NATIONAL BREAST
CANCER CENTRE
Incorporating the
Ovarian Cancer Program

Breast fine needle aspiration cytology and core biopsy: a guide for practice

RCPA
The Royal College of Pathologists of Australasia

Breast
Cancer
Network
Australia

Breast fine needle aspiration cytology and core biopsy: a guide for practice

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This document provides recommendations regarding appropriate practice, to be followed subject to the clinician's judgement and the patient's preference in each individual case.

The information contained in this document is designed to assist decision making and is based on the best evidence available at the time of production.

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FOREWORD

Breast fine needle aspiration (FNA) cytology and core biopsy are practised widely throughout Australia by clinicians of different disciplines. While there may be particular requirements for practice at the local level, there are no nationally agreed recommendations to guide practice in this area.

Breast fine needle aspiration cytology and core biopsy: a guide for practice ('the guide') has been developed by a multidisciplinary project team coordinated by the National Breast Cancer Centre (NBCC). The guide is intended to assist all clinicians involved in the investigation of women with breast symptoms or image-detected breast lesions. However, it is not intended as a training manual for those learning to perform FNA cytology or core biopsy. The guide is based on evidence where available and on expert consensus opinion. Given that the available literature does not meet the rigour required to develop clinical practice guidelines as outlined by the National Health and Medical Research Council (NHMRC),[1] the guide simply provides a series of recommendations and suggestions for practice.

The vast majority of breast cancers occur in women. Therefore, the term 'women' and feminine pronouns are used throughout the guide. However, the information and principles outlined in the guide are also applicable to men with breast lesions.

We are confident the successful implementation of the recommendations in the guide will foster high standards of investigation of women with breast lesions throughout Australia.

ABBREVIATIONS

ACN	Australian Cancer Network
ADH	atypical ductal hyperplasia
AH	atypical hyperplasia
ALH	atypical lobular hyperplasia
ASUM	Australasian Society for Ultrasound in Medicine
BIRG	Breast Imaging Reference Group
DCIS	ductal carcinoma in situ
ER	oestrogen receptor
FNA	fine needle aspiration
H&E	haematoxylin and eosin
IBUS	International Breast Ultrasound School
LCIS	lobular carcinoma in situ
NBCC	National Breast Cancer Centre
NHMRC	National Health and Medical Research Council
PPV	positive predictive value
PR	progesterone receptor
QA	quality assurance
RANZCR	Royal Australian and New Zealand College of Radiologists
RCPA	Royal College of Pathologists of Australasia

KEY RECOMMENDATIONS

The following table provides a summary of the key recommendations presented in this document. These recommendations are based either on the best available evidence where that exists, or the consensus opinion of experts. These recommendations should be considered in the investigation of breast symptoms or image-detected breast lesions. To understand each recommendation in context, please refer to the appropriate chapter.

BREAST FNA AND CORE BIOPSY: A GUIDE FOR PRACTICE

Key recommendations
Chapter 1. General principles of investigation
• FNA cytology and core biopsy form an integral component of the triple test and should always be interpreted in correlation with the clinical and imaging findings.
• Best practice is most effectively achieved in a multidisciplinary team environment that includes those responsible for the performance, interpretation and correlation of the tests and for patient care.
• Adequate clinical examination and imaging investigation of both breasts should be performed prior to FNA cytology or core biopsy of palpable and impalpable lesions.
• It is recommended that one person is nominated as the managing clinician to take responsibility for coordinating the investigation of any breast lesion, correlating the cytological/histological results with the clinical and imaging findings, and communicating the results to the woman.
Chapter 2. Indications for FNA cytology and core biopsy
• Core biopsy is the investigation of choice in the evaluation of microcalcifications.
• Core biopsy, unlike FNA cytology, yields tissue fragments allowing architectural features of the lesion to be identified to determine whether ductal carcinoma in situ (DCIS) or invasive carcinoma is present.

- Definitive diagnosis of some lesions can be difficult to make on the basis of FNA cytology. These include atypical ductal hyperplasia (ADH), low-grade DCIS, some tubular carcinomas and some invasive lobular carcinomas.
- A core biopsy showing only DCIS does not exclude the possibility of invasive disease.

Chapter 3. Communicating effectively with women undergoing FNA cytology and core biopsy

- Adequate information should be provided to the woman about the nature of the procedure and its interpretation, benefits, limitations, complications and implications, in a reassuring and appropriate manner that is understandable to the woman.
- The woman should be informed as to how and when she will be given the results, which should be provided in a timely manner.
- The provision of results indicating a malignancy should be coordinated by the managing clinician. It is highly desirable that such results be given in person and when the woman has a support person present, if she so chooses.

Chapter 4. Performing FNA cytology and core biopsy

- The clinician's patient load and experience in performing FNA cytology and core biopsy have been demonstrated to influence performance. It is recommended that all clinicians performing these procedures regularly audit their sampling accuracy for malignant lesions and the rate of inadequate specimens submitted.
- Imaging guidance, ultrasound or stereotactic mammography, is required to ensure accuracy of sampling when lesions are impalpable, small or difficult to palpate.

Chapter 5. The specimen: request, preparation and processing

- Microcalcifications found in histological sections should be matched with the microcalcifications seen on the specimen radiograph.
- The use of a standardised request form is recommended for all FNA cytology and core biopsy specimens.

- It is recommended that cyst fluid is sent for cytological evaluation if it is bloody/serosanguinous, if there is a residual palpable mass or solid lesion on ultrasound, or if imaging studies indicate that the cyst is complex.
- When performing a core biopsy for microcalcifications, the specimen should be radiographed. Both the specimen radiograph and specimen should be sent to the pathology laboratory with a report confirming the presence of microcalcification/s within the cores of tissue.

Chapter 6. Pathology reporting

- It is recommended that FNA cytology and core biopsy be reported by cytopathologists/pathologists actively involved and experienced in reporting breast aspirates, and preferably participating in a multidisciplinary team.
- It is recommended that the reporting cytopathologist/pathologist uses the diagnostic categories outlined in the chapter to report their findings. The use of descriptive diagnostic categories enhances communication within the multidisciplinary team.

Chapters 7 & 8. Common pitfalls in the reporting of FNA cytology and core biopsy

- It is important all members of the multidisciplinary team are aware of the common pitfalls in the interpretation of FNA cytology and core biopsy.
- Maintaining strict cytological criteria for malignancy should keep false positive diagnoses to a minimum.
- Application of the triple test should reduce the incidence of missed cancers when there is a false negative FNA cytology or core biopsy result.
- A commitment to obtaining and assessing follow-up data is necessary to improve patient care and to understand and evaluate diagnostic pitfalls, in particular false negative diagnoses.

Chapter 9. Training and quality assurance

- Regular audit and review of results should be conducted within each practice providing FNA cytology and core biopsy services, to identify and address the need for additional training of staff.

INTRODUCTION

Dr Julienne Grace

BACKGROUND

For decades, small samples of tissue have been obtained using a needle to diagnose lesions in many anatomical locations.[2] Breast lesions were identified as particularly suitable for the technique due to their accessibility.[2] The use of smears obtained by aspiration for diagnostic purposes was reported as early as 1933, when Stewart's series of 2,500 specimens included almost 500 breast lesions.[3] The publication of cytology results for a series of 2,111 fine needle aspiration (FNA) samples by Franzen and Zajicek in 1968 established the technique as a vital part of the assessment of breast lesions.[4]

FNA cytology and core biopsy were originally used to diagnose palpable breast lesions. Both methods have a high degree of sensitivity and specificity. FNA cytology is an excellent method for diagnosing palpable lesions; its sensitivity has been reported to be between 89% and 98%[5] and its specificity between 98% and 100%.[6]

Following the introduction of mammographic screening, FNA cytology and core biopsy are now also used to diagnose impalpable breast lesions. The sensitivity and specificity of stereotactic FNA cytology with impalpable lesions have been reported to be 77–100% and 91–100% respectively.[6] The use of core biopsy has increased, especially in the evaluation of lesions that are associated with high inadequacy rates with FNA cytology – such as mammographically detected lesions that are very small, suspected radial scars or microcalcifications.[6] Both the sensitivity and specificity of core biopsy for the diagnosis of impalpable lesions are usually reported to be at least 90%.[2] In a multidisciplinary breast setting it has been shown that ultrasound-guided core biopsy has a sensitivity of 82% and a specificity and a positive predictive value (PPV) for malignancy of 100%.[7] In general, core biopsy has been shown to be superior for the confirmation of benign lesions, as the rate of samples reported as unsatisfactory is less than for FNA cytology (12.5% versus 34.2%).[5]

Unlike studies about FNA cytology where the procedure has been used in large series of palpable and image-detected lesions, most studies about core biopsy include selected cases. Rosen (1999)[8] reports that core biopsy is accurate for the

diagnosis of most breast lesions, but fails to identify 6–12% of mammographically detected microcalcifications and under-diagnoses ductal carcinoma in situ (DCIS). Rosen also states that most follow-up studies of the results of core biopsies are inadequate at present.[7]

In the United Kingdom, 62% of cancers detected in 1996–1997 in the National Health Service Breast Screening Programme were diagnosed preoperatively by FNA cytology or core biopsy.[9] Even though this is still short of the National Health Service Breast Screening Programme target of 70%, Britton and McCann (1999)[9] argue that it represents an improvement over previous years, and an improvement that is likely to continue as a result of improved technological expertise by the radiographers, radiologists and pathologists involved.

When the UK National Health Service Breast Screening Programme was established, FNA cytology was the method of choice in the assessment of image-detected lesions. However, in recent years there has been an increase in the use of core biopsies to facilitate a preoperative diagnosis.[9] There are two principal explanations for this trend. One is the increased rate of inadequate specimens in impalpable lesions, sampled by FNA cytology. The other is the lack of expertise among pathologists in the interpretation of fine needle aspirates. The first explanation may be due to lack of technical skill or the nature of the lesion. The experience and skill of the operators and pathologists and the nature of the lesion will affect the choice of biopsy technique.

FNA cytology and core biopsy are complementary procedures.[6,10] Pinder and associates (1996)[10] and Masood (1996)[6] have stated there is insufficient evidence to decide if one method is better than another. These authors recommend the use of the appropriate combination of FNA cytology and/or core biopsy as the best approach for the diagnosis of breast lesions at different settings.[6,10]

AUSTRALIAN EXPERIENCE

In Australia, FNA cytology and core biopsy have been in use for many years to diagnose palpable breast lesions. Svante Orell can be credited with promoting FNA cytology of the breast in Australia since the 1970s, and the *Manual and Atlas of Fine Needle Aspiration Cytology*[11] by Orell and associates constitutes a milestone for FNA cytology.

Since the introduction of the national mammographic screening program BreastScreen Australia in 1991, large numbers of impalpable breast lesions have

been detected. The first National Accreditation Requirements for the program, developed in 1991, emphasised the need for improved preoperative diagnosis of benign and malignant lesions. Consequently, stereotactic and ultrasound-guided core biopsy have become much more widely used in the assessment of image-detected lesions. Improvements in imaging equipment are also likely to have contributed to this trend.

The standards for BreastScreen Australia 2002[12] further require its services to minimise unnecessary investigations, by setting performance objectives for preoperative diagnosis. A preoperative diagnosis of cancer is defined as a malignant result on FNA cytology or core biopsy, which is consistent with suspicious or malignant imaging findings. Current National Accreditation Standards for BreastScreen Services[12] specify that:

- at least 75% of cancers are diagnosed without the need for diagnostic excisional biopsy
- the rate of FNA cytology specimens reported as inadequate/insufficient is less than 25%
- the false negative rate for FNA cytology procedures is less than 6%
- the rate of core biopsy specimens reported as false negative or inadequate is less than 15%
- the false positive rate for FNA cytology procedures and core biopsy is less than 1%
- the false positive rate for core biopsy is less than 0.5%.

The standards were reviewed in 1994 and in 2000. The revised standards were considered and ratified by the BreastScreen Australia National Advisory Committee in July 2001.

NEED FOR RECOMMENDATIONS FOR FNA CYTOLOGY AND CORE BIOPSY

Breast changes can be detected as a mammographic lesion at screening, as a breast symptom found by the woman or as a sign found by her doctor. The investigation of these changes using the triple test approach will often involve FNA cytology or core biopsy to help determine the nature of the lesion (see Chapter 1).

It is likely that standards of FNA cytology and core biopsy practice will vary between clinicians and practice settings. While some data about standards of practice in FNA cytology and core biopsy exist within the national mammographic screening program,[11] the availability of data outside the program is limited.

The pathology reporting of breast cancer: a guide for pathologists, surgeons and radiologists, first published in 1997 by the Australian Cancer Network (ACN) Pathology Working Party and revised in 2001, provides best practice recommendations in relation to pathology reporting of surgical breast cancer specimens.[13] No national recommendations currently exist for breast specimens obtained using FNA cytology or core biopsy.

OBJECTIVES AND TARGET AUDIENCE

The objective of this guide is to assist clinicians, including surgeons, pathologists, radiologists and breast physicians, to achieve and maintain best standards of practice in FNA cytology and core biopsy of both palpable and impalpable breast lesions. The guide includes recommendations covering all aspects of the practice of these procedures, including:

- the indications, advantages, disadvantages and complications of both procedures
- techniques
- reporting
- training and continuing education
- quality assurance.

The relevance of the different sections of the guide to individual clinicians will vary according to each clinician's involvement in the various steps of the process.

This document in not intended to be prescriptive, but to offer guidance to practice. It is anticipated that achieving and maintaining high standards of practice in FNA cytology and core biopsy will result in more effective investigation, greater diagnostic accuracy and better overall outcomes for women.

CHAPTER 1 GENERAL PRINCIPLES OF INVESTIGATION

Fine needle aspiration (FNA) cytology and core biopsy are essential tools in the diagnosis and management of breast disease. Accurate diagnosis depends on a number of factors, such as awareness of correct techniques and their application, use of the most appropriate test for a particular clinical situation, the sensitivity and specificity of the techniques and interpretation of results in the clinical setting.

THE MULTIDISCIPLINARY APPROACH

The effective diagnosis and management of breast cancer relies on the specialist skills of many disciplines. The benefits of a multidisciplinary approach to the treatment of women with breast cancer are well recognised, in Australia and internationally.[14, 15, 16, 17]

While there are limited data objectively demonstrating the benefits of a multidisciplinary approach to the assessment of breast lesions, it is widely accepted that the best approach is to bring together all clinicians with relevant expertise, including those responsible for the performance, interpretation and correlation of the tests and for patient care.

It is preferable that one clinician ('the managing clinician') takes responsibility for coordinating the investigation of any breast lesion and for communicating the results to the woman. The managing clinician should be nominated before any imaging, FNA cytology or core biopsy is performed.

THE TRIPLE TEST

FNA cytology and core biopsy results should always be interpreted in the context of the triple test.[5, 11]

The triple test is the recommended approach for the investigation of palpable or impalpable breast lesions detected by imaging. It comprises the following components:

- clinical breast examination and medical history
- imaging – mammography and/or ultrasound
- non-excision biopsy – FNA cytology and/or core biopsy.

The triple test is positive if **any** of the three components is positive, and negative if all the components are negative. The triple test has a sensitivity (true positive rate) of 99.6%, and a specificity of 93%.[18] Irwig and Macaskill (1997)[18] have developed models to illustrate the accuracy of the triple test results for clinically and mammographically detected breast lesions (see Appendix B).

It is the responsibility of the managing clinician to correlate the cytological/histological results with the clinical and imaging findings. Accurate interpretation requires a close working relationship between the managing clinician, the radiologist and the pathologist. When a discrepancy between the triple test components occurs, further investigation is mandatory. This may include excision biopsy.

ADVANTAGES OF THE TRIPLE TEST APPROACH

Within both the screening and the diagnostic setting, the effective investigation of breast lesions using the triple test approach aims to ensure that the majority of changes are diagnosed without the need for excision biopsy while maintaining a high accuracy for the detection of cancer.

