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Pathology: the science behind the cure

Standards and datasets for reporting cancers

Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening

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Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendices G and H) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Other, non-core, data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholders were contacted to consult on this document:

- the Association of Breast Pathology
- the Association of Breast Surgery
- the British Society of Breast Radiology
- NHS England.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset.

The information used to develop this dataset was obtained by undertaking a systematic search of PubMed. Key terms searched included ‘breast core biopsy’, ‘vacuum-assisted

biopsy' and 'vacuum-assisted excision'; dates searched were between January 2019 and April 2025. Published evidence was evaluated using modified SIGN guidance (see Appendix Q). Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence will be identified by College members via feedback received during consultation.

A formal revision cycle for all cancer datasets takes place on a 3-yearly basis. However, each year, the College will ask the authors of the dataset, in conjunction with the relevant sub-specialty adviser to the College, to consider whether the dataset needs to be revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for 2 weeks for Fellows' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group and will be placed on the College website for consultation with the membership from 18 March to 15 April 2026. All comments received from the Working Group and membership will be addressed by the author to the satisfaction of the Chair of the Working Group and the Clinical Leads for Guideline Adjudication.

The NHS Breast Screening Programme is grateful to the members of the Guidelines Working Group of the UK National Coordinating Committee for Breast Pathology for their work in updating the guideline. The NHS Breast Screening Programme will reference this updated guidance in its future publications.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team and are available on request. The authors have declared no conflicts of interest.

1 Introduction

The aim of assessment is to obtain a definitive and timely diagnosis of all potential abnormalities detected during screening.[1] This is best achieved by using 'triple assessment', comprising imaging (usually mammography and ultrasound), plus clinical examination and image-guided needle biopsy for histological examination, if indicated.

Definitive non-operative diagnosis of malignancy allows rapid referral for treatment, ideally in 1 operative procedure. Definitive non-operative diagnosis of benign conditions is equally useful, usually leading to discharge from the clinic and return to routine recall.

In the early days of breast screening, fine needle aspiration cytology (FNAC) was the procedure of choice, but it is now recommended that needle core biopsy (NCB) or vacuum-assisted biopsy (VAB) is used for assessment of significant screening detected abnormalities.[1] This is because current evidence suggests that core biopsy has greater sensitivity and specificity in evaluating microcalcification, asymmetry and architectural distortion than does FNAC.[2] It also aids definitive benign diagnosis.

Invasive carcinoma can be distinguished from ductal carcinoma in situ (DCIS) on core biopsy (but not with FNAC). Oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) status can be assessed on core biopsies because invasive carcinoma can be recognised. Histological grade can be more accurately assessed on core biopsy.

FNAC may be used in addition to core biopsy if an urgent diagnosis is required or if core biopsy is not possible.[1] FNAC should not be used alone in the assessment of lesions in the breast detected by screening mammography, unless core biopsy is contraindicated.

The purpose of these guidelines is to provide pathologists with an update on the role of non-operative diagnosis in breast screening assessment, and on the handling and reporting of biopsy specimens. A similar approach is recommended for symptomatic breast lesions. The document concentrates on NCB and VAB, both first line and for subsequent vacuum-assisted excision (VAE). It also describes the mechanisms used to assess and assure the quality of non-operative diagnosis in breast screening.

This document constitutes the 6th edition of guidelines for non-operative diagnosis in breast cancer screening. It updates and replaces the previous guidelines published in 2021.[3]

1.1 Key changes to previous guideline

Key changes made to the previous guideline are outlined in the table below.

Section	Explanation
2	Simplification of information provided on image guidance for breast biopsy to increase relevance to primary users
3.8.3	Microinvasive carcinoma should now be categorised as B5a whether or not there is associated DCIS
Appendix C	This section has been updated and expanded to provide useful information on interpretation of figures from the national pathology data review (formerly national pathology audit)
Appendix F	A reference table is now provided to show B codes for selected core biopsy diagnoses

1.2 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are breast radiologists, radiographers, clinicians and administrative staff working in the breast screening programme.

2 Use of non-operative diagnostic techniques

Detailed guidance on assessment procedures is provided in the National Health Service Breast Screening Programme (NHSBSP) guidelines, *Clinical guidance for breast cancer screening assessment (4th edition)*.[1]

All cases should be thoroughly assessed prior to needle biopsy. The radiological findings can be categorised into 5 categories according to the British Society of Breast Radiology classification:

1. normal/no significant abnormality
2. benign findings
3. indeterminate/probably benign findings
4. findings suspicious of malignancy
5. findings highly suspicious of malignancy.

The number is preceded by U for ultrasound assessment, M for mammography, MRI for magnetic resonance imaging and R can be used for overall radiological assessment.[4] In

some centres, Breast Imaging Reporting and Data System (BI-RADS) categories are used to classify lesions. These categories map approximately to the categories 1 to 5 in the list above. All needle sampling procedures carried out on screen detected abnormalities must be discussed at a multidisciplinary meeting, where findings from all modalities are discussed and further management is decided. These guidelines also detail the methods of choice for sampling the different types of mammographic abnormality.

This approach must be adhered to in the National Breast Screening Programme, as it is recognised that very rare false positive interpretation of needle biopsy specimens can occur. All cases should be subject to multidisciplinary review to ensure concordance before proceeding to definitive treatment.

Both NCB and VAB procedures may result in removal or destruction of the mammographically detected lesion. The lesion may therefore not be identified in a subsequent VAE or operative specimen. Reporting in this situation is dealt with in the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*[5] and Appendix C.

2.1 Multidisciplinary discussion

Core biopsy results should not be interpreted in isolation. The multidisciplinary meeting should make a judgement about whether the biopsy is concordant with radiological and clinical findings, and whether the biopsy is representative of the lesion. If there is discordance, further management must be discussed. When the imaging findings are suspicious for malignancy and the biopsy is normal or benign, management should be reviewed at a multidisciplinary meeting and a decision made whether to repeat the sampling procedure or to refer for open biopsy or localisation biopsy.

In cases where there is disagreement between modalities and a failure to achieve consensus after multidisciplinary discussion, repeat core biopsy, VAB or surgical biopsy are likely to be the most appropriate courses of action. No more than 2 non-surgical needle biopsy procedures from the same area, carried out on separate occasions, should normally be needed to achieve a non-operative diagnosis of a screen detected abnormality. Frozen section for the diagnosis of screen detected lesions is inappropriate.

Evidence from published series of multiple NCB sampling has shown that for certain types of mammographic abnormality, particularly moderate to low-level suspicion microcalcification, a larger volume of tissue is required for accurate diagnosis.[6] For such

lesions, where the use of conventional 14 G core biopsy carries a high risk of an equivocal result, use of larger volume sampling techniques may increase the accuracy of biopsy.

VAB has a lower equivocal sample rate and increased accuracy in the detection of small invasive tumours associated with an area of DCIS.[7–9] VAB may also be useful after a B1 or B4 diagnosis on 14 G core biopsy. Guidelines propose more thorough sampling or excision, using VAE as an alternative to diagnostic surgical biopsy for the majority, although not all, of B3 lesions.[10]

2.1 Image guidance for breast biopsy

NCB is now considered to be the minimum standard for breast biopsy with FNAC reserved for sampling axillary lymph nodes and/or breast cysts in some centres.[11] Core biopsy provides more reliable results and more information on which to base the diagnosis and subsequent management options. FNAC may still rarely be used for some small breast lesions, in patients with implants, or for lesions difficult to access with a larger core device. Predictive biomarker assessment may sometimes be carried out on FNA specimens in patients with significant comorbidity. Increasingly, VAB is used in circumstances where core biopsy may not be reliable and is regarded as the gold standard for sampling calcifications.

2.1.1 When to use ultrasound guidance

Most soft tissue lesions in the breast are visible using modern high-frequency ultrasound apparatus. Ultrasound is, therefore, the imaging method of choice for sampling non-palpable soft tissue lesions and allows real-time demonstration of the needle traversing the lesion. Some clusters of microcalcification, particularly coarser comedo type calcification, are visible on high frequency ultrasound and may therefore be sampled by ultrasound guidance.

2.1.2 When to use stereotactic guidance

X-ray stereotaxis is used for image-guided biopsy of most indeterminate and suspicious microcalcifications, areas of parenchymal distortion/stellate lesions and small soft tissue masses that cannot be adequately visualised by ultrasound. It is common practice to ultrasound areas of microcalcification detected on mammography. As for ultrasound guided cores for microcalcification, the specimens should be X-rayed to confirm sampling of the microcalcification.

Tomosynthesis is a digital mammography technique that involves acquisition of images from a limited angle rotation of the X-ray source around the breast. This enables viewing of the breast in the conventional image planes in multiple sections, similar to computed tomography. This allows for separation of overlapping structures that make up the conventional 2-dimensional mammography image and improves detection of abnormalities, while decreasing false positive findings.

A small number of women are being offered magnetic resonance imaging (MRI) as part of their family history screening plan. MRI detects a small number of significant abnormalities that are not seen on either mammography or ultrasound and, therefore, require MRI guided biopsy. The technology for MRI-guided breast biopsy is well established, and the skills required are more widely available. NHSBSP protocol requires that all MRI guided breast biopsy is performed using VAB techniques.

2.2 Sampling techniques and procedures

These include:

- FNAC
- NCB
- VAB.

All these procedures can be carried out by members of the breast team who have had specialist training in image guided breast biopsy: a radiologist, advanced practitioner or breast clinician. For simplicity radiologist or assessing clinician is used below. Ultrasound guided NCB is the technique of first choice for sampling impalpable breast lesions, as it is easier to perform, more comfortable for the patient and less time consuming than the X-ray guided techniques (see section 2.1 above). In practice, ultrasound guided NCB is also used for most palpable lesions.

2.3 Core biopsy: general principles

Core biopsy of the breast is a safe and effective method for obtaining a non-operative diagnosis of breast lesions. It should be performed with a spring-loaded device, usually 14 G diameter.

It is the operator’s responsibility to confirm the patient’s identification and label the specimen pot before leaving the room.

2.4 Ultrasound guided core biopsy

The lesion is demonstrated and surrounding breast tissue immobilised. Local anaesthetic is infiltrated both superficially and deeply down to and around the lesion. The core biopsy needle is advanced until the tip is a few millimetres proximal to the edge of the lesion. The core biopsy gun is then fired, and the needle is visualised passing through the lesion. An image showing the needle passing through the lesion is usually recorded.

The needle is withdrawn and the specimen is delivered into fixative. 2 or 3 passes are usually sufficient in most cases to obtain diagnostic material from soft tissue mass lesions.

2.5 Stereotactic-guided core biopsy

During stereotactic core biopsy, the position of the lesion on the stereotactic views is used to determine the position of the needle guide on the X and Y axes. This means that, when a needle of known length is introduced through the guide into the breast, the centre of the needle sampling trough will correspond to the chosen target.

X-ray guided biopsy using tomosynthesis is also now available. The technique is largely similar to stereotactic biopsy except that the image to select the target is acquired by continuous X-ray source arc rotation rather than from 2 images taken at 15-degree angles. When available, it is a quicker localisation technique and facilitates biopsy of lesions only seen on tomosynthesis images. Pathologists should also be aware that contrast-enhanced mammography guided biopsies are in use in some centres and may become more common in the future.

The specimen X-rays should be made available to the reporting pathologist. If multiple biopsies are taken for microcalcification, it is helpful to separate the cores with calcification from those without so that, if microcalcification is not present in the initial levels, the pathologist knows which blocks to request further levels from.

2.6 Large volume sampling techniques

2.6.1 Vacuum-assisted biopsy

There are several systems available for VAB, but all operate under similar principles. Vacuum biopsy is now recommended and preferred for sampling many types of abnormality that require stereotactic X-ray guided biopsy, such as calcification, and is currently obligatory for MRI guided breast biopsy. It is acknowledged that capacity for specific VAB modalities remains variable across services.

The biopsy probe incorporates a vacuum channel, which applies negative pressure to the biopsy port and thereby sucks the adjacent breast tissue into the port for sampling. The biopsy probe is introduced into the breast and positioned using image guidance. Deep local anaesthetic is used.

The vacuum is activated and sucks breast tissue into the biopsy port. A rotating or oscillating cutting cylinder then passes down within the probe and separates the biopsy material from the surrounding tissue. The biopsy specimen is delivered by withdrawing the cutting cylinder while applying negative pressure. Unlike NCB, the needle probe remains within the breast during the whole procedure. Multiple specimens can be obtained and the probe can be rotated in the breast so that the biopsy port is applied to different areas of the surrounding breast tissue.

The advantages of this system are the ability to obtain a larger volume of tissue for histological examination and the rapid evacuation of any haematoma that collects at the site of the biopsy. This ensures that the specimens obtained are of good quality and not compromised by the presence of haematoma. The larger gauge vacuum probes can retrieve 400 mg of breast tissue per core sample.

Guidance is that diagnostic samples of potentially borderline lesions, e.g. microcalcification and architectural distortion, should aim to retrieve around 2 g of tissue. For VAE of B3 lesions, removal of about 4 g of tissue is recommended.[9] This weight of 4 g refers to the weight of the VAE alone and not the combined weight including the previous diagnostic biopsy. If the lesion is small, it may be possible to remove it with some surrounding tissue in a sample that weighs less than 4 g. It should also be noted that samples of the same size may have varying weights depending on, for example, whether the tissue is predominantly fatty or densely glandular.

Of note, the number of cores equivalent to these weights depends on the system manufacturer of the probe rather than purely on the gauge of the needle.

2.6.2 Marker placement

It is recommended that a marker should be placed at the biopsy site for all VAB procedures, after gaining informed consent from the patient. Markers that contain a metal component and can also be seen on ultrasound are preferred, as these facilitate easier subsequent localisation for surgery, if needed. If not, they provide future reference as to where prior biopsy has been performed.

A marker is mandatory if there is any risk that the whole of the target lesion might be removed by the needle biopsy. The pathology department should ideally be made aware of any subsequent biopsy that may contain a marker, as this may influence how the tissue is prepared for sectioning.

2.7 Complications of NCB

NCB and FNAC are remarkably complication free, although common side effects include mild bleeding, bruising and discomfort. Some less common problems should also be considered. Pain after the procedure and fainting during it are occasional side effects. Pneumothorax is very rare. Other side effects that may affect histological interpretation of subsequent specimens are described below.

2.7.1 Haematoma

Where possible, all imaging investigations should be complete before sampling is performed, as haematoma formation, if it occurs, can cause confusion on subsequent imaging and biopsy. The overall rate of haematoma formation after biopsy is approximately 6%; haematoma is usually not clinically significant.[12] Although data is limited, VABs appear to have a higher rate of haematoma formation than other techniques.

2.7.2 Removal of lesion by core biopsy

Small lesions including foci of microcalcification may, particularly if extensively sampled, be removed by core biopsy. This possibility increases when greater numbers of core samples are taken or with VAB. It is recommended that markers are inserted at the site of biopsy at the time of the biopsy to ensure that the site can be identified subsequently.

On occasion, a small, sole invasive focus (with or without surrounding DCIS) may be removed in the needle biopsy samples with no further invasion in the subsequent excision specimen. In such circumstances, the core biopsy sample should be used to provide information on histological grade and tumour type. Further information on reporting in this situation can be found in the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5]

2.7.3 Epithelial cell displacement

Epithelial displacement can be seen following needle core or VAB sampling of both benign lesions (such as intraductal papillomas) and malignant neoplasms. In this context, the absence of surrounding myoepithelium should not alone be interpreted as evidence of invasion. Small clusters of cells are seen, sometimes showing degenerate features,

usually with associated fibrosis and inflammation consistent with the site of previous biopsy. The track is often linear. Displacement is rarely recognised more than a few millimetres from the source of the cells. The clinical significance of this phenomenon is not yet clear.

3 Core biopsy reporting guidelines

This section of this document is designed to assist in classification of NCB and VAB samples. The diagnostic terminology and entities referred to are described in more detail in the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5] Since the last edition of these guidelines was published, the UK National Screening Committee has given its support to the use of digital pathology for the reporting of breast cancer screening specimens.[13]

3.1 Core biopsy specimen information and handling

Proper interpretation of core biopsies requires details of the patient's history and clinical and radiological findings. It is essential that this information is provided on the request form (paper or electronic). Although increasingly this information will be available in the patient's electronic record, it should still be summarised on the request for reasons of efficiency.

The information provided with the request should include:

- full patient and demographic details
- the laterality and location of the lesion(s)
- the clinical impression
- radiological details (mass lesion, deformity, calcification, etc.).

It is essential that the patient and clinical details, including the location of the biopsy on the specimen pot and request form are correct and match. Particular care is needed if multiple biopsies are taken from the same patient. It is also essential that the details are checked in the pathology laboratory before handling the specimen, and when reporting.

3.1.1 Specimen imaging

A radiograph should be taken of all biopsies performed from microcalcifications to determine their presence in the sample. Whenever possible, a radiological comment regarding the presence of microcalcification representative of the mammographic lesion should be provided to the pathologist, along with the specimen X-ray. It is also useful if the

number of cores retrieved is recorded on the request form to enable correlation at macroscopic examination.

The pathologist must be able to view the core biopsy X-rays on a monitor of suitable quality.[14] However, it is the responsibility of the radiologist and the multidisciplinary team (MDT) to decide whether the calcification in the mammogram correlates with the calcification seen histologically.

3.1.2 Fixation and laboratory handling

Biopsies should be placed immediately in a formalin fixative solution and sent promptly to the laboratory. Optimal fixation is essential, particularly for ER and HER2 analysis, for which a minimum of 6 hours and a maximum of 72 hours are recommended.[5] Occasionally, molecular diagnostic testing is performed on core biopsy specimens. This has implications for scheduling of laboratory work. Specimens may be fixed rapidly with the aid of microwave techniques, but such techniques must be validated, including assessment of immunohistochemistry.

There are different approaches to the macroscopic description of core biopsies and VABs. Some laboratories record the number of cores and the length of each. This has the advantage that the number of cores taken in the clinic can be confirmed and allows the number and length of cores to be checked on the histological slides.

Some radiology departments weigh VABs to ensure an adequate amount of tissue has been obtained. The weight can be estimated from the number of cores and the type of device.[10] An alternative approach to the handling of cores is to put the cores into containers in the clinic, so that in the laboratory the cores can be placed directly into the cassette without further handling. This reduces the risk of loss of tissue but precludes macroscopic description.

After processing, it is essential to ensure that the biopsy is properly embedded and that the block is adequately cut into when the sections are taken. Haematoxylin and eosin-stained sections from 1 level are usually sufficient for core biopsies from mass lesions, but core biopsies taken for the investigation of microcalcification should have a minimum of 3 levels examined. In problematic cases, further levels and immunohistochemical studies may be helpful.

Information from all core biopsies of screen detected lesions should be entered on the National Breast Screening System (NBSS – see Appendix D).

[Level of evidence – GPP.]

3.2 RCPath dataset items

The RCPath dataset proformas include a subset of data items included in the NHSBSP form. RCPath dataset items should be collected in all cases of invasive cancer or carcinoma or in situ. For cases being collected through the breast screening programme, it is acceptable to complete the breast screening form, but for cases outside the screening programme, the RCPath dataset should be followed if the NHSBSP form is not being used for all cases. The use of reporting templates is at the discretion of the reporting pathologist; however, all mandatory dataset items should be included.

3.2.1 Recording basic clinical information

Centre/location

Give the name of the assessment centre, clinic, department, etc, and where the specimen was obtained.

Side

Indicate right or left. For specimens with biopsies from multiple sites, use a separate form for each site.

Localisation technique

Choose 1 of the following terms:

- palpation
- ultrasound guided
- stereotactic
- MRI.

Number of cores

If known, indicate the number of core biopsy samples taken.

Presence of calcification on specimen X-ray

If the biopsy is performed for investigation of radiological calcification, indicate whether there is calcification visible on the specimen radiograph, if known. State if the radiograph has not been seen.

[Level of evidence C – The presence of microcalcification within the biopsy is important information that contributes to the discussion at the multidisciplinary meeting about

whether the sample includes the desired lesion and informs assessment of the adequacy of the biopsy.]

