

**MULTI-DISCIPLINARY ASPECTS OF QUALITY ASSURANCE IN THE  
DIAGNOSIS OF BREAST DISEASE  
EUSOMA**

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on behalf of EUSOMA Working Party

**This is a revised version of the original EUSOMA Position paper published in 2001  
(European Journal of Cancer, 2001; 37: 159-172).**

## 1. Introduction

It is four years since the first EUSOMA position paper on this subject (1). During that time its aims and ideals have been widely accepted, namely that training, audit and documented quality measures should become just as routine for breast diagnosis as for breast screening, as they will ultimately affect a greater number of women. The European Parliament has strongly supported this viewpoint following the third edition of the European Guidelines (2), it has requested this fourth edition co-ordinated by EUREF working in conjunction with the European Breast Cancer Network, updated and enhanced by the addition of published EUSOMA documents on diagnosis and breast care. The goal has been a larger and more comprehensive work covering quality of symptomatic as well as screening service provision.

This chapter attempts to lay out in a setting suitable for European usage, those aspects of quality assurance, quality objectives and outcome measures that are required to provide a satisfactory breast diagnostic service. Published guidelines for quality assurance in mammography screening already exist at European level and at a national level in several Member States. This document is intended to enhance and strengthen any such guidelines already used at a local level, not to conflict with them.

Modern diagnosis of breast disease is a multidisciplinary activity requiring trained and experienced professionals using specialised equipment with up to date sampling and other diagnostic techniques. Triple assessment, i.e. clinical examination, imaging, and cytological / histological sampling is still regarded as the gold standard. As far as possible we have tried to avoid screening or treatment issues unless of particular relevance to diagnostic activity. We have also chosen not to attempt to define clinical protocols.

Screening is predominantly a radiological procedure with particular emphasis placed on the optimal balance of sensitivity and specificity. Many abnormalities are impalpable and priority is given to maximising the cancer detection rate while minimising anxiety and reducing the benign biopsy rate by paying sufficient attention to the accuracy of non-operative diagnostic techniques. The radiologist has the role of prime responsibility in screening.

In symptomatic activity the clinician has the role of prime responsibility. Usually, this person is either the referring General Practitioner, or the surgeon or radiologist that the patient is referred on to for further investigations. The clinician may also be regarded as any medical professional who is trained and skilled specifically in clinical examination of the breast. In these circumstances however the role of imaging, interpretation and cytological/histological sampling procedures will still be paramount as supportive diagnostic activities.

Practices are likely to vary across Member States according to healthcare environments and the availability of trained personnel, however these variations must not be allowed to interfere with the achievement of set targets and outcome measures. Any variation to standard procedures in the diagnostic work-up should be tolerated only if documented audit demonstrates satisfactory outcomes and provision of care.

It is strongly recommended that all women with breast symptoms should be referred to a specialist breast unit, the requirements for which have already been laid out by EUSOMA (3), (see chapter 9 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and

diagnosis). However it is important to recognise that in a decentralised healthcare setting many women will not undergo more than basic imaging following a General Practitioner referral, and the benefits of full multidisciplinary assessment will not be available to them, or indeed necessary for many of them. These chapter will therefore attempt to cover all pertinent aspects of basic diagnosis as well as assessment and underline the importance of ensuring that women who do require further assessment are not denied it. In order to ensure this, agreed protocols should be set up between basic breast imaging units and specialist breast assessment units. Throughout this text the terms patients and women are referred to at various points as appropriate. It is recognised that on occasions, male patients will also require the services of a diagnostic breast clinic.

Asymptomatic women do not necessarily require initial clinical examination or other imaging investigation apart from mammography if taking part in a breast screening programme. However it is regarded as good practice that all women with breast symptoms undergo a clinical examination prior to any further investigation requested, and that this be performed by a suitably trained and experienced clinician.

## **2. Training and Quality Assurance**

The key professional personnel involved in breast diagnosis are the surgeon (clinician), radiologist, radiographer, histo/cytopathologist, nurse counsellor and physicist. All such personnel must hold the requisite professional qualifications in their own country and have undergone specific training in the field of diagnosis/diagnostic imaging of the breast. They should regularly participate in Continuing Medical Education and update courses, take part in any existing external quality assessment schemes and possess any necessary Certificate of Competence.