In cases where cancer is reported, such an approach allows for preoperative counselling of the woman regarding treatment options, and may assist in the planning of single-stage surgery.[10, 11, 19] In cases where a benign diagnosis is reported or confirmed and where the need for excision biopsy, is eliminated, the woman can be reassured and appropriate management options discussed.

The aims of the triple test are to:

- maximise the diagnostic accuracy in breast disease
- maximise the preoperative diagnosis of cancer
- minimise the proportion of excision biopsies for diagnostic purposes
- minimise the proportion of benign excision biopsies for diagnostic purposes.

FACTORS INFLUENCING THE USE OF FNA CYTOLOGY AND CORE BIOPSY

FNA cytology and core biopsy are complementary procedures.[6, 10] Both procedures have advantages and disadvantages (see Chapter 2).

Generally, the advantages of FNA cytology are: the possible availability of results within a few hours, few complications and good patient acceptability.[5] In addition, with careful selection of suitable lesions, and when performed and examined by experienced operators and cytologists, FNA cytology is highly specific for the detection of malignant cells.

There is some evidence that, compared with FNA cytology, core biopsy has higher sensitivity and specificity and a lower rate of samples reported as unsatisfactory,[5,6,9] particularly for image-detected lesions. Most importantly, core biopsy but not FNA cytology enables invasive cancer to be differentiated from DCIS, but it is still difficult to distinguish atypical ductal hyperplasia from low-grade in situ carcinoma.[20] However, core biopsy requires local anaesthesia and may result in more discomfort post-procedure, and its results usually take longer to be obtained. Disposables and equipment required to perform FNA are less expensive than for core biopsy.

When FNA cytology is combined with core biopsy, the rate of preoperative diagnosis of image-detected lesions has been reported to be up to 90%.[10] Factors that may influence the relative use of FNA cytology and core biopsy include the characteristics of the breast lesion being investigated, the experience and preference of the clinician performing the procedure, the preference of the managing clinician, the availability of pathologists with experience in cytology.

MAXIMISING DIAGNOSTIC ACCURACY

A thorough clinical examination and necessary imaging investigations should be performed prior to FNA cytology or core biopsy of breast lesions, whether palpable or impalpable. Haematoma associated with the sampling procedure may compromise the interpretation of subsequent clinical examination or imaging studies. If work-up of further palpable and impalpable lesions found during examination is necessary, it may proceed immediately, avoiding the inconvenience for the woman of additional visits.

The level of suspicion of the imaged breast lesion should be considered in the diagnostic process. The standardised report and classification system for breast imaging developed for use outside the national mammographic screening program (BreastScreen Australia) and supported by the Breast Imaging Reference Group of the Royal Australian and New Zealand College of Radiologists (RANZCR), is described in *Breast imaging: a guide for practice.*[21]

The proposed classification system for use in diagnostic breast imaging provides a means of indicating the level of suspicion/significance of lesions. The categories are:[21]

No significant imaging abnormality detected	(Category 1)
Benign findings	(Category 2)
Indeterminate/equivocal lesion	(Category 3)
Suspicious features of malignancy	(Category 4)
Malignant	(Category 5)

FNA cytology or core biopsy of a palpable lesion may require image-guided localisation, regardless of which sampling technique is selected. The use of image guidance for either FNA cytology or core biopsy increases the likelihood of obtaining a representative sample from the lesion. The use of image guidance may be influenced by:

- the clinical ability to define the lesion from the adjacent breast tissue
- the size of the lesion
- the proximity of the lesion to the chest wall
- the proximity of the lesion to a breast prosthesis
- the expertise of the operator.

Guidance techniques are discussed in Chapter 4.

Summary

- FNA cytology and core biopsy are complementary techniques. Factors that may influence the relative use of FNA cytology and core biopsy include the characteristics of the breast lesion being investigated, the experience and preference of the clinician performing the procedure and the clinician managing the patient, the availability of pathologists with experience in cytology.
- By performing these procedures as part of the triple test, clinicians aim to minimise the proportion of excision biopsies and the proportion of benign excision biopsies for diagnostic purposes, and to maximise the preoperative diagnosis of cancer.

CHAPTER 2 INDICATIONS FOR FNA CYTOLOGY AND CORE BIOPSY

Both fine needle aspiration (FNA) cytology and core biopsy have roles to play in the evaluation of breast lesions. Both have been shown to have high specificity and sensitivity when used for palpable and impalpable lesions. They are complementary, although one may be more appropriate than the other in a given clinical situation.

Both FNA cytology and core biopsy can be performed as outpatient procedures. If hormone receptor studies are needed, they can be performed on both types of specimen. Complications, other than bruising, are rare (see Chapter 4). A benign diagnosis allows surgery to be avoided in the majority of cases, while a positive diagnosis of carcinoma allows preoperative discussion with the woman regarding management options and treatment planning. Single-stage surgery may be planned in many cases, and women for whom surgery is inappropriate may have their disease diagnosed and management planned. Frozen section is avoided when malignancy is confirmed preoperatively, but may be of value when results of FNA cytology and core biopsy are inconclusive.

The decision to use either FNA cytology, core biopsy or both will be influenced by various factors, which may include the following:

- the size of the lesion
- the clinical characteristics of palpable lesions
- the characteristics of the lesion identified on imaging, eg mass, architectural distortion, asymmetric density, microcalcifications
- the likelihood of achieving a definitive diagnosis
- the woman's ability to tolerate more than one procedure
- the expertise of the clinician performing the procedure
- the preference of the managing clinician
- the availability of pathologists with experience in cytology
- the need for hormone receptor assay or tumour marker studies in inoperable tumours
- consideration of subsequent surgical management
- the need for a rapid result.

If a cytoscientist or pathologist is present at the aspiration procedure, the adequacy of the sample can be assessed immediately. If an inadequate specimen is obtained, FNA sampling may be followed by core biopsy.

ADVANTAGES AND DISADVANTAGES OF FNA CYTOLOGY

The reliability of FNA cytology depends on the skills of the aspirator, the cytopathologist and the histological type of the lesion. The age of the patient, size of the lesion and method of detection (clinically detected or image-detected) also influence reliability.

The relative advantages of FNA cytology, compared with core biopsy, include:

- the sampling procedure for FNA cytology is quicker to perform than core biopsy
- in most instances FNA cytology does not require local anaesthetic
- FNA cytology is generally less traumatic than core biopsy and may be more appropriate for women taking anticoagulant medication
- FNA cytology is associated with a low complication rate
- FNA cytology results are available relatively quickly (within a few hours in some centres); the presence of a cytopathologist may facilitate an immediate result
- relatively inexpensive to perform.

The relative disadvantages of FNA cytology, compared with core biopsy, include:

- FNA cytology requires training in the preparation of quality smears
- considerable cytology expertise is required to interpret FNA cytology
- FNA cytology is generally inappropriate for the assessment of microcalcifications
- FNA cytology does not enable the pathologist to distinguish between DCIS and invasive carcinoma
- definitive diagnosis of some lesions can be difficult to make on the basis of FNA cytology. These include atypical ductal hyperplasia (ADH), low-grade DCIS, some tubular carcinomas and some invasive lobular carcinomas

- FNA cytology may not be the sampling technique of choice for lesions that are relatively hypocellular and yield scanty epithelial material. These include sclerotic fibroadenomas, sclerosing ductal carcinoma, and infiltrating lobular carcinoma.

ADVANTAGES AND DISADVANTAGES OF CORE BIOPSY

The relative advantages of core biopsy, compared with FNA cytology, include:

- core biopsy is the investigation of choice in the evaluation of microcalcifications[22]
- core biopsy can be used when FNA cytology fails to correlate with clinical findings or imaging studies, as may occur with an inadequate cytology specimen (eg fewer than three to six epithelial groups per slide).[23] If the cytological findings do not correlate with the clinical and/or imaging findings, further investigation should be performed
- core biopsy yields tissue fragments allowing architectural features of the lesion to be identified to determine whether DCIS or invasive carcinoma is present
- core biopsy is useful in the evaluation of lesions likely to be low histological grade and in those presenting as architectural distortions, for which FNA cytology may fail or has failed to provide a diagnosis
- core biopsy may be preferred when appropriate cytological expertise is not available
- compared with FNA cytology, core biopsy may achieve higher specificity and sensitivity. Limited data suggest it may increase the probability of obtaining a satisfactory and representative sample, particularly for image-detected lesions [5,6,9]
- tissue is usually available for adjunctive tests (ER, PR and Her2).

Potential disadvantages of core biopsy include the following:

- the reliability of core biopsy depends on the skill of the operator
- false negatives may result from: (i) a 'clear miss', that is the lesion not being sampled, or (ii) artefactual distortion of the lesion and/or cores making definitive interpretation of the pathology changes on excision impossible

- it is not always possible to immediately assess the adequacy of core biopsy performed for a mass lesion or architectural distortion. In the case of microcalcifications the specimen can be radiographed to confirm whether representative microcalcifications are present
- compared with FNA cytology, core biopsy is associated with an increased risk of complications, including haematoma,[8] haemorrhage and needle tract implantation of tumour cells.[2, 24, 25] These are more likely to occur if a large number of core biopsies are performed
- core biopsy requires the use of a local anaesthetic
- the mammographic lesion may not be identified in subsequent open biopsy, due to complete removal of the lesion or in the presence of inflammation and fibrosis due to biopsy[26]
- core biopsy may interfere with the interpretation of the subsequent excision biopsy, particularly with grading and the estimation of the size of the lesion. This is particularly relevant in the case of small lesions
- core biopsy requires adequate fixation and processing, and generally requires a minimum of one working day before results can be available[footnote]
- core biopsy is generally more expensive than FNA cytology.

GUIDE TO SELECTING FNA CYTOLOGY OR CORE BIOPSY

There are no absolute rules determining whether FNA cytology or core biopsy is the more appropriate investigation. The following is a general guide only and reflects the opinion of the guide project team members.

Indications for FNA cytology

FNA cytology may be indicated in the following clinical situations:

- investigation of palpable masses, regardless of whether they are considered benign or malignant
- investigation of impalpable image-detected masses that are considered likely to be benign or with typically malignant features

Imprinting of cores, which requires cytological expertise, may provide an immediate result. However, further trials of imprinting are required before it can be recommended for routine practice. Findings from different studies are conflicting.[27, 28, 29, 30, 31] While some show the benefits of imprinting, others have found the technique to have problems, including artefactual distortion and specimen dry-out.

- investigation of suspected local recurrence of breast cancer, as suggested by the presence of palpable masses, impalpable image-detected masses, or lymph node involvement
- evaluation of cystic lesions with atypical imaging features
- confirmation of a diagnosis of breast cancer when core biopsy is not available, not possible or contraindicated.

Indications for core biopsy

Core biopsy may be indicated in the following clinical situations:

- investigation of lesions with suspicious features identified on imaging that cannot be identified on ultrasound
- further evaluation of a benign cytological pattern in the presence of a suspicious lesion on imaging
- further evaluation of a lesion for which cytology results are atypical or suspicious
- when a single surgical procedure is the desired outcome (for example wide excision and axillary dissection). It must be noted that a core biopsy showing only DCIS does not exclude the possibility of the presence of invasive carcinoma in the lesion
- evaluation of microcalcifications that are radiologically indeterminate, suspicious or typically malignant. In such cases core biopsies should be radiographed prior to histological processing to confirm adequate sampling of the lesion
- evaluation of suspicious architectural distortion at a site of previous malignancy
- evaluation of an area that has been treated with radiation.

POTENTIAL COMPLICATIONS OF FNA CYTOLOGY AND CORE BIOPSY

Displacement of the epithelium and needle tract implantation are potential complications of core biopsy and, to a lesser extent of FNA cytology.

Displacement of the epithelium

Displacement of both benign and malignant epithelium into other structures may have diagnostic or treatment implications. Displacement may occur into stroma, other ducts, skin or vascular and lymphatic spaces.

Displacement of epithelium may occur with any procedure involving a needle, including the insertion of local anaesthetic and guidewires. However, it is more common with larger gauge needles, such as those used in core biopsy. Few appropriately designed studies have evaluated the risk of an adverse event due to displacement of malignant epithelium by FNA cytology or core biopsy.

Needle tract implantation

The biological significance of needle tract implantation in the breast is not known at this time, though there is evidence from studies of other cancer types indicating that the risk of malignancy is increased in those tissues. Rosen (1997)[2] reported several cases where fragments of breast carcinoma were found in the needle tract following 14-gauge core biopsy. Rosen also reported one case of carcinoma cells in the skin of a mastectomy specimen.[2]

Summary

There are no absolute rules determining when FNA cytology or core biopsy is the more appropriate investigation. Both have been shown to have high specificity and sensitivity when used for palpable and impalpable lesions. They are complementary, although one may be more appropriate that the other in a given clinical situation.

Core biopsy can be used when FNA cytology fails to correlate with clinical findings or imaging studies. If the cytological findings do not correlate with the clinical and/or imaging findings, further investigations should be performed.

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CHAPTER 3 COMMUNICATING EFFECTIVELY WITH WOMEN UNDERGOING FNA CYTOLOGY AND CORE BIOPSY

The investigation of a breast change can be a highly stressful experience for a woman, whether she receives a benign result or a result that requires further investigation.[32, 33, 34, 35, 36] The best way to prepare a woman is to make sure she feels she has received all the information needed, and that all her questions have been answered, while showing regard for her emotional concerns.[37, 38] In addition to the communication principles outlined below, the publication *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*[38] includes detailed strategies that may be helpful for all women undergoing FNA cytology and/or core biopsy (see Appendix C).

PREPARING WOMEN FOR FNA CYTOLOGY AND CORE BIOPSY

The practice of FNA cytology or core biopsy carries the obligation to carefully explain to the woman, prior to the procedure, the roles these tests play in the management of a breast condition. It should be emphasised that:

- the test forms part of the overall assessment of the woman's breast condition, taking into account the clinical and imaging components of the triple test
- the test in itself does not necessarily give a definitive diagnosis.

When providing information, the clinician should use language that is easily understood by the woman. Medical jargon and difficult terms should be explained. The individual's language and cultural needs must be considered.

It is highly desirable that discussion involves the following information:

- the purpose of the test
- how, and by whom, the test is to be performed
- how long it will take
- whether any clinical conditions are present that may preclude the test being performed (eg comorbid medical problems, allergies, current use of anticoagulant medication)

- an assessment of the degree of pain or discomfort that is to be expected during and after the test procedure, including the need for anaesthetic
- potential complications of the test, such as bruising
- how the results will be interpreted in the context of the triple test
- limitations of the accuracy of the test; the woman should understand that the test in itself may not provide a diagnosis and that other tests may be necessary
- how the results will influence the management of the condition
- how the results will be communicated to the woman
- costs of the test to the woman.

Clearly such a discussion will depend on which test is to be used and how it is to be performed. In addition to a verbal explanation, it is useful to supply an information sheet briefly summarising the points listed above and supplemented with simple diagrams (Appendix D). Such a written document provides a useful permanent reference, as many women may not recall all the information they have been given verbally.[39] Special strategies may be needed when providing information to women from culturally and linguistically diverse backgrounds. It is advisable that a professional interpreter, either on site or via telephone, is used when providing information to women with limited English.[37, 38]

THE CONSENT PROCESS

The clinician should encourage the woman to ask questions until she is satisfied with her understanding of the information provided, before she gives consent for the procedure. Clear communication is the key to avoiding misunderstandings between the doctor and the woman. The principles of providing information to facilitate informed consent are outlined in the NHMRC's *General guidelines for medical practitioners on providing information to patients.*[37]

For consent to be valid, it must be a voluntary choice, free of coercion and given after receiving adequate and appropriate information at the individual's level of comprehension. Women from linguistically diverse backgrounds may face language difficulties and special attention should be paid to ensure that they understand consent. The woman should be asked if she requires further information or is satisfied with the information that she has received. If so, consent should be obtained to proceed with the test.

The woman has the choice as to whether the test is performed or not, and the option to withdraw consent at any stage. If she does choose to withdraw consent, the ramifications of that decision should be explained and a plan for further follow-up outlined. The entire discussion should be carefully documented. The woman needs to be provided with adequate information, and the clinician needs to ensure that the woman understands the information she receives.