Histological calcification

Indicate whether calcification has been identified in the sample and, if present, whether it is associated with benign or malignant disease, or both. Examination of further levels should be performed if calcification in a pattern consistent with that seen on the specimen X-ray is not apparent on histological examination of initial levels. Calcifications less than 100 μm in diameter are not detectable radiologically.[15] It is good practice for the cores containing calcification to be sent in a separate pot as this can reduce the processing workload required in the laboratory. In some circumstances, X-ray of paraffin blocks can also be helpful to aid subsequent histological detection of calcifications. If calcifications obliterating ducts with dense periductal inflammation are noted, deeper levels to look for viable epithelial lining should be considered. This can aid detection or exclusion of obliterative ('burnt out') DCIS.

3.2.2 Histological/cytological opinion

Record as B1–B5 for diagnostic biopsies (core biopsies or first line VAB) or C1–C5 for cytology specimens, as indicated. For further information, see sections 3.3 to 3.8 on core biopsy reporting categories and Appendix A on FNAC reporting.

3.2.3 Tumour classification

If present, record the presence and type of invasive malignancy. If there is no invasive malignancy, record the presence and type of in situ carcinoma.

3.2.4 Grade

Record the tumour grade using the Elston and Ellis method. Accurate grading is important to guide neoadjuvant treatment decisions. For further details on grading, see section 3.8 and the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5]

[Level of evidence B – Invasive tumour grade is a recognised important prognostic factor that is used in treatment planning; accurate assessment is expected.]

3.2.5 ER status, PR status, HER2 status

ER status predicts response to endocrine therapy. The data for PR and response to hormone therapy is less clear, but assessment of PR status is recommended by NICE and is a requirement for some clinical trial recruitment.[16] Overexpression of HER2 protein in

breast cancer is predictive of response to HER2 targeted treatment. Accurate assessment of ER, PR and HER2 status also guides neoadjuvant treatment decisions. NICE recommends testing the status of all 3 markers on the initial histological specimen at the time of initial histopathological diagnosis.[16]

[Level of evidence A – ER status predicts response to endocrine therapies. Overexpression of HER2 predicts response to HER2 targeted treatments.]

Pathologist

The name of the pathologist giving the opinion, who must be registered at the screening office.

Date

Enter the date of issuing the report.

Case for review

This is a field to indicate that a specimen has been sent for a further opinion or that the case is a particularly interesting example.

Recording the opinion

See the section on reporting categories, below.

Comment field

This free text field is included for extra information to be recorded.

3.3 Core biopsy reporting categories

5 reporting categories are used for diagnostic biopsies. They should not be used for excision specimens, including those performed by vacuum-assisted techniques. It is important to remember that histological examination of core biopsy samples is performed to fulfil the assessment process role by giving a pathology category classification (B1–B5). It is not designed to give a definitive diagnosis, although this is possible in most cases.

Thus, while most core biopsy samples can be readily categorised as normal, benign or malignant, it must be recognised that a small proportion (less than 10% in most units) of samples cannot.

In recognition of this, the following reporting guidelines have been devised and should be used for all screen detected lesions. It is recommended that this approach also be adopted for symptomatic practice. It is important to remember that although there are 5 reporting categories similar to those used in FNAC, these are not equivalent.

A table containing selected core biopsy diagnoses and their corresponding diagnostic categories (B codes) is presented in Appendix F. These categories only take account of the histological nature of the specimen, and not the clinical or imaging characteristics. A lesion, for example, should not be classified as benign (B2) simply because radiological–pathological correlation appears appropriate, if only normal histology is seen. Similarly, there should not be equivocation over the category of a biopsy in this situation (e.g. 'B1/2' classification.) Reporting in this way affects audit of individual and unit data in the breast screening programme.

Similarly, it is not feasible for pathology interpretation to judge independently whether a sample is adequate and is from the mammographic lesion. This judgement requires multidisciplinary discussion. For these reasons, there is no inadequate biopsy category for core biopsy specimens.

For VAE of a lesion that has already been diagnosed on a previous biopsy, a B category is not appropriate. VAE is regarded as equivalent to a surgical diagnostic biopsy.

The B category of a diagnostic biopsy should not be changed because a later VAE or surgical excision gives a different diagnosis, unless there was an error in the interpretation of the diagnostic biopsy. In the case of an error, any revised report should make clear that there has been a change.

Sometimes pressure is put on pathologists to issue provisional reports before multidisciplinary meetings or to help meet clinical targets. This is discouraged and not considered good practice. Issuing verbal reports before the report is authorised also confers risk to patient management and is discouraged.[17]

Sometimes it is necessary to send slides and/or blocks to another centre for example for a second opinion, for assessment of markers such as HER2 or if patient care is transferred. Such transfers should be undertaken promptly using a trackable transport system. Mechanisms must be in place for rapid communication of any results or diagnostic disagreement.[18]

3.4 B1 normal tissue

This indicates a core of normal tissue, whether or not breast glandular structures are present. This category is, therefore, equally appropriate for a core including normal breast ducts and lobules or mature adipose tissue or stroma only. A B1 report should include a

description of the components present and comment should be made regarding the presence of breast epithelial structures.

Normal histology may indicate that the lesion has not been sampled. This is, however, not necessarily so. In the case of certain benign lesions, such as hamartomas and lipomas, apparently normal histological features would be expected on core biopsy. Minor architectural distortions seen mammographically may also result in minimal changes such as a slight increase in stromal fibrous tissue on biopsy.

A minor degree of fibrocystic change is usually best categorised as B1. In these circumstances, it is the remit of the multidisciplinary meeting to determine if the lesion of interest has been sampled, if the core biopsy can be considered representative, and if a B1 result can explain the clinical and radiological findings. Lactational change should be categorised as B1.

Cores with B1 diagnoses may contain microcalcification of sufficient size to be radiologically visible, e.g. within involutional lobules or in the stroma. It is important in these cases that discussion between pathology and radiology colleagues is undertaken to confirm whether the microcalcification in the histological specimen is representative of that seen on the mammogram.

Foci of calcification within involuted lobules are common and may be too small to be visible mammographically. Therefore, a report that merely records the presence of this calcification, without additional comment on its nature, size and site, may be misleading and lead to false reassurance. The resolution of digital mammography is lower than film/screen mammography, but calcifications of similar size are more visible and easier to detect on digital mammography.[19]

The pathologist should not categorise a biopsy as B1 because they think the biopsy may not reflect the clinical or radiological abnormality.[20] The latter is the function of MDT discussion. The pathologist should describe the histological features and base the B category on these features. Nevertheless, the pathologist may make a comment in the report that the biopsy may not be representative of the lesion. It is the role of the MDT to judge whether the core biopsy is adequate.

Exceptionally, some specimens may be classified as uninterpretable because of, for example, excessive crush artefacts or because the sample consists of blood clot only. Such samples should also be classified as B1.

3.5 B2 benign lesion

A core is classified as B2 (benign) when it contains a benign abnormality. This category is appropriate for a range of benign lesions, including fibroadenomas, fibrocystic change, sclerosing adenosis, benign squamous metaplasia and duct ectasia, and extends to include other non-parenchymal lesions, such as abscesses and fat necrosis. A fully represented small papilloma or radial scar without epithelial atypia may also be categorised as B2.[10]

In some cases, it may be difficult to determine whether a specific lesion is present, for example, if minor fibrocystic changes are seen. The multidisciplinary approach is once again vital in these cases to determine whether the histopathological features are in keeping with the radiological and clinical findings. It may be appropriate and prudent to classify the lesion as B1 rather than B2, if only very minor changes are present.

Sometimes skin or nipple lesions will be sampled. If a definite benign diagnosis is possible, then B2 categorisation is appropriate. Sometimes a definite diagnosis is difficult, e.g. some adnexal tumours may be difficult to categorise on core biopsy, in which case B3 may be more appropriate.

3.6 B3 lesion of uncertain malignant potential

This category mainly consists of lesions that provide benign histology on core biopsy, but either are known to show heterogeneity or to have an increased risk of associated malignancy (albeit lower than for B4). The level of risk is very different for the different entities. The management of B3 lesions is discussed in detail in a separate document.[10] More comments about management are included in section 3.6.9.

It is essential that a search is made for epithelial atypia and that such atypia is reported, even if there is another reason for a B3 categorisation, as the risk of malignancy associated with atypical intraductal epithelial proliferation (AIDEP) is relatively high.[21] For all B3 diagnoses, a comment should be made about whether epithelial atypia is present. Use of a reporting template may improve recording of presence or absence of atypia in B3 lesions.

3.6.1 Atypical intraductal epithelial proliferation

There is a range of intraductal epithelial atypia, short of that required for a definite diagnosis of DCIS, that is best classified as B3 with epithelial atypia or B4. Different

patterns of atypia may be seen resembling atypical ductal hyperplasia (ADH), flat epithelial atypia, apocrine atypia and atypia that does not conform to any of these patterns.

A common pattern resembles what would be called ADH on a surgical specimen: a monomorphic proliferation of evenly spaced cells with small regular nuclei that raises the possibility of low grade DCIS, but has insufficiently developed features or insufficient extent for this diagnosis.[5] These range in severity, from those that are insufficient for a definite diagnosis of DCIS but highly suspicious, to those that only show a minor degree of atypia, normally architectural, which requires further assessment and judgement of appropriate categorisation as B3 with epithelial atypia or B4; most are best classified as B3 with epithelial atypia.

The definition of ADH is derived from surgical resection specimens and relies on a combination of architectural, cytological and size extent criteria. For this reason, accurate diagnosis of ADH is not possible on core biopsy, and the term AIDEP should be used.

It has, however, been shown that core biopsy samples that include atypical intraductal epithelial proliferative foci, of insufficient extent for classification as DCIS, may form, on subsequent surgical resection, part of an established in situ neoplastic lesion, with or without associated invasion.[21]

This view is based on studies that describe the subsequent surgical diagnoses in cases described as ADH in non-operative core biopsy. The upgrade rate of AIDEP varies depending on the type of core biopsy specimen, being greater with small samples.[10] This is not surprising as ADH is defined as an intraductal epithelial proliferation showing the features of low-grade DCIS, but in fewer than 2 duct spaces or of less than 2 mm in maximum dimension.

The limited tissue sampling that can be undertaken by core biopsy guns (often by stereotactic methods for foci of microcalcification) may thus provide insufficient material for definitive diagnosis of low-grade DCIS if only a few ducts spaces are obtained. In these cases, a diagnosis of AIDEP should be made, along with a classification of B3 with epithelial atypia or, less commonly, B4 suspicious for malignancy, depending on the severity and extent of the lesion.

Immunohistochemistry for basal cytokeratins (such as CK14 and CK 5/6) and ER can play a useful role in assessing epithelial proliferations. The epithelial cells in DCIS and ADH/AIDEP are typically completely negative for basal cytokeratins and uniformly positive

for ER. Usual type epithelial hyperplasia shows patchy expression of basal cytokeratins and ER.

The surrounding myoepithelial cells are usually positive for basal cytokeratins. However, there are pitfalls. Occasionally, DCIS is positive for basal cytokeratins, but this is usually high grade. Columnar cell change and apocrine change are both negative for basal cytokeratins, so assessment of atypia in these lesions must rely on morphology. For a more detailed discussion, see the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5]

3.6.2 Flat epithelial atypia

Columnar cell lesions are discussed in greater detail in the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5] Most columnar cell change, with or without hyperplasia, shows no atypia and is best categorised as B2 (or sometimes as B1 if it is very focal).

Flat epithelial atypia is categorised as B3 with epithelial atypia on core biopsy. The diagnosis of flat epithelial atypia shows poor concordance – interobserver variability is high.[22] The risk of upgrade to malignancy with flat epithelial atypia alone also appears to be low compared to other B3 lesions with atypia.[23] If there is a more complex architecture (usually cribriform or micropapillary), the considerations in the above section on atypical intraductal proliferations apply.

Flat epithelial proliferations with high-grade nuclei should be categorised as B4 if the changes are limited, and as high-grade DCIS (B5a) only if the features are sufficient for an unequivocal malignant diagnosis.

3.6.3 Lobular neoplasia

A pathologist may consider a small to medium cell regular dyscohesive epithelial proliferation within lobules to represent classical lobular neoplasia: either atypical lobular hyperplasia (ALH) or lobular carcinoma in situ (LCIS). It should be classified as B3 with epithelial atypia.

The distinction between ALH and LCIS cannot always be reliably made on core biopsy, so the overarching term ‘lobular neoplasia’ is preferable. If preferred, sub-categorisation into ‘at least ALH’ and ‘LCIS’ can be made, but there appears to be no significant difference in upgrade rate (i.e. risk of adjacent DCIS or invasive carcinoma), so there is no clinical benefit to this distinction in core biopsy.

Classical lobular neoplasia does not have the same management implications as a diagnosis of DCIS or invasive malignancy and does not per se require therapeutic excision. Lobular neoplasia is, however, often a coincidental finding in a core biopsy from a screen detected lesion, and multidisciplinary discussion is essential as the abnormality identified radiologically may not be represented. These cases must be managed cautiously.[10]

Pleomorphic LCIS is best classified as B5a (see below in 3.8.4). Occasionally, lobular neoplasia shows marked distension of the acini, often with necrosis, but without marked nuclear pleomorphism.[24] There are only limited data on the behaviour of this variant,[25,26] which is now called florid LCIS, but in view of the overlap of features with the DCIS, it is best classified as B4.

There are limited data on the optimum management of both pleomorphic and florid LCIS, but the WHO Classification of Tumours recommends excision for both when diagnosed on core biopsy.[27]

E-cadherin immunohistochemistry can be useful to help distinguish lobular neoplasia and DCIS in difficult cases. DCIS typically shows complete membrane expression, whereas lobular neoplasia usually shows reduced, absent or otherwise abnormal E-cadherin membrane expression. In cases where E-cadherin is unhelpful, beta-catenin (negative in lobular proliferations) may resolve the issue. Basal cytokeratins are typically absent in lobular neoplasia, as described above for DCIS. On occasions, it may be difficult to classify an epithelial proliferation as either lobular neoplasia or low-grade DCIS. In these circumstances, a B4 classification may be appropriate.

3.6.4 Phyllodes tumour

The presence of cellular stroma within a fibroepithelial lesion on core biopsy suggests a differential diagnosis of either cellular fibroadenoma or benign phyllodes tumour. However, definitive categorisation is not possible on core biopsy alone. Such lesions should be designated as B3 fibroepithelial lesions, with a statement indicating that a phyllodes tumour cannot be excluded.

As cellular fibroadenoma is relatively common, it is important to search for additional histological features that favour a diagnosis of phyllodes tumour in these cellular fibroepithelial lesions.[28,29] Features that support phyllodes tumour include:

- stromal overgrowth: defined as a ×40 field of stroma lacking glandular elements on core biopsy

- fragmentation: stromal fragments with epithelial components at one or both ends
- mitoses: while 1–2 mitoses per 10 high-power fields (2 mm²) may be seen in both fibroadenoma and phyllodes tumour, the presence of 3 or more mitoses per 10 high-power fields more strongly favours phyllodes tumour. However, caution is advised against overinterpreting juvenile fibroadenomas as phyllodes tumours based solely on mitotic activity.

If multiple supportive features are present, a definitive diagnosis of phyllodes tumour may be possible. However, given that phyllodes tumours account for approximately 1 in 40 fibroepithelial lesions in European populations,[30] overinterpretation of minor changes may lead to unnecessary surgical excision of numerous fibroadenomas.

When features suggest a benign phyllodes tumour, classification as a B3 fibroepithelial lesion remains appropriate. Marked stromal atypia is usually accompanied by other features of phyllodes tumour and may raise the level of suspicion. In such cases, reporting as B3 with a comment indicating possible borderline or malignant phyllodes tumour is advised. In select cases, B4 or even B5 categorisation may be warranted. Notably, marked atypia should be distinguished from the presence of bizarre stromal giant cells, which may occur in fibroadenomas, phyllodes tumours, or other lesions and do not in themselves indicate malignancy.

An important diagnostic pitfall is that some phyllodes tumours contain areas that closely resemble typical fibroadenomas. Clinical features, particularly large or increasing tumour size, should be considered and discussed at multidisciplinary meetings to guide management decisions.

3.6.5 Papillary lesions

Papillary lesions may show significant intralesional heterogeneity and the limited sampling achieved with core biopsy may miss areas of in situ carcinoma. Papillary lesions with or without atypia should be categorised as B3, unless any atypical proliferation is of sufficient extent (>3 mm) to warrant classification as B5a. On rare occasions, when a very small lesion is seen within the diameter of the core, a benign B2 classification may be considered. It is important that even focal epithelial atypia is sought, as the chance of malignancy in the subsequent excision specimen is much higher than in lesions without atypia (30–40% versus 5–10%).[31]

Immunohistochemistry for myoepithelial markers can be helpful. Benign papillomas contain a myoepithelial layer, both at the edge and within the lesion between the

epithelium and the fibrovascular core. However, in papillary carcinoma in situ, myoepithelial cells are usually absent within the lesion.

Myoepithelial cells may be seen surrounding papillary DCIS but are usually absent at the periphery of encapsulated papillary carcinoma. Papillomas with involvement by DCIS typically show retention of a myoepithelial layer. Basal cytokeratins and ER are useful for distinguishing usual type epithelial hyperplasia and DCIS, as discussed above.

Nipple adenomas often show papillary features and so are usually best classified as B3.

3.6.6 Radial scar

Biopsies that show features of radial scar, namely fibroelastotic stroma containing entrapped glands with surrounding myoepithelial layer, should be categorised as B3. In the case of a small radial scar, fully represented within the core biopsy and without epithelial atypia, B2 categorisation is appropriate.[10] If reliable distinction from tubular carcinoma is not possible, then immunohistochemistry with a panel of myoepithelial markers is valuable. As described above for papillary lesions, epithelial atypia should be sought, as the chance of malignancy in the subsequent excision specimen is much higher if atypia is present.[31]

3.6.7 Mucocoele-like lesions

Mucin in the stroma (a mucocoele-like lesion) can be associated with benign cysts, AIDEP/ADH, DCIS and invasive carcinoma, particularly of mucinous type. The risk of malignancy appears to be low if there is no atypia on the core biopsy.[32]

3.6.8 Rare lesions

Some rare lesions are best classified as B3 on core biopsy, such as adenomyoepithelioma, microglandular adenosis, apocrine adenosis, granular cell tumour, spindle cell lesions such as fibromatosis and myofibroblastoma and vascular lesions that are difficult to classify. Some bland vascular lesions are appropriately categorised as B2, but if there is doubt then categorise as B3 without epithelial atypia.

3.6.9 Management of B3 lesions

As with all non-operative diagnoses, multidisciplinary discussion is important. Multidisciplinary guidelines propose excision or more thorough sampling using VAE as an alternative to diagnostic surgical biopsy in the majority of lesions with a B3 diagnosis made with core biopsy or VAB.[10] It is recommended that the VAE removes about 4 g of tissue as an indication of adequate sampling. This weight of 4 g refers to the weight of the VAE

alone and not the combined weight including the previous diagnostic biopsy. Smaller lesions may be completely excised in less than 4 g of tissue.

This approach is recommended for AIDEP, flat epithelial atypia, classical lobular neoplasia, papilloma without epithelial atypia, radial scar with or without epithelial atypia, and mucocoele-like lesion with or without epithelial atypia.

Surgical excision is recommended for papillomas with epithelial atypia, as the distinction between ADH and DCIS within a papilloma is based on extent (3 mm). This cannot be assessed reliably if the lesion is removed as multiple separate pieces.

Surgical excision is usually the appropriate management for cellular fibroepithelial lesions, spindle cell lesions, including fibromatosis and myofibroblastoma, vascular lesions that are difficult to classify, adenomyoepithelioma and microglandular adenosis. There are detailed management flow charts in the B3 guidelines.[10]

The findings in second line VAE specimens should be reported in conjunction with the findings of the core biopsy or diagnostic VAB (or both if this is the third specimen), e.g. regarding assessment of the extent of AIDEP and thus whether the overall lesion is sufficient in the two specimens for diagnosis of low-grade DCIS.

A comment should be made as to whether similar changes are present in both specimens and whether there are signs of previous biopsy in the later specimen(s) to indicate sampling of the appropriate site. If a marker clip reaction is identified, this should be documented. Subsequent management should be based on the final diagnosis taking all specimens into account.

For reporting purposes, VAE specimens are treated like surgical biopsies, therefore a B code is not appropriate.

