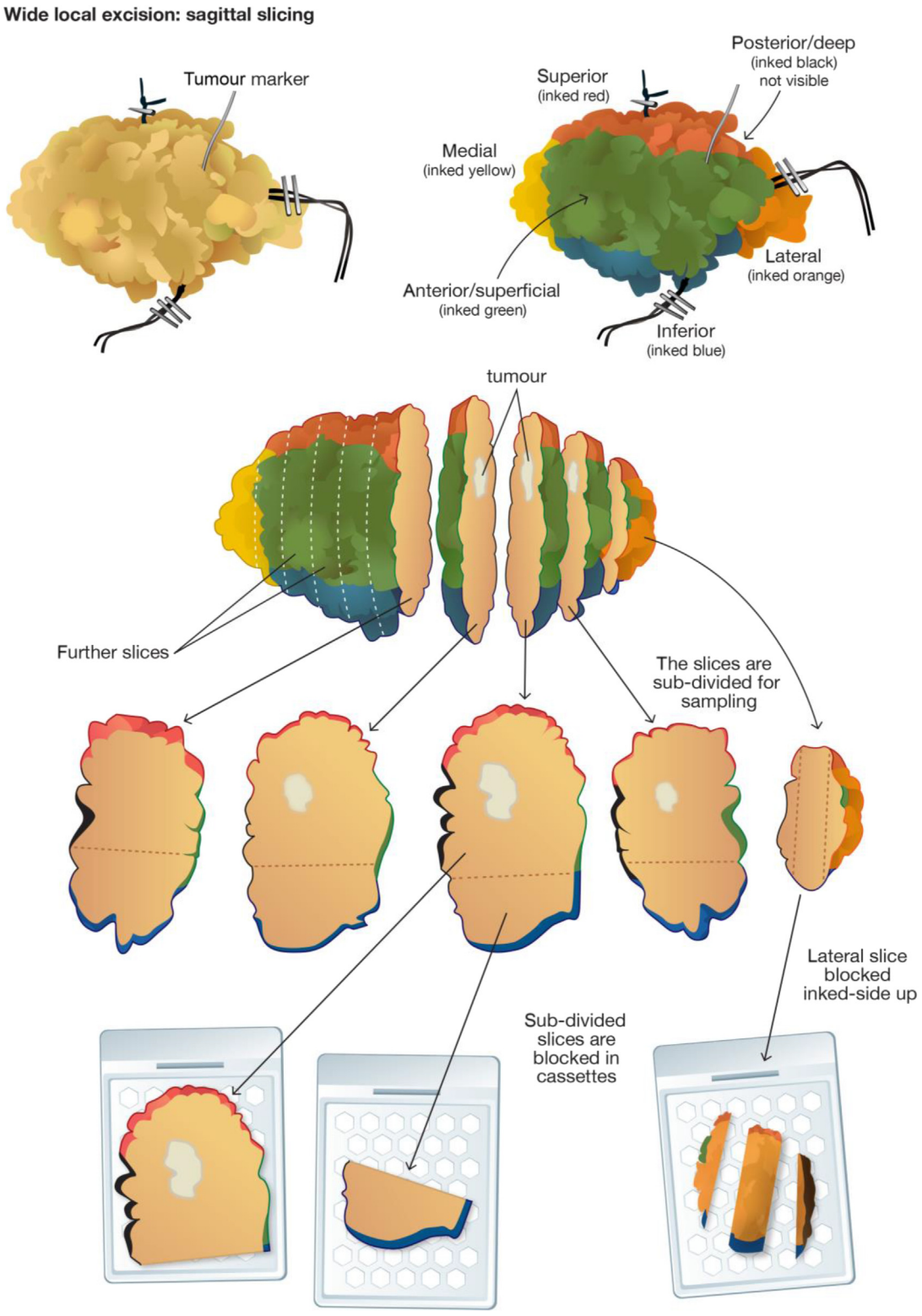


Figure 4

Invasive lobular carcinoma may be further sub-classified into classical, solid, alveolar or pleomorphic lobular carcinoma.

A wide variety of other histological types are identified and these histological patterns are associated with different prognosis. These tumours include tubular carcinoma (more common in the screening population and associated with an excellent outcome), mucinous carcinoma (more common in elderly women, again associated with good outcome) and medullary-like carcinoma (a tumour with high-grade

pathological features but better prognosis than would be expected from the histological grade).

Rarer types of invasive carcinoma within the breast include micropapillary carcinoma, often associated with lymphovascular channel involvement and local recurrence, squamous carcinoma and adenoid cystic carcinoma.

A full list of the many and varied types of invasive carcinoma can be found in the WHO Classification of breast tumours.

All invasive breast carcinomas will be graded using the Modified Bloom and Richardson score.

Grading system

This classifies invasive carcinomas in to three groups, grade 1 having the best prognostic outlook and grade 3 the poorest. Specialist breast pathologists in the UK regularly take part in a National Quality Assurance system to ensure that they are grading appropriatly and consistently.

Molecular subtyping using hierarchical clustering emerged as a new way to classify breast cancers. This has translated in to surrogates in clinical practice with **luminal A** carcinomas (lower grade ER and PR positive, HER2-negative and low proliferation), **luminal B** carcinoma (higher grade ER positive, PR and HER2 positive or negative high proliferation), **HER2-positive** and **basal** (triple negative).

Younger individuals, particularly with triple negative disease, may require genetics referral for assessment of risk and genetic testing.