In Australia, the format of consent sought, verbal or written, varies between clinicians and practice settings and according to the procedure to be performed. For both FNA cytology and core biopsy, verbal consent is typically sought; however, at BreastScreen Australia Services and in some other settings, written consent is obtained.

COMMUNICATING THE RESULTS

The woman should be informed as to how and when she will be given the results. Women report experiencing considerable anxiety while waiting for the results of assessment of a breast change,[35, 36] so results should be given as soon a possible. The managing clinician, who takes the responsibility for correlating the cytological/histological results with the clinical and imaging findings, should inform the woman of the result and its significance. It is also the responsibility of the managing clinician to inform the woman's general practitioner of the results, if agreed to by the woman.

Clinicians should ensure they have systems in place to remind them when results are due, whether they have been received and how and when they have been communicated to the woman. The provision of results indicating a malignancy should be coordinated by the managing clinician. It is highly desirable that such results be given in person and when the woman has a support person present, if she so chooses. Strategies recommended in the NHMRC's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer* [38] may also apply to women undergoing FNA cytology and/or core biopsy (Appendix C).

Summary

- When providing information, the clinician should use language that is easily understood by the woman, with consideration of her language and cultural needs.
- The woman should be encouraged to ask questions to satisfy her understanding of the information provided, before she gives consent for the procedure. Clear communication is the key to avoiding misunderstandings between the doctor and the woman.
- Clinicians should establish reminder systems tracking when FNA cytology and core biopsy results are due, whether they have been received and how/when they have been communicated to the woman.

CHAPTER 4 PERFORMING FNA CYTOLOGY AND CORE BIOPSY

WHO PERFORMS THE INVESTIGATION

Fine needle aspiration (FNA) cytology and core biopsy may be performed by radiologists, surgeons, pathologists, breast physicians, radiation and medical oncologists and, in some rural or remote areas, general practitioners. Training in needle techniques, specimen handling and preparation of cytological smears or core samples are prerequisites for performing FNA cytology and core biopsy. It is advantageous for a pathologist experienced in reporting cytology or a cytoscientist to be present when an aspirate is taken, to advise on whether adequate material has been obtained.

The clinician's patient load and experience in performing FNA cytology and core biopsy have been demonstrated to influence performance.[5, 40, 41] It is recommended that all clinicians performing these procedures regularly audit their sampling accuracy for malignant tissue and the rate of inadequate specimens submitted.

PLANNING THE PROCEDURE

Having selected FNA cytology or core biopsy as the most appropriate procedure (see Chapter 2), the operator must plan the approach and select which guidance or localisation method is to be used. In addition, the operator should ensure, in conjunction with the multidisciplinary team, that the patient's further surgical management is not compromised by the procedure.

Choosing the guidance technique

Available guidance methods are:

- clinical guidance for palpable lesions
- ultrasound and stereotactic mammographic guidance for impalpable and palpable lesions that can be visualised by the imaging technique.

For lesions that are easy to palpate, clinical guidance is the method of choice because it is quick, accurate, and cost-effective. For lesions that are difficult to palpate, imaging guidance should be used to ensure accuracy of sampling. If a

breast prosthesis is present, imaging guidance should be used to minimise the risk of prosthesis damage. Imaging guidance may also be preferred for palpable lesions, as it can reduce sampling errors and avoid complications.

Some lesions are only visible on either mammography or ultrasound. If a lesion is visible on both mammography and ultrasound, ultrasound is generally preferred to stereotactic mammographic guidance, as it is quicker and easier to use. Ultrasound guidance also allows the operator to view the sampling procedure in real time and readily sample different parts of the lesion, eg central or peripheral. Normal breast ultrasound imaging equipment is used to guide tissue sampling. Stereotactic mammographic guidance involves the use of either an upright add-on attachment affixed to a normal mammographic unit, or a dedicated prone localisation table. A digital imaging facility is an optional component of both add-on and dedicated units.

Some comparative advantages and disadvantages of the guidance techniques are summarised in Table 4.1.

Table 4.1. Comparison of guidance techniques

	Guidance techniques		
Parameters	**Clinical**	**Ultrasound**	**Stereotactic**
Speed	+++	+++	+ if not digital ++ if digital
Ease and comfort of the woman	+++	+++	+ if upright ++ if prone
Ease and comfort of the clinician performing the procedure	+++	+++	+ if upright ++ if prone
Flexibility of approach	+++	+++	++
Complication rate	+	+	+

Code: +++ high, ++ moderate, + low

Aspiration vs capillary technique for FNA cytology

Most operators use a suction or aspiration technique for FNA cytology, using a syringe alone or with a syringe holder. Extension tubing may also be used. The use of suction has been shown to reduce the rate of inadequate/non-diagnostic sampling from benign lesions.[42] The aspirator may choose to convert from a non-

aspiration technique if the lesion yields limited cellular material or if the lesion feels fibrous.

Some operators prefer a non-suction or capillary technique, which has the advantages of enhancing fingertip sensitivity and needle control and reducing the risk of blood contamination. Conversion to an aspiration technique is recommended if the lesion is fibrous or yields limited cellular material.

Preparation of equipment

A list of required equipment for each sampling method and guidance technique appears in Appendix F.

TAKING THE TISSUE SAMPLE

Sampling techniques

A description of how to perform the following procedures appears in Appendix G:

FNA cytology:

- clinically guided
- ultrasound-guided
- sterotactically guided.

Core biopsy:

- clinically guided
- ultrasound-guided
- sterotactically guided.

Post sampling checklist

At the end of the FNA cytology or core biopsy procedure, it is important the operator checks that the following steps have been complete:

- all specimens, including slides and specimen jars, are clearly labelled (see Chapter 5)
- the request form is completed, including the patient's details, clinical and imaging information, history of hormone replacement therapy or pregnancy, the provisional diagnosis, and the adequacy of sampling, if known. A checklist of items recommended for inclusion in the request form appears in Chapter 5

- a copy of the specimen radiograph (if taken) accompanies the request
- the woman is properly informed of the possible complications of the procedure, how to recognise them, and strategies to minimise or avoid them
- the woman is aware of the arrangements for receiving the results of the procedure.

Specimen handling

Techniques of slide preparation, fixing and handling of specimens are detailed in Chapter 5.

COMPLICATIONS OF FNA CYTOLOGY AND CORE BIOPSY

Both fine needle aspiration cytology and core biopsy are associated with low rates of complications. The complications and strategies to minimise or avoid their occurrence are outlined in Table 4.2.

Table 4.2 Complications of FNA cytology and core biopsy and strategies to minimise or avoid them

Complication	Comment	Strategies to minimise or avoid complications
Pain	Discomfort is common but pain is typically minimal	Can be minimised by: fully explaining the procedure; using local anaesthesia as required with FNA cytology, and routinely with core biopsy; and (in some cases) using analgesic and anxiolytic medication
Bruising	Minimal bruising is common	Bruising may be difficult to avoid entirely, especially in older women.

Haematoma	Uncommon; likelihood increased by the use of anticoagulants, including aspirin	Both can be minimised by compressing the biopsy site both in between sampling and at the completion of the procedure. When large core biopsies are performed or the lesion is thought to be vascular, then it is recommended local anaesthesia be used with a vasoconstrictor
Infection	Rare	Can be avoided by careful skin cleansing and by use of sterile disposable items and equipment
Fainting	Uncommon May present special difficulty when using upright stereotactic systems	Can be minimised by treating anxiety, fully explaining the procedure, providing analgesia or anaesthesia where appropriate, and performing the procedure with the patient lying down
Pneumothorax	A rare complication, but the most serious one. The risk is increased in very thin women or if the lesion is close to the chest wall, in the upper inner quadrant or high in the axilla	Can be avoided by taking care not to angle the sampling needle towards the chest wall, but rather parallel to it. Pneumothorax can be minimised by monitoring the needle position with imaging

Summary

- When sampling a palpable lesion, clinical guidance is the method of choice as it is quick, accurate and cost-effective. Imaging guidance may also be used for any palpable lesion, as it can reduce sampling errors and avoid complications.
- Clinicians performing FNA cytology or core biopsy should be aware of potential complications, and routinely implement strategies to minimise or avoid them.

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CHAPTER 5 THE SPECIMEN: REQUEST, PREPARATION AND PROCESSING

Accurate interpretation of fine needle aspiration (FNA) cytology and core biopsy specimens depends on correct specimen preparation as well as the availability of adequate clinical and radiological information.

THE REQUEST FORM

It is recommended that a standardised request form be used if possible for all FNA cytology and core biopsy specimens. An example is included in Appendix E.

The request form for FNA cytology and core biopsy should include the following information:

- patient's name, date of birth, unit number or medical record number, if available
- name and address of the managing clinician/s
- name and address of requesting clinician
- name of the clinician who performed the procedure
- side of lesion
- site of lesion and distance from nipple, eg 'right upper outer quadrant at 11 o'clock, 60 mm from nipple'. Distance from nipple is particularly important when more that one lesion is present
- clinical features of lesion such as size, shape and texture
- imaging findings, regardless of whether the lesion is palpable or impalpable
- in the case of core biopsy for calcifications, a copy of the specimen radiograph should accompany the request form
- an indication as to the likely diagnosis. This can be either a judgement as to whether the lesion is expected to be benign or malignant, or a description of a specific lesion (eg fibroadenoma)
- relevant clinical history, including:
    - any previous history of breast cancer, melanoma or other malignancy
    - treatment for prior breast disease, eg radiotherapy, chemotherapy
    - history of hormone replacement therapy, pregnancy or lactation

- request for oestrogen receptor (ER)/progesterone receptor (PR)/assay if appropriate, eg for a woman with advanced breast cancer.

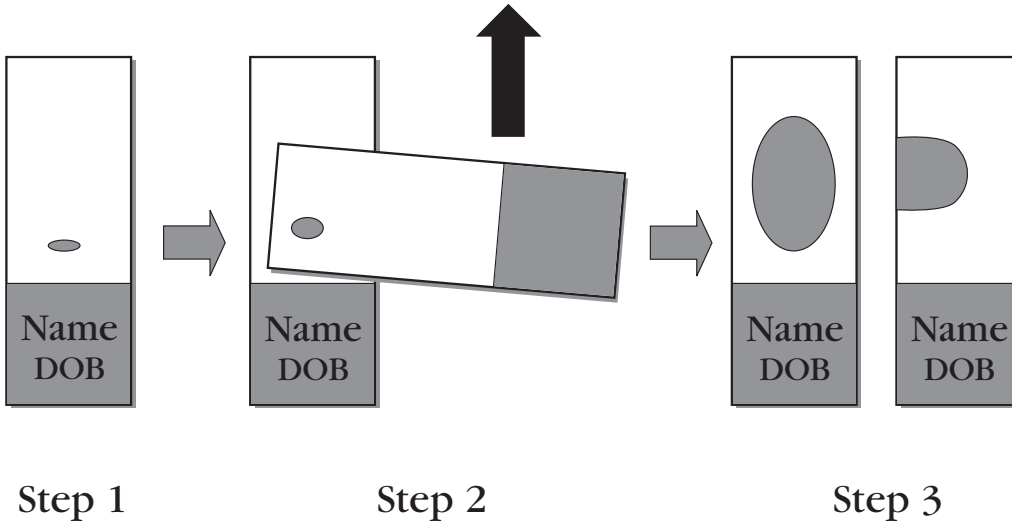
PREPARATION AND PROCESSING OF FNA CYTOLOGY SPECIMENS

The principal aims for FNA cytology slide preparation is to make a thin smear that is not subject to crush artefact, and to allow rapid air-drying of air-dried slides and rapid fixation of wet-fixed slides.

One commonly used method of preparing slides is as follows:

Expel a drop of the aspirated fluid onto two of the pre-labelled glass slides. If all the material is expelled onto one slide, it can be split simply by touching the second slide to the surface and separating them again. The material can be spread in several ways. The quickest (and probably easiest) method is illustrated in Figure 1.

Figure 1. A method for preparing slides for FNA cytology



Note: No excessive downward pressure or surface squash should be used as this will distort the cells and may render the slides uninterpretable.

For other methods, either ask the pathologist or refer to the references provided.

If slides are prepared by non-laboratory staff, the clinician obtaining the specimen should ask the pathologist to indicate their preferred method of preparation.

The following items should be available and prepared before the procedure:

- frosted ended slides labelled with the patient's name and date of birth. The use of two identifiers is recommended, especially if more than one woman is to have an aspirate at the same clinic
- fixative solutions
- a rapid Romanovsky stain, such as DiffQuik®, if the material is to be assessed for adequacy at the time of the aspirate. Any wet-fixed slides can be stained later in the laboratory
- a balanced salt solution in which the needle can be rinsed
- slide trays or plastic slide carriers for transport.

Fixation and staining of slides for FNA cytology

Practice varies according to the preferences of pathology laboratories. For example, the pathology laboratory may specify air-dried or wet-fixed smears or a combination of both.

The use of spray fixatives for wet-fixed smears is generally not acceptable, as fixation may be uneven, particularly in thick areas. If held too close, the material may be dispersed across the slide. If spray fixatives are used the laboratory should be informed, as the use of spray fixatives also necessitates an additional process to remove Carbowax because the persistent presence of Carbowax interferes with the Papanicolaou stain.[43, 44]

It is important that both wet-fixed and air-dried slides are fixed quickly to avoid artefact.

In cases in which the specimen is bloody and/or higher volume, part of the syringe contents should be expelled onto a slide and slides smeared as noted above. The bloody or fluid specimens are best dried more rapidly. The best method to achieve this is to use a standard hair dryer on a low heat setting. The remainder of the specimen may be expelled into a sterile container and submitted – rapidly – to the pathologist or pathology laboratory for further processing.

Consultation with the pathology laboratory regarding their preferred method of preparation is essential for anyone performing FNA cytology.

The following description of procedures for slide fixation and staining is a commonly used one and is provided as an example. It is important that the laboratory that will be doing the processing is consulted to identify its preferred method of preparation.

Fixation of slides for FNA cytology

Slides may be fixed as follows:

1. Wet-fixed slides: Immediate placement into a Coplin jar containing either 95% ethanol or Carnoy's solution. (If Carnoy's or modified Carnoy's solution is used, then the slides should be transferred to 95% ethanol after five minutes, to avoid excessive cell shrinkage).

2. Air-dried slides: Rapid air-drying either by gently waving the slide in the air or by using a hair drier on a cold or low heat setting. Blowing from the mouth should not be used to air-dry slides. It is important to ensure the slide is dry before it is fixed. The slide can then either be placed in methanol for at least 30 seconds, or transported to the laboratory where it can be fixed at a later stage.

Staining of slides for FNA cytology

A rapid Romanovsky stain, such as DiffQuik®, can be used if the material is to be assessed for adequacy at the time of the aspirate. Any wet-fixed slides can be stained later in the laboratory.

One method of staining slides is as follows:

1. Air-dried slides can be stained at the time of the procedure using a rapid Romanovsky-type stain. If using DiffQuik®, after fixation in methanol the slide is dipped in Solution I and then into Solution II. The number of dips is roughly 10 and 14 respectively but will vary according to personal preference and the duration of the dips.

2. After rinsing in water, the slide can be viewed under the microscope and assessed for adequacy.

3. Wet-fixed slides are stained with a Papanicolaou stain.

Processing needle-rinse material from FNA

After the slides have been made, material remaining in the needle and syringe may be utilised for further studies such as ER and PR assays. Needle contents may be extracted by rinsing with a balanced salt solution, and used in cytospin or cell block preparations. If a cell block is required, a separate pass can be placed into the solution.

Processing cyst fluids obtained via FNA

Although it is not standard practice to submit cyst fluid from cysts for cytological evaluation, cyst fluid should be sent for cytological evaluation if any of the following apply:

- it is bloody or serosanguinous
- there is a residual palpable mass or solid lesion on ultrasound[45]
- imaging studies indicate that the cyst is complex.

Further information regarding the management of breast cysts is available in *The investigation of a new breast symptom: a guide for general practitioners.*[45]

PROCESSING OF CORE BIOPSY SPECIMENS

Core biopsy of mass lesion

Three to four hours fixation in 10% buffered formalin is usually appropriate for core biopsies before they are routinely processed. However, practices may vary between laboratories.