3.7 B4 suspicious

This category is used uncommonly (<1% of biopsies). Technical problems such as crushed or poorly fixed cores that contain probable carcinoma but cannot provide the definitive diagnosis are best categorised as B4. Similarly, small groups of apparently neoplastic cells contained within blood clot or adherent to the outer aspect of the sample should be classified as B4. Very small foci suspicious of invasive carcinoma in which there is insufficient material to allow immunohistochemical studies may also reasonably be assigned to this category.

A complete single duct space bearing an unequivocal high-grade atypical epithelial proliferative process can be classified as B5a – malignant – in situ. However, care must be taken if one or only part of a duct space is seen containing a highly atypical epithelial process, particularly if no necrosis is present. This may be regarded as suspicious rather than definitively malignant. In particular, great care should be taken if the epithelial cells show any features of an apocrine phenotype, which may represent an atypical apocrine proliferation rather than DCIS. In this context strong complete membrane positivity for HER2 supports the diagnosis of DCIS.

Another lesion that can be allocated to this category is a non-high-grade intraductal proliferation with a significant degree of atypia probably representing intermediate or low-grade DCIS, where relatively few involved duct spaces are represented in the biopsy. A pragmatic approach is usually required by reporting an atypical intraductal proliferation and qualifying this according to the degree of suspicion, i.e. ‘at least ADH, probably low-grade DCIS’, and, based on the extent or severity of atypia, allocating the case either to the B3 or to B4 category.

As discussed in the section above on lobular neoplasia, lesions that are difficult to classify as LCIS or DCIS, as well as florid LCIS, are often best classified as B4.

The management of cases classified as B4 will usually be either diagnostic excision biopsy of the area or repeat core biopsy or VAB to obtain definitive diagnosis. Definitive therapeutic surgery should not be undertaken as a result of a B3 or B4 core biopsy diagnosis except after a definite diagnosis of a phyllodes tumour.

3.8 B5 malignant

This category is appropriate for cases of unequivocal malignancy on core biopsy. The B5 category is further subdivided into B5a, B5b and B5c.

B5a is the appropriate classification for unequivocal DCIS of all grades and pleomorphic LCIS, the report stating whether the lesion is DCIS or LCIS (classical lobular neoplasia is categorised as B3). Encapsulated papillary carcinoma and solid papillary carcinoma are both classified as B5a.

B5b is used for all invasive primary breast carcinomas and rare invasive malignancies, including malignant phyllodes tumours, lymphomas and metastatic tumours.

B5c is used when it is not possible to say whether the carcinoma is invasive or in situ. This category should be rarely applied. It is only used when there are large fragments of

carcinoma with no surrounding stroma. Malignant papillary lesions should not routinely be classified as B5c. The edge of a papillary lesion is usually assessable in a core biopsy that permits classification as B5a. Again, malignant papillary lesions should only be classified as B5c in the rare circumstance where no surrounding stroma is present in the biopsy. Fragments of papillary carcinoma are usually best categorised as B5a.

If there is unequivocal DCIS and features suspicious of invasion, but not sufficient for a definite diagnosis of invasive carcinoma, then B5a categorisation should be used.

3.8.1 Category B5a: DCIS

One of the benefits of core biopsy compared with FNAC is that it can allow distinction between in situ and invasive carcinoma. However, as a result of the biopsy missing an area of invasion, approximately 20–30% of patients with a core biopsy diagnosis of DCIS will have invasive carcinoma identified in the subsequent excision specimen.[33]

The nuclear grade of the DCIS should be indicated on the core biopsy (see the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*).[5] Architecture and the presence of necrosis may also be noted. The presence or absence of associated calcifications should be recorded, particularly if the biopsy was for investigation of calcification.

Paget's disease of the nipple should also be categorised as B5a. Immunohistochemistry can be helpful. Paget's disease is usually luminal cytokeratin and HER2 positive. Bowen's disease expresses basal cytokeratins. Melanoma is HMB45 and melan-A positive. S100 can be positive in Paget's disease as well as melanoma.

3.8.2 Malignant papillary lesions

Encapsulated papillary carcinoma should be categorised as B5a. Encapsulated papillary carcinomas usually lack a myoepithelial layer and probably represent an indolent form of invasive carcinoma.[34]

Regardless of whether these are invasive lesions or in situ cancers, the clinical outcome is good with adequate local therapy alone, similar to DCIS. Hence the current recommendation is that these lesions should be categorised as B5a. It is recommended that the pathology report describes the lesion so that it is clear that it is not conventional DCIS.

3.8.3 Foci of invasive carcinoma 1 mm or smaller

Microinvasive carcinoma is an entity requiring full assessment of the overall lesion. It cannot be definitively diagnosed on core biopsy.

If the core biopsy shows a small area of invasion less than or equal to 1 mm, it is recommended that levels are examined to see if the area is larger than 1 mm.

Unequivocal invasive carcinomas 1 mm or less in diameter should now be categorised as B5a whether or not there is associated DCIS. These guidelines apply to all types of microinvasive carcinoma, including microinvasive lobular carcinoma.

If there is DCIS and an area suspicious for invasion, but no definite invasion, then categorisation as B5a is appropriate. If there is an area less than or equal to 1 mm suspicious of invasion but no definite invasion and no DCIS, then categorisation as B4 is appropriate.

B5c should not be used for invasive carcinoma less than or equal to 1 mm.

It is important that the lesions discussed in this section have the histological features carefully described in the report so that it is clear what is present in the biopsy.

3.8.4 Lobular neoplasia

Pleomorphic LCIS shows marked nuclear pleomorphism like that seen in high-grade DCIS. It can be confused with DCIS, particularly when associated with necrosis and calcification. These lesions should be categorised as B5a, as the current recommended management is similar to high-grade DCIS.

Immunostaining with E-cadherin will often help differentiate between high-grade DCIS and pleomorphic LCIS. In exceptional circumstances, lobular neoplasia may be impossible to distinguish from small cell solid DCIS. Staining for E-cadherin and β-catenin should be helpful to differentiate between the two. Membrane expression of E-cadherin and β-catenin is typically absent or reduced in lobular neoplasia and present in DCIS.

Classical lobular neoplasia (ALH/LCIS, see section 3.6.3) should be categorised as B3 with epithelial atypia.

3.8.5 Category B5b: invasive carcinoma

A major advantage of core biopsy over FNAC is the ability to diagnose invasion positively.

Invasive carcinoma can be unequivocally identified in core biopsy with a positive predictive value (PPV) of almost 100%. False positive diagnosis is very rare.[35] As noted above,

however, the negative predictive value for invasion is only 80% when only DCIS is identified.[36]

Rarely, carcinoma is seen only in lymphovascular spaces. Provided the changes are sufficient for an unequivocal diagnosis, this should also be categorised as B5b.

3.9 Assessment of prognostic and predictive factors

All invasive carcinomas should be graded and typed on core biopsy, where possible. Evidence suggests that concordance between grade on core biopsy and that in the definitive excision specimen can be achieved in approximately 70% of cases.[37,38] Although not mandatory, inclusion of the individual factors used to assess grade (gland formation, nuclear pleomorphism and mitotic activity, e.g. T3 P2 M1) is considered best practice.

It should, however, be made clear to the clinicians that the grade may differ (almost invariably by only 1 level) from that in the subsequent resection specimen. A phrase such as ‘provisional (core) grade’ is suggested. In particular, mitotic count may be lower in the core biopsy than in the excision specimen, therefore leading to underestimation of grade on the core.[39] Assessment of histological grade can also be performed on core biopsy of nodal metastases. The latter should only be used if the amount of tumour tissue is too small on the breast core or if the breast core biopsy sample is technically suboptimal (e.g. due to poor fixation).

Assessment of histological type is useful to identity patients with invasive lobular carcinoma, who may be offered MRI if they are considering breast conserving surgery to identify multifocal disease.

Core biopsy may be the only opportunity to assess grade and type in the neoadjuvant setting when there may not be any residual tumour in the surgical specimen.

ER and HER2 assessment on core biopsy has been shown to correlate well with subsequent surgical excision specimens.[40] There is poorer correlation with PR. Of note, there is emerging evidence that including HER2 low status in studies of correlation between core biopsy and excision specimens reduces concordance.[41,42] NICE recommends that ER, PR and HER2 are assessed on the core biopsy to facilitate planning of patient management.[16] In line with ASCO/CAP and NICE guidelines, PR testing could be considered as good practice for UK laboratories and included as a part of the biomarker panel, especially if resources permit.[16,43] However, at present, given the lack of consensus agreement, it has not been included in the RCPath dataset as a mandatory item.

ER is not part of the minimum dataset for DCIS, but is assessed in some centres, particularly if it will influence treatment, for example in a patient who is not fit for surgery or where adjuvant hormone therapy is being considered.

As with determination on excision biopsy samples, a standard protocol and method of assessment should be used. For best results, the core biopsy should be fixed for at least 6 and no more than 72 hours. For detailed guidance on assessment of ER, PR and HER2, please refer to the *Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer*.[5]

For patients to be recommended neoadjuvant chemotherapy or primary endocrine treatment based on core biopsy features, the biopsy must contain sufficient carcinoma for definitive diagnosis, assessment of histological grade and reliable determination of ER, PR and HER2 status.

Other diagnostic and predictive markers such as Ki67, PD-L1, PIK3CA, AKT, NTRK, IDH2 and others may also be requested on core biopsy tissue. There is evidence that commonly requested gene expression tests are reliable in core biopsy tissue.[44,45]

3.10 Rare malignancies

Spindle cell carcinomas and metaplastic carcinomas should be designated as B5b. The use of an antibody panel, including a range of anti-cytokeratin antibodies (high and low molecular weight cytokeratins and a broad-spectrum antibody), will assist in diagnosis. When a definite histological diagnosis cannot be made, the abnormality should be reported as spindle cell lesion of uncertain histogenesis or nature and classified as B3 or B4.

3.10.1 Lymphoma

If suspicion of lymphoma is raised histologically, the case should ideally be referred to a specialist integrated haematopathology diagnostic service for full diagnostic and molecular workup. Malignant lymphoma should be classified as B5b. Most of these lesions are of high-grade B-cell morphology and may mimic epithelial malignancy. As in other organs, the cells frequently show less cohesion and a higher nuclear to cytoplasmic ratio and do not demonstrate the architectural features of carcinoma. The correct diagnosis is supported by immunohistochemistry (CD45, CD20, CD3, CD30, etc.) to differentiate from an epithelial or other malignancy such as melanoma (and demonstrate the appropriate phenotype).

Low-grade lymphomas may be more difficult to distinguish from a chronic inflammatory process. Infiltration of the lobular epithelium should be sought and if the degree of lymphoid infiltrate is high, it should raise the possibility of a neoplastic process. A panel of lymphoid markers is necessary to demonstrate the phenotype of the cells present to allow correct diagnosis.

3.10.2 Metastasis to the breast

Metastasis to the breast from primary malignancies elsewhere is well recognised, although in practice rarely biopsied if the diagnosis is recognised clinically. A full clinical history is essential to avoid misdiagnosis of a metastatic adenocarcinoma as a primary carcinoma.

A wide range of tumours can metastasise to the breast, but the most frequently seen are lymphomas, carcinomas of the lung, ovary (serous papillary), kidney and prostate, neuroendocrine tumours/carcinomas and malignant melanoma. The diagnosis should be considered if the features of a malignancy are not typical of mammary origin.[46]

Immunohistochemistry is often helpful, but no marker is completely sensitive or specific, so it is important to use a panel of antibodies. Breast carcinoma usually expresses cytokeratin 7 and 18 (and not cytokeratin 20), GATA3, and TRPS1. SOX10 can be helpful in triple negative breast cancer. Approximately 80% of primary breast tumours are ER positive. TTF1 is useful for identifying pulmonary and thyroid carcinoma, WT1 for identifying ovarian carcinoma, synaptophysin, chromogranin and INSM1 for neuroendocrine lesions and S100, Melan-A and HMB45 for identifying melanoma. PAX8 is a useful marker of gynaecological, renal and thyroid carcinomas. Further help dealing with this situation can be found in the dataset for histopathological reporting of cancer of unknown primary and malignancy of unknown primary origin.[47]

3.10.3 Sarcomas

Primary breast sarcomas are rare. Mammary sarcomas most commonly originate in association with malignant phyllodes tumour or as part of a metaplastic carcinoma, but in a core biopsy the epithelial component may not be represented. The most common associated sarcomas are liposarcoma, fibrosarcoma, osteosarcoma, chondrosarcoma and rhabdomyosarcoma.

Angiosarcoma is the most common primary breast sarcoma and most commonly arises in the dermis after previous radiotherapy. It may be the cause of false negative diagnosis, as it may be relatively subtle.

Primary and secondary leiomyosarcoma may be found in the breast.

All these lesions can be difficult to diagnose definitively in core samples. If unequivocal malignancy is present, they should be categorised as B5b. A high index of suspicion and judicious use of immunohistochemistry can facilitate or support a diagnosis.

3.11 Problems and pitfalls in diagnosis

There are recognised problem areas and potential pitfalls in core needle biopsy diagnosis.[48,49]

3.11.1 Minor degrees of epithelial atypia

Mild atypia of epithelium within lobular units is one of the most common problems encountered in core biopsy samples. Care must be taken not to overdiagnose such minimal degrees of atypia, which may represent usual epithelial hyperplasia (UEH), apocrine change or reactive changes, e.g. adjacent to a previous sampling procedure.

Conversely, more severe degrees of atypia must be sought that may reflect cancerisation of lobules by high-grade DCIS. The degree of atypia should be helpful in distinguishing the process, and the nuclear chromatin and presence of mitoses (although rarely seen) may aid in the diagnosis.

Similarly, UEH and other forms of benign hyperplasia – such as that of gynaecomastoid type – are commonly seen in cores from benign fibroadenomas. This often shows apparent dyscohesion due to the trauma of the core biopsy sampling process, and ‘telescoping’ of the epithelium is seen within the duct spaces, thus resembling a hyperplastic process.

As with UEH in surgical excision specimens, the lack of uniformity and distribution/streaming of the epithelial cells with bland nuclear features and paucity of mitoses is of assistance in reaching a diagnosis. AIDEP should not be diagnosed in these cases unless uniformity of nuclear size and shape and regular, evenly placed nuclei are seen. UEH of gynaecomastoid type with a micropapillary architecture should not be mistaken for micropapillary ADH/DCIS.

As discussed above, immunohistochemistry for basal cytokeratins and ER can be helpful in distinguishing UEH from DCIS.

3.11.2 Apocrine atypia and apocrine DCIS

Apocrine atypia, particularly in association with a sclerosing lesion, such as sclerosing adenosis, may be especially difficult to identify correctly in non-operative diagnostic samples.[50]

In core biopsy, large nuclei, often with prominent nucleoli, may be mistaken for DCIS if pleomorphism is also present. The typical granular eosinophilic cytoplasmic appearance of apocrine cells should be sought.

Pure apocrine DCIS is relatively rare and pleomorphic apocrine LCIS is even less common. When an atypical apocrine proliferation is seen within ducts in a core biopsy, additional features of malignancy – such as significant atypia, intraluminal necrosis and the presence of mitoses, as well as multiple duct involvement – should be sought for confirmatory evidence. In addition, multiple duct involvement indicating a more extensive lesion may provide further supportive evidence.

Mild or moderate degrees of apocrine proliferation with atypical features in a duct space should be assessed with caution; it may be prudent not to record a definite diagnosis, but to classify such a process as B3 of uncertain malignant potential. Conversely, papillary apocrine change should not be mistakenly classified as other than benign.

3.11.3 Lactational change

Focal lactational change may be seen in women who are neither lactating nor pregnant and indeed are nulliparous and/or postmenopausal. The involved acini are usually lined by plump vacuolated cells with a ‘hobnail’ architecture, but may less frequently appear atypical with irregular, large or pyknotic nuclei. The epithelial cells may appear degenerative and, rarely, the benign nature of the process may be mistaken for cancerisation of lobules by DCIS. The recognition of the vacuolation of the cytoplasm and the typical hobnail architecture will enable the correct diagnosis to be established.

3.11.4 Sclerosing lesions (including complex sclerosing lesion/radial scar) versus tubular carcinoma

There is a risk of overdiagnosis of invasive carcinoma when confronted by sclerosing lesions in a core biopsy, particularly as the normal lobular arrangement may be less apparent than on an excision biopsy specimen. Immunohistochemical staining for myoepithelial markers can be useful in this situation although interpretation of these markers can sometimes be difficult.

3.11.5 Stromal proliferations and spindle cell lesions

Spindle cell proliferations may cause difficulties in diagnosis in core biopsy samples. The most common lesion seen on core biopsy is scarring. Usually, associated changes such as fat necrosis or haemosiderin-laden macrophages are present and enable a diagnosis and categorisation as B2. Occasionally, scarring may show atypical spindle cells, and a definite benign diagnosis may not be possible on core biopsy.

Myofibroblastoma is composed of short bundles of bland spindle cells with intervening eosinophilic collagen bundles and sometimes adipose tissue. The cells typically express CD34 and desmin as well as myoepithelial markers.

Fibromatosis is a bland spindle cell proliferation that is best categorised as B3. Nuclear expression of β-catenin is frequently seen but is not specific and β-catenin immunohistochemistry can be difficult to interpret in this situation. Cytokeratins and CD34 are not expressed. Molecular testing for CTNNB1 mutation is helpful in uncertain cases.

Metaplastic carcinoma should be considered when dealing with spindle cell lesions, as it can show a wide range of appearances, including resembling fibromatosis. Evidence of epithelial differentiation must be sought. This may range from small cohesive foci to conventional carcinoma. Immunohistochemistry for a panel of cytokeratins, including both luminal and basal cytokeratins, should be performed.

Occasionally, a phyllodes tumour may show only spindle cells on core biopsy. Evidence for an epithelial component should be sought, e.g. by performing additional levels. CD34 expression supports the diagnosis of phyllodes tumour.

Primary sarcomas of the breast are very rare; the most common of these is angiosarcoma. Skin lesions such as dermatofibroma and melanoma need to be considered in the differential diagnosis of spindle cell lesions.

When a definitive histological diagnosis cannot be made, the abnormality should be reported as a spindle cell lesion of uncertain nature and classified as B3 or B4.

3.11.6 Radiation-induced changes

Radiotherapy changes to the breast may be difficult to differentiate from foci of recurrent or residual carcinoma, both in situ and invasive. The radiation induces a degree of atypia of the breast epithelium, but also in the histiocyte population, which is prominent as a result of the radiotherapy and recent surgery. If the pathologist is confident that atypia is radiation-induced, a B2 category is appropriate.

The macrophages may also show degenerative features. Thus, carcinoma cells can conversely mimic macrophages. Immunocytochemistry can be helpful in difficult cases, as irradiated neoplastic cells retain cytokeratin expression, while macrophages demonstrate a histiocytic phenotype, e.g. CD68 reactivity.

3.11.7 Invasive lobular carcinoma

Small foci of invasive lobular carcinoma can be missed in histological sections and be dismissed as chronic inflammation or stromal cells. The targetoid infiltrative pattern of classical lobular carcinoma and the characteristic intracytoplasmic vacuolation may be of assistance, but a reactive lymphocyte process can also have a periductal or perilobular distribution. Cytokeratin immunohistochemistry to demonstrate the neoplastic cells is of value in difficult cases, but recognition of the abnormal cell proliferation requires vigilance, as the features can be subtle.

4 Axillary lymph node assessment and preoperative sampling

Axillary nodal status remains the most powerful prognostic factor in patients with invasive carcinoma of the breast.[51] Sentinel node biopsy has become the standard method for staging of disease. Those patients with involved nodes may then require further treatment of the axilla. Neoadjuvant chemotherapy will often be given after a preoperative diagnosis of nodal metastasis. Thus, accurate preoperative nodal assessment is essential.

All patients seen in symptomatic and screening assessment clinics who have suspicious mammographic and/or ultrasound findings should have detailed ultrasound assessment of the axilla.[4] Level 1 axillary nodes, easily visualised in most patients, can be assessed for risk of metastatic involvement.[52]

Morphological lymph node abnormality is more predictive of metastatic involvement than cortical thickening. When axillary lymph nodes are involved, ultrasound and needle biopsy or FNA will detect disease in over 80%.[53] The chances of detection are higher in high-grade invasive breast cancer and when there are 4 or more nodes involved. The yield from sampling morphologically normal lymph nodes with no cortical thickening is very low and is not recommended.