In addition to the chapter on training in the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis, a further document on the training of health professionals in breastcare has been prepared by EUSOMA and will published soon. It is to be hoped that over the next few years there will be a move towards certification/accreditation for all professional staff and units participating in this activity, supported by EUREF and EUSOMA.

A full and comprehensive quality assurance programme must be in place with clearly documented local quality control procedures and quality assurance manuals. As far as the imaging aspects of breast diagnosis are concerned – i.e. radiographic and radiological – these must comply with the technical and professional requirements laid out in chapters 2, 3 and 4 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis

It is essential that there be a nominated person with responsibility for the physico-technical quality control aspects of every unit participating in breast diagnosis, at whatever level. Similarly, each service must have a Clinical Director or one member of the professional team acting as Lead Clinician with responsibility for overall performance and quality of the service, and with the requisite authority to make changes, take equipment out of service, and suspend elements of the programme if necessary, while essential service improvements are carried out.

### 3. Imaging Procedures

All breast units carrying out screening, diagnostic or assessment work must be in possession of local imaging protocols agreed by and made available to all clinic staff and forming part of the local QA manual, which should be based on national or European documents, containing accepted and published values.

Mammography and ultrasound either alone or in combination remain the primary diagnostic imaging methods used for the breast. Protocols should be in place to discourage inappropriate referrals for breast imaging, e.g. breast pain, and to ensure that women with symptoms highly suggestive of breast pathology, e.g. a lump or skin / nipple dimpling or distortion have access to urgent investigation. Women with a family history of breast cancer should be referred to a specialist clinic with access to further genetic counselling should this be considered necessary.

If mammography is required, a two view examination should be performed using the standard lateral oblique and cranio caudal projections. The use of mammography prior to the age of 35 is of limited diagnostic use and carries a higher theoretical risk from ionising radiation. Mammography in this age group should only be used in particular circumstances such as a strong clinical suspicion of malignancy and when specifically authorised by the radiologist in charge. Where clinical findings are sufficiently suspicious, it may be advantageous to carry out oblique mammographic views in this age group to search for radiological signs which may be relatively subtle to demonstrate sonographically, e.g. distortion or microcalcification.

Ultrasound is the initial diagnostic method of choice if breast imaging is required below the age of 35. Other imaging techniques such as magnetic resonance imaging (MRI) of the breast have specific indications and do not form part of the initial diagnostic investigation at present (see section 11). If a woman complains of, or is found to have a discrete mass or other significant clinical sign in her breast which is not demonstrable mammographically, it is essential that she be referred for an ultrasound examination as part of standard triple assessment procedures. This will reduce the possibility of missed malignancy with negative mammography. Even if a clinical mass is demonstrated mammographically, ultrasound examination is still advised in order to further demonstrate imaging characteristics of the mass, or possible tumour extent, multi-focality and axillary node enlargement in cases of malignant disease. In women with a positive finding on breast MRI, but an initially negative ultrasound examination, a focused second look breast ultrasound may be helpful in a substantial number of cases. The primary requirement of ultrasound investigation is to provide an image of good contrast and resolution, and a high level of anatomical representation. Additional ultrasound techniques such as Doppler imaging, blood pool imaging, 3D and 4D analysis, elastography (strain imaging) and panoramic representations may further enhance diagnostic information but have not yet been proven necessary for basic diagnosis.

Mammography is associated with a variable false negative rate in the order of 10% - 20%, but this may be as high as 50% if the image quality is compromised for any reason including the age of the patient and the density of the breast. Assessment of microcalcification is likely to require magnification views, and these should be performed in orthogonal projections, i.e. true lateral and cranio caudal in order to maximise the diagnostic information available. Initial work up of asymmetries, distortion and possible masses will require further views to be performed which may include paddle compression spot views,

although it should be appreciated that the use of paddle compression may prove unhelpful and even misleading in cases where breast cancer presents as subtle asymmetries or an area of increased density.