It is common practice to stain a minimum of three to six levels of section at approximately 50-m intervals. However, further levels may be required.

Core biopsy of microcalcifications

When performing a core biopsy for microcalcifications, the specimen should be radiographed.

Both the specimen radiograph and specimen should be sent to the pathology laboratory with a report confirming the presence of microcalcification/s within the cores of tissue.

Microcalcifications identified histologically should be matched with those detected radiologically. If calcifications are not identified after six levels of

section, further levels through the block should be performed until the calcifications are found. Occasionally calcifications fall out of the biopsy before or during processing and cannot be located. There may be a need to cut deeper levels, X-ray blocks, etc to find the microcalcification/s that correspond to those seen on the radiograph. However, very small microcalcifications (<100–m) may be seen in the histological sections, but may be too small to be resolved radiologically.[46] It is important to match the histological and radiological microcalcifications with those shown radiologically to be of concern. Note that the sections should be polarised, especially if there are cysts, as calcium oxalate crystals (which are birefringent) are not basophilic and may be obscured by debris. Most microcalcifications consist of calcium phosphates and are basophilic.

Fixation and processing of core biopsy specimens containing microcalcifications is described below.

Fixation and processing specimens with microcalcification

The following steps are recommended when fixing and processing core biopsy specimens from microcalcification/s:

1. Fixation in 10% buffered formalin for 3–4 hours is usually adequate.

2. Tissue is routinely processed. While practices vary, more common practices include the following:

- cutting approximately 10 serial ribbons and staining several ribbons at regular intervals, for example, 1, 5 and 10, **or**
- staining at least three levels with haematoxylin and eosin (H&E).

Summary

- Consultation with the pathology laboratory regarding its preferred method of preparation is essential for anyone performing FNA cytology. The pathology laboratory may specify air-dried smears, wet-fixed smears, or a combination of both.
- A specimen radiograph should accompany core biopsy specimens for microcalcifications, together with a comment from the radiologist regarding the presence or absence of calcifications.
- If ER and PR studies are requested from FNA cytology, a cell block containing adequate cellular material is required. ER and PR studies can be performed on smears only in laboratories experienced with this technique.

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CHAPTER 6 PATHOLOGY REPORTING

WHO SHOULD REPORT ON FNA CYTOLOGY OR CORE BIOPSY?

It is recommended that FNA cytology or core biopsies are reported by cytopathologists or pathologists who are experienced and regularly involved in reporting on these types of specimens.[47] Reporting accuracy for both FNA cytology and core biopsy is enhanced if the reporting pathologist has knowledge of the relevant clinical and imaging findings, including past and present treatment. Such an understanding is facilitated by good communication within the multidisciplinary team.

FNA cytology

No evidence is currently available on the number of aspirate examinations and reports per month or year sufficient to maintain an individual's skills. It is suggested that an inexperienced pathologist initially reports with an experienced pathologist until an acceptable concordance is reached.

The performance of the cytopathologist should be monitored against associated clinical, imaging and surgical findings.[48] Participation in internal and external quality assurance (QA)/review and audit processes is recommended (see Chapter 8).

Core biopsy

Core biopsy pathology must be correlated with the clinical and imaging findings, and the results later reviewed in conjunction with associated surgical pathology or clinical and imaging findings. Participation in internal and external QA/review and audit processes is recommended (see Chapter 8).

COMPONENTS OF THE REPORT

FNA cytology and core biopsy reports should include the following components.

Patient and clinical details

- clinical notes and imaging findings, transcribed from the request form (see Chapter 5).

Specimen and technical details

- the date and time of specimen collection and its receipt at the pathology laboratory
- a brief description of the material received, including:
    - the number of FNA cytology slides, including the number of air-dried and wet-fixed slides, and the volume and description of fluid received, if any
    - the number of core biopsies or tissue fragments
    - the presence or absence of microcalcification in the specimen radiograph of core biopsies taken from the site of image-detected microcalcification
- stains used, including any special procedures.

Microscopic report

Microscopic report for FNA cytology:

- a statement indicating the adequacy of the specimen for cytological assessment
    - various criteria to define an adequate sample have been proposed, eg samples have been defined as adequate when there are at least three to six epithelial groups per slide.[23] The adequacy will depend on the type of lesion, eg no ductal cells are expected from a lipoma. The cytological findings should correlate with the clinical and imaging findings
    - if the sample is unsatisfactory for cytological assessment, the report should explain why – eg scant cellularity, drying artefact, epithelial cells obscured by blood or inflammatory cells
- a description of cell types present, noting the presence of malignant, atypical or benign cells, and significant background cells
- indication of whether there are any diagnostic features consistent with a specific diagnosis, eg fibroadenoma or malignant background features, such as mucin or necrosis.

Microscopic report for core biopsy:

- a brief microscopic description of the tissue received
- description of any abnormal findings, both benign and malignant

- indication of the presence or absence of microcalcifications of sufficient size to be radiologically detected and their correlation with the specimen radiograph. Calcifications of > 100-μ assessed histologically are not visible on core biopsy specimen radiographs and may not represent the mammographically detected calcification[46]
- findings should be correlated with the clinical and imaging findings. Note that lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH) are incidental findings and are not usually detected on imaging.

Diagnostic category

Communication within the multidisciplinary team is enhanced by the use of standardised diagnostic categories. A diagnostic category is selected from the following five standard options when reporting either FNA cytology or core biopsy samples:

Diagnostic category#	**Corresponding numerical code***
• Inadequate/insufficent^	1
• Benign	2
• Atypical/indeterminate	3
• Suspicious of malignancy	4
• Malignant	5

The diagnostic category represents the interpretation of the findings on the slides for that case, but may or may not be representative of the underlying target lesion. This depends on sampling. The diagnostic category may be qualified with further comments as considered appropriate by the reporting pathologist.

* The numerical code should not be used without a diagnostic category (see *Standardised Reporting* p. 44).

^ The numerical code of 'one' corresponds to the diagnostic category inadequate/insufficient.

Some pathologists recommend this category be termed 'non-diagnostic' or 'non-representative', and there may be cogent reasons for doing so. An aspirate may be non-diagnostic for reasons other than inadequate or insufficient material.

Predictive/prognostic markers

- Indication of whether predictive/prognostic markers such as ER and PR assays have been performed, and the results.

A description of each diagnostic category for FNA cytology and core biopsy follows. For all categories, it is important that there is adequate material on which to base a diagnosis and that it is representative of the lesion of interest.

REPORTING CATEGORIES FOR FNA CYTOLOGY

The following categories apply to FNA cytology:

Inadequate/insufficient (corresponding numerical code = 1)

This category is used when the smears are too sparsely cellular or distorted to allow a microscopic diagnosis, or the aspirate is inconsistent with the clinical and imaging findings. Since this is a subjective diagnosis, an explanation of why the sample is inadequate/insufficient should be given.

Artefacts – such as crushing, excessive thickness, blood, or problems from fixation and processing – may make a smear uninterpretable and therefore inadequate for diagnostic purposes.

A specimen is satisfactory/sufficient if the lesion is properly sampled, the cytology findings are consistent with the clinical and imaging findings, and the smears can be interpreted. Special circumstances in which this may be the case include:

- an acellular or sparsely cellular sample may be representative if it is from a scar
- a lipoma or fatty lesion yields plentiful fat but no epithelial cells.

If a specimen is considered to be non-representative and does not correlate with the clinical or imaging findings, repeat FNA or core biopsy is recommended.

Benign (corresponding numerical code = 2)

This diagnostic category is used when the sample is adequate and shows no evidence of malignancy.

Specific features diagnostic of fibroadenoma, fat necrosis, simple cyst, etc may be present. However, a specific diagnosis may not always be possible.

Whenever a discrepancy between the triple test components occurs, further investigation is mandatory.

Atypical/indeterminate (corresponding numerical code = 3)

The most common circumstances in which this category is considered appropriate involves smears with benign features but also showing features which may be seen with malignancy, such as loss of cohesion or nuclear atypia. Another possible circumstance include a lesion in which the cellularity is low with subtle cytologic atypia.

Aspirates showing papillary features or having mucin may also be placed in this category, depending on the circumstances.

Suspicious of malignancy (corresponding numerical code = 4)

This diagnostic category is used when the smears show features suggestive of, but not diagnostic of, malignancy. The malignant cells may be too scanty, obscured by artefact, or show atypical features more marked than in the atypical or indeterminate category, but not diagnostic of malignancy.

Malignant (corresponding numerical code = 5)

This diagnostic category is used when the aspirate is clearly malignant. This diagnostic category includes invasive breast carcinoma, DCIS, and other malignancies. While invasive breast carcinoma and DCIS cannot be reliably distinguished, cytological correlation with clinical and imaging findings is helpful in diagnosing a predominantly invasive or DCIS component.

The type of malignancy (carcinoma, sarcoma, and lymphoma) and any specific features (eg malignant squames or mucin) should be noted.

The nuclear grade of carcinomas may be commented upon. In addition, if available and specifically requested, predictive/prognostic markers (including ER and PR) may be performed in special circumstances.

REPORTING CATEGORIES FOR CORE BIOPSY

Core biopsies are usually reported according to the specific diagnosis for the type of lesion sampled (fibroadenoma, atypical ductal hyperplasia, ductal carcinoma in situ, invasive ductal carcinoma).

Although not routinely recommended, the use of diagnostic categories in certain circumstances might be appropriate, particularly in cases where a specific diagnosis cannot be rendered for whatever reason. This would be considered to be a rare occurrence. Circumstances in which this may occur are:

Inadequate/insufficient

This diagnostic category is used when the epithelium present is too distorted or its volume is too scanty for diagnosis, or when the specimen does not correlate with the imaging or clinical findings (eg no calcification seen in a lesion for which microcalcification was reported at imaging, or only non-specific benign tissue present for a lesion described as suspicious on imaging). There is no consensus definition of specimen adequacy.

Since this is a subjective diagnosis, it should be accompanied by an explanation of why the sample is inadequate/insufficient. Further investigation or follow-up is recommended.

Benign

This diagnostic category is used when a specific benign diagnosis, for example fibroadenoma or papilloma, cannot be made. Any specific benign diagnosis should be recorded together with the imaging correlation. Follow-up recommendations, if relevant, should be included.

Atypical/indeterminate

This diagnostic category is used for:

- atypical intraductal proliferative processes, including atypical ductal hyperplasia
- atypical changes in papillomas
- architectural and cytological changes in sclerosing lesions and microglandular adenosis where it is not possible to absolutely exclude invasive carcinoma
- worrying findings about which it is not possible to make a specific diagnosis in the tissue received.

Following an atypical/indeterminate diagnosis, further investigation – usually by excision biopsy – should be recommended.

Suspicious of malignancy

This diagnostic category is used when there are changes suspicious of DCIS or invasive breast carcinoma. However, these changes are insufficiently well seen for a specific diagnosis because the lesion present is too scanty or obscured by artefactual changes.

Malignant

This diagnostic category is used for DCIS, invasive breast carcinoma and other malignancies. There may be circumstances in which the ACN Guidelines for the Reporting of Breast Carcinoma[13] might be appropriate in biopsy specimens. However, because of significant discordance between biopsy and excision specimens, this is not routinely recommended.

Subsequent correlation with the pathology of the excisional biopsy should be made in the biopsy report of the latter.

Specific considerations for the reporting of DCIS, invasive breast carcinoma and other malignancies are described below.

FURTHER CONSIDERATIONS FOR REPORTING MALIGNANCIES IDENTIFIED ON CORE BIOPSY

Ductal carcinoma in situ

Nuclear grade, the presence or absence of necrosis, type/architecture and the site and type of microcalcification should be reported according to ACN recommendations:[13]

Where possible, nuclear grade should be reported as low, intermediate or high, based on the criteria advocated by Elston and Ellis for grading invasive carcinoma.[49, 50] It may not be possible to grade very small tumours accurately. If this is the case it should be noted in the report.

Invasive breast carcinoma

- Tumour type should be reported where possible. If this is not possible based on the sample received, features present should be described
- While the volume of cancer will often be too small for accurate grading, the nuclear grade, presence or absence of tubule formation and the frequency of mitosis can predict a high- or low-grade carcinoma, and should be noted. The Elston and Ellis criteria should be used[50]

- Vessel invasion, that is the presence of nests of tumour cells in endothelial-lined spaces, should be assessed and reported
- The presence of necrosis and microcalcification should be recorded
- The presence of any DCIS, ADH, ALH or LCIS in the cores should be noted
- For small tumours, if the core biopsy measurement is the only measurement then the maximum length of tumour can be estimated from the core specimen
- Immunohistochemistry for ER/PR may be required if pre-surgical treatment is to be given or selection for trial participation is being made
- Depending on the institutional policy, need, cost and availability, other prognostic/proliferative markers may be performed.

Other malignancies

- Melanoma is one of the most common neoplasms to metastasise to the breast, and may be seen within breast tissue or an intramammary lymph node
- Metastatic tumours are occasionally present as the first evidence of an occult primary source, usually from a primary lung tumour or melanoma
- While less than 0.5% of all malignant lymphomas involve the breast, these may result in a palpable or imaging-detected lesion. It is important that benign, sometimes reactive, intramammary lymph nodes are not interpreted as lymphoma (flow cytometry may be required to confirm or help exclude lymphoma)
- The incidence of sarcoma is small compared with primary breast cancer. Angiosarcoma is the most common form of breast sarcoma. Metaplastic carcinoma may be interpreted as sarcoma.

STANDARDISED REPORTING FOR FNA CYTOLOGY AND CORE BIOPSY

It is essential that the report for FNA cytology or core biopsy is brief, easy to understand, and contains sufficient specific details to facilitate decisions about subsequent treatment. The report must also facilitate the ongoing collection and evaluation of performance data. Standardised reporting helps to achieve this.

The information to be included in standardised reports for FNA cytology and core biopsy is outlined in Appendix H.

Numerical coding should not substitute the reporting categories, and should not be included in the main body of the report. However, because of the usefulness of numerical coding for statistical purposes, the numerical coding that corresponds to the category in the report could be included as an adjunct:

Diagnostic category	Corresponding numerical code
• Inadequate/insufficent	1
• Benign	2
• Atypical/indeterminate	3
• Suspicious of malignancy	4
• Malignant	5

PITFALLS OF FNA CYTOLOGY AND CORE BIOPSY

Potential false positive and false negative diagnoses for FNA cytology and core biopsy are outlined in Chapters 7 and 8.

Summary

- Reporting accuracy for both procedures is enhanced if the reporting cytopathologist/pathologist has knowledge of the relevant clinical and imaging findings, including past and present treatment. This is facilitated by good communication within the multidisciplinary team.
- Diagnostic pitfalls are reduced if:
  - the reporting pathologist has knowledge of the relevant clinical and imaging findings and clinical history, including past and present treatment. This is facilitated by good communication with the multidisciplinary team
  - reporting pathologists are experienced and their performance is monitored and peer reviewed
  - sampling is both accurate and adequate.

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CHAPTER 7 COMMON PITFALLS IN THE INTERPRETATION OF FNA CYTOLOGY

It is important that all members of the multidisciplinary team are aware of the common pitfalls in the interpretation of FNA cytology of the breast. This chapter is not meant to be an aid to diagnosis, but rather to provide an understanding of the reasons for false negative and false positive diagnoses and ensuring that appropriate additional investigations are undertaken.

This chapter is primarily addressed to clinicians recommending patient management on receipt of a FNA cytology report, and is intended to assist them in the interpretation of pathology reports by highlighting the most common pitfalls. It is also particularly relevant to those who principally perform FNA cytology – ie radiologists, breast physicians and surgeons with experience in radiological interpretation. It will also assist pathologists by providing a reminder of the conditions that require special care at reporting.

FALSE POSITIVE DIAGNOSES IN FNA CYTOLOGY

False positive diagnoses in FNA cytology occur at a rate of less than 1%, and are frequently due to difficulties with interpretation. The most commonly encountered pitfalls are listed below (the list is not all-inclusive).