Both core biopsy and FNA may be used to sample abnormal axillary nodes. FNA is preferred for smaller nodes and for nodes close to vessels. Core biopsy may be preferred

when the lymph node is large (>20 mm) or when FNA is negative, inadequate or equivocal from clearly radiologically abnormal nodes. The sensitivity of core biopsy for malignancy in lymph nodes is generally higher than for FNA.[53,54] For this reason (and the ability to perform immunohistochemistry), it is now the standard in many centres.

The lymph node targeted on ultrasound is frequently not the sentinel node subsequently targeted at surgery.[52] In the case of positive nodes identified preoperatively, techniques for targeting the sampled node during surgery are available, such as marker clips and tattoo ink.[55]

Specificity is high for both NCB and VAB, but false positive diagnosis has been described with FNAC of axillary nodes and is likely to be more frequent with FNAC than with core biopsy, as is well recognised in sampling of lesions in the breast. About half of nodal metastases can be detected, but the sensitivity depends on how patients are selected and the number of passes. Sensitivity increases with increasing nodal disease burden.[56]

Given the necessary expertise, FNA may allow equivalent sensitivity at a lower cost. FNA is preferred by some units due to the proximity of large vessels and nerves and the speed of the procedure. Core biopsy provides sections for ready identification of a small volume of disease and allows immunohistochemistry in cases of equivocal morphology. With FNAC it is helpful to prepare material for immunocytochemistry, as this may be useful on occasions. Needle washings can be used for this. Limited volume disease can be missed with either technique.

Lymph node FNA and core biopsy in breast cancer patients is intended for assessment of the presence or absence of metastatic carcinoma. If there is suspicion of malignant lymphoma (axillary lymphadenopathy in the absence of a known cause or malignancy in the breast), the patient should be referred for assessment in line with local protocols for diagnosis of malignant lymphoma.

All patients with primary invasive breast cancer with negative results for metastatic disease on FNA or core of the axillary nodes are candidates for sentinel node biopsy or other axillary procedure for definitive staging.

4.1 L codes for FNAC

For FNAC assessment of axillary lymph nodes, the following diagnostic categories may be used but are not mandatory and can be replaced by C codes. LC codes map directly to the corresponding C code when entering data on NBSS.

LC1 Inadequate: no lymphoid cells or technically inadequate.

LC2 Benign: benign lymphoid cells regardless of whether specific reactive features are seen or not.

LC3 Atypia: atypical cells present, lymphoid or other of uncertain nature and significance. LC3 can be used for atypical lymphoid proliferations – usually low-grade lymphomas where immunohistochemistry and flow samples are not available.

LC4 Suspicious for malignancy: either metastasis or lymphoma. Usually, only occasional cells present either singly or in small groups.

LC5 Malignant: metastatic carcinoma or other malignancy (including lymphoma).

4.2 L codes for NCB

For NCB assessment of axillary nodes, the following diagnostic categories may be used but are not mandatory and can be replaced by B codes. LB codes map directly to the corresponding B code when entering data on NBSS.

LB1 Inadequate: no lymph node/lymphoid tissue. Lymph node tissue with artefact that prevents interpretation should be categorised as LB1.

LB2 Benign: either normal lymph node or lymph node with benign changes such as reactive hyperplasia, dermatopathic lymphadenopathy, foreign body reaction, granulomatous inflammation, etc.

LB3 Atypia: lymphoid tissue with atypical cells present, lymphoid or other of uncertain nature and significance.

LB4 Suspicious for malignancy, including metastatic carcinoma or other malignancy (including lymphoma).

LB5 Malignant, metastatic carcinoma or other malignancy (including lymphoma).

In instances where there is a discrepancy between the lymph node cytology or biopsy and the radiological impression, repeat FNAC or core biopsy can be helpful as lymph node involvement may be focal.

The utility of axillary ultrasound and needle biopsy should continue to be reviewed, based on current recommended practice in relation to sentinel node biopsy and axillary dissection.

4.3 Pitfalls

The primary aim of preoperative assessment of axillary nodes in patients with breast cancer is to detect nodal metastases from the mammary carcinoma. It is important to recognise other diagnoses and avoid misdiagnosis.

Other malignancies may involve the nodes. To avoid misdiagnosis, it is useful to compare the morphology of the neoplastic cells present in the lymph node FNA or core biopsy with the tumour in the preoperative core biopsy of the breast, as metastases are usually similar to the primary tumour.

If the tumour has a different appearance or has features unusual for a mammary carcinoma, metastasis from other sites should be considered. Melanoma should be in the differential diagnosis. Malignant lymphoma must also be considered. Immunohistochemistry, particularly on core biopsy, can often resolve these differential diagnoses.

Benign lymph node inclusions are a diagnostic pitfall. Melanocyte rests are the most common, but epithelial inclusions and, rarely, mesothelial inclusions can occur.

Macrophages as part of reactive conditions, such as dermatopathic lymphadenopathy or granulomatous lymphadenitis, may mimic carcinoma cells. Immunohistochemistry for epithelial markers and macrophage markers such as CD68 can be helpful.

Lymphocytic infiltrates from inflammatory disorders affecting adjacent structures including the skin may mimic a lymph node.

Small metastases should be reported as malignant. If there are only a few cells in the metastasis, it is suggested that this is indicated in the report so that it can be discussed at the multidisciplinary meeting. Occasionally, after a diagnosis of malignancy on the core or FNAC of the axillary nodes, the surgical specimen may show no nodal metastasis. The original core biopsy or FNAC should be reviewed to confirm the original diagnosis. If the carcinoma is small on the core or there are only scanty cells on the FNAC, it may be reasonable that no metastases are found in the surgical specimen. If the patient has had preoperative systemic treatment, a fiducial marker may be present or there may be features suggesting treated carcinoma, such as fibrosis. In the case of preoperative systemic treatment, it is not necessary to review the original core biopsy or cytology findings.

Sometimes, nodes low in the axilla are missed at surgery – ultrasound of the axilla should be considered to search for such nodes.[57]

5 Criteria for audit

The following are recommended by the RCPath as key assurance and key performance indicators:[58,59]

- cancer resections should be reported using a template or proforma, including items listed in the English COSD, which are, by definition, core data items in RCPath cancer datasets. English trusts were required to implement the structured recording of core pathology data in the COSD
  - standard: 95% of reports must contain structured data
- histopathology cases that are reported, confirmed and authorised within 7 and 10 calendar days of the procedure
  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days.

Please see also Appendix C (Quality Assurance) for details on auditing core biopsy performance.

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Appendix A FNAC reporting guidelines

This section of the document is designed to assist classification and reporting of FNAC samples. It should, however, be noted that FNAC alone is not an appropriate method of assessment of abnormalities detected by breast screening. FNAC does provide the advantage of providing a rapid diagnosis compared with core biopsy and may be used in conjunction with core needle biopsy where the necessary expertise exists. It can also be used for assessment of symptomatic patients.

Reporting categories

In ideal circumstances, one should aim for a definitive benign or malignant diagnosis. The proportion of cases where this is possible will increase with experience of both the pathologist and aspirator.

C1 inadequate

The designation of an aspirate as inadequate is, to a certain extent, a subjective matter and may depend on the experience of the aspirator and/or the interpreter. It is generally based on the presence of sufficient numbers of epithelial cells to provide a sample adequate for confident assessment. There are several reasons for labelling a smear as inadequate. These fall into 3 main groups:

- hypocellularity
- error in aspiration, spreading or staining
- excessive blood.

In some cases, diagnostic information may be present and may be conveyed in the accompanying text description, e.g. adipose tissue fragments could support a clinical diagnosis of lipoma. Aspirates from certain lesions, such as cysts, abscesses, intramammary lymph nodes, fat necrosis and nipple discharge specimens, may not contain epithelial cells but should not be classified as inadequate.

Preparative artefacts include:

- crush: when too much pressure is used during smearing
- drying: when the dry smears are allowed to dry too slowly (dry smears should be dried quickly; wafting in the air can speed up drying) or when the wet fixed smears have been allowed to dry out before fixation

- thickness of smear: when an overlay of blood, protein rich fluid or cells is obscuring the picture, making assessment impossible.

It is helpful to make a comment explaining why the specimen is inadequate.

C2 benign

This category indicates an adequate sample showing no evidence of malignancy or specific lesions regarded as atypical and, if representative, a negative report can be issued.

The aspirate in this situation is poorly to moderately cellular and tends to consist mainly of regular duct epithelial cells. These are generally arranged as monolayers with characteristic benign cytological features. The background is usually composed of dispersed individual and paired naked nuclei. Should cystic structures be a component of the aspirated breast, a mixture of foamy macrophages and regular apocrine cells may be part of the picture. Fragments of fibrous and/or fatty tissue are common findings.

A positive diagnosis of specific conditions, e.g. fibroadenoma, fat necrosis, granulomatous mastitis, breast abscess, lymph node etc, may be suggested if sufficient specific features are present to establish the diagnosis with confidence. This may be helpful in multidisciplinary correlation.

Care should be taken when correlating cytology features and radiology. For example, a few cohesive groups of epithelial cells in an aspirate from a well-defined lesion thought to be a cyst may not be representative of the lesion.

C3 atypia probably benign

The aspirate here can have all the characteristics of a benign aspirate, as described in the previous paragraph. There are, however, also certain features not commonly seen in benign aspirates.

These could be any, or a combination, of the following:

- nuclear pleomorphism
- some loss of cellular cohesiveness
- nuclear and cytoplasmic changes resulting from, for example, hormonal (pregnancy, pill, hormone replacement therapy) or treatment influences (see section 4.3 for diagnostic pitfalls)
- increased cellularity accompanying the above features.

In addition, specific lesions that are regarded as showing an increased risk of malignancy can be identified on FNAC and should be reported as C3. These include papillary lesions and suspected phyllodes tumours. In both examples, there may not be any cytological atypia, but the possibility of malignancy in a focal area of these lesions warrants a report of C3.

C4 suspicious for malignancy

This category should be used for aspirates where there are atypical features, such that the pathologist is almost certain that they come from a malignant lesion, but a confident diagnosis cannot be made.

This may be for 3 main reasons:

- the specimen is scanty, poorly preserved or poorly prepared, but some cells with features of malignancy are present
- the sample may show some malignant features without overt malignant cells present – the degree of abnormality should be more severe than in the previous category
- the sample has an overall benign pattern with large numbers of naked nuclei and/or cohesive sheets of cells, but with occasional cells showing distinct malignant features.

If an aspirate is reported as C4 because of low cellularity, repeat aspiration is often helpful. If, however, the aspirate is cellular but considered to be suspicious of malignancy, it is unlikely that repeat aspiration will be helpful.

Definitive therapeutic surgery should not be undertaken as a result of a C3 or C4 diagnosis.

C5 malignant

This indicates an adequate sample containing cells characteristic of carcinoma, or other malignancy.

The pathologist should feel at ease in making such a diagnosis. Malignancy should not be diagnosed based on a single criterion. Combination of the features listed in Table 1 will be necessary to achieve this diagnosis.

Calcification

FNAC should not be carried out on mammographic calcifications in the absence of a mass detected on ultrasound or clinical examination. The reasons for this are twofold: it is difficult to confirm that calcification is present in the sample and it is not possible to reliably

distinguish between in situ and invasive malignancy on FNAC, rendering a C5 diagnosis in these circumstances of limited use in planning treatment.

General diagnostic patterns

The essential role of cytological diagnosis is to distinguish benign from malignant processes. The common general criteria used are illustrated in Table A1. It is important to bear in mind that the morphological and histological patterns seen in both benign and malignant breast disease are quite varied; this is reflected in the cytological appearances. For this reason, it is useful to have a working understanding of breast histology before approaching breast FNAC. This knowledge can improve recognition of rare lesions and reduce numbers of false positive and false negative diagnoses.

Table A1: Diagnostic criteria for the recognition of benign and malignant conditions.

Criterion	Benign	Malignant
General characteristics		
Cellularity	Usually poor or moderate	Usually high
Cell-to-cell cohesion	Good with large defined clusters of cells	Poor, with cell separation resulting in dissociated cells with cytoplasm or small groups of intact cells
Cell arrangement	Even, usually in flat sheets (monolayers)	Irregular with overlapping and three-dimensional arrangement
Cell types	Mixtures of epithelial, myoepithelial and other cells with fragments of stroma	Usually uniform cell population
Bipolar (elliptical) bare nuclei	Present, often in high numbers	Not conspicuous
Background	Generally clean except in inflammatory conditions	Occasionally with necrotic debris and sometimes inflammatory cells, including macrophages
Nuclear characteristics		
Size (in relation to red blood cell diameter)	Small	Variable, often large, depending on tumour type
Pleomorphism	Rare	Common
Nuclear membranes (Papanicolaou stain)	Smooth	Irregular with indentations
Nucleoli (Papanicolaou stain)	Indistinct or small and single	Variable but may be prominent, large and multiple

Chromatin (Papanicolaou stain)	Smooth or fine	Clumped and may be irregular
Additional features	Apocrine metaplasia, foamy macrophages	Mucin, intracytoplasmic lumina

Nipple discharge cytology

Nipple discharge cytology specimens are rarely taken in breast screening patients. However, nipple discharge is the principal complaint in about 5% of symptomatic patients. Nipple discharge may be divided into physiological and pathological categories.

Physiological discharge is usually bilateral and from multiple ducts.

Pathological discharge is usually unilateral, from a single duct, spontaneous and persistent. Most pathological nipple discharge has a benign cause, with intraductal papilloma and duct ectasia being the most common. A few percent of patients have an associated carcinoma.[1]

Nipple discharge cytology is no longer recommended because it has poor sensitivity.[1,2] If there is an underlying carcinoma, it is usually detected by clinical or radiological examination (mammography and retroareolar ultrasound), although sensitivity for these conventional imaging techniques is also low.[2] In rare circumstances, a small proportion of such carcinomas are not apparent clinically or radiologically. Some of these occult carcinomas may be detected by nipple discharge cytology.

There is no standard reporting system for nipple discharge cytology. The C1 to C5 system for FNAC can be adapted, but the categories are not completely equivalent. The criteria used to judge an FNAC as inadequate do not apply to nipple discharge specimens, as epithelial cells are not normally seen. A nipple discharge specimen is only inadequate if it is poorly prepared, preventing assessment.

Specimens frequently contain only acellular material, foamy macrophages and anucleate squames. This appearance should be categorised as benign.

It is important to comment on the presence or absence of epithelial cells and red blood cells. Categorisation of epithelial clusters is difficult. They often have a rounded papillary outline; most epithelial groups have some degree of nuclear atypia, usually mild. This atypia may be degenerative, but occasionally this appearance is seen with low grade DCIS.

An unequivocally malignant nipple discharge specimen is rare. It is much more common to see features suspicious for malignancy. Features of malignancy are similar to those seen in FNAC: a cellular sample with groups of cells and single cells with moderate to marked nuclear atypia.

Assessing the PPV of the above categories is difficult because some studies only include patients with surgical excision and no follow up of the other patients. Also, criteria for surgery are not uniform and differ between series. The definition of positive cytology is variable. It is not surprising, therefore, that the sensitivity of suspicious or malignant cytology varies in some series between 17 and 70%.[3,4] Clearly, there is a high false-negative rate.

As with FNAC, the triple approach should be applied. If there is concern about a clinical or radiological abnormality, then core biopsy is often indicated. From a practical perspective, suspicious or malignant nipple discharge cytology results are useful, as further investigation is necessary. Management of patients with mildly atypical epithelial groups with normal clinical and radiological findings is difficult as the risk of malignancy is low.

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Appendix B Cytological features of specific lesions diagnosed on FNAC

Benign lesions

Fibroadenoma

Typical fibroadenomas are characterised by 3 features: numerous staghorn branching groups of epithelial cells, frequent bipolar bare nuclei and stromal fragments resembling the stroma seen on histology of fibroadenomas.

On occasion, aspirates from fibroadenoma may contain atypical epithelial cells, but identification of the pattern at low power examination will prevent false positive diagnoses (C3 and above). Fortunately, this usually happens in actively growing lesions in teenage women, rather than in the screening age range.

The clue to the diagnosis is the presence of ‘stripped’ bipolar nuclei. Smears containing these in significant numbers should not be diagnosed as malignant unless there are clear features of a benign epithelial lesion (with benign epithelial clumps) and also malignant clumps and dissociated malignant cells recognisable as a distinctly separate cell population.

These smears, where the needle has passed through both a benign and a malignant lesion, may be very difficult to classify, but the 2 distinct populations of epithelial cells should aid their recognition.

Smears from some malignant tumours contain bare nuclei. These bare or stripped nuclei are not bipolar and have obvious malignant features identical to coexisting intact tumour cells. Often in fibroadenomas, 2 cell types can be recognised in the cell clumps, even in the atypical examples.

It is recognised that LCIS, DCIS and invasive carcinoma may arise in fibroadenomas, like any other breast tissue. The presence of significant atypia in a fibroadenoma-like lesion should result in a C3 or C4 diagnosis.

Apocrine cells

Apocrine cells in smears may appear pleomorphic and may dissociate. Degenerate apocrine cells in cyst fluids may also have an atypical appearance. Recognition of the dusty blue cytoplasm, with or without cytoplasmic granules with air dried slides or pink

cytoplasm on wet fixed slides, coupled with the prominent central nucleolus, is the key to identifying cells as apocrine.

Awareness of the marked pleomorphism, which may occur in degenerate apocrine cells, and careful assessment of the cellularity and chromatin pattern, should allow the distinction from the rare apocrine carcinoma. If there is doubt about the nature of apocrine cells, it is better to err on the side of caution and give a suspicious or atypical report.

One particularly difficult lesion is atypical apocrine change in sclerosing adenosis, especially if this is associated, as it often is, with a complex sclerosing lesion or radial scar, giving a mammographically worrying appearance.

In this case, the highly pleomorphic apocrine cells may not always appear obviously apocrine in smears. Features that may be helpful are the abundant cytoplasm with granules and the absence of necrosis. Spindling of cells in the centre of the clumps (myoepithelial cells from the sclerosing adenosis), surrounded by or intermingled with the atypical apocrine cells, may be seen.

Papilloma

Aspiration of papillomas usually produces cellular aspirates with staghorn clusters of cells similar on low power appearance to those seen in fibroadenomas, although they may appear 3 dimensional with well-defined edges. In some cases, connective tissue cores may be seen within these clusters. These may be diagnostic of papilloma but are not a common feature.

Fibroadenomas do not contain large numbers of foam cells. Bare nuclei are seen in papilloma but there are generally not as many as in fibroadenomas. Apocrine metaplasia may also be present.

While it is important clinically to distinguish papilloma from encapsulated papillary carcinoma, this may not be possible on cytological grounds. Some features of malignancy, such as nuclear pleomorphism, increased nuclear cytoplasmic ratio and cellular crowding or overlapping, may occur with some benign forms of papilloma. No single feature can differentiate the 2 conditions.

Papillary lesions with no epithelial cell atypia should be reported as C3 on FNAC. If there is epithelial cell atypia of a significant degree or loss of cohesion not due to overspreading, a report of C4 is appropriate. Due to limited sampling, it is difficult to make a C5 diagnosis on papillary lesions on FNAC.

Atypical lobular hyperplasia and lobular carcinoma in situ

It is not possible to reliably distinguish ALH and LCIS (and even invasive lobular carcinoma) on fine needle aspiration smears alone. The difference between LCIS and ALH is one of extent of lobule involvement seen in histological sections and is not based on the cytological appearances of the cell.

The cells are similar or identical in morphology. The cytological features of ALH have been well described.[1] Cytologically dissociated small epithelial cells with rounded or squared-off nuclei are seen. These are present singly or in small groups with nuclear moulding.

The cells may contain intracytoplasmic lumina (private acini), seen best on mucin staining where they appear like a ‘bull’s eye’ with an alcian blue stained microvillous membrane and a periodic acid Schiff-stained mucin droplet in the centre.

ALH and LCIS are usually seen as an incidental finding in association with another lesion, which can result in complex appearances in fine needle aspiration smears.