For many years digital mammography has had an established role for rapid spot-view imaging in stereotactic procedures. There is now increasingly widespread use of full-field digital mammography (FFDM) although clinical comparative and logistical evaluations are underway, the largest being the ACRIN, (DMIST) trial in the United States. The technique is known to have high image quality and is likely to become established due to multiple current advantages such as image manipulation, transmission and data display. On-line computer aided detection is available, and shown to provide advantages under certain conditions. FFDM in the majority of cases obviates the need for analogue microfocus magnification views of microcalcification, as on-screen magnification normally provides sufficient detail in order to base a clinical decision as to whether to proceed to tissue sampling techniques. FFDM also carries potentially significant advantages for technological developments such as tomosynthesis dual energy techniques and 3D reconstruction. As in the reading of film screen mammography, and possibly of even more importance, sufficient care must be given to ensure low incident light levels in the reporting room as the light output of the monitors is considerably less than a conventional x-ray viewing light box.

Women with breast implants should be advised that these may significantly reduce the efficacy of subsequent mammography and that mammographic imaging should be performed in clinics where ultrasound is available as it may frequently be required as an additional imaging technique. Magnetic resonance imaging is now recognised as the method of choice for investigating significant abnormalities in the breast in the presence of implants and for the assessment of possible intracapsular or extracapsular implant rupture.

It is preferable to perform clinical examination prior to any image guided interventional sampling procedure so that subtle clinical signs are not disturbed by haematoma formation. For similar reasons it is preferable to perform any necessary basic imaging procedures such as mammography/ultrasound prior to any clinically guided sampling. If facilities and staffing allow, it may be logistically advantageous to perform sampling of clinically palpable lesions under image guided control in order to have visual confirmation of accuracy.

Communication at all times is an essential part of the process and this must exist between the members of the imaging team e.g. radiographer/radiologist, as well as with the patient and the referring clinician. It is still the case that a number of breast cancers fail to be detected each year due to insufficient attention being paid to the symptomatic details being provided by the patients.

#### **4. Diagnostic Breast Imaging Unit**

In a decentralised healthcare setting there may be multiple clinics or offices present within a geographical area offering mammography and/or ultrasound examination of the breast. Some of these may be operating to significantly lower volume levels than that currently regarded as acceptable by specialist units. There are numerous problems with low volume throughput in breast imaging and a decentralised approach must not be allowed to jeopardise production of examinations having adequate image quality. The highest possible image quality is necessary to maximise diagnostic information and provide suitable levels of sensitivity and specificity. Inadequate quality of equipment, inadequate

processing facilities, under used processing facilities, lack of a quality control programme and poorly trained and experienced radiological or radiographic staff will adversely affect optimum performance and interpretation of breast images. Minimum standards must be set in place so that this is not allowed to happen.

This section will describe certain requirements to be provided by any unit offering diagnostic imaging services. This should be regarded as the most basic level of quality needed for adequate service provision. The next section will describe requirements for a fuller and more comprehensive breast assessment unit.

The end point of the Diagnostic Imaging Unit is to correctly identify and classify imaging characteristics, and should not include further formal assessment with tissue/cytology sampling, with the exception of simple cyst aspiration. Further investigations should be performed at or in conjunction with a specialist breast assessment unit as laid out in the next section. This will ensure that cellular or tissue samples are analysed by a trained and recognised pathologist adhering to pathology quality assurance requirements. Feedback from the result of any such further investigations should be made available to the diagnostic unit for completion of the quality process.

#### 4.1 Mammography Equipment

Dedicated mammographic and film processing equipment must be available with the facility to produce low dose with high contrast and spatial resolution examinations. An adequately high optical density is required for satisfactory image interpretation due to the proven relationship between optical density and small cancer detection rates (4). Equipment should be up to date, of recognised manufacturer, suitable for its purpose, and subject to regular maintenance and quality control checks as laid out in chapter 2 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis. For example it is not suitable to use a mammography machine without a foot operated compression system. All equipment in the unit must be subject to regular radiographic quality control checks and performance tests by a medical physicist suitably trained and experienced in mammography. Consistent breaching of quality control levels should lead to suspension of the equipment from use by the nominated person charged with the overall responsibility for quality assurance of the unit.

The following are essential targets to be achieved, fuller requirements are laid out in chapter 2 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis.