Conditions associated with false positive diagnoses include:

- **Fibroadenoma with atypical features.** This is the lesion most commonly mistaken for cancer, especially when there is sub-optimal cell preservation, as the epithelial cells may be large and dissociated.[51] However the presence of bare bipolar nuclei should prevent a diagnosis of malignancy.
- **Mass or thickening associated with lactation.** A clinical history is most important to prevent a false positive cytological diagnosis. During pregnancy, lactation, or post lactation, most of the cells are acinar and dispersed with prominent nucleoli. However, the presence of abundant cytoplasm, vacuolation and a lipo-proteinaceous background should prevent misdiagnosis, especially when used in conjunction with the triple test.

- **Radial scar with hyperplasia.** Ductal hyperplasia is usually an incidental histological finding, but when associated with radiological findings suggestive of malignancy (eg a radial scar), differentiation from a well differentiated carcinoma can be difficult. Bare bipolar nuclei are usually a feature. It is important that a definite diagnosis of malignancy is not made if bare bipolar nuclei are present with the atypical cells.
- **Papilloma.** It is not possible to reliably distinguish between papilloma, atypical papilloma,[5] intracystic papillary carcinoma and invasive papillary carcinoma on cytological material alone. Core biopsy may provide a definitive diagnosis in some papillary lesions. The clinical and imaging findings may also overlap. Excision biopsy is recommended following a diagnosis of a papillary lesion on FNA cytology.
- **Radiation changes.** The more widespread use of breast conserving surgery has resulted in an increased use of breast irradiation. Radiation-induced epithelial atypia is common in benign breast tissue after treatment. A diagnosis of malignancy should be made only if all cytological criteria are met. Similar problems may arise following chemotherapy.[5]
- **Fat necrosis.** Mesenchymal cells or histocytes may resemble abnormal epithelial cells but the presence of inflammatory cells, foamy macrophages and multinucleated histiocytic giant cells should avoid a false positive diagnosis. This is one lesion for which the result of the triple test may be misleading, as fat necrosis is a lesion that can mimic carcinoma both clinically and on imaging.[5]
- **Atypical apocrine cells.** Apocrine carcinoma is rare, whereas apocrine cells in fibrocystic change are common. The differential diagnosis between apocrine metaplasia and apocrine carcinoma can occasionally be difficult.
- **Gynecomastia.** The cellularity of the smears is highly variable, and epithelial atypia is common. Bare bipolar nuclei are present and a diagnosis of malignancy should not be made unless all the cytological criteria are met.
- **Phyllodes tumour.** This is a stromal neoplasm with a biphasic pattern. In some cases, the associated epithelial hyperplasia may result in a false positive diagnosis. Again, the presence of bare bipolar nuclei and assessment of the stromal fragments should prevent a malignant diagnosis.[5]

- **Adenomyoepithelioma.** This is a rare tumour, for which large atypical epithelioid cells and spindled cells are common features. Bare bipolar nuclei are usually numerous and should prevent a definitive diagnosis of malignancy.
- **Tubular adenoma.** This is much less common than fibroadenoma but is cellular and shows marked dispersal, microacini and prominent nucleoli. Bare bipolar nuceli are present.
- **Granular cell tumour.** This is a rare soft tissue tumour which can occur in the breast. Dispersed cells with granular cytoplasm, combined with suspicious radiological features, make this lesion a pitfall. However, the granular cells do not show malignant criteria.

Maintaining strict cytological criteria for malignancy will assist in keeping false positive diagnoses to a minimum.

FALSE NEGATIVE DIAGNOSES IN FNA CYTOLOGY

False negative diagnoses in FNA cytology are more common than false positive diagnoses, and have been reported to be between 3% and 24%.[52, 23] Sampling error is the most common reason for a false negative diagnosis. FNA cytology is highly dependent on the skill and experience of the aspirator.[5] A false negative result can also be due to interpretation error. The most commonly encountered pitfalls are listed below (the list is not all-inclusive).

Situations and conditions associated with false diagnoses in FNA cytology include:

- Some lesions may be more difficult to sample. Examples of situations that may result in sampling difficulty include:
    - small malignant lesions are a special problem, particularly those that are well differentiated and sclerotic, as the cell yield is low and cells may be difficult to distinguish from benign cells. This may result in a false negative diagnosis
    - for mass lesions that are difficult to feel, such as those deep in the breast, ultrasound guided FNA cytology may be useful
    - if the lesion is close to the chest wall, it may be difficult to obtain sufficient cells. Ultrasound guidance may increase the yield.
- Well-differentiated grade 1 carcinomas may be difficult to diagnose, as the cell yield may be poor or there may be only mild cellular atypia

- Infarcted papilloma. Infarction causes cell dispersal. Recognition of degenerate columnar forms should prevent a diagnosis of malignancies
- Invasive lobular carcinomas may yield few cells, which are often difficult to distinguish from benign cells.[11] They are often mixed with benign ductal elements
- Low-grade DCIS, some tubular carcinoma and cribriform carcinoma may yield deceptively 'benign' aspirates
- Inflammatory carcinomas by definition show involvement of the dermal lymphatics by carcinoma. An adequate sample can be difficult to obtain and ultrasound guidance is advised if no definite mass is palpable
- Necrosis may be present in the centre of a high-grade carcinoma. It is important to sample the edge of such a lesion, either by increasing the amplitude of the needle passes to achieve passage of the needle through the lesion, and/or by specifically aiming for the edge of the lesion as palpated or with image guidance. The use of a needle without aspiration may also be useful
- Sclerosis is a potential cause of a low cell yield
- Papillary carcinomas may yield numerous cells, but differential diagnosis of most papillary lesions requires excision and examination of the whole lesion and capsule
- Mucinous tumours are often well differentiated and the cell yield may be poor. The presence of mucin raises the possibility of a mucinous tumour.[6]

Application of the triple test should reduce the incidence of missed cancers when there is a false negative cytology result.

TECHNIQUES FOR REDUCING FALSE POSITIVE AND FALSE NEGATIVE RESULTS IN FNA CYTOLOGY

To reduce false positive and false negative results in FNA cytology, it is recommended that:

- a multidisciplinary approach with appreciation of the importance of the clinical and imaging findings (triple test) is adopted
- imaging is used to sample lesions difficult to localise or palpate
- there is adequate training of operators

- a minimum of three passes is considered standard practice. The presence of a pathologist or cytoscientist at the procedure is helpful to assess adequacy of the specimen, otherwise multiple passes are required. If the specimen is still inadequate, core biopsy should be performed
- slides are well spread, well prepared and well fixed
- there is adequate training of cytopathologists in cytology as well as histology
- services and individuals participate in quality assurance programs.

Summary

- FNA cytology is highly dependent on the skill and experience of the aspirator.
- False positive diagnoses are rare, and most are due to difficulties in lesion interpretation.
- False negative diagnoses are uncommon. In the Breast Screen setting, the accreditation standard is a false negative rate of less than 6%[12]. It is recommended that, for all pathology services, attempts are made to monitor the false negative rate. Causes include sampling errors and errors of interpretation usually involving types of pathology known to be difficult (eg invasive lobular carcinoma).
- The risk of false positive and false negative results in FNA cytology may be minimised by the adoption of a multidisciplinary approach in both specimen sampling and the interpretation of results, ensuring adequate training and experience of staff involved at all stages of the process, a policy of routinely correlating cytology findings with clinical and imaging findings, consistent collection of follow-up data, and participation of services and individuals in QA programs.

CHAPTER 8 COMMON PITFALLS IN THE INTERPRETATION OF CORE BIOPSY

As with FNA cytology, pitfalls in the interpretation of core biopsy are reduced when the pathologist works within a multidisciplinary team and has knowledge of the relevant clinical and imaging findings and clinical history, including past and present treatment. This chapter primarily addresses clinicians who are required to recommend patient management on receipt of a core biopsy report, and is intended to assist them in the interpretation of pathology reports by highlighting the most common pitfalls. As with FNA cytology, it is also relevant to those clinicians who perform core biopsy and to pathologists by providing a reminder of the conditions that require special care at reporting.

A commitment to obtaining and assessing follow-up data is necessary to improve patient care and to understand and evaluate diagnostic pitfalls, in particular false negative diagnoses.

FALSE POSITIVE DIAGNOSES IN CORE BIOPSY

The rate of false positive diagnoses on core biopsy are rare (less than 1%)[20] Difficulties in interpretation that may result in over-diagnosis include:

- ADH may be interpreted as low-grade DCIS.[20] Conversely, DCIS (with or without invasive carcinoma) is found in approximately 50% of the lesions diagnosed on core biopsy as ADH. Excision biopsy is therefore recommended when ADH is diagnosed[53, 54]
- LCIS, which is usually an incidental finding, may be interpreted as DCIS of solid type
- Florid epithelial hyperplasia may be interpreted as DCIS
- Duct ectasia/stasis with inflammation may be interpreted as comedo necrosis in DCIS. Both lesions can be associated with microcalcification.

The proliferative components of complex sclerosing lesions or radial scars may be interpreted as tubular carcinoma in core biopsies. Epithelial hyperplasia, sometimes with focal necrosis or LCIS, can be interpreted as DCIS or invasive carcinoma. Radial scars may be associated with atypia, tubular carcinoma, infiltrating lobular and infiltrating ductal carcinomas, and DCIS.[55] Whilst it has been accepted that these lesions require complete excision,[56, 57, 58, 59, 60] there is some evidence to suggest that radial scars diagnosed on core biopsy (especially

large bore core biopsies) can be managed conservatively. A recent well controlled prospective Australian study has shown that a radial scar can be more accurately diagnosed by core biopsy when performed under specific conditions. These conditions involve the taking of cores centrally and across the dimensions of the lesion with the most accurate results obtained when a mean of 5 cores were taken.[61] In addition a large core biopsy (ABBI / Site select) which completely excises the lesion may not require further excision. The incidence of ADH, DCIS and invasive carcinoma increases with the size of the radial scar and the age of the patient.[57, 62]

- Adenosis:
    - microglandular adenosis may mimic tubular carcinoma and is a risk factor for carcinoma. The use of immunohistochemistry aids diagnosis
    - florid adenosis and sclerosing adenosis with epithelial or myoepithelial hyperplasia may mimic DCIS or invasive carcinoma
    - DCIS and LCIS may arise in, or be involved in, sclerosing adenosis. The use of immunohistochemistry is helpful in this situation
    - excision is recommended if there is microglandular adenosis or atypical epithelial hyperplasia.
- Extrusion of mucin into stroma from a ruptured benign mucinous cystic lesion or minor papillary elements attached to fragments of the cyst wall may be interpreted as mucinous carcinoma. Detached epithelial cells should be seen amongst the mucin to diagnose carcinoma
- Atypical apocrine lesions.

FALSE NEGATIVE DIAGNOSES IN CORE BIOPSY

False negative diagnoses are uncommon.[63] Reported false negative rates range from less than 1% to 2%.[20, 64]

More common are benign diagnoses not concordant with the imaging findings; that is, the core biopsy is not representative of the imaging appearance. Missed cancers are greatly reduced when a repeat biopsy/excision is performed if the tissue is considered unrepresentative after imaging review.[65, 66]

The non-representative sample rate in cancers has been reported to be between 11% and 39%.[65, 66]

A sample that is non-representative may result from:

- movement of the lesion in the breast. Dense stroma or areas of dense calcification in fatty breast tissue may be pushed away by the sampling device
- the artefactual dispersion of microcalcifications by the technical procedure.

False negative histological diagnoses can result from either technical factors or a misinterpretation of the histology.

The most common technical factors are:

- artefactual distortion of the biopsy tissue, which may result in failure to recognise a carcinoma microscopically, especially if only a small volume of tissue is present
- failure to examine sufficient levels microscopically.

Difficulties in interpretation that may result in underdiagnosis are:

- core biopsies that show only DCIS, 15–20% of core biopsies identified as DCIS show invasive carcinoma on subsequent biopsy[2]
- microcalcification associated with extensive periductal mastitis may make recognition of DCIS difficult
- end-stage periductal mastitis, which may produce an appearance that can mimic DCIS with extensive periductal fibrosis
- papillary and associated lesions, such as adenomyoepitheliomas and ductal adenomas. Excision biopsy is recommended
- solid DCIS and low-grade DCIS, which may be underdiagnosed as LCIS and ADH respectively.

DIAGNOSTIC PROBLEMS

The following may be difficult to distinguish as benign or malignant on core biopsy:

- phyllodes tumours and some fibroadenomas
- spindled and soft tissue tumours
- residual or recurrent carcinoma (or even benign cells) after radiotherapy/chemotherapy
- atypical papillary or mucinous cells
- atypical lymphoid cells or a reactive intramammary lymph node.

TECHNIQUES FOR REDUCING FALSE POSITIVE AND FALSE NEGATIVE DIAGNOSES IN CORE BIOPSY

The following strategies and techniques are recommended to reduce false positive and false negative diagnoses in core biopsy:

- adequate training of all staff
- a multidisciplinary approach: correlation of the microscopic findings with the results of the clinical and radiological assessment; and recommendation of further biopsy, core or excision, and/or follow-up if there is lack of correlation
- assessing the adequacy of the biopsy, including an X-ray of the cores in calcified lesions
- examining sufficient levels microscopically (see Chapter 5)
- appropriate use of immunohistochemistry
- recommending local excision of all atypical lesions
- repeating the core biopsy if the sample is non-representative
- collecting follow-up data, as this is essential to assess and improve performance standards (see Chapter 9).

Summary

- False positive diagnoses are rare (<1%).
- False negative diagnoses are uncommon (<1–2%). However, the non-diagnostic/non-representative sample rate in cancers has been reported to be between 11% and 39%.
- The risk of false positive and false negative results in core biopsy may be minimised by the adoption of a multidisciplinary approach in both specimen sampling and the interpretation of results, ensuring adequate training and experience of staff involved at all stages of the process, a policy of routinely correlating pathology findings with clinical and imaging findings, consistent collection of follow-up data, and participation of services and individuals in QA programs.

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CHAPTER 9 TRAINING AND QUALITY ASSURANCE

FNA cytology and core biopsy are highly operator- and interpreter-dependent procedures. The skill and experience of the operator are very important for obtaining an adequate and representative specimen. The skill and experience of the reporting cytopathologist or histopathologist are also very important, for accurate reporting of FNA cytology and core biopsy respectively.[40, 67, 41, 68] Clinicians performing and reporting FNA cytology and core biopsy should have a sufficient caseload to maintain their clinical skills.

CONTINUING EDUCATION AND TRAINING OPPORTUNITIES

Training and continuing education in the performance of FNA cytology and core biopsy are currently fragmented in Australia. Radiologists, pathologists, surgeons and breast physicians receive training in performing FNA cytology and core biopsy within training programs for their speciality. These specialists are trained in clinical settings through on-the-job training with supervision of trainees, or attend centres known for their expertise in the performance of FNA cytology and/or core biopsy where they observe and receive one-on-one training.

Admission to Fellowship of the Royal College of Pathologists of Australasia requires that candidates have demonstrated competence in all aspects of histopathology and diagnostic cytology, including familiarity with breast pathology and the practice of FNA cytology. In addition, cytopathologists are encouraged to pursue post-fellowship training. Appropriate post-fellowship qualifications are offered by the Royal College of Pathologists of Australasia and the International Academy of Cytology.

Currently, no formal postgraduate courses on FNA cytology or core biopsy are provided by medical colleges in Australia, with the exception of pathology. However, individual tuition may be available on request and by prior arrangement from specialist breast clinics. Individual BreastScreen Australia Screening and Assessment Services may offer training for professionals working within the BreastScreen Australia Program.

Seminars including workshops on ultrasound-guided and stereotactic breast biopsies are held periodically, often as part of international surgical or radiological meetings. The Australasian Society for Ultrasound in Medicine, the

Breast Imaging Reference Group of the RANZCR and the International Breast Ultrasound School provide information on upcoming workshops. Useful contacts for training in Australia are listed in Appendix I. This list includes some of the organisations that provide opportunities for training Australia-wide. Training may also be available at individual clinics not included in the list.