Atypical ductal hyperplasia

ADH is most often encountered in breast screening in patients who present with microcalcification on mammography. As stated earlier, FNAC is of very limited or no benefit in this situation and, if not carried out, the potential pitfalls can be avoided.

Most cases of DCIS detected by breast screening are of the comedo or large cell type. These do not present a problem, because if they are aspirated the characteristic features of malignant cells are present along with necrosis and dissociation.

The difficulty comes in the distinction of low-grade DCIS of cribriform or micropapillary type from ADH. Cytology cannot reliably distinguish between ADH and low-grade DCIS.

Low-grade cribriform or micropapillary DCIS does not produce necrosis or large numbers of dissociated cells and is mainly recognised by its architectural pattern within the cell clusters. ADH is similar but, unlike the monotony of the cell clusters in cribriform DCIS, the clusters of ADH still show a biphasic pattern, at least in part. They differ from the cell groups found in benign breast lesions in that they have a 3-dimensional appearance and usually show some cytological atypia, which may be severe in some cases.

Columnar cell change

This may produce dissociation; some authors have noted that the cells may resemble lobular carcinoma cells. Some of the cells are columnar in nature, resembling bronchial

epithelial cells. Again, this change is most often seen in association with mammographic microcalcification, and FNAC should not be performed in these circumstances.

Lactational change

Even in the screening age group, focal lactational changes can occur. This is uncommon but can produce occasional dissociated cells within an otherwise benign appearing smear. The dissociated cells may possess nucleoli and have larger nuclei than the surrounding benign cells.

They do, however, have a moderate quantity of pale blue cytoplasm on Giemsa staining with lipid droplets in the cytoplasm. Caution in interpreting occasional dissociated cells in an otherwise benign pattern should be exercised, even in the screening age range. In these cases, it is necessary to ask specifically: could these be lactational or secretory cells?

Outside the screening age, a history of pregnancy or lactation should always be sought, and clinicians should always tell the pathologist of lactation or pregnancy.

Radiotherapy changes

These can lead to a false positive cytological diagnosis, especially when the history of previous irradiation is not provided. However, the aspirate is usually not very cellular and the interpretation of poorly cellular smears, especially with a history of irradiation, should be undertaken with caution, as in item 3 (spreading artefacts). Irradiation can cause marked nuclear pleomorphism and dissociation. Mammography may also be unhelpful (or even false positive) in this situation, which may lead to an inaccurate clinical impression.

Intramammary lymph nodes

These should not cause a problem if the pathologist recognises the cells as lymphoid. Awareness that these can occur and can be aspirated should be enough to avoid an error.

Lymphomas may be more difficult to distinguish from carcinoma, but the lack of clumps should suggest the possibility. Careful assessment including immunocytochemistry should distinguish the occasional carcinoma showing almost complete dissociation with a plasmacytoid appearance.

Degenerate cells in cyst fluids

Degeneration of cells within cysts or nipple discharge specimens can give pleomorphic appearances, especially when these are larger apocrine cells. Cautious interpretation of cells within degenerate cysts is advised.

Uncommon lesions

Granulomatous mastitis

Epithelioid macrophages in granulomatous mastitis can mimic carcinoma cells. They are associated with other inflammatory cells in the smear and numerous macrophages may be seen. The smear is also very cellular. In the presence of inflammation and a cellular smear, the finding of multinucleate macrophages should alert the observer to the possibility of granulomatous mastitis.

The rare cribriform carcinomas with multinucleate giant cells do not usually contain other inflammatory cells. They are, therefore, distinguishable from granulomatous mastitis by their dimorphic picture of small malignant cells in clumps and singly, and more basophilic osteoclast-like giant cells with larger nuclei and prominent nucleoli. Mononuclear forms of the multinucleate cells may also be present.

Granular cell tumour

This can present a worrisome appearance in smears: there may be marked dissociation of cells with pink cytoplasm, which, although they have small nuclei generally, may contain occasional larger nuclei, giving a pleomorphic appearance. However, the cells do not look epithelial and benign epithelial clumps are seen between the dissociated cells of the tumour. The cells have eosinophilic granular cytoplasm on Papanicolaou or haematoxylin and eosin staining, and a mottled pale mauve cytoplasm on Giemsa stains, similar in appearance to apocrine cells.

Adenomyoepithelial lesions

These lesions can show malignant cytological features because of dissociation of pleomorphic cells, which are in fact myoepithelial. However, obvious benign clumps and bipolar bare nuclei are present. Malignancy can arise within these lesions.

Collagenous spherulosis

This lesion produces rounded globules staining a granular purple colour on Giemsa stains with surrounding spindle cells. There is a resemblance to adenoid cystic carcinoma, with which the lesion can be confused. The globules can also be seen in papilloma and ductal adenoma. Biopsy in these rare conditions is advised.

Potential false negative diagnosis

The most common cause of false negative cytological diagnosis is an aspiration miss. There are, however, types of carcinomas that by their nature may lead to a false negative cytological diagnosis.

Tubular carcinoma

Tubular carcinoma cells often have much in common with benign breast epithelial cells, including uniformity, nuclear size and, often, absence of immediately obvious nuclear abnormalities. Knowledge of the mammographic findings, a lack of bare nuclei, individual cells with cytoplasm and occasional tubular profiles are pointers to the diagnosis. Paradoxically, the nuclei are often more regular and orderly than benign ductal epithelium and there is a single cell population in the clumps.

Often, it is not possible to give an unequivocal diagnosis, but care should always be taken in interpreting smears from stellate opacities to avoid false negative results from this type of tumour. It should be noted that tubules can occasionally be obtained from benign lesions, including radial scars, tubular adenomas and fibroadenomas.

Lobular carcinoma

Aspirates from lobular carcinoma are often difficult to interpret. The cellularity of these specimens is usually less than that seen in carcinoma, NST and, due to the growth pattern of this tumour, there is often a mix of benign and malignant cells in an aspirate.

Several patterns can be observed, ranging in cytological appearance from benign looking uniform cells to atypical cells not dissimilar to those seen in invasive carcinoma, NST. The presence of small 3-dimensional collections of cells with only slightly enlarged nuclei is helpful.

Many cells with intracytoplasmic lumina (private acini), in association with the above features, is suggestive of lobular carcinoma. Nuclear irregularities and small protrusions from the nucleus (‘noses’) may also be seen.

Apocrine carcinoma

This rare type of carcinoma produces cellular smears. Difficulty in interpretation is related to the subtle appearance of the neoplastic apocrine cells and their resemblance to benign apocrine cells with degenerative changes. Clustering of cells and papillary formations are seen in benign as well as malignant lesions and are of little help.

The key feature of a malignant aspirate is the uniform cell population with nuclear atypia, which should not be confused with degenerative changes. Necrosis is also a helpful feature. Until one is aware of the marked atypical changes associated with apocrine cells in fibrocystic change, the diagnosis of apocrine carcinoma should always be approached with caution.

DCIS

It should be noted that DCIS and invasive carcinoma, NST cannot be distinguished accurately by cytology alone. While some cases of DCIS are overtly malignant, low-grade DCIS may present difficulties. A clue in some cases can be obtained from the architectural pattern within the rigid and monomorphic clumps.

Carcinoma with extensive fibroelastosis

These tumours may give sparsely cellular smears, which can lead to difficulties in diagnosis. Often, it is not possible to be definitive and the need for caution in the interpretation of poorly cellular smears is again emphasised.

Other unusual lesions

Silicone, soya oil or paraffin granuloma

This may occasionally be problematic because of cell dissociation, but the appearances are made easier with the recognition of multinucleate cells and oil or silicone droplets in the cytoplasm of the macrophages. Clinical data will be helpful here. Clinicians should understand the need to supply the pathologist with proper clinical information on all breast lumps sampled by FNAC.

Benign stromal lesions

These lesions are occasionally aspirated when they produce an irregular mass on mammography or palpation. One of the more usual lesions to be mistaken for carcinoma radiologically is fibromatosis. Nodular fasciitis may, however, also be sampled. On aspiration, there are small numbers of stromal cells that are dissociated from each other. The cells are spindle in shape and have regular nuclear characteristics.

Phyllodes tumours

The benign variants of phyllodes tumour may not be recognised as such on fine needle aspiration and may give a picture similar to fibroadenoma. Clues to the diagnosis include the presence of intact stromal cells, occasionally with nuclear abnormalities, and the finding of pieces of cellular mucoid connective tissue in the aspirate. Fibroadenomas can

also show both these features, however. The recognition of benign phyllodes tumours often depends on clinical and sonographic features.

Occasionally, phyllodes tumours can also produce a false positive diagnosis of malignancy. Malignant phyllodes tumours show a pattern of benign appearing epithelial clumps, with spindle cells showing obvious malignant nuclear features.

Metastatic tumours

Metastatic tumours in the breast should always be considered in FNAC where a peculiar pattern unusual for breast tumours is seen. Melanoma and small cell carcinoma are the most common. In melanoma, pigment and large intranuclear cytoplasmic inclusions may be visible.

Ovarian metastases are often papillary with psammoma bodies (an uncommon feature of breast tumours). Large clear cells full of glycogen may suggest a renal metastasis. Squamous carcinoma cells may be from a primary breast lesion but may also be from a metastatic lesion, etc. The triple approach may often resolve this problem.

Lymphoma

The recognition of the lymphoid nature of an apparent primary breast tumour depends on the recognition of the spectrum of lymphoid cell types and the absence of clumps of cells. Immunocytochemistry may be necessary in some cases.

New onset peri-implant collection can raise suspicion of breast implant-associated anaplastic large cell lymphoma. This is characterised by a cellular pleomorphic lymphoid population with background macrophages and lymphocytes. These cells are typically CD30 positive, ALK negative and these seroma fluid samples should be processed to prioritise generation of a cell block to enable immunocytochemistry for diagnosis. Referral to a regional lymphoma specialist diagnostic service should also be considered.[2]

Malignant stromal tumours

The most common sarcoma to be aspirated from the breast is angiosarcoma. This can show variable cytological features but is often accompanied by a large amount of blood. Clumps of cells may occasionally be seen but the pattern is often that of malignant appearing spindle or ovoid cells.

Sarcomas also give a picture of dissociated malignant spindle cells. The major diagnostic dilemma is between spindle cell carcinoma and sarcoma. When this is a problem, immunocytochemistry for epithelial markers may be necessary.

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Appendix C Quality assurance

Background

Accurate non-operative diagnosis is an essential component of a successful breast screening programme. Accurate diagnosis of malignancy allows for patients with cancer to have a therapeutic procedure as the first surgical procedure. Accurate diagnosis of benign lesions means that most patients avoid surgery completely, which is important in reducing the morbidity associated with screening.

Screening detects many borderline lesions and, although it is not possible to achieve 100% diagnostic accuracy, it should be possible to achieve performance in line with that of other similar units. To this extent, comparisons using standard reports are invaluable, but only as part of an effective overall screening quality assurance (QA) programme.

Definitions

The definitions shown in Table C1 are intended to relate to the clinical evaluation of the effectiveness of core biopsy, and not specifically to evaluation of the laboratory component. Thus, normal (B1) core biopsy results are not excluded from the calculations, as in some evaluations in the literature. Pathologists wishing to evaluate their statistics purely to see their own accuracy in diagnosis may wish to calculate the figures slightly differently.

Table C1: Definitions of QA standards for core biopsy.

QA standard	Definition
Absolute sensitivity	The number of carcinomas diagnosed as such (B5), expressed as a percentage of the total number of carcinomas sampled
Complete sensitivity	The number of carcinomas that were not definitely negative on core, expressed as a percentage of the total number of carcinomas
Specificity (full)	The number of correctly identified benign lesions (the number of B2 results minus the number of false negatives), expressed as a percentage of the total number of benign lesions sampled
PPV of a B5 diagnosis	The number of correctly identified cancers (number of B5 results minus the number of false-positive results), expressed as a percentage of the total number of positive results (B5)
PPV of a B4 diagnosis	The number of cancers identified as suspicious (number of B4 results minus the number of false suspicious results), expressed as a percentage of the total number of suspicious results (B4)

PPV of a B3 diagnosis	The number of cancers identified as atypia (number of B3 results minus the number of benign atypical results), expressed as a percentage of the total number of atypical results (B3)
False negative case	A case that over the next 3 years turns out to be carcinoma, having had a negative (B2) core result; this will by necessity include some cases where a different area from the lesion was sampled but who present with an interval cancer
False positive case	A case that was given a B5 result who turns out at open surgery to have a benign lesion, including atypical hyperplasia
False negative rate	The number of false-negative results, expressed as a percentage of the total number of carcinomas sampled
False positive rate	The number of false-positive results, expressed as a percentage of the total number of carcinomas sampled

How to calculate quality assurance statistics (biopsy quality assurance)

Pathology statistics for the National Health Service Breast Screening Programme (NHSBSP) can be produced automatically from data input onto the NBSS database, which cross-references the core biopsy result with the histology or subsequent outcome. Accurate data entry is, therefore, essential to provide meaningful statistics. An NBSS report can generate the wide bore needle statistics (biopsy quality assurance [BQA]), which are used to monitor performance for QA purposes.

Further rules used in deriving QA statistics

Cases with both a non-invasive and invasive cancer should count as invasive unless they are in opposite breasts, in which case they should be counted twice (once for each breast).

In cases with a malignant and a benign diagnosis, the malignant result overrides the benign result unless they are from opposite breasts.

Cases with open episodes are listed at the bottom of the report.

Tables C2 and C3 can be produced for internal QA purposes for all clients, all tests and all clients and tests combined. These can be run at screening service, laboratory, clinical team or individual pathologist level. Client-level data collates all the pathology samples that an individual client had and considers the most significant biopsy result. This provides information about a service's performance. All client data are used for the standards in Table C4. If a patient has lesions in both breasts, these are counted as 2 clients. The number of tests is expected to be greater than the number of clients because some lesions will have more than 1 biopsy taken. Test-level data gives the outcome for all biopsies for

each lesion and is used as an indicator of individual pathologist performance (see information below on pathology data review).

The tables can also be produced for any date range (using the date of biopsy or, if not available, the date of reporting), any geographic location, the method of localisation (palpable, ultrasound or stereotactic) and by radiological appearances (spiculated mass, rounded opacity, microcalcification, stellate lesion or asymmetrical density).

It is possible to request a report that lists the screening numbers of clients involved in any of the cells in Table C3. For example, a list of cases in cell box 65 is produced with the title: 'Cases with B4 results not biopsied but with closed episodes – please check'. Note that all cases in box 61 are regarded as malignant and that all cases in box 66 are regarded as benign.

Table C2: Core BQA standard report.

	Core biopsy diagnosis											
Final histology	B5	B5a	B5b	B5c	B4	B3	B3 with atypia	B3 with-out atypia	B3 not specified	B2	B1	Total
Total malig-nant	Box 1	Box 2	Box 3	Box 4	Box 5	Box 6	Box 7	Box 8	Box 9	Box 10	Box 11	Box 12
Invasive	Box 13	Box 14	Box 15	Box 16	Box 17	Box 18	Box 19	Box 20	Box 21	Box 22	Box 23	Box 24
Non-invasive	Box 25	Box 26	Box 27	Box 28	Box 29	Box 30	Box 31	Box 32	Box 33	Box 34	Box 35	Box 36
Total benign	Box 37	Box 38	Box 39	Box 40	Box 41	Box 42	Box 43	Box 44	Box 45	Box 46	Box 47	Box 48
Benign, proven malig-nancy*	Box 49	Box 50	Box 51	Box 52	Box 53	Box 54	Box 55	Box 56	Box 57	Box 58	Box 59	Box 60
No further histology	Box 61	Box 62	Box 63	Box 64	Box 65	Box 66	Box 67	Box 68	Box 69	Box 70	Box 71	Box 72
Total B results	Box 73	Box 74	Box 75	Box 76	Box 77	Box 78	Box 79	Box 80	Box 81	Box 82	Box 83	Box 84
* Box 49 is definite malignancy on core biopsy followed by normal or benign surgery												

The BQA report produces Tables A to F. Table C2 shows the format of BQA Table D. Calculations in Table C3 are for BQA Table D.

Table A: Total screened, total assessed, total biopsies

Table B: WBN/VAB to VAE

Table C: WBN/VAB to surgery

Table D: WBN/VAB to VAE or surgery

Table E: Sensitivity, specificity, positive predictive value (PPV), etc.

Table F: VAE to surgery

The entry in each box in Table C2 is calculated from the numbers of core biopsies with a B code (B1, B2, etc.) and cross-referenced with the worst histology diagnosis.

The table and calculations (see below) should be produced for all core biopsy tests (headed ‘all tests’) and for all clients (headed ‘all clients’). The report for all clients records the most significant biopsy result (with the highest B number) if there are 2 or more biopsy results. Only closed episodes should be used.

The figures in the tables are then used to calculate values for each of the BQA measures. The calculations are shown in Table C3 (the numbers in bold correspond to the box numbers in Table C2).

It is recognised that specificities and false negative rates are approximate and will be more accurate the longer the date range of analysis is from the date of calculation.

Table C3: Calculation of biopsy performance measure.

Absolute sensitivity (this assumes that all B5 results without further histology are carcinomas)	$\frac{\mathbf{(1+61)}}{\mathbf{12+61}} \times 100$
Complete sensitivity	$\frac{\mathbf{(1+5+6+61)}}{\mathbf{12+61}} \times 100$
Specificity (biopsy cases only)	$\frac{\mathbf{46}}{\mathbf{48}} \times 100$
Specificity (full) (this assumes that all B3 cases with no further histology are benign)	$\frac{\mathbf{(46+70)}}{\mathbf{(48+66+70+71)}} \times 100$
PPV (B5 diagnosis)	$\frac{\mathbf{(73-37)}}{\mathbf{73}} \times 100$
PPV (B4 diagnosis)	$\frac{\mathbf{77-41-65}}{\mathbf{(77-65)}} \times 100$

PPV (B3 diagnosis)	$\frac{\mathbf{6}}{\mathbf{78}} \times 100$
False negative rate	$\frac{\mathbf{10}}{\mathbf{12+61}} \times 100$
False positive rate	$\frac{\mathbf{37}}{\mathbf{12+61}} \times 100$
B1 core biopsy rate	$\frac{\mathbf{83}}{\mathbf{84}} \times 100$
B1 core biopsy rate from cancers	$\frac{\mathbf{11}}{\mathbf{12+61}} \times 100$
Suspicious rate	$\frac{\mathbf{77+78}}{\mathbf{84}} \times 100$
Core biopsy miss rate from cancers	Sum of false negative rate and B1 core biopsy rate from cancers

Interpreting figures from the National Breast Screening Pathology Data Review

The annual National Breast Screening Pathology Data review of non-operative diagnosis report aims to inform pathologists of both their individual data and the range in screening service/laboratory BQA statistics, to allow comparison against relevant standards and to facilitate comparison of departmental results with other services and comparison of their individual results with those of other pathologists. The report will also allow assessment of performance against standards indicated in this document (see Table C4).

Pathology outcomes for non-operative reporting are obtained from the national breast screening system (NBSS) system. BQA reports from core biopsies followed by VAE and/or surgery outcomes have been generated for the most significant non-operative core biopsy result for a patient (known as client-level data) to assess laboratory quality data, and all non-operative core biopsy results (known as test-level data) to assess individual pathologist data. As ‘laboratory’ was added as a primary reporting item to the BQA report in December 2022, this enables the extraction of the reporting laboratories directly from the BQA reports. Some services have recorded the hospital trust as the laboratory in the biopsy results on NBSS, meaning that if the trust operates more than 1 laboratory, the laboratory data will be incorrect, as all results are aligned to the hospital trust.

Breast screening services retain responsibility for accurately inputting the data onto NBSS and should work collaboratively to resolve such queries in real time so that inaccurate data

is not added to the system; as an example, some services could not map the pathologists on their BQA report to the laboratory shown on the report, suggesting either a pathologist or laboratory recording error. SQAS should work with their services to amend these on the NBSS.

Each laboratory is given a unique code starting with the breast screening service (BSS) cipher.

Results by laboratory

The guidance document *Breast Screening: quality assurance guidelines for breast pathology services*[1] sets 30 cases as the minimum number to be reported by an individual pathologist over a 3-year period, so it is deemed appropriate to use this as a minimum inclusion criteria for laboratory. The reporting laboratory is taken directly from BQA reports (as recorded on NBSS), rather than laboratory provided by the service.