##### 4.1.1 Targets

###### Analogue targets

High contrast/spatial resolution > 12lp/mm

Optical density 1.4 – 1.9

Mean glandular dose for standard breast per film <2.5mGy

Daily processor control maintenance 100%

###### Digital targets

Contrast – to – noise ratio sufficiently high

Mean glandular dose for standard breast < 2.5mGy

Weekly homogeneity check

Regular monitor check

## 4.2 Ultrasound equipment

Breast ultrasound should only be carried out by members of medical staff specifically trained and experienced in this procedure. It should not be carried out by General Practitioners, gynaecologists, surgeons, radiologists, or radiographers who have not undergone such specific training and who do not participate in regular performance or audit of this activity. It is regarded as best practice that whenever possible the ultrasound examination should be carried out by a trained and specialist radiologist. The operating frequency of the ultrasound machine must be at least 7.5 MHz, and should preferably operate at 10 MHz or higher. Suitable recording facilities for sonographic images must be available and used to record all significant findings with images clearly annotated to show side, size, depth and position of the lesion.

## 4.3 Radiographic staff

Mammograms should be performed by suitably trained and experienced radiographic staff fulfilling all necessary training and working professional requirements and holding any relevant Certificate of Competence as previously described. In Units where no mammographically certificated radiographer is employed, the member of staff performing the mammograms must have undergone full training in the radiographic aspects of mammography, comply with all requirements as laid down for radiographic staff, including any necessary external quality assessment schemes and update courses and take the lead in regular radiographic quality control procedures. For the purpose of this document such a person will be referred to as the radiographer.

It is the radiographer's responsibility within the team to produce an optimum image with regard to positioning and technical aspects and in a manner acceptable to women. All obvious clinical abnormalities including the presence of a palpable lump felt by the radiographer during mammographic positioning, obvious distortion, skin abrasions and other significant cutaneous abnormalities should be recorded and this information made available for the radiologist at the time of film reading. The radiographer must inform the woman about the procedure, how it is to be performed, how she will get her result, and in what time scale. The radiographer in charge of the unit is responsible for ensuring that a regular quality control programme is carried out and is responsible for reporting breaches of quality to the radiologist in charge.

In order to limit unnecessary exposure to ionising radiation and the creation of unnecessary anxiety, the technical retake level where repeat mammograms are necessary for positioning or technical faults must be kept to an absolute minimum, preferably below 1% but no more than 3%. All such retakes should be documented for audit purposes. Positioning performance requirements for adequate mammographic examinations are laid out in chapter 3 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis and must be adhered to. The minimum requirements for positioning of the standard lateral oblique projection are that the pectoral muscle must be displayed down to nipple level, the inframammary fold should be visible and the nipple should be in profile. Skin folds, movement and other artefacts should be absent. An external quality assessment scheme should be in place so that peer review of adequate positioning is performed and satisfactory results obtained in at least 97% of images. All films must be appropriately named, dated and marked correctly for side.

In order to maintain the skills and expertise required to carry out optimum mammography and be a useful member of the multidisciplinary team, the radiographer must be involved in performing at least 20 mammographic studies per week, preferably more.

### 4.3.1 Targets

Technical repeat rate minimum level <3% - expected <1%

More than 97% of women will have an acceptable examination according to the positioning and exposure criteria given.

100% of women will be informed by the radiographer of the method and timescale for receiving her results.

Minimum 20 mammographic studies per week to be performed by each radiographer.

#### 4.3.2 Basic quality control

The following is a basic summary of routine quality control tests to be performed by the radiographer, fuller details are available in chapter 2 and 3 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis

##### Daily Analogue Tests

Mechanical, safety and function checks

Standard density consistency tests

Reproducibility of mAs values

Sensitometry

Clean x-ray cross over rollers

Screen inspection and cleaning

Cassette inspection for wear and tear

##### Daily Digital Tests

Monitor check

##### Weekly Analogue Tests

Automatic exposure control check

Image quality

##### Weekly Digital Tests

Homogeneity (image quality) check

3-6 monthly tests (performed by radiographer or physicist)

Sensitivity and radiation absorption of cassettes

Film screen contact

Calibration of densitometer

#### 4.4 Radiological staff

The radiologist must be specifically trained and experienced in breast imaging. This should include a knowledge of technical requirements of mammography equipment, processing, exposure factors and all those other factors of importance that are necessary in the production of good image quality. If possible, radiologists involved in symptomatic activity should also participate in local screening programmes both for the reading of screening films and the assessment of screen-detected abnormalities.