Other training opportunities are available internationally. For example, the Nottingham International Breast Education Centre in the United Kingdom provides theoretical and practical training for all health care professionals involved in breast cancer screening and symptomatic breast disease diagnosis and management.

It is essential that attendance at a course or workshop is not understood to guarantee proficiency in the practice of FNA cytology and/or core biopsy, and that theoretical knowledge is reinforced in practice. In each individual practice setting, regular audit and review of results should be conducted. This will allow for additional training and continuing education requirements to be identified and addressed. Training and continuing education should be part of ongoing quality improvement programs.

QUALITY ASSURANCE

Internal and external QA measures aim to monitor and improve standards of practice. In breast cancer diagnosis, the pathology laboratory is the key to data collection in terms of tissue diagnosis.

The following activities are valuable in monitoring diagnostic accuracy:

Internal QA within the pathology laboratory

- Monitoring of performance indicators (see Table 8.1 and Appendix J) - although the indicators in Appendix J refer to image-guided aspirates in specialised centres and may not be directly applicable to other clinical situations
- Determining individual statistics for pathologists, radiologists, and other clinicians in terms of unsatisfactory sample rates
- Determining individual statistics for the laboratory/pathologist in terms of reporting categories, predictive value of malignant diagnoses and false negative rates

- Conducting microscopic review sessions for pathologists, including correlation between FNA cytology and core biopsy material with subsequent excisional biopsy
- Providing in-house training/continuing education sessions for pathologists and trainees.

External QA for the pathology laboratory

- Participation in slide circulation schemes of FNA cytology and core biopsy cases
- Comparison of the pathology laboratory's performance with that of State/Territory, national and other pathology laboratories.

External QA for clinicians

- Providing feedback to clinicians about their performance, from State/Territory BreastScreen Australia programs, other breast centres and pathology laboratories
- Establishing training and education programs in the technical aspects of FNA cytology and core biopsy with the assistance of State/Territory BreastScreen Australia Programs, pathology laboratories and relevant professional colleges.

CURRENT PRACTICE

Within BreastScreen Australia, services are required to collect data on screen-detected lesions for which FNA cytology or core biopsy has been carried out. National accreditation standards have been developed using these data (Table 8.1). Performance indicators for each service are evaluated annually, and must meet national accreditation standards.

Table 8.1: Minimum standards for FNA cytology and core biopsy for BreastScreen Australia Program, 2002

	Minimum standards	
Performance indicator	**FNA cytology**	**Core biopsy**
Absolute sensitivity	> 60%	> 70%
Complete sensitivity	> 80%	> 80%
Positive predictive value (PPV)/malignant	> 98%	> 99%
False positive rate	< 1%	< 0.5%
False negative rate	< 6%	N/A
Inadequate sample rate	< 25%	
False negative or inadequate rate	N/A	<15%

Note: Refer to Glossary for definition of terms

Summary

- Internal and external quality assurance measures are necessary to monitor and improve standards of practice in the FNA cytology and core biopsy diagnosis of breast lesions.
- FNA cytology and core biopsy are highly operator- and interpreter-dependent procedures. Clinicians performing and reporting FNA cytology and core biopsy should have a sufficient caseload to maintain their clinical skills.

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CHAPTER 10 NEW TECHNOLOGIES AND EMERGING TRENDS

New breast biopsy techniques have been developed in recent years. Vacuum-assisted techniques and large core biopsy techniques are currently practised only at specialist breast clinics. The adoption of these new technologies requires expertise in the area, and there may be cost implications regarding the consumables, clinicians' time, and other resources required. The criteria for selecting lesions appropriate for these techniques, and the appropriate clinical settings in which they should be performed, are still under investigation.

DIRECTIONAL VACUUM-ASSISTED BIOPSY

Directional vacuum-assisted biopsy was developed with the intention of making core biopsy simpler to perform and the diagnosis more accurate, particularly for 'difficult' impalpable lesions. 'Difficult' lesions can be grouped into those that are difficult to sample, such as microcalcifications and small mass lesions less than 1 cm in maximum diameter, and those that are difficult for the pathologist to interpret, such as AH and low-grade DCIS lesions.

This technique can be used with ultrasound or mammographic stereotactic guidance. The needle size is typically 11-gauge. As the needle or biopsy device does not need to be removed to remove the tissue sample, multiple samples can be readily obtained from the area of interest after a single needle insertion. The lumen of the needle or biopsy device can be used to inject local anaesthesia into the tissues around the biopsy site. It can also be used to insert a small staple or clip at the biopsy site for future reference, particularly if the whole of the lesion has been removed by the core biopsy. Directional vacuum-assisted biopsy is associated with a low complication rate. A full description of the technique is readily available in the literature (see *Further reading* at the end of this chapter).

LARGE CORE BIOPSY

Large core biopsy techniques, which take one-piece tissue samples typically of 15mm, have been used in recent years.[69] They have been developed based on the principle that larger samples allow greater certainty of histologic diagnosis and reduce sampling error.

Large core biopsy techniques should be used only for lesions that are clearly visible by mammogram. These techniques require a team approach and must include staff members with radiological and surgical skills as a minimum. A dedicated stereotactic prone table is necessary. Large core biopsy is associated with a low complication rate. Its role in the treatment of small lesions is under investigation.

FURTHER INFORMATION

Information about directional vacuum-assisted biopsy and large core biopsy techniques is included in the *New technologies in breast cancer diagnosis: Information update* (September 2000), available from the NBCC website (www.nbcc.org.au).

Summary

- New breast biopsy techniques, including vacuum-assisted techniques and large core biopsy techniques, are currently practised only at specialist breast clinics.
- The nature of the lesions to be assessed using these techniques and the clinical settings where these procedures should be performed are still under investigation.
- The adoption of these new technologies requires expertise in the area. There are also cost implications.

FURTHER READING

Leibman AJ, Frager D, Choi P. Experience with breast biopsies using the Advanced Breast Biopsy Instrumentation system. *AJR Am J Roentgenol* 1999;172:1409–12.

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Parker SH, Dennis MASAT. Ultrasound-guided mammotomy. A new breast biopsy technique. *J Diagnostic Medical Sonography* 1996;12:113–8.

Philpotts LE, Shaheen NA, Carter D, Lange RC, Lee CH. Comparison of rebiopsy rates after stereotactic core needle biopsy of the breast with 11-gauge vacuum suction probe versus 14-gauge needle and automatic gun. *AJR Am J Roentgenol* 1999;172:683–7.

LIST OF TABLES

APPENDIX A DEVELOPMENT OF THE GUIDE

PROCESS FOR THE DEVELOPMENT OF THE GUIDE

The Royal College of Pathologists of Australasia (RCPA) and the National Breast Cancer Centre (NBCC) agreed on the need for recommendations about FNA cytology and core biopsy which are relevant and applicable to the current Australian setting.

A multidisciplinary project team, including pathologists, radiologists, breast surgeons, a breast physician, a rural general practitioner and a consumer representative, reviewed relevant international recommendations about FNA cytology and core biopsy. This review determined that existing recommendations required significant modification in order to be relevant and applicable to the Australian setting. The project team agreed on the need to develop a guide for the practice of FNA cytology and core biopsy that would be appropriate for Australia.

The topics to be covered by the guide were identified by the project team. The members of the team agreed to be involved in the writing process and to be responsible for the development of particular chapters. Various drafts of the guide were reviewed by members of the project team. Chapters and appendices were discussed at meetings and agreed on by the whole project team.

The project team reviewed available literature up until mid 2000. Where evidence existed, it was appraised and considered for relevance and, where appropriate, incorporated into the guide. However, due to the paucity of relevant research data relating to several areas covered in the guide and due to the inclusion of sections that are essentially descriptive, an expert consensus approach was adopted for some aspects of the guide.

CONSULTATION PROCESS

A draft of *Breast fine needle aspiration cytology and core biopsy: a guide for practice* was circulated to the following professional colleges and organisations on 31 May 2001 for review over a six-week period:

- Australian Cancer Network (ACN)
- Australasian Society of Breast Physicians (ASBS)

- Australian Society of Cytology (ASC)
- Breast Cancer Network Australia (BCNA)
- BreastScreen Australia
- Cytopathology Quality Assurance Program, RCPA
- Faculty of Radiation Oncology, RANZCR
- InterCollegiate Committee, BreastScreen Australia
- Medical Oncology Group of Australia (MOG)
- Royal Australasian College of Surgeons (RACS)
- Rural Faculty, Royal Australian College of General Practitioners (RACGP)
- The Royal Australian and New Zealand College of Radiologists (RANZCR)
- The Royal College of Pathologists of Australasia (RCPA).

International experts in the field of pathology and radiology were also invited to review the guide. These were pathologist Professor Jerry Waisman (New York University, US), and radiologists Dr Robin Wilson (Nottingham International Breast Education Centre, United Kingdom) and Dr Laura Liberman (Memorial Sloan-Kettering Cancer Center, US).

In addition, a notice indicating the availability of the draft guide for review was included in the June issue of the NBCC's publication, *BreastFax.* A copy of the draft guide was sent to additional individuals/organisations who requested the document.

Comments were received from the following:

- ACN
- ACS
- ASBS
- Breast Cancer Network Australia
- BreastScreen Australia
- Dr Sanjiv Jain, ACT Pathology, ACT
- InterCollegiate Committee, BreastScreen Australia
- Associate Professor Jonathan Osborne, State Radiologist, BreastScreen Queensland
- RCPA
- RANZCR

- RACS
- Ms Deidre Rennick, Consellor, BreastScreen NSW (SouthWest)
- Sydney Square Breast Clinic, NSW
- St Vincent's Breast Centre, Queensland
- The Cytopathology Quality Assurance Program, RCPA
- The Faculty of Radiation Oncology, RANZCR
- The Rural Faculty, RACGP
- Dr Robin Wilson, Nottingham International Breast Education Centre, UK
- Professor Jerry Waisman, New York University, US.

DISSEMINATION OF THE GUIDE

Copies of the guide will be disseminated to relevant professional groups and organisations. The guide will also be available at the NBCC's web site (www.nbcc.org.au). The guide will be promoted through presentations at relevant professional meetings and conferences and submissions to professional journals.

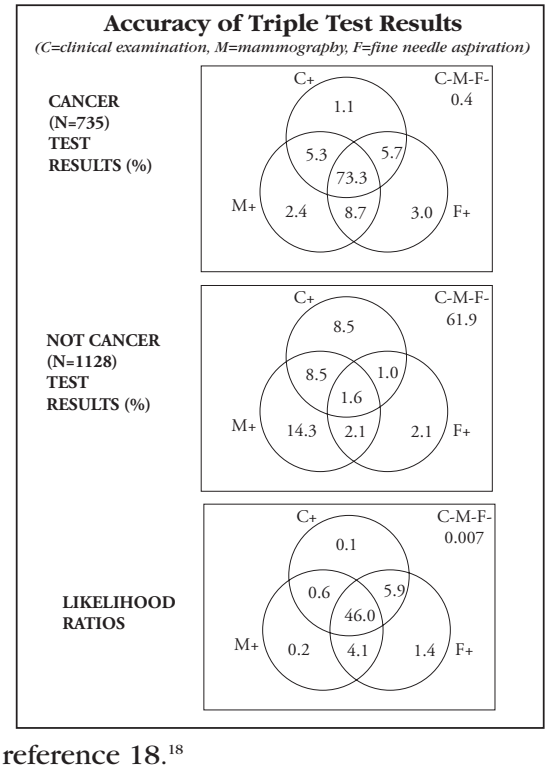
EVALUATION

Recommendations for pathology requesting and reporting are a key aspect of the guide. An evaluation process will be considered to determine the impact of the guide on the quality of pathology requests and reports.

APPENDIX B THE CONTRIBUTION OF CLINICAL EXAMINATION, FNA CYTOLOGY AND MAMMOGRAPHY TO THE DIAGNOSIS OF A BREAST CHANGE

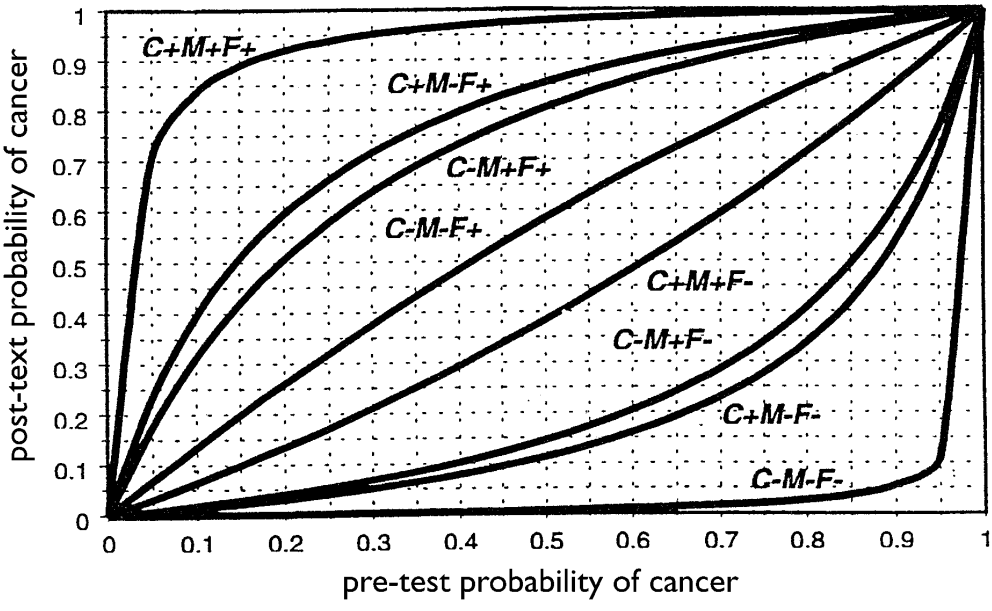
The contribution of each component of the triple test to the diagnosis of a breast change can be determined by examining the proportion of cancers detected by various combinations of test results. The accuracy of clinical examination, mammography and FNA cytology and the probability of cancer with different clinical examination, mammographic and FNA cytology results are shown in Figures B1 and B2 respectively. Details about the construction of these figures are available in the report *Evidence relevant to guidelines for the investigation of breast symptoms.*[18]

Figure B1. Accuracy of clinical examination, mammography and fine needle aspiration



Reproduced from reference 18.[18]

Figure B2. Probability of cancer with different clinical examination, mammography and fine needle aspiration results



Reproduced from reference 18.[18]

APPENDIX C SUMMARY OF USEFUL STRATEGIES TO PREPARE WOMEN FOR FNA CYTOLOGY AND CORE BIOPSY

The following tables have been reproduced from *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer,*[38] which were developed for women with breast cancer. However, many of the strategies described could be used for women who do not receive a positive diagnosis. The tables below summarise useful strategies that could be used when preparing women for FNA cytology and core biopsy and when giving test results. The topics covered include: preparing women for potentially threatening medical procedures; dealing with cultural issues; general interactional skills; and telling a woman she has breast cancer, a recurrence or metastasis.

Table C1. Recommended steps involved in adequately preparing a woman for a potentially threatening medical procedure

These steps are recommended in conjunction with the general interactional skills summarised in Table C3.

Before the procedure

- Explain why the procedure is needed, and the expected outcome
- Ask how much detail the woman would like to know about the procedure before explaining it. The information may include:
    - where the procedure might take place, and who will perform it
    - any tests needed before the procedure
    - what the woman will need to do before the procedure
    - what the woman is likely to experience during and after the procedure
- Encourage the woman to talk about her concerns, such as pain, fear, death, embarrassment
- Ask the woman what she thinks she can do to cope
- Enquire about, and reinforce, previous coping strategies (eg relaxation techniques and imagery).

During the procedure

- Provide information about what will be done and how it will feel
- Give the woman control, where possible (eg ask her to tell you when she is ready to begin)
- Encourage the use of coping strategies.

After the procedure

- Encourage the use of coping skills (eg relaxation techniques and imagery)
- Encourage the woman to state her needs and reframe her complaints into requests
- Arrange follow-up and support.