Data tables are provided in the companion spreadsheet, which show overall numbers of cases for the 3-year period by laboratory.

Results for smaller laboratories tend towards extreme values, making interpretation difficult. The predominant reason for excluding small volume laboratories is that analysis of units with such small numbers would not provide meaningful results.

Results by pathologist

Pathologists are excluded from the analysis if they have reported fewer than 30 tests in a 3-year period. The threshold of 30 biopsies was chosen to reflect national guidance,[1] which states that those reporting fewer cases should consider whether they are receiving sufficient exposure to maintain expertise. This is particularly true if all consultants in a department between them report less than 30 cases in a 3-year period. Further investigation into the use of these laboratories in the screening programme is warranted.

Results by pathologist are more skewed than for total laboratory results, owing to the smaller number of cases.

BQA activity data at pathologist level are reported by test, assessing all core biopsy results issued by the reporting pathologist. The data analysed by pathologist (by test) has different denominators to those reported in the previous section (client level data), as some clients will have had multiple tests. In such cases, the test results will be considerably different to the final (worst) client result. Assessing all test results maximises the number of cases for each pathologist and makes sure that all biopsy results are captured for each.

Although the guidance clearly states that results by client should be used to assess the quality of the screening service and the related laboratory, if an individual pathologist is a low or high outlier for any of the measures, a similar approach and suggested actions to that for service level outlier status described below (and the same considerations) may be applied.

Multidisciplinary nature of the data

The national pathology data review presents an opportunity for breast screening pathologists to examine both their individual and their laboratory's results and to identify and address variation in practice as required. However, in some instances, it is recognised that a significant contributing factor to variation is data quality. This may be challenging for pathologists to tackle due to the complexities around data entry in different services, both at service as well as individual level. However, it is important to address these problems to ensure that true variation in clinical practice can be correctly identified in the future.

It must also be remembered that the data presented is not purely reflective of the pathologists' adherence to reporting of specimens in line with national guidance. The data are multifactorial, and some elements are outside the control of the pathology department; for example, the accuracy of the operator (biopsy taker) to sample the index lesion, the radiological threshold for sampling, and the availability and use of vacuum-assisted techniques significantly impact many parameters. Sharing the results with other breast screening colleagues, particularly radiologists, is recommended.

It should be noted that the BQA reporting outcome for both client and test results triangulates the biopsy result to the subsequent VAE or surgery histology for the client and not an individual lesion. Therefore, in the instance of multiple lesions (all test data), this may not accurately reflect practice when looking at some of the metrics. However, assessing test level data for the pathologist maximises their number of cases and makes sure that all biopsy results are captured for each pathologist.

Governance

All pathologists working within the NHS Breast Screening programme should review the national pathology data and use the results to inform personal development, including local audit. However, caution should be applied when working with small numbers, as the analyses may not be meaningful.

The lead breast screening pathologist should identify the appropriate actions for their department and/or staff and develop an action plan that should be presented and signed

off at an internal meeting. The internal monitoring of actions should align with trust clinical governance arrangements. Any professional performance issues identified should be followed up in line with Trust protocols for professional competence.

The lead breast screening pathologist should inform the director of breast screening of the planned actions and the impact this may have on the screening programme and to agree any joint areas of work. Actions pertaining to the operator (biopsy taker) should be led by the director of breast screening/lead radiologist, as appropriate.

The director of breast screening and the lead breast screening pathologist should present the action plan to the local commissioning programme board, which will require regular updates so it can be assured that the agreed actions have been followed up in a timely manner.

If the screening service is supported by more than 1 laboratory, the director of breast screening should collate the action plans into a single service improvement plan, to be monitored through the local commissioning programme board.

The regional screening QA service (SQAS) should provide professional advice and support to the providers and commissioners on the accurate interpretation and actioning of this report and to the lead pathologist regarding any recommendations and internal audits.

Regional commissioners should investigate the reporting of breast screening biopsies by low volume laboratories and ascertain whether the continued commissioning of these laboratories is justified and, if so, to assure themselves that these facilities are offering the required level of service stipulated. SQAS can provide further advice on the standards of service delivery required.

Data sources and methodology

The NBSS is the computer system used by all 77 screening services in England to record outcomes of women invited for screening. This includes information at all stages in the pathway through screening: invitation, attendance, assessment and treatment. Pathology outcomes for non-operative reporting are obtained from the NBSS system. BQA reports have been generated for the most significant non-operative biopsy result (known as client level), and for all biopsy results (known as test level) in this report.

A 3-year period is examined to provide an adequate number of cases for statistical analyses. The pathology data review standard operating procedure (SOP) and supplementary training slides are shared annually with administrative staff across the 77

breast screening services and the SQAS[1] teams in each region, with an aim to clearly define the roles and responsibilities required to complete each BQA task for the national pathology data review. Instructions included how to run the BQA reports, resolve exceptions and to ensure that the number of instances of false positives, benign proven malignancy and B5b to non-invasive cases were accurate and that each laboratory and pathologist on the BQA report could be correlated. A data collection table was populated to include the reporting pathologist, their GMC number, their respective laboratory and their total biopsies they had reported. A second table was populated with each laboratory shown on the BQA report and their total biopsies reported. A third table was populated with the total instances and the outcome of the review for each case.

Breast screening staff assigned to BQA work were responsible for running the reports, validating their data and completing the tables. All data was signed off by the director of breast screening and the lead breast screening pathologist before submission to SQAS. SQAS checked and validated the reports and were instructed to ensure that all reports received were accurate before submission for national analysis.

The BQA reports were run on NBSS by laboratory and pathologist for all clients and for all tests at all screening services. The client report gives the most significant (‘worst’) wide bore needle biopsy outcome for each woman biopsied and cross-references this with the subsequent histology from VAE or surgery outcome. Cases with both invasive and non-invasive tumours found in the same breast are recorded as invasive, as only the worst result is included. If more than 1 lesion is biopsied from opposite sides (invasive 1 side and non-invasive on the other side) they are both included (1 for each breast). The tests report gives the outcome of all wide bore needle tests for each lesion in both breasts.

Service-level and laboratory-level BQA results were calculated from the BQA report for all clients. Pathologist level BQA results were calculated from the BQA report for all tests. England averages for all clients and for all tests were calculated from the total client tables and total tests tables respectively, for each service.

Pathologist level BQA results include consultant pathologists reporting in both NHS and private sector pathology laboratories providing routine services to the NHS breast screening programme. Where a pathologist reported cases from more than 1 breast screening service, their results were amalgamated across England, as were the laboratories.

Funnel plots are used throughout the data review document. These charts are helpful in showing where variation is significantly different. Each chart has 5 lines: upper control limits at the 95% and 99.7% levels, lower control limits at the 95% and 99.7% levels, and the average. Laboratory level results and pathologist level results are compared to the England average. Any data points within the control limits are deemed to be subject to natural variation. Data points outside of the 95% control limits are significantly different and are deemed to be a result of special cause variation. This is even more so for the 99.7% control limits. Where this occurs, investigations should take place to determine the nature and cause of this variation. Breast screening services and pathologists with results falling outside of the control limits are referred to as outliers. It is important to note that outlier performance should not be assumed to be worse (or better) than the average; the data simply indicate that the performance is significantly different to that which could be explained by chance alone. Outlier status may also not necessarily equate with clinical relevance.

Where there are national standards, these are used to inform the interpretation of client level data only. There are currently no standards for all tests data.

Analysing reporting categories B1–B5

The data review compares the proportion of all clients whose outcomes were reported as B1–B5. Laboratories are encouraged to review the statistics in conjunction with overall screening key performance indicators (KPIs) for their related pathology service. Review of indicators such as referral rates, PPV of recall, proportion of women assessed proceeding to biopsy and overall cancer detection rates may help to explain the patterns of pathology reporting.

The outcomes of individual pathologists within a laboratory should be reviewed to identify any trends in reporting that may be significant. However, if all the pathologists reporting biopsies from a single screening centre are outliers for a particular performance measure, this may reflect wider screening practice rather than histopathology reporting alone.

Performance quality measures – Standards (by client)

Acceptable (replaces minimum) and achievable (replaces preferred) standards are presented in Table C4. These standards are applicable to client level data only.

Table C4: Thresholds for core biopsy performance

	Acceptable (%)	Achievable (%)	Rate for England 2021–2024 (%)*	Current median (%)* 2021 – 2024
AS for all carcinomas	>96	>98	96.9	97.2
AS for DCIS after maximum of 2 attempts	>85	>90		
Complete sensitivity	>99	>99.5	99.9	100
Specificity (full) (SPEC) (including non-biopsied cases)	>75	>85	76.1	77.6
PPV B5 (+PV)	>99.5	>99.9	99.99	100
False-positive rate (F+)	<0.2	<0.1	0.01	0
False-negative rate (B2 from cancer)	<0.5	<0.2	0.08	0
B1 core biopsy rate from cancers	<0.5	<0.3	0.06	0
Miss rate (B1 + B2) from cancer at first attempt	<5	<1	0.14	0
Suspicious rate (B3 + B4)	<10	<5	9.5	8.9
B3 rate	4 to 9	4.5 to 8.5	9.1	8.4
B4 rate	<1.5	<1	0.4	0.3
PPV B4	–	–	78.7	83.3
PPV B3	–	–	13.4	12.2

*Figures from National Breast Screening Pathology Audit for the period 1 April 2021 to 31 March 2024.

AS: Absolute sensitivity; DCIS: Ductal carcinoma in situ

These standards are under continuous review. Any revisions would apply to data relating to the period following the publications of any revised guidance.

Interpretation of data

Total core biopsy results

The proportion of total core biopsy results that are reported as B1 to B5 will be dependent on a variety of factors, including the population case mix, the accuracy of the operator to target the appropriate area of suspicion, the degree of specificity of the operator, the threshold for biopsy of lesions at assessment and the accuracy of the pathologist in classifying specimens according to these guidelines.

Graphs showing the proportion of all core biopsy tests reported as B1 to B5 (rather than by client) provides information around frequency of repeat sampling and potential impact on pathology quality data.

B1 and B2 rates

High outliers for B1 or B2 rates (or both) should assess the proportion of B1 to B3 outcomes in comparison to the national average. An audit of a sample of B1 and B2 lesions (proportionate to the service size) should be undertaken to ensure that reporting complies with national guidance and to ensure that the B2, benign, category is not applied when the B1 category, normal, would be more appropriate, or vice versa.

High outliers for B1 core biopsy rates may be attributable to a low threshold for performing needle core biopsies; it is, therefore, advisable to examine the proportion of women undergoing NCB tests at the service in comparison to the national average. These data may help to triangulate the relationship with radiology.

The PPV of referral for assessment at the service is defined as the number of cancers expressed as a proportion of all women referred for assessment. This should be examined to establish whether there is a tendency to biopsy lesions with a very low suspicion of malignancy mammographically. Following this review of PPV of referral data and the service biopsy rate (both are available on BSIS), within the context of these data on B1/B2 biopsy data, the service should review its referral and assessment protocols to reduce the number of unnecessary referrals and biopsies. Consideration could be given to taking all recalls (whether discrepant or otherwise) through an arbitration process. It is also sensible to examine the miss rate (B1+B2) from cancers (below). This may be higher than expected, suggesting that the operator (biopsy taker) mistargeted the lesion.

Negative predictive value (B2, all clients)

Definition: The number of lesions that are not cancer that are identified as B2 expressed as a percentage of the total number of B2 results.

NHSBSP standard: none.

This is intimately linked to the false negative rate (B2 from cancers), whereby if the false negative rate is 0% then the negative predictive value is 100%.

False negative rate (B2 from cancer, all clients)

Definition: Number of false negative results expressed as a percentage of the total number of carcinomas sampled.

NHSBSP standard (by client): <0.5% (acceptable), <0.2% (achievable).

This indicator measures the percentage of all cancers on VAE or surgical histology for which there was a B2 result non-operatively. This indicator is closely related to the negative predictive value, as the numerator is the number of malignancies categorised as B2 non-operatively.

Low outlier status (provided in the companion spreadsheet) represents optimal performance by the operator for accurately targeting the lesion and the pathologist for correctly recognising and diagnosing benignity.

Core biopsy miss rate (B1 and B2 from cancer, all clients)

Definition: Number of cancers with prior core biopsies that were categorised as B1 or B2.

NHSBSP standard (client): <5% (acceptable), <1% (achievable).

It is good practice that a review at the MDT meeting is undertaken for any cancers which had a B1 outcome reported non-operatively. Although it is conceivable that the diagnosis was missed by the pathologist who reported the core as B1, the lesion reported by the image reader may not have been sampled. Hence, the reasons and justifications for the MDT decision not to repeat the core biopsy should be examined.

Specificity (biopsy cases only) (all clients)

Definition: The number of correctly identified benign lesions (B2) excised as VAE or surgical biopsies expressed as a percentage of the total number of benign VAE and surgical specimens.

NHSBSP standard: none.

Full specificity (all clients)

Definition: Number of correctly identified benign lesions (the number of B2 results minus the false negatives) expressed as a percentage of the total number of benign lesions biopsied.

NHSBSP standard (client): >75% (acceptable), >85% (achievable).

The NHSBSP assesses full specificity for all benign lesions (including those without final histology) and specificity for cases that have undergone biopsy only. Services with high specificity (for biopsy cases only) effectively means that a high proportion of cases that were proven benign at open biopsy had a B2 reporting outcome non-operatively.

Being a high outlier for full specificity could be due to greater use of the B2 reporting category with possible underuse of the B3 category. Services with high specificity (biopsy only) are often outliers for reporting in the B2 and/or B3 categories. If B3 is seldom used, the MDT meeting decision could be influencing the decision to refer the woman to surgical excision biopsy. The availability of VAB may also be influential in this measure.

As full specificity is likely to be high with accurate identification of benignity, high outlier status for this measure is not problematic. Low outliers should examine the B1 core biopsy rate, as this may be high and could indicate either suboptimal or mis-sampling by the operator (biopsy taker), although conversely this may represent a low threshold for sampling by the radiologist, consultant practitioner or advanced practitioner.

The proportion of women assessed undergoing needle tests should be compared to other services and the national average (see earlier interpretation of B1 and B2) and the PPV of referral (the number of cancers expressed as a proportion of all women referred from screening for assessment) should be examined, as this may indicate if a low threshold for sampling is a contributory factor. If the PPV of referral is low, this may be due to radiological aspects of performance (PPV of referral and biopsy rates are available on BSIS).

However, variation in the way pathologists report cases as B1 or B2 may be significant, especially when histological changes are minor or there is discordance with the clinical findings.

Services which have a low rate of specificity may also have a rate of benign biopsy outside the QA acceptable standard of <1.5 per 1,000 screened. It is worth assessing the benign biopsy rate in conjunction with specificity, as high rates may indicate an overuse of the B3 reporting category in these circumstances.

B3 rate (all clients)

Definition: the number of B3 diagnoses expressed as a percentage of the total number of core biopsy results.

NHSBSP standard (client): acceptable 4% to 9%; achievable 4.5% to 8.5%.

B3 with and without atypia (all clients)

It is mandatory on NBSS for all B3 core biopsy results to include a record of whether there is, or is not, associated epithelial atypia and the nature of that atypia (ductal, lobular or flat epithelial atypia).

The data recording of associated atypia in B3 lesions has historically shown wide variation. It is essential that communication between pathologists and all staff entering data into NBSS be improved to facilitate accurate recording of this data field and that staff understand that the epithelial atypia result (present or absent) and epithelial proliferation result must align.

To support data entry accuracy, pathologists should ensure clarity in core biopsy reports. Any laboratory that is an outlier in this measure should review the interpretability of their reports and consider performing an audit of data accuracy.

B3 lesions, both with and without atypia recorded, having no further investigation by VAE or surgery has historically reduced each year. The lack of further investigation remains unlikely in view of recommended clinical management. This may reflect misuse of the appropriate forms on NBSS which now exist for VAE specimens; for example, the data may be completed as for VAB rather than VAE.

It is essential that biopsy takers clearly record their intent as to whether they are performing a VAB or VAE and the pathologists in receipt of the specimen are informed about what procedure has been undertaken, so that the information is reported correctly. This will then facilitate accurate entry of data to NBSS.

If a laboratory is an outlier for B3 diagnoses, either with or without atypia, it is important that the performance of individual pathologists within the specific laboratory is analysed on this indicator. Sometimes an individual may appear to be an outlier as these, often more difficult cases may more frequently be reported by the most experienced pathologist. Similarly, if reviewed by several pathologists, inaccuracies in data recording may play a role (i.e. if several pathologists names are on the histology report, they may all erroneously be attributed to a particular individual). Alternatively, outlier status could indicate a particular trend in reporting B3 lesions by the team, which may need further investigation and/or input from the SQAS team. It can be helpful to examine whether it is an individual or the whole pathology reporting team which demonstrates outlier performance.

PPV B3 (all clients)

Definition: This indicator measures the percentage of total B3 results which are malignant on a VAE or surgical specimen.

NHSBSP standard: none.

Low outliers for PPV B3 should triangulate this information with overall use/percentage of the B3 category and with benign biopsy rates. A low threshold for reporting biopsies as B3 will result in a high B3 rate and potentially a subsequent increased benign biopsy rate and a low PPV for B3. It should be noted that, historically, benign biopsy rates only included surgical specimens and rates may now appear low because of the increased use of VAE rather than diagnostic surgery. It is worthwhile confirming that VAE procedures for B3 lesions have been correctly identified and coded. This may result in no apparent further diagnostic intervention following a B3 result, for example if incorrectly labelled as 'biopsy' and thus given a B code on data entry.

High outliers for PPV B3 should examine the number and type of non-operative biopsies (core needle biopsy or VAB) undertaken at assessment, as adequate diagnostic work up in the first instance may have prevented an unnecessary surgical diagnostic excision biopsy (i.e. non-therapeutic) with malignant histology.

PPV B3 with and without atypia (all clients)

Definition: This indicator measures the percentage of total core biopsy B3 lesions with atypia results which are malignant on a VAE and/or a surgical specimen and the percentage of total B3 without atypia results that are malignant on VAE or a surgical specimen.

NHSBSP standard: none.

The accuracy of recording these data fields will clearly influence the PPV of B3 lesions with and without atypia. Any laboratory that is an outlier in this measure should undertake an audit of data accuracy.

B4 rate (all clients)

Definition: The number of B4 diagnoses expressed as a percentage of the total number of core biopsy results.

NHSBSP standard (client): acceptable <1.5%; achievable <1%.

PPV B4 (all clients)

Definition: The percentage of total B4 results which are malignant on a VAE or surgical specimen.

NHSBSP standard: none.

This metric identifies the percentage of all B4 core biopsy results that were subsequently malignant on a VAE or surgical specimen. Most services and laboratories report very few specimens as B4, on both an annual basis and over a longer, aggregated period. Caution must, therefore, be exercised when reviewing this outcome measure.

A high PPV B4 could indicate over-caution in reporting of malignancy, while a low PPV may indicate a low threshold for reporting the suspicious category. It is advised that the proportion of B3 and PPV of B3 lesions are examined to assess whether there is an excess use of this category. If the PPV of the B3 category is high, this may represent over-caution by the pathologist or suboptimal sampling by the operator.

Absolute sensitivity (all clients)

Definition: Number of carcinomas diagnosed as such (i.e. B5 category) expressed as a percentage of the total number of carcinomas sampled.

NHSBSP standard (client): >96% (acceptable), >98% (achievable).

Complete sensitivity (all clients)

Definition: Number of carcinomas that were not definitely negative (not B1 or B2) on core biopsy, expressed as a percentage of the total number of carcinomas.

NHSBSP standard (client): >99% (acceptable), >99.5% (achievable).

Low outliers for absolute sensitivity should examine the rates of complete sensitivity. If this is not also low, or conversely, if the screening unit identified as being a high outlier, the pathologist may possibly be ‘under calling’ B5 cases, i.e. classifying lesions as B3 or B4 (number can be found within PPV B3 and PPV B4 data). This is problematic, as it may result in unnecessary further procedures. However, this may not always be related to histopathology; accuracy of targeting the lesion may be relevant. Methodology may also play a role in this, such as the use of 14- or 16-gauge core biopsy rather than appropriate use of VAB. If absolute and complete sensitivity are low, the B1 core biopsy rate from cancers and the false negative rate should be examined, as cancers may have been reported non-operatively as B1 or B2. This requires investigation by the radiologists and pathologists jointly, as it may result from either inaccuracy of identification or targeting of the index lesion or from missed diagnosis by the pathologist. It is also important to review the MDT decision making process to identify why no further needle biopsies were undertaken.