Margins

With regard to margin assessment, depending on local protocol, the surgeon may perform a single wide local excision or wide local excision associated with cavity shavings. The shavings may or may not be orientated. It is important that the team adheres to local protocols to allow accurate assessment of the pathological specimen. The team should regularly assess the number of cases requiring re-excision and, audit the local recurrence rate.

In the definitive surgical pathology report margin assessment will give an indication of the distance of in situ and invasive malignancy from the margin and refer to the appropriate margin.

There is some debate on what constitutes a positive or negative margin in the setting of in situ and invasive malignancy.

In some units a positive margin is regarded as 'tumour on ink'. This refers to the tissue ink used by the pathologist at the time of dissection. Unfortunately, this definition is not as simple as suggested by the wording. Ink may 'leak' into the specimen and be present at sites which do not represent a surgical margin. There may be marked diathermy artefact making assessment of the margin difficult. In relation to DCIS, this is further complicated by the fact it is a discontinuous lesion, often with no gross abnormality.

The Association of Breast Surgeons recommends a margin of 1 mm for invasive carcinoma and DCIS.

The American Guidelines suggest '**tumour on ink'** for invasive carcinoma and a distance of 2 mm for ductal carcinoma in situ.

A local protocol should be agreed and followed, individual case discussion is essential.

With the evolution of **oncoplastic techniques** surgical margin assessment can be further complicated. It is reported that the requirement for re-excision is lower in oncoplastic techniques as a larger volume of tissue is often excised. However, it must be remembered that the aim of breast cancer surgery is to remove any malignancy and that oncological safety is paramount.

Lymph nodes

The pathology report will include the assessment of axillary nodes.

Previously all women with invasive breast carcinoma underwent axillary clearance. As this is associated with morbidity and is unnecessary in many women the technique of sentinel node biopsy has become the surgical option of choice.

The pathology report will comment on the type of axillary surgery, the number of nodes involved and classify nodal involvement as individual tumour cells (ITCs — deposits less than 0.2 mm), micrometastases (greater than 0.22 mm, less than 2 mm) and macrometastases (greater than 2 mm). A comment will also be made if there is extranodal extension of carcinoma.

There have been major changes in the management of the axilla over the last 10 years with an aim to minimizing treatment and thus morbidity.

In the UK the POSNOC Trial is currently recruiting cases with 1—2 involved axillary nodes to assess if further axillary treatment is necessary.

Neo-adjuvant therapy

Neo-adjuvant chemotherapy and endocrine therapy may be considered in certain cases, aiming to reduce tumour volume allowing for less extensive breast surgery and less extensive axillary surgery.

Prior to embarking on neo-adjuvant therapy a radiological clip should be inserted in the breast lesions to allow tumour bed identification.

The post-surgery pathology report will comment on the presence or absence of a microscopic response to the neo-adjuvant therapy. There may be a complete pathological response with no remaining viable carcinoma or varying degrees of residual tumour within the breast and axillary nodes.

There is a variety of grading systems available to assess the extent of response (Miller and Payne, Residual Cancer Burden).

Breast cancer prognostic indices

For many years a variety of algorithms have been used to assess risk and prognosis in breast cancer patients. This initially involved such indces as the Nottingham Prognostics Index, based on conventional pathological prognostic factors. Over time these algorithms have been refined, with biomarker status oestrogen and progesterone receptor HER2, Ki67, age and clinical factors being included in the algorithms (PREDICT, ADJUVANT, IHC4).

Ki67 is an immunohistochemical test which assesses proliferation. There has been much debate on the use of Ki67 in prognostication of the breast carcinoma. There has been much criticism as it is felt that Ki67 staining and counting is not reproducible between pathology laboratories. In addition there is no clear cut-off as to what constitutes a high/low Ki67. It is also suggested that a change in Ki67 while on treatment (pre and on-treatment assessment) will provide an indication of the likelihood of response to therapy. Ki67 assessment is not currently

included in the Royal College of Pathology minimum data set for breast cancer reporting.

A variety of **molecular tests** are now available to assess risk in specific situations. The aim of such tests is to provide risk stratification, avoiding unnecessary treatment in many women and personalizing treatment to allow the best outcomes with minimal toxicity. Many of these molecular tests are expensive and are not appropriate for every individual, however they are indicated in specific sub-groups to assess risk and allow improved treatment pathways.

In the United Kingdom the Oncotype Dx Test which assesses 21 genes is used in a specific group of hormone receptor positive, node negative individuals to define treatment pathways. Currently a variety of commercial tests (MAMMAPRINT, PAM 50 and many others) are available and a NICE assessment of the appropriateness of each test is underway.

It must be noted that prognostication and prediction is improved by combining conventional prognostic factors with certain molecular tests. We must be aware that molecular testing is expensive and not indicated in every case, but does provide useful information in certain clinical situations. It is our duty as clinicians to keep up to date with these advances and work as a team to decide which tests are appropriate for which patient taking pathological factors and other patient related factors in to account. This will allow the best treatment pathway for the individual and appropriate use of health service resources.

For molecular testing to be undertaken good quality tissue and tissue targeting is required for accurate molecular profiling.

The management of breast disease is an evolving field. We are working towards minimizing surgical intervention, personalized treatment and avoiding morbidity. Due to improvements in diagnosis and treatment, many types of breast cancer should be regarded as a chronic disease, with excellent long term outcomes.

As a clinical team it is vital that we work together to improve outcomes and minimize morbidity in our patients. ◆

FURTHER READING

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