Reproduced from the NHMRC National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.*[38]

Table C2. Recommended steps involved in dealing with cultural issues

- If the woman is not proficient in English, book a trained interpreter from the Translating and Interpreting Services (TIS) - phone: 13 14 50 (24 hours a day, 7 days a week, Australia wide)
- Explain the role of the interpreter and ensure that the woman agrees to their presence
- Talk directly to the woman rather than the interpreter, keep sentences short, and pause after a few seconds to allow for interpretation
- Provide culturally appropriate health care workers, if possible
- Provide a female medical professional or nurse, if possible
- Explain how confidentiality is achieved within the medical setting
- Ask how the woman feels about her disease and treatment, and what meaning it has for her within her culture
- Assess the woman's understanding of her disease, treatment and prognosis
- Ask about cultural or religious issues that may influence treatment
- Offer to discuss issues and treatment options with the woman's family
- Explain the importance of social support, and encourage the woman to seek support from family, friends, support services and local cancer organisations

- Provide written information in the appropriate language, if available
- Arrange follow-up and support
- Always be aware of culturally specific and individually specific values, beliefs and modes of behaviour.

Reproduced from the NHMRC National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.*[38]

Table C3. General interactional skills

The following skills should be considered in any consultation with a woman with breast cancer:

Supportive communication

- Ask the woman if she would like someone to be with her during the consultation
- Show regard and concern for the woman by using appropriate verbal and non-verbal behaviour, including sitting attentively and facilitating the woman's responses
- Use verbal and non-verbal behaviours appropriate to the woman's age and cultural background
- Express empathy, and listen actively
- Allow and encourage the woman to express her feelings (eg by crying, talking about concerns, fears, anger, anxieties etc.)
- Handle embarrassing or disturbing topics directly and sensitively.

Delivering medical information in plain English

- Assess the woman's understanding before providing additional information
- Explain difficult terms and avoid medical jargon
- Use explicit categorisation (provide information clearly grouped in specific topics).

Strategies to aid recall and understanding

- Actively encourage questions and seek understanding
- Make use of simple diagrams and pictures where appropriate
- Repeat and summarise important information

- Reinforce important information by using one or more of the following aids:
  - writing down relevant information
  - taping the consultation as needed and if wanted
  - sending the woman a summary letter as follow-up.

Ongoing support

- Assess the woman's level of family or social support
- Provide the names and contact details of relevant persons or organisations from whom more information can be obtained
- Refer to a specialist breast nurse or other relevant professional for support as required.

Reproduced from the NHMRC National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.*[38]

Table C4. Recommended steps for telling a woman she has breast cancer, a recurrence or metastasis

These steps are recommended in conjunction with the general interactional skills summarised in Table C3.

1. Prior to discussing diagnosis, recurrence or metastases

- Ensure the news is given in person, in a quiet, private place and allow enough uninterrupted time
- Encourage a second person to be present if appropriate
- Arrange to provide other methods to convey the information (eg written materials, video tapes, tapes of consultations, etc).

2. When providing the information

- Assess the woman's understanding of her condition and the woman's personal preference for information
- Briefly explain the process by which the diagnosis was reached
- Provide information simply and honestly, using lay terms without using euphemisms
- Avoid conveying the notion that 'nothing can be done'
- Clearly indicate that the woman will have the final decision regarding her care.

3. Emotional and supportive role

- Encourage the woman to express her feelings (eg by crying freely, talking about concerns, fears, anger, anxieties, etc) and respond to her feelings with empathy
- Address disturbing or embarrassing topics directly, and with sensitivity
- Assess the type and level of assistance that may be required, such as financial, transport or childcare assistance
- Provide information about support services.

4. Concluding the discussion

- Summarise the main points of the consultation, and assess the woman's understanding
- Ask if there is anything further the woman would like to discuss
- Offer assistance to tell others difficult news
- Indicate your availability for contact to address any questions or concerns, and arrange a further appointment to review the situation within a stated time period (eg within 24 hours to two weeks).

5. After discussing a diagnosis, recurrence or metastasis

- Document information given to the woman and family members
- Let others, particularly the woman's general practitioner, know the extent of information given and your perception of the woman's understanding.

Reproduced from the NHMRC National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.*[38]

APPENDIX D EXAMPLES OF INFORMATION SHEETS FOR WOMEN UNDERGOING FNA CYTOLOGY OR CORE BIOPSY

The following information sheets have been prepared as examples to assist clinicians to develop written information for women.

The text of these examples has been adapted from information available from a sample of State and Territory BreastScreen program,[70,71,72,73] and from the NBCC's publication *Breast changes: what you need to know.*[74]

Example of an information sheet for women undergoing fine needle aspiration cytology

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Fine needle aspiration cytology

Fine needle aspiration (FNA) cytology, also known as FNA biopsy, is used to investigate a breast change as part of what is known as the triple test. The triple test is the recommended way of investigating a breast change or symptom.

The triple test includes three main steps:
1. clinical breast examination and medical history
2. imaging tests, that is mammography and/or ultrasound
3. fine needle aspiration (FNA) cytology and/or core biopsy

Although none of these tests is 100% accurate, their combined use gives the best chance of detecting or excluding breast cancer.

FNA cytology involves placing a thin needle into the breast to obtain a small sample of cells from the lump or area of concern. An experienced clinician – who may be a radiologist, surgeon, breast physician, or pathologist – takes the sample. If the lump cannot be easily felt, ultrasound or mammography may be used to help the doctor guide the needle into the correct area of the breast. The needle is typically inserted several times. The choice between ultrasound and mammography will depend on which method is available or which method makes the area being studied easier to see. The test itself takes only one to two minutes. However, should mammography or ultrasound be used, you may be in the biopsy room for up to 30 minutes to make sure an adequate sample is obtained.

The sample obtained is then sent to a pathologist, who will study the cells under a microscope and provide a detailed report on the type of cells present. In some situations the sample can be immediately checked to see if enough cells have been obtained, and a provisional result may be available immediately after the test. The final result will be available within a few days. It is important to confirm when and how your results will be made available.

The test may be uncomfortable, but is rarely painful. It will sometimes cause bruising, and infection is rare. If after having the test the area is uncomfortable it is recommended you take paracetamol to ease the discomfort. Aspirin is not recommended as it could make the bruising worse. Firm pressure may also be used to ease any discomfort and reduce swelling.

Definition of terms:

Cyto = cell

Cytology = study of cells

Mammography = X-ray of the breast

Text adapted from information sheets from various State and Territory BreastScreen programs,[70, 71, 72, 73] and from the National Breast Cancer Centre's publication *Breast changes: what you need to know.*[74]

Example of an information sheet for women undergoing core biopsy

Core biopsy

Core biopsy is used to investigate a breast change as part of what is known as the triple test. The triple test is the recommended way of investigating a breast change or symptom.

The triple test includes three main steps:
1. clinical breast examination and medical history
2. imaging tests, that is mammography and/or ultrasound
3. non-excision biopsy, that is fine needle aspiration (FNA) cytology and/or core biopsy.

Although none of these tests is 100% accurate, their combined use gives the best chance of detecting or excluding breast cancer.

Core biopsy involves making a very small cut in the skin and removing several narrow sections of tissue from a lump or area of concern through the same cut, using a large needle. This is done under a local anaesthetic which is a substance that numbs the area. An experienced clinician – who may be a radiologist, surgeon, breast physician or pathologist – takes the tissue sample.

If the lump cannot be easily felt, ultrasound or mammography may be used to help the doctor guide the needle into the right area of the breast. The choice between ultrasound and mammography will depend on which method is available or which method makes the area being studied easier to see. The test will usually take between 30 minutes and one hour to complete.

After the procedure is completed the biopsy area will be covered with some tape or a dressing. The dressing can be removed the following day. A very small and fine scar may be left.

The sample obtained is then sent to a pathologist, who will study it under a microscope and provide a detailed report on the type of tissue present. The results should be available within a few days. It is important to confirm when and how your results will be made available.

A core biopsy may be uncomfortable. However, as a local anaesthetic is given before the test is done, it is rarely painful. If after having the core biopsy the area is uncomfortable, it is recommended you take paracetamol to ease the discomfort. Some bruising may occur. Aspirin is not recommended as it could

make the bruising worse. Firm pressure may also be used to ease any discomfort and reduce swelling. Infection is rare.

Definition of terms:

Mammography = X-ray of the breast

Text adapted from information sheets from various State and Territory BreastScreen programs,[70, 71, 72, 73] and from the National Breast Cancer Centre's publication *Breast changes: what you need to know.*[74]

APPENDIX E EXAMPLE OF A PATHOLOGY REQUEST FORM FOR FNA CYTOLOGY AND CORE BIOPSY

PATHOLOGY REQUEST

Date: ____ / ____/ ____

Patient Name:_____

Date of Birth: ___/___/___

Address: _____

_____

_____

Affix sticler here (UMRN)

Operator - Name/Coded ID/Provider Number: _____

Requesting clinician – Name/Coded ID/Provider Number: _____

☐ urgent request ☐ routine request

If urgent, relay report by: mobile phone no _____ fax no _____

_____

Request ☐ cytology ☐ histology ☐ receptors ☐ other_____

Specimen

Date: ____ / ____/ ____ Time: _____

- Site sampled: ☐ breast ☐ lymph node ☐ skin ☐ other _____
- Site position: side + 'o'clock' _____ distance from nipple _____

Guidance: ☐ palpation ☐ stereotaxis ☐ ultrasound

continued over

Site of lesion (specify on diagram)

Specimen radiology:

□ done

□ accompanies specimen

□ microcalcification present

History:

Medical history: _____

_____

Clinical findings: _____

_____

Imaging findings:

□ Mammography performed:

- □ stellate lesion
- □ circumscribed opacity
- □ asymmetric density
- □ microcalcifications
- □ microcalcifications & mass
- □ disturbance of architecture
- □ other (specify) _____

□ Ultrasound performed

- □ simple cyst
- □ complex cyst
- □ well defined hypoechoic
- □ ill defined hypoechoic
- □ microcalcifications & mass
- □ disturbance of architecture
- □ other (specify)_____

Provisional diagnosis:_____

_____

_____

Copies of report to: _____

Managing clinician: _____

APPENDIX F EQUIPMENT REQUIRED FOR FNA CYTOLOGY AND CORE BIOPSY

FNA CYTOLOGY

Most operators do not routinely use local anaesthesia for cytology sampling, although it may be indicated if the lesion is tender near the nipple or at the woman's request.

A 23- to 25-gauge needle is typically used for cytology sampling. Depending on the guidance technique selected and the operator's preference, the type of needle varies from a simple venipuncture needle to a specifically designed biopsy needle. The length of the needle will also vary.

Most operators use a suction or aspiration technique, using a syringe alone or with a syringe holder. Extension tubing may also be used. Some operators prefer a non-suction or capillary technique, which has the advantages of enhancing fingertip sensitivity and needle control, and reducing the risk of blood contamination. The use of suction has been shown to reduce the insufficiency rate for benign lesions.[42]

In the case of ultrasound-guided procedures, a protective cover is required for the probe and gel or other coupling fluid. If gel is used, care should be taken to avoid contamination of the needle by gel. Removal of all gel from the skin is recommended before inserting the needle. For a stereotactic procedure, sterile needle guides are used.

Clinicians performing either procedure need to be aware of standard precautions to prevent needlestick injury or contamination with body fluids.

Contents of tray or trolley for FNA cytology sampling

The following items are typically required for FNA cytology sampling:

- sampling needle:
  - venipuncture needle or specifically designed biopsy needle – depends on the guidance technique and preference of the operator
  - typically 22–25-gauge
  - length – depends on the guidance technique and preference of the operator

- syringe (10–20 ml)
- syringe holder +/- extension tubing
- alcohol or iodine preparation cleansing agent
- swabs
- gloves
- adhesive dressing
- pencil for labelling slides, pen for labelling specimen containers
- local anaesthesia, needles and syringe if required
- glass slides and transport medium, if required
- protective cover for ultrasound probe, if ultrasound-guided procedure
- gel or other coupling fluid, if ultrasound-guided procedure
- needle guides, if mammography-guided procedure.

CORE BIOPSY

For core sampling, 14-gauge needles are the most commonly used needles. The needle type and length will vary depending on the guidance technique and whether a disposable unit is used, or a disposable needle is used in conjunction with an automated Tru Cut® device. Vacuum-assisted biopsy devices, typically using 11-gauge needles, may be used in some specialised centres.

Local anaesthetic is routinely used for core biopsy procedures, because the 14-gauge or larger needles require a small stab incision to be made in the skin to allow free movement of the cutting blade. Local anaesthetic is also commonly injected more deeply around the lesion for image-guided procedures. A vasoconstrictor can be used to reduce bleeding.

Contents of tray or trolley for core biopsy sampling

The following items are typically required for core biopsy sampling:

- biopsy needle:
  - 14-gauge needle or larger
  - length and type depends on the guidance technique and preference of the operator
- automated Tru Cut® or other firing device
- scalpel blade

- alcohol or iodine preparation cleansing agent
- swabs
- local anaesthesia
- needles and syringes for anaesthetic
- gloves
- wound cover
- specimen container
- label or pen for labelling specimen containers
- protective cover for ultrasound probe, if ultrasound-guided procedure
- gel or other coupling fluid, if ultrasound-guided procedure
- needle guides, if mammography-guided procedure.

APPENDIX G SAMPLING TECHNIQUES FOR FNA CYTOLOGY AND CORE BIOPSY

CLINICALLY GUIDED FNA CYTOLOGY

The following description represents one approach to taking the tissue sample using FNA cytology under clinical guidance:

1. The woman is placed in a comfortable position, usually supine
2. The skin over the lesion is cleansed
3. Local anaesthetic (if required) is injected into the skin over the lesion
4. The lesion is immobilised between the thumb and forefinger of one hand. The needle is introduced with the other hand. Depending on operator preference, the needle may be introduced either (i) on its own, (ii) with the syringe attached or (iii) with the syringe and holder attached
5. When the needle tip is felt to be at the edge of the lesion, negative pressure is applied while entering the lesion and actively performing passes through the lesion
6. Rapid multiple passes are made through the lesion, varying the angling of the sampling only if necessary. If blood is seen in the hub, sampling should be ceased as excessive blood reduces the quality of the sample
7. The negative pressure is released while the needle is still in the lesion. The needle is then withdrawn and the material is expelled from the needle onto a labelled glass slide using the syringe
8. The needle may be rinsed in transport medium, eg for receptor studies.

Typically more than one sample/pass of the lesion is required for diagnosis, irrespective of guidance modality. The number of samples/passes necessary can be determined by the immediate examination of the slides under the microscope. If immediate examination is not possible, at least three passes are taken. Typically, any further sampling has little additional yield.

ULTRASOUND-GUIDED FNA CYTOLOGY

The following description represents one approach to taking the tissue sample using FNA cytology under ultrasound guidance:

1. The woman is positioned supine or supine oblique with her arm placed above her head so as to reduce breast movement and thickness
2. The skin over the lesion is cleansed and local anaesthetic injected as required. It is recommended that any gel be cleaned from the skin before inserting the needle. Some operators hold the probe with one hand and introduce the needle with the other
3. Some operators prefer to have an assistant hold the ultrasound probe over the lesion so as to enable one hand to be free to keep the breast from moving, while the other is used to introduce the needle. Other operators hold the probe with one hand and introduce the needle with the other
4. The needle should be introduced so its long axis is in line with the long axis of the probe face. With this approach the full length of the needle, including the tip, is visualised at all times. The needle angle should be kept as parallel to the probe face and chest wall as possible, so as to aid visualisation and reduce the risk of accidental pneumothorax
5. When the needle tip is seen at the leading edge of the lesion, negative pressure is applied and sampling is carried out as described above
6. A hard copy image may be taken to record the position of the tip of the needle within the lesion.