False positive rate (all clients)

Definition: A potential false positive is any case with a B5 core biopsy followed by a normal or benign surgery (or rarely a normal or benign VAE).

NHSBSP Standard (client): <0.2% (acceptable); <0.1% (achievable).

BQA downloads have historically produced inaccurate false positive rates because of the way NBSS analyses data for those cases where cancers have been completely removed by core biopsy (whether followed by normal or benign VAE or surgical excision) or where there has been complete pathological response following neoadjuvant therapy. In addition, some clients are not correctly allocated on NBSS if they firstly have malignant axillary only surgery followed by non-malignant breast surgery (for example, treated by neoadjuvant chemotherapy with complete pathological response or lesion entirely removed at biopsy).

Breast screening guidance requires that genuine false positives are reported as screening incidents and subject to duty of candour programmes. Should this occur, services should ensure, as per routine practice, that the relevant stakeholders are informed.

Specificity and the PPV of B5 are the only performance measures affected by the number of false positives. The total benign lesions include B5 to benign cases for specificity and the PPV B5 measures the percentage of total B5 results which are subsequently malignant in a surgical specimen.

Recording false positives

Following MDT review, pathology specimens may be reviewed and diagnoses amended with a supplementary report issued. Rarely, this can lead to an initial B5 outcome being reclassified as B3 or B4 on a supplementary pathology report. In this circumstance, it is essential that the original malignant biopsy outcome is retained and not deleted or altered on NBSS. The supplementary report should be added to NBSS as an additional reported test.

While genuine false positives may lead to harm, situations where a malignancy is downgraded in retrospect but prior to further clinical management (i.e. no harm to the patient has occurred) still need to be recorded in the breast screening programme. There is need for total transparency in the frequency of this phenomenon occurring.

Benign proven malignancy

Definition: A ‘benign proven malignancy’ is any case with a B5 core biopsy followed by a normal or benign surgery, or a B1 to B4 core biopsy followed by a VAE E5 and then

normal or benign surgery. The number of benign proven malignancy results is expressed as a percentage of the total number of carcinomas sampled.

NHSBSP standard: none.

The benign proven malignancy cases are recorded within the BQA tables but do not form part of the total number of biopsies.

Education and training

The Training and Education Subgroup of the National Coordinating Committee for Breast Pathology is responsible for organising breast screening pathology courses. A number of regular breast pathology educational courses take place each year in the UK. Additional experience may be gained by secondment to neighbouring centres of expertise and by participating in EQA schemes. Pathologists involved in the breast screening programme should also attend regular breast pathology QA meetings.

It is recognised that courses can only provide baseline knowledge and that acceptable levels of performance, particularly in core biopsy and cytological diagnosis, can only be realistically achieved by experience in routine practice. Regular self-audit of non-operative diagnosis results should be undertaken and is of educational value.

Reference

1. NHS England. *Breast screening: quality assurance guidelines for breast pathology services.* Accessed January 2026. Available at: www.gov.uk/government/publications/breast-screening-quality-assurance-guidelines-for-breast-pathology-services/breast-screening-quality-assurance-guidelines-for-screening-pathology-services

Appendix D Recording of data on the National Breast Screening System

The NBSS provides an interface for recording of pathology data related to breast screening patients. As most pathologists prefer to provide the data as a component of their histopathology report, rather than enter the data directly onto the system, the information must be provided in a clear and interpretable manner for easy extraction. For patients with complex or multiple abnormalities, steps should be taken to ensure that data is recorded accurately for the correct lesions. The data required for NBSS are listed in appendices E and F. It is hoped that future versions of NBSS will include methods to extract relevant data directly into NBSS from pathology data systems.

Lesion identification

This should be done by the radiologist at the time of assessment. For convenience, with patients who have more than 1 abnormality, the most suspicious or main lesion should be recorded as lesion 1 and other lesions recorded separately. Where lymph node assessment and needle biopsy is carried out, this should be recorded. Pathologists should clearly record information for each lesion that has been sampled so that transcription of the data is straightforward.

Cytology form

The method of localisation should be indicated. Options available are palpation, stereotactic, prone stereo, X-ray, ultrasound or MRI. There is an option of ‘not stated’ but it should not be necessary to use this. The specimen type should also be recorded. It is important to select ‘Node aspirate’ if the sample is from an axillary node. The cytology classification (C1–C5 or LC1–LC5) must be included in the cytopathology report.

Core needle biopsy form

The core needle biopsy form has scope to record more data in relation to the lesion. Pathologists are encouraged to record as much data as possible, which will help with future analysis and audit.

The first part of the form includes details of method of localisation:

- intention with regard to diagnostic
- therapeutic with regard to vacuum-assisted specimens (i.e. VAB or VAE)

- whether the sample was from a node
- whether the presence or absence of calcification on specimen X-ray is completed at the time of sampling.

If the pathologist has access to NBSS, it is possible to check this information for correlation. Misclassification here risks affecting NBSS data quality and data review metrics.

The information for the section headed ‘Pathology result’ should be provided by the pathologist, including specimen number, name of reporting pathologist and the B category. In the rare instance when it is not possible to distinguish between invasive and in situ disease, it should be recorded as ‘Not assessable’ rather than ‘Not stated’.

The above fields are mandatory for all biopsies. The remaining fields are optional but should be completed if possible. There are options for recording more information regarding benign and malignant lesions, as well as grading and hormone receptor and HER2 status, if performed on the core biopsy.

If the intention of a VAB is diagnostic rather than excision, the NBSS VAB form should be completed with a B category. If a B3 lesion such as a radial scar or papilloma has been excised or more thoroughly sampled as a VAE, then the diagnosis should be entered on the NBSS VAE form. The use of the terms VAB and VAE relies on the intention of the clinician when performing the procedure and should be provided by them on the request form. If the intention is diagnostic, typically fewer cores are sampled, which should be given a B code. A VAE is performed when the intention is to exclude associated or adjacent malignancy and generally more extensive sampling takes place. Some VAEs will not excise the whole lesion, but it should be noted that the same is true for some surgical diagnostic excisions. A proforma can be used for reporting VAEs (Appendix I). For reporting purposes, these are treated like surgical biopsies and no B category is needed. As in a surgical biopsy, classical or pleomorphic LCIS in a VAE is recorded as malignant, despite the differences in management of these variants.[1]

However, on NBSS, an ‘E’ code will be entered by the screening office with 2 main options: E2 for benign pathology and E5 for malignant pathology. This is similar to the H2 for benign pathology and H5 for malignant pathology coding on surgical specimens.

Pathologists should record clearly on the report whether the diagnosis is benign or malignant, but do not need to provide an ‘E’ code on the pathology report. There are also

NBSS codes for use by the screening office if the specimen cannot be reported (E0) or where the specimen is reported as containing normal breast tissue only (E1).

Regardless of how data are entered on to NBSS, pathologists should be involved in quality assurance of the information entered on to the system on a regular basis.

Using the core biopsy reporting form

The core biopsy reporting forms used may be the separate reporting form or the form generated specifically by the NBSS, which comes with the patient details already filled in by the computer. These both essentially request the same information.

The forms are typically submitted along with the sample and a separate local specimen request form and may be used directly or, more usually, the information is provided as part of the overall histology report. In the latter case, it is helpful to maintain the same terminology and order of data items for the screening unit staff to simplify transposition of the information to NBSS.

How the national screening system treats this information has been included in Appendix C. Information on the nature of the mammographic abnormality and clinical characteristics should be provided by the breast screening assessing clinician requesting the pathology examination.

Reference

1. Public Health England. *Breast screening: How to record vacuum-assisted excisions*. 2018. Available at: www.gov.uk/government/publications/breast-screening-how-to-record-vacuum-assisted-excisions/breast-screening-how-to-record-vacuum-assisted-excisions

Appendix E Recommended SNOMED codes for breast pathology

Neoplasms

The following are SNOMED3 equivalents of the ICD-O codes that are recognised internationally. Codes marked with an asterisk (*) are proposed codes that have not yet been formally included in ICD-O.

The licensing rights to SNOMED are held by IHTSDO.

Morphological codes	SNOMED code	SNOMED CT terminology	SNOMED CT code
Adenocarcinoma not otherwise specified (NOS)	M-81403	Adenocarcinoma, no subtype (morphologic abnormality)	1187332001
Adenoid cystic carcinoma	M-82003	Adenoid cystic carcinoma (morphologic abnormality)	11671000
Adenoma of nipple	M-85060	Adenoma of the nipple (morphologic abnormality)	65787003
Adenomyoepithelioma (benign)	M-89830	Adenomyoepithelioma (morphologic abnormality)	128765009
Adenomyoepithelioma (malignant)	M-89833	Adenomyoepithelioma with carcinoma (morphologic abnormality)	703644009
Angiosarcoma	M-91203	Haemangiosarcoma (morphologic abnormality)	39000009
Apocrine carcinoma	M-85733	Adenocarcinoma with apocrine metaplasia (morphologic abnormality)	22694002
Atypical medullary carcinoma	M-85133	Atypical medullary carcinoma (morphologic abnormality)	128698005
Carcinoma with osteoclast-like giant cells	M-80353	Carcinoma with osteoclast-like giant cells (morphologic abnormality)	128631001
Cribriform carcinoma	M-82013	Cribriform carcinoma (morphologic abnormality)	30156004
DCIS	M-85002	Intraductal carcinoma, noninfiltrating, no ICDO subtype (morphologic abnormality)	1162814007
Ductal adenoma	M-85030	Intraductal papilloma (morphologic abnormality)	5244003

Ductal carcinoma/NST	M-85003	Infiltrating duct carcinoma (morphologic abnormality)	82711006
Encysted papillary carcinoma	M-85042	Noninfiltrating intracystic carcinoma (morphologic abnormality)	703545003
Fibroadenoma	M-90100	Fibroadenoma, no ICDO subtype (morphologic abnormality)	1156873009
Fibroadenoma juvenile	M-90300	Juvenile fibroadenoma (morphologic abnormality)	46212000
Fibromatosis-like carcinoma	M-85723	Adenocarcinoma with spindle cell metaplasia (morphologic abnormality)	68358000
Granular cell tumour	M-95800	Benign granular cell tumour (morphologic abnormality)	1336225003
Haemangioma	M-91200	Haemangioma, no ICDO subtype (morphologic abnormality)	253053003
Hamartoma	M-90203	Hamartoma (morphologic abnormality)	51398009
Inflammatory carcinoma	M-85303	Inflammatory carcinoma (morphologic abnormality)	32968003
Intraductal papilloma	M-85030	Intraductal papilloma (morphologic abnormality)	5244003
Intraductal papilloma with DCIS	M-85032	Noninfiltrating intraductal papillary adenocarcinoma (morphologic abnormality)	30566004
Invasive micropapillary carcinoma	M-85073	Invasive micropapillary carcinoma of breast (morphologic abnormality)	703578005
Invasive papillary carcinoma	M-85033	Intraductal papillary adenocarcinoma with invasion (morphologic abnormality)	64524002
LCIS	M-85202	Lobular carcinoma in situ (morphologic abnormality)	77284006
Lipoma	M-88500	Lipoma morphology (morphologic abnormality)	134328007
Lobular carcinoma	M-85203	Lobular carcinoma (morphologic abnormality)	89740008
Low-grade adenosquamous carcinoma	M-85703	Adenocarcinoma with squamous metaplasia (morphologic abnormality)	15176003
Lymphoma NOS	M-95903	Malignant lymphoma, no ICDO subtype (morphologic abnormality)	1163043007

Medullary carcinoma	M-85103	Medullary carcinoma (morphologic abnormality)	32913002
Metaplastic carcinoma NOS	M-85753	Metaplastic carcinoma (morphologic abnormality)	128705006
Metastatic carcinoma	M-80106	Carcinoma, metastatic (morphologic abnormality)	79282002
Mixed carcinoma	Specify subtypes		
Mucinous carcinoma	M-84803	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Myoepithelial carcinoma	M-89823	Malignant myoepithelioma (morphologic abnormality)	128884000
Myofibroblastoma	M-88250	Myofibroblastoma (morphologic abnormality)	128738002
Neuroendocrine carcinoma (poorly differentiated)	M-80413	Small cell carcinoma (morphologic abnormality)	74364000
Neuroendocrine tumour (well differentiated)	M-82403	Well-differentiated neuroendocrine tumour (morphologic abnormality)	1286768001
Nodular fasciitis	M-88280	Nodular fasciitis (morphologic abnormality)	703616008
Paget’s disease of nipple	M-85403	Paget's disease, mammary (morphologic abnormality)	2985005
Papillary carcinoma in situ	M-85032	Noninfiltrating intraductal papillary adenocarcinoma (morphologic abnormality)	30566004
Papilloma multiple	M-85050	Intraductal papillomatosis (morphologic abnormality)	32296002
Phyllodes benign	M-90200	Phyllodes tumour, benign (morphologic abnormality)	16566002
Phyllodes malignant	M-90203	Phyllodes tumour, malignant (morphologic abnormality)	87913009
Phyllodes borderline	M-90201	Phyllodes tumour, borderline (morphologic abnormality)	71232009
Pleomorphic carcinoma	M-80223	Pleomorphic carcinoma (morphologic abnormality)	16741004
Pleomorphic LCIS	M-85192	Pleomorphic lobular carcinoma in situ (morphologic abnormality)	444591006
Secretory carcinoma	M-85023	Juvenile carcinoma of the breast (morphologic abnormality)	41919003

Signet ring carcinoma	M-84903	Signet ring cell carcinoma (morphologic abnormality)	87737001
Spindle cell carcinoma	M-80323	Spindle cell carcinoma (morphologic abnormality)	65692009
Squamous cell carcinoma	M-80703	Squamous cell carcinoma (morphologic abnormality)	1162767002
Syringomatous adenoma of nipple	M-84070	Syringoma (morphologic abnormality)	71244007
Tubular adenoma	M-82110	Benign tubular adenoma (morphologic abnormality)	1156654007
Tubular carcinoma	M-82113	Tubular adenocarcinoma (morphologic abnormality)	4631006
Undifferentiated carcinoma	M-80203	Carcinoma, undifferentiated (morphologic abnormality)	38549000

Other conditions

Term	SNOMED code	SNOMED CT terminology	SNOMED CT code
Abscess	M-41610	Abscess (morphologic abnormality)	44132006
Accessory/ectopic breast	D4-48012	Accessory breast (disorder)	18166000
Apocrine metaplasia	M-73310	Apocrine metaplasia (morphologic abnormality)	81274009
Atypical apocrine hyperplasia	M-73315	Atypical apocrine metaplasia (morphologic abnormality)	103673004
Atypical ductal hyperplasia	M-72175	Atypical intraductal hyperplasia (morphologic abnormality)	6660000
Atypical lobular hyperplasia	M-72105	Atypical lobular hyperplasia (morphologic abnormality)	33889003
Calcification	M-55400	Pathologic calcification, calcified structure (morphologic abnormality)	18115005
Collagenous spherulosis	M-72171	Collagenous spherulosis (morphologic abnormality)	447298005
Columnar cell atypia	M-67020	Columnar cell atypia (morphologic abnormality)	55465005
Columnar cell lesions	M-74240	Blunt duct adenosis (morphologic abnormality)	58811002
Complex sclerosing lesion	M-78731	Radial scar (morphologic abnormality)	133855003

Cyst NOS	M-33400	Cyst (morphologic abnormality)	367643001
Duct ectasia	M-32100	Dilatation (morphologic abnormality)	25322007
Epithelial hyperplasia without atypia	M-72170	Intraductal hyperplasia (morphologic abnormality)	67617000
Excision margins tumour free	M-09400	Surgical margin uninvolved by tumour (finding)	55182004
Fat necrosis	M-54110	Fat necrosis (morphologic abnormality)	79682009
Fibrocystic change	M-74320	Non-proliferative fibrocystic disease (morphologic abnormality)	133852000
Fibromatosis	M-76100	Angiomatosis (morphologic abnormality)	14350002
Fistula	M-39300	Acquired fistula (morphologic abnormality)	51711001
Foreign body reaction	M-44140	Foreign body giant cell granuloma (morphologic abnormality)	37058002
Galactocoele	M-33220	Galactocele associated with childbirth (disorder)	87840008
Gynaecomastia	M-71000	Hypertrophy (morphologic abnormality)	56246009
Infarction	M-54700	Infarct (morphologic abnormality)	55641003
Inflammation acute	M-41000	Acute inflammation (morphologic abnormality)	4532008
Inflammation chronic	M-43000	Chronic inflammatory morphology (morphologic abnormality)	409777003
Inflammation granulomatous	M-44000	Granulomatous inflammation (morphologic abnormality)	6266001
Involutional change	M-79140	Menstrual involution of breast (morphologic abnormality)	33429008
Juvenile hypertrophy	D7-90404	Pubertal breast hypertrophy (disorder)	198113009
Lactational change	M-82040	Lactating adenoma (morphologic abnormality)	128651002
Metaplasia atypical	M-73005	Atypical metaplasia (morphologic abnormality)	125544002
Metaplasia chondroid	M-73600	Cartilaginous metaplasia (morphologic abnormality)	112671001

Metaplasia epithelial (clear cell, etc)	M-73200	Epithelial metaplasia (morphologic abnormality)	54725001
Metaplasia osseous	M-73400	Osseous metaplasia (morphologic abnormality)	38109001
Metaplasia squamous	M-73220	Squamous metaplasia (morphologic abnormality)	83577005
Microglandular adenosis	M-72480	Microglandular hyperplasia (morphologic abnormality)	2953007
Microglandular hyperplasia	M-72450	Adenofibromyomatous hyperplasia (morphologic abnormality)	88000003
Morphological description only	M-09350	Morphologic description only (finding)	85728002
Mucocoele-like lesion	M-33440	Mucous cyst (morphologic abnormality)	19633006
Normal: NOS	M-00100	Normal tissue (finding)	30389008
PASH	M-72430	Stromal hyperplasia (morphologic abnormality)	75235002
Plasma cell mastitis	M-43060	Plasma cell inflammation (morphologic abnormality)	26246006
Pregnancy	M-68080	Pregnancy pattern (morphologic abnormality)	68737009
Radial scar	M-78731	Radial scar (morphologic abnormality)	133855003
Radiotherapy effect	M-11600	Radiation injury (morphologic abnormality)	81018009
Sclerosing adenosis	M-74220	Fibrosing adenosis (morphologic abnormality)	50916005
Surgical wound or cavity	M-14020	Surgical wound (morphologic abnormality)	112633009
Weddelite	M-55400	Pathologic calcification, calcified structure (morphologic abnormality)	18115005

Appendix F B codes for selected core biopsy diagnoses

Diagnosis	B code	Comment
Abscess	B2	
Adenomyoepithelioma	B3	If no atypia or overt malignancy; rarely may be B5
Angiosarcoma	B5b	
Apocrine adenosis (sclerosing adenosis with apocrine change), cytological atypia	B3 with epithelial atypia	
Apocrine adenosis (sclerosing adenosis with apocrine change), no atypia	B2	
Apocrine metaplasia	B2	
Apocrine proliferation, atypical	B3 with epithelial atypia	Unless amounts to definite apocrine DCIS, when B5a
Atrophic breast tissue	B1	
Atypical intraductal epithelial proliferation (AIDEP)	B3 with epithelial atypia	
Cellular fibroepithelial lesion, phyllodes cannot be excluded	B3	
Collagenous spherulosis	B2	
Columnar cell change	B2	
Columnar cell hyperplasia	B2	
Complex sclerosing lesion/radial scar	B3 with or without epithelial atypia	
Cyst	B2	
DCIS	B5a	Includes DCIS in a papilloma and solid papillary carcinoma in situ
Duct ectasia	B2	
Ductal adenoma	B2	
Encapsulated papillary carcinoma	B5a	Unless overt or conventional invasion when B5b