A dedicated mammographic film viewer must be available and films should be read in a suitable room with control of background lighting. This is even more crucial for the reading of digital examinations on soft copy due to the lower light output of monitors compared to light boxes for analogue films. It is the responsibility of the radiologist to ensure that the mammograms are of adequate diagnostic standard, particularly with regard to positioning and film density. Where films are inadequate, they

must be repeated. The radiologist must also ensure that feedback is provided to the radiographer on image quality. The report provided by the radiologist must state quite clearly the nature of any abnormality present, its side, site, size, description and extent. The radiologist should make clear the implication of the imaging findings and should recommend the most suitable necessary further investigation or sampling procedure.

If a significant finding is present, carrying a high risk of malignancy, it is the responsibility of the reporting radiologist to ensure that the woman is aware that further investigation or management will be required. For this reason it is recommended that wherever possible the radiologist should be available within the unit during the mammographic examination so that any necessary procedure such as an ultrasound can be performed while the woman is still present. This will avoid the need for a separate return visit, and allow the radiologist to pass on any necessary information to the woman, with due regard paid to the importance of not creating unnecessary anxiety. Under such circumstances it is obviously beneficial if nurse counselling is available at that time.

#### 4.5 Basic Requirements of a Diagnostic Mammography Unit

Ultimately it is hoped that all clinics offering breast diagnostic services will be subject to accreditation/certification procedures. Until that time the following criteria are proposed in line with the Certification Protocols (chapter 11 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis).

The following basic criteria will be required from a Diagnostic Mammography Unit, which should:

- A. Perform at least 1,000 mammograms per year.
- B. Have dedicated equipment specifically designed for application in diagnostic mammography and ultrasound e.g. mammography system with magnification ability and dedicated processing, and be able to provide adequate viewing conditions for mammograms.
- C. Comply with the physico-technical protocol in chapter 2 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis.
- D. The radiographer, technologist or other member of staff performing the mammographic examination must have had at least 40 hours of training specific to the radiographic aspects of mammography and regularly participate in External Quality Assessment Schemes where available and radiographic update courses. This person must also take the lead in the radiographic aspects of quality control.
- E. Employ a trained radiologist, i.e. a person who has had at least 60 hours of training specific to mammography and who in volume requirements reads at least 500 mammograms per year.
- F. Keep a record of mammogram results and monitor numbers of women referred for further assessment.
- G. Provide feedback of further assessment outcomes to the unit radiologists.

Volume requirements as stated in this section and the following section are regarded as the absolute minimum required to allow the production of adequate diagnostic quality images. Greater number may not guarantee higher quality, but are more likely to be associated with a significantly higher level of professional skill and physico-technical excellence. For this reason, higher volume throughputs are strongly recommended, there being scientific data demonstrating improved performance of radiologists' reading in excess of 2000 mammograms per annum (5).

In all cases a mammogram refers to a full set of mammograms performed on a woman, and should not under any circumstances for the purposes of numerical advantage be counted in terms of individual mammographic exposures.

## **5. Breast Assessment Unit**

While basic diagnostic imaging in the form of mammography/ultrasound may be sufficient for many women, those with significant symptoms, clinical findings, or mammographic findings need further workup which will require more specialist equipment and staff. A protocol should be in place with referring General Practitioners so that women with a clinical finding carrying a significant risk of malignancy should be referred directly for assessment at a specialist breast unit. Such clinical findings will include a discrete new palpable mass, nipple discharge – particularly if single duct and unilateral, nipple retraction, nipple eczema, skin distortion such as tethering, dimpling or a change in breast shape, palpable axillary lymphadenopathy or inflammatory change. In this setting the woman will undergo a process of triple assessment i.e. clinical, imaging and cytological/histological investigation, performed by a specialist multidisciplinary team with access to more sophisticated imaging equipment