STEREOTACTICALLY GUIDED FNA CYTOLOGY

The following description represents one approach to taking the tissue sample using FNA cytology under stereotactic guidance:

1. Mammogram films are used to select the best approach to the lesion – typically the shortest
2. The woman is positioned accordingly and compression is applied to the breast using a biopsy plate. An exposure is taken to check that the lesion has been accurately positioned
3. Stereotactic views are taken and the x, y and z coordinates of the lesion are calculated
4. The skin is cleansed and local anaesthesia is injected as required

5. The needle is passed through the needle guides and introduced into the breast at the site determined by the coordinates
6. Stereotactic images are taken to confirm that the needle tip is accurately placed
7. If the position is correct, the z coordinate is changed to approximately +5 mm, negative pressure is applied and the needle is moved back and forth through the lesion several times
8. The negative pressure is released and the needle is removed. The sample is then assessed
9. A hard copy image may be taken to record the position of the tip of the needle within the lesion.

CLINICALLY GUIDED CORE BIOPSY

The following description represents one approach to taking the tissue sample using core biopsy under clinical guidance:

1. Patient positioning, skin cleansing and lesion fixation are the same as for a cytology procedure. However, local anaesthesia is always used in the skin and immediate subcutaneous tissue
2. The position of the skin entry site for a core biopsy should be carefully planned in consultation with the surgeon
3. Using a scalpel blade, a small cut is made at the selected entry point and the needle is introduced through this entry point
4. When the tip of the needle is felt to be at the leading edge of the lesion, the firing mechanism is released and the sample taken
5. The needle is removed and the sample extracted
6. The procedure is then repeated. Typically three to five samples are taken through different parts of the lesion to ensure adequacy of sampling.

The number of cores will be the result of various issues, including lesion characteristics, imaging findings, ability to localise, guidance modality, patient tolerance, and the confidence in the adequacy of the sample. Generally between three to five cores will be taken.

ULTRASOUND-GUIDED CORE BIOPSY

The following description represents one approach to taking the tissue sample using core biopsy under ultrasound guidance:

1. The woman is positioned supine or supine oblique, and an assistant may hold the ultrasound probe, as for a cytology procedure
2. The route of approach to the lesion is planned. If malignancy is suspected, the operator may wish to plan the most appropriate approach in consultation with the managing surgeon
3. The skin is cleansed, local anaesthesia is injected into the skin and a small stab incision is made. Deep tissue anaesthesia may also be used as appropriate. It is recommended that any gel is cleaned from the skin before inserting the needle
4. The needle needs to be introduced so its long axis is in line with the long axis of the probe, and as parallel to the chest wall as possible. The area beyond the needle tip should be visualised prior to firing to reduce the risk of a pneumothorax, because the needle is typically thrown forward 15-22 mm
5. After each sampling, the needle is removed and the tissue extracted. To ensure adequacy of sampling, typically three to five core samples are taken through different parts of a mass lesion. A greater number of samples may be required for other lesion types
6. A hard copy image may be taken to record the position of the needle within the lesion.

For very small lesions, it may be preferable to take the sample using a vacuum-assisted technique, so as to allow for a marker to be left in situ if the entire lesion has been removed by sampling.

STEREOTACTICALLY GUIDED CORE BIOPSY

The following description represents one approach to taking the tissue sample using core biopsy under stereotactic guidance:

1. Breast immobilisation and positioning are performed as for stereotactic cytology procedures. The approach may be determined in consultation with the managing surgeon
2. The skin is cleansed and local anaesthesia is injected into the skin and into the deeper tissues, as required

3. Once the needle has been placed in the breast, stereotactic images are taken to confirm the accuracy of positioning. When using the Tru Cut® device or similar, positioning should be precise, particularly for microcalcifications and small mass lesions
4. The needle tip is withdrawn approximately 5 mm back from the centre of the lesion prior to firing, if the lesion is small. This positioning will place the lesion within the central area of the tissue sample after firing
5. The automated core device is fired
6. If a mass lesion or architectural disturbance is being sampled, the position of the needle relative to the lesion is evaluated by post-firing stereotactic exposures, so as to confirm adequacy of sampling. Hard copy images may be taken to record the position of the needle within the lesion. To ensure adequacy of sampling, typically three to five cores are taken through different parts of a mass lesion or architectural disturbance
7. After each sampling, the needle is removed and the sample is extracted.

If microcalcifications are being sampled, post-firing exposures can be replaced by core specimen radiographs. The core radiograph will confirm whether adequate samples of the microcalcifications have been obtained. To ensure adequacy of sampling, typically three to five core samples are taken and then radiographed.[75] If the core radiograph does not show microcalcification, more cores are taken immediately.

For very small lesions, it is preferable to take the sample using a vacuum-assisted technique, so as to allow for a marker to be left *in situ* if the entire lesion has been removed by sampling.

APPENDIX H EXAMPLES OF STANDARDISED REPORTS FOR FNA CYTOLOGY AND CORE BIOPSY

It is recommended that a standardised report format be used for reporting FNA cytology and core biopsy specimens. The use of standardised reporting helps ensure that pathology reports are concise, comprehensive and easy to understand.

EXAMPLE OF REPORT FOR FNA CYTOLOGY

It is recommended that the following items be included in a standard report of a FNA cytology specimen:

- patient identification details
- specimen identification – laboratory/specimen numbers
- requesting doctor, aspirator, reporting pathologist
- copies of reports to [names]
    - clinical notes and imaging findings, including:
    - side of lesion – whether left or right
    - site of lesion – either quadrant or o'clock position
    - distance from nipple, if more than one lesion is being analysed
    - nature of lesion, including clinical and imaging features
    - collection guidance – palpation, ultrasound, stereotaxis
    - pregnancy – yes/no
- time and date of collection
- time and date of laboratory receipt
- description of material received, including number of slides received, number of air-dried and wet-fixed slides; and if the material received was cyst fluid, a statement indicating this. If the pathologist did the aspiration, a brief description of the texture of the lesion and aspirated material is recommended

- specific findings: a brief description of the microscopic appearance of the smears and their adequacy. Specific inclusion of cellularity, pattern, cytologic appearance and background is recommended.
- diagnostic category. The report should include one of the following:
    - Inadequate/insufficient
    - Benign
    - Atypical/indeterminate
    - Suspicious of malignancy
    - Malignant
- descriptive diagnosis, including non-specific statements such as 'benign ductal cells' and 'macrophage reaction only', and specific diagnoses such as 'fibroadenoma' and 'breast carcinoma'
- numerical coding could be included as an adjunct
- comment or recommendation, if applicable
- name of reporting cytopathologist
- date of report
- numerical coding could be included as an adjunct.

EXAMPLE OF REPORT FOR CORE BIOPSY

It is recommended that the following items be included in a standard report of a core biopsy specimen:

- patient identification details
- specimen identification (laboratory/specimen numbers)
- requesting doctor
- reporting pathologist
- copies of reports to [names]
- clinical notes and imaging findings, including:
    - tissue sampled
    - side of lesion – whether left or right
    - site of lesion – either quadrant or o'clock position
    - distance from nipple – if more than one lesion is being analysed
    - nature of lesion including clinical and imaging features
    - pregnancy – yes/no

- collection details, including:
  - collected by [name]
  - time and date of collection
  - localisation – palpation, ultrasound, stereotactic
- laboratory details, including:
  - specimen receipt – date and time
  - specimen X-ray – yes or no
  - microcalcification seen – yes or no
- macroscopic description, including
  - side and site of core biopsy
  - number of cores or tissue fragments
- microscopic report, including:
  - microcalcification (yes, no or not applicable)
  - diagnostic category. The report should include one of the following:
    - Inadequate/insufficient
    - Benign
    - Atypical/indeterminate
    - Suspicious of malignancy
    - Malignant
- descriptive diagnosis, including non-specific statements such as benign breast change, and specific diagnoses such as fibroadenoma and breast carcinoma.

  If invasive carcinoma is present, list, if possible:
  - type
  - grade – because of the small volume, this may be an estimate of low, intermediate or high
    - tubule formation – description
    - nuclear grade – description
    - mitoses – description
  - size – an indication of the size present in the cores received. The tumour should equal, or be greater than, this size

- lymphatic/vascular involvement
- oestrogen receptor status (if requested)

If DCIS is present, list, if possible:

- type – architecture, including the presence or absence of necrosis and the presence or absence of microcalcification and its type
- nuclear grade
- approximate volume in cores, for example the approximate number or percentage of ductules involved

- comment or recommendation, if applicable
- name of reporting pathologist
- date of report.

APPENDIX I CONTACTS FOR TRAINING IN FNA CYTOLOGY AND CORE BIOPSY

- Australasian Society for Ultrasound in Medicine (ASUM)
  Contact details for ASUM are available at
  www.medeserv.com.au/asum/open/home.htm
- Australasian Society of Breast Physicians
  In Australia the Society can be contacted at the
  Calvary Breast Clinic, telephone 07 4031 6482, fax 07 4041 1105
- Breast Imaging Reference Group (BIRG) – The Royal Australian and New Zealand College of Radiologists
  Contact details for members of the BIRG are available at
  www.racr.edu.au/open/breast_contacts.htm
- BreastScreen Australia
  Contact details for the State/Territory Programs are available at
  www.breastscreen.info.au/further/index.htm
- International Breast Ultrasound School (IBUS)
  Contact details for IBUS and information about
  IBUS workshops and seminars are available at www.ibus.org
- Royal Australasian College of Surgeons
  Contact details for the College are available at
  www.racs.edu.au/index.cfm
- Royal Australian and New Zealand College of Radiologists
  Contact details for the College are available at
  www.racr.edu.au/open/contact.htm
- Royal College of Pathologists of Australasia
  Contact details for the College are available at
  www.rcpa.edu.au

APPENDIX J PERFORMANCE INDICATORS FOR FNA CYTOLOGY AND CORE BIOPSY

A review of 31 articles reporting the results of a total of 17,108 FNA cytologies and core biopsies was undertaken by Britton (1999).[19] Britton points out that as the research projects reviewed have mostly been conducted by leaders in their field, the results are likely to be better than those obtained at other centres.[19] Analysis of the accumulated data from these 31 articles is presented in Table J1.

A comparison of performance indicators for FNA cytology and core biopsy at 85 of the 95 screening centres within the United Kingdom National Health Service Breast Screening Programme is presented in Table J2.

Table J1. Analysis of the accumulated data from 31 series by Britton[19]

	Stereotactic guidance		Ultrasound guidance	
	FNA cytology (%)	Core biopsy (%)	FNA cytology (%)	Core biopsy (%)
Absolute sensitivity	62.4	90.5	83.1	96.7
Complete sensitivity	83.1	94.6	95.1	98.5
Specificity	86.9	98.3	84.0	98.7
Positive predictive value malignant	99.3	99.5	98.3	100
False positive rate	0.5	0.4	1.4	0
Inadequate rate	6.4	1.0	12.8	0.05
Inadequate rate in cancers	5.0	1.5	2.1	0

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Table J2. Comparison of performance indicators for FNA cytology and core biopsy at the National Health Service Breast Screening Programme (NHSBSP)9

Performance indicator	NHSBSP target	FNA cytology		Core biopsy (all)		Core biopsy (five category classification only)	
		Median	Range *(IQ range)*	Median	Range *(Q range)*	Median	Range *(IQ range)*
Absolute sensitivity	> 60%	53.6	0–89.7 *38.9–65.6*	75.0***	0–100 *62.7–80.4*	69.7***	0–100 *54.1–80.0*
Complete sensitivity	> 80%	81.8	15.4–97.2 *74.1–88.1*	76.6***	0–100 *67.5–85.7*	76.4***	0–100 *67.7–88.4*
Full specificity	> 60%	57.8	20.0–80.7 *46.1–67.3*	84.2***	33.3–100 *72.4–92.3*	84.4***	33.3–100 *76.1–92.0*
PPV category 5 outcome	> 95%	100.0	75.0–100 *100–100*	100.0	91.2–100 *100–100*	100	93.3–100 *100–100*
False positive rate	< 1%	0	0–6.3 *0–0*	0	0–7.7 *0–0*	0	0–3.7 *0–0*
False negative rate	< 5%	6.3	0–26.7 *3.1–10.5*	13.0***	0–100 *8.5–20.5*	13.1***	0–100 *7.2–20.3*
Inadequate rate	< 25%	23.2	4.7–75.8 *17.7–29.3*	10.6***	0–40 *5.1–21.3*	9.0***	1.4–40 *3.6–18.4*
Inadequate rate in cancers	-	10.6	0–76.9 *6.2–18.2*	7.4**	0–42.9 *0.9–12.9*	4.9*	0–30.4 *2.4–13.8*

*:P<0.05, P>=0.01; **:P<0.01, P>=0.001; ***:P<0.0001

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GLOSSARY

Absolute sensitivity

The number of malignant diagnoses expressed as a percentage of the total number of confirmed malignancies sampled.

Benign diagnosis

Where the FNA cytology or core biopsy shows no evidence of malignancy and this correlates with benign clinical and imaging findings.

Complete sensitivity

The number of confirmed malignancies in which there was an abnormality on FNA cytology or core biopsy, expressed as a percentage of the total number of confirmed malignancies. Where an abnormality is classified as atypical/indeterminate, suspicious of malignancy or malignant. Non-diagnostic/non-representative samples are excluded.

Core biopsy

The use of a 10–14-gauge needle, typically to obtain a tissue sample for histological examination.

Displacement of epithelium

The removal of breast epithelium from the normal location.

False negative case

A case with a proven malignant diagnosis with a previous benign pathology report. Non-diagnostic/non-representative cases are excluded.

False negative rate

The number of false negative reports expressed as a percentage of the total number of malignancies sampled.

False positive case

A case with a proven benign diagnosis with a previous malignant pathology report.

False positive rate

The number of false positive reports expressed as a percentage of the total number of malignancies sampled.

FNA cytology

The use of a needle, typically 22-gauge or smaller gauge, to obtain a cell sample for cytological examination. Also referred to as fine needle aspiration biopsy (FNAB) or fine needle cytology (FNC).

Frozen section

An intraoperative rapid histopathological examination of fresh tissue. The technique involves freezing a small sample, cutting very thin sections with a microtome and staining the sections for microscopy. It is most often used to confirm or exclude malignancy and where the result may help the surgeon decide the subsequent operative procedure.

Inadequate sample rate

The number of inadequate samples expressed as a percentage of the total number of lesions sampled. The definition of 'inadequate' varies; for the purposes of this document, 'inadequate' is equivalent to the report category 'non-diagnostic/non-representative'.

Inadequate sample rate in cancers

The number of malignancies preceded by a non-diagnostic report category expressed as a percentage of the total number of malignancies sampled.

Managing clinician

The clinician who takes responsibility for correlating the cytological/histological results with the clinical and imaging findings. This could be the woman's general practitioner, a surgeon to whom the woman has been referred or an other clinician.

Needle tract implantation

The insertion of epithelium, either benign or malignant, along the needle tract following a needle biopsy procedure.

Non-diagnostic specimen

A specimen that does not permit a microscopic diagnosis, either because the material present is too distorted or its volume is too scanty.

Non-representative specimen

A specimen that is inconsistent and does not correlate with the clinical and imaging findings.

Positive diagnosis of carcinoma

One in which there is an FNA cytology or core biopsy diagnosis of malignancy that correlates with malignant clinical and/or imaging findings.

Positive predictive value of a malignant diagnosis

The number of correctly identified malignancies, that is the number of malignant reports minus the number of false positive reports, expressed as a percentage of the total number reported as malignant.

Preoperative diagnosis of cancer

A malignant result on FNA cytology or core biopsy, which is consistent with suspicious or malignant imaging findings. A malignant result includes DCIS and invasive carcinoma.

Specificity

The number of correctly identified benign lesions, that is the number of benign reports minus the number of false negative reports, expressed as a percentage of the total number of benign lesions sampled.

Triple test

The recommended approach for the investigation of a breast change or symptom. It includes clinical breast examination and medical history, imaging tests (mammography and/or ultrasound) and FNA cytology and/or core biopsy. Also referred to as triple assessment.

Unsatisfactory specimen

A specimen that does not permit a microscopic diagnosis, either because the material present is too distorted or its volume is too scanty. Unsatisfactory is equivalent to the report category 'non-diagnostic/non-representative'.

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