Fat necrosis	B2	
Fibroadenoma	B2	
Fibrocystic change	B1 or B2	Depends on degree, minor changes best classified as B1
Fibromatosis	B3	
Fibrosis, e.g. scarring	B1 or B2	Minor degrees of fibrosis should be classified as B1
Flat epithelial atypia	B3 with epithelial atypia	
Foreign body reaction, e.g. implant/silicone	B2	
Galactocoele	B2	
Granular cell tumour	B3	
Gynaecomastia	B2	
Haemangioma	B2 or B3	Depends on size of lesion and whether any atypical features
Haematoma	B2	If extensive, rather than just minor blood clot
Hamartoma	B1 or B2	May only see normal tissue on core and best then classified as B1
In situ lobular neoplasia (atypical lobular hyperplasia or classical LCIS)	B3 with epithelial atypia	
In situ lobular neoplasia (florid LCIS)	B4	
In situ lobular neoplasia (pleomorphic LCIS)	B5a	
Infarction	B2	
Inflammation, acute, chronic or granulomatous	B2	
Insufficient for diagnosis or artefact precluding assessment	B1	
Intraductal papilloma	B2 or B3	It is anticipated most will be B3 (with or without epithelial atypia), but if small and completely within the width of the biopsy then B2 appropriate.
Intramammary lymph node	B2	
Invasive carcinoma (any type)	B5b	Does not apply to microinvasive carcinoma, which should be classified as B5a
Juvenile fibroadenoma	B2	

Lactational change	B1	
Leiomyoma	B2 or B3	If any atypical features, call B3
Lipoma	B1	Cannot be definitely diagnosed on core but may be reported as consistent with lipoma, if fat only present.
Lymphoma	B5b	
Melanoma	B5b	
Metastatic carcinoma	B5b	
Microglandular adenosis	B3	
Microinvasive carcinoma	B5a	
Mucocoele-like lesion	B3 with or without epithelial atypia	
Myofibroblastoma	B3	
Neurofibroma	B2 or B3	If any atypical features, call B3
Nipple adenoma	B3 with or without epithelial atypia	
Nodular fasciitis	B3	
Normal tissue, with or without breast epithelial elements	B1	
Papillary carcinoma in situ or papilloma with definitive DCIS or solid papillary carcinoma in situ	B5a	Unless overt invasion when B5b
Papilloma	B3 with or without epithelial atypia	
Periductal mastitis	B2	
Phyllodes tumour (benign or borderline)	B3	The majority of definite phyllodes tumours, but with no malignant features on core, should be classified as B3. Occasionally may be B4
Phyllodes tumour (malignant features evident)	B5b	If unequivocal malignant features
Pseudoangiomatous stromal hyperplasia (PASH)	B2	

Radial scar	B2 or B3 with or without epithelial atypia	It is anticipated most will be B3, but if small and completely within the width of the biopsy then B2
Radiation-induced atypia	B2	
Sarcoma	B5b	
Scarring, e.g. from previous surgery or biopsy	B2	
Schwannoma	B2 or B3	If any atypical features, call B3
Sclerosing adenosis	B2	
Spindled cell lesion of uncertain nature	B3	
Surgical or previous biopsy site reaction	B2	
Suspicious for malignancy	B4	
Tubular adenoma	B2	
Usual epithelial hyperplasia	B1 or B2	Depending on extent, if only focal/mild, best regarded a B1
Vascular lesion (indeterminate)	B3	

Appendix G Reporting proforma for breast core biopsy

Surname: ..... Forenames: ..... Date of birth: .....

Sex: ..... Hospital: ..... Hospital no.: .....

NHS no.: ..... Date of surgery: ..... Date of report: .....

Authorisation: ..... Report no: ..... Date of receipt: .....

Pathologist: ..... Surgeon: .....

Side: Left □ Right □

Quadrant: Upper outer quadrant □ Lower outer quadrant □

Upper inner quadrant □ Lower inner quadrant □

Retroareolar □

Number of cores if known: .....

Specimen type: NCB □

VAE biopsy □

Vacuum-assisted diagnostic biopsy □

Vacuum-assisted biopsy – not further specified □

Calcification present on specimen X-ray? Yes □ No □ Radiograph not seen □

Comment: .....

Histological opinion: B1 (Normal) □

B2 (Benign) □

B3 (Uncertain malignant potential with epithelial atypia) □

B3 (Uncertain malignant potential without epithelial atypia) □

B4 (Suspicious) □

B5a (Malignant in situ) □

B5b (Malignant invasive) □

B5c (Malignant not assessable) □

If biopsy taken for assessment of calcification:

Histological calcification: Not identified □ Benign □ Malignant □ Both benign and malignant □

In situ carcinoma: Not identified □ Ductal □ Lobular □

DCIS grade: High □ Intermediate □ Low □ Cannot be assessed □

Invasive carcinoma: Not identified □ Present □

Type: No special type (ductal NST) □

Pure special type (90% purity; specify components present below) □

Mixed tumour type (50–90% special type component; specify components present below) □

Other malignant tumour (please specify): .....

Specify type component(s) present for pure special type and mixed tumour types†:

Tubular/cribriform □ Lobular □ Mucinous □ Medullary/atypical medullary □

Ductal/no special type □ Other □ (please specify): .....

Invasive carcinoma grade: 1 □ 2 □ 3 □ Cannot be assessed □

Oestrogen receptor status: Positive (≥ 1%) □ Negative (<1%) □

Percentage positive tumour cells =……

On-slide positive control material: Present □ Absent □

PR status: Positive (≥ 1%) □ Negative (<1%) □

Percentage positive tumour cells =……

On-slide positive control material: Present □ Absent □

HER2 IHC score: 0 negative □ 1+ negative □ 2+ Borderline □ 3+ Positive □

Not performed □

FISH/CISH ratio: .....

Status: Amplified □ Non-amplified □ Borderline □ Not performed □

HER2 copy no.: …… Chromosome 17 no.: ……

Final HER2 status: Positive □ Negative □

SNOMED codes: T ……. M ……

Date reported: ..... Pathologist: .....

Appendix H Reporting proforma for breast core biopsy in list format

Element name	Values	Implementation comments	COSD v9
Side	Single selection value list: • Left • Right		pCR0820 Left = [L] Left Right = [R] Right Not selected = [9] Not known
Quadrant	Single selection value list: • Upper outer quadrant • Lower outer quadrant • Upper inner quadrant • Lower inner quadrant • Retroareolar		
Number of cores if known	Free text		
Specimen type	Single selection value list: • NCB • VAE biopsy • Vacuum-assisted diagnostic biopsy • Vacuum-assisted biopsy – not further specified		pCR0760 All values = [BU] Biopsy NOS
Calcification present on specimen X-ray?	Single selection value list: • Yes • No • Radiograph not seen		
Comment	Free text		

Histological opinion	Single selection value list: • B1 (Normal) • B2 (Benign) • B3 (Uncertain malignant potential with epithelial atypia) • B3 (Uncertain malignant potential without epithelial atypia) • B4 (Suspicious) • B5a (Malignant in situ) • B5b (Malignant invasive) • B5c (Malignant not assessable)		pBR4260 B1 = [B1] Unsatisfactory/ normal tissue only B2 = [B2] Benign B3 (Uncertain malignant potential with epithelial atypia) = [B3b] Uncertain malignant potential with epithelial atypia B3 (Uncertain malignant potential without epithelial atypia) = [B3a] Uncertain malignant potential without epithelial atypia B4 = [B4] Suspicious B5a = [B5a] Malignant in-situ B5b = [B5b] Malignant invasive B5c = [B5c] Malignant not assessable
Histological calcification	Single selection value list: • Not identified • Benign • Malignant • Both benign and malignant		
In situ carcinoma	Single selection value list: • Not identified • Ductal • Lobular		
DCIS grade	Single selection value list: • High • Intermediate • Low	Not applicable if ‘In situ carcinoma’ is ‘Not identified’ or ‘Lobular’ only.	pBR4160 High = [H] High Intermediate = [I] Intermediate Low = [L] Low

	• Cannot be assessed		Cannot be assessed = [X] Not assessable Not applicable = Leave COSD value blank
Invasive carcinoma	Single selection value list: • Not identified • Present		
Type	Single selection value list: • No special type (ductal NST) • Pure special type (90% purity; specify components present below) • Mixed tumour type (50–90% special type component; specify components present below) • Other malignant tumour		
Other malignant tumour, please specify	Free text	Only required if 'Type, Other' – Malignant tumour' is selected.	
Specify type component(s) present for pure special type and mixed tumour types	Single selection value list: • Tubular/cribriform • Lobular • Mucinous • Medullary/ atypical medullary • Ductal/no special type • Other	Only required if 'Specify type component(s) present for pure special type and mixed tumour types, Other' is selected.	
Other, please specify	Free text		

Invasive carcinoma grade	Single selection value list: • 1 • 2 • 3 • Cannot be assessed		pCR0860 1 = [G1] Well differentiated 2 = [G2] Moderately differentiated 3 = [G3] Poorly differentiated Cannot be assessed = [GX] Grade of differentiation is not appropriate or cannot be assessed
Oestrogen receptor status	Single selection value list: • Positive (≥ 1%) • Negative (<1%)		pBR4220 Positive = [P] Positive (> or = 1%) Negative = [N] Negative <1% Not performed = [X] Not performed
Percentage positive tumour cells	Free text		
On-slide positive control material	Single selection value list: • Present • Absent		
PR status	Single selection value list: • Positive (≥ 1%) • Negative (<1%)		
Percentage positive tumour cells	Free text		
On-slide positive control material	Single selection value list: • Present • Absent		
HER2 IHC score	Single selection value list: • 0 negative • 1+ negative • 2+ Borderline • 3+ Positive		pBR4280 0 = [N1] Negative (0) 1+ = [N2] Negative (1+) 2+ = [B] Borderline (2+)

	• Not performed		3+ = [P] Positive (3+) Not performed = [X] Not performed
FISH/CISH ratio	Free text		
FISH/CISH status	Single selection value list: • Amplified • Non-amplified • Borderline • Not performed		pBR4310 Amplified = [P] Positive (Amplified) Non-amplified = [N] Negative (Non-amplified) Borderline = [B] Borderline Not performed = [X] Not performed
HER2 copy no.	Free text		
Chromosome 17 no.	Free text		
Final HER2 status	Single selection value list: • Positive • Negative		
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables		pCR6410
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables		pCR6420

Appendix I Reporting proforma for VAE

Surname: ..... Forenames: ..... Date of birth: .....

Sex: ..... Hospital: ..... Hospital no.: .....

NHS no.: ..... Date of surgery: ..... Date of report: .....

Authorisation: ..... Report no: ..... Date of receipt: .....

Pathologist: ..... Surgeon: .....

Localisation type: .....

Side: Left □ Right □

Quadrant: Upper outer quadrant □ Lower outer quadrant □

Upper inner quadrant □ Lower inner quadrant □

Retroareolar □

Number of cores if known: .....

Specimen type: VAE biopsy □

Calcification present on specimen X-ray? Yes □ No □ Radiograph not seen □

Comment:

.....

Histological opinion: Normal □

Benign □

Malignant in situ □

Malignant invasive □

Histological description:

If biopsy taken for assessment of calcification:

Histological calcification: Not identified □ Benign □ Malignant □ Both benign and malignant □

For benign lesions:

Epithelial atypia: Not present □

Present without atypia □

Present with atypia – ductal □

Present with atypia – FEA □

Present with atypical lobular hyperplasia □

In situ carcinoma: Not identified □ Ductal □ Lobular□

DCIS grade: High □ Intermediate □ Low □ Cannot be assessed □

Invasive carcinoma Not identified □ Present □

Type: No special type (ductal NST) □

Pure special type (90% purity; specify components present below) □

Mixed tumour type (50–90% special type component; specify components present below) □

Other malignant tumour (please specify): .....

Specify type component(s) present for pure special type and mixed tumour types:

Tubular/cribriform □ Lobular □ Mucinous □ Medullary/atypical medullary □

Ductal/no special type □ Other □ (please specify): .....

Invasive carcinoma grade: 1 □ 2 □ 3 □ Cannot be assessed □

Oestrogen receptor status: Positive (≥ 1%) □ Negative (<1%) □

Percentage positive tumour cells =……

On-slide positive control material: Present □ Absent □

PR status: Positive (≥ 1%) □ Negative (<1%) □

Percentage positive tumour cells =……

On-slide positive control material: Present □ Absent □

HER2 IHC score: 0 negative □ 1+ negative □ 2+ Borderline □ 3+ Positive □

Not performed □

FISH/CISH ratio: .....

Status: Amplified □ Non-amplified □ Borderline □ Not performed □

HER2 copy no.: …… Chromosome 17 no.: ……..

Final HER2 status: Positive □ Negative □

SNOMED codes: T ……. M …..……

Date reported: ..... Pathologist: .....

Appendix J Reporting proforma for VAE in list format

Element name	Values	COSD v9
Side	Single selection value list: • Left • Right	
Quadrant	Single selection value list: • Upper outer quadrant • Lower outer quadrant • Upper inner quadrant • Lower inner quadrant • Retroareolar	
Number of cores if known	Free text	
Specimen type	Single selection value list: • VAE biopsy	
Calcification present on specimen X-ray?	Single selection value list: • Yes • No • Radiograph not seen	
Comment	Free text	
Histological opinion	Single selection value list: • Normal • Benign • Malignant in situ • Malignant invasive	
Histological calcification	Single selection value list: • Not identified • Benign • Malignant • Both benign and malignant	
For benign lesions	Single selection value list: • Epithelial atypia: Not present • Present without atypia • Present with atypia – ductal • Present with atypia – FEA	

	• Present with atypical lobular hyperplasia	
In situ carcinoma	Single selection value list: • Not identified • Ductal • Lobular	
DCIS grade	Single selection value list: • High • Intermediate • Low • Cannot be assessed	
Invasive carcinoma	Single selection value list: • Not identified • Present	
Type	Single selection value list: • No special type (ductal NST) • Pure special type (90% purity; specify components present below) • Mixed tumour type (50–90% special type component; specify components present below) • Other malignant tumour	
Other malignant tumour, please specify	Free text	
Specify type component(s) present for pure special type and mixed tumour types	Single selection value list: • Tubular/cribriform • Lobular • Mucinous • Medullary/atypical medullary • Ductal/no special type • Other	
Other, please specify	Free text	
Invasive carcinoma grade	Single selection value list: • 1 • 2 • 3 • Cannot be assessed	

Oestrogen receptor status	Single selection value list: • Positive (≥1%) • Negative (<1%)	
Percentage positive tumour cells	Free text	
On-slide positive control material	Single selection value list: • Present • Absent	
PR status	Single selection value list: • Positive (≥1%) • Negative (<1%)	
Percentage positive tumour cells	Free text	
On-slide positive control material	Single selection value list: • Present • Absent	
HER2 IHC score	Single selection value list: • 0 negative • 1+ negative • 2+ borderline • 3+ positive • Not performed	
FISH/CISH ratio	Free text	
Status	Single selection value list: • Amplified • Non-amplified • Borderline • Not performed	
HER2 copy no.	Free text	
Chromosome 17 no.	Free text	
Final HER2 status	Single selection value list: • Positive • Negative	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables	

Appendix K Reporting proforma for breast FNAC

Surname: ..... Forenames: ..... Date of birth: .....

Sex: ..... Hospital: ..... Hospital no.: .....

NHS no.: ..... Date of surgery: ..... Date of report: .....

Authorisation: ..... Report no.: ..... Date of receipt: .....

Pathologist: ..... Surgeon: .....

Side: Left □ Right □

Location: Upper outer quadrant □ Lower outer quadrant □

Upper inner quadrant □ Lower inner quadrant □

Retroareolar □

Cytological opinion: C1 □ (Inadequate/unsatisfactory)

C2 □ (Benign)

C3 □ (Uncertain)

C4 □ (Suspicious)

C5 □ (Malignant)

Comment:

.....

.....

SNOMED codes: T …… M ……

Date reported: ..... Pathologist: .....

Appendix L Reporting proforma for breast FNAC in list format

Element name	Values	COSD v9
Side	Single selection value list: • Left • Right	pCR0820 Left = [L] Left Right = [R] Right Not selected = [9] Not known
Quadrant	Single selection value list: • Upper outer quadrant • Lower outer quadrant • Upper inner quadrant • Lower inner quadrant • Retroareolar	
Cytological opinion	• C1 (Inadequate/unsatisfact-ory) • C2 (Benign) • C3 (Uncertain) • C4 (Suspicious) • C5 (Malignant)	pBR4240 C1 = [C1] Inadequate / unsatisfactory specimen C2 = [C2] Benign C3 = [C3] Uncertain C4 = [C4] Suspicious of malignancy C5 = [C5] Malignant
Comment	Free text	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables	pCR6410
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables	pCR6420

Appendix M Reporting proforma for axillary FNAC

Surname: ..... Forenames: ..... Date of birth: .....

Sex: ..... Hospital: ..... Hospital no.: .....

NHS no.: ..... Date of surgery: ..... Date of report: .....

Authorisation: ..... Report no.: ..... Date of receipt: .....

Pathologist: ..... Surgeon: .....

Side: Left □ Right □

Location: Axillary LN □

Cytological opinion: LC1 □ (Inadequate/unsatisfactory)

LC2 □ (Benign)

LC3 □ (Uncertain)

LC4 □ (Suspicious)

LC5 □ (Malignant)

Comment:

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SNOMED codes: T ……. M ……..……

Date reported ..... Pathologist .....

Appendix N Reporting proforma for axillary FNAC in list format

Element name	Values	COSD v9
Side	Single value selection list: • Left • Right	pCR0820 Left = [L] Left Right = [R] Right Not selected = [9] Not known
Location	Single value selection list: • Axillary LN	
Cytological opinion	• LC1 (Inadequate/unsatis-factory) • LC2 (Benign) • LC3 (Uncertain) • LC4 (Suspicious) • LC5 (Malignant)	pBR4250 LC1 = [C1] Inadequate / unsatisfactory specimen LC2 = [C2] Benign LC3 = [C3] Uncertain LC4 = [C4] Suspicious of malignancy LC5 = [C5] Malignant
Comment	Free text	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables	pCR6410
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables	pCR6420

Appendix O Reporting proforma for axillary core biopsy

Surname: ..... Forenames: ..... Date of birth: .....

Sex: ..... Hospital: ..... Hospital no.: .....

NHS no.: ..... Date of surgery: ..... Date of report: .....

Authorisation: ..... Report no.: ..... Date of receipt: .....

Pathologist: ..... Surgeon: .....

Side: Left □ Right □

Location: Axillary LN □

Opinion LB1 □ (Inadequate/Unsatisfactory)

LB2 □ (Normal/Benign)

LB3 □ (Uncertain)

LB4 □ (Suspicious)

LB5 □ (Malignant)

Comment:

.....

.....

.....

.....

.....

.....

SNOMED codes: T …… M ……

Date reported: ..... Pathologist: .....

Appendix P Reporting proforma for axillary core biopsy in list format

Element name	Values	COSD v9
Side	Single value selection list: • Left • Right	pCR0820 Left = [L] Left Right = [R] Right Not selected = [9] Not known
Location	Single value selection list: • Axillary LN	
Cytological opinion	• LB1 (Inadequate/unsatisfactory) • LB2 (Normal/Benign) • LB3 (Uncertain) • LB4 (Suspicious) • LB5 (Malignant)	pBR4270 LB1 = [LB1] Inadequate / unsatisfactory LB2 = [LB2] Normal/benign LB3 = [LB3] Uncertain LB4 = [LB4] Suspicious LB5 = [LB5] Malignant
Comment	• Free text	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables	pCR6410
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables	pCR6420

Appendix Q Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	At least 1 high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target population or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high- quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix R AGREE II guideline monitoring sheet

The guidelines of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of these guidelines that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Foreword, 1
2 The health question(s) covered by the guideline is (are) specifically described	1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	1
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	1
10 The methods for formulating the recommendations are clearly described	1
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword, 1
12 There is an explicit link between the recommendations and the supporting evidence	2, 3, 4
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	1, 2, 3, 4, Appendices A to F
16 The different options for management of the condition or health issue are clearly presented	2, 3, 4

17 Key recommendations are easily identifiable	2, 3, 4
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A to Q
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	5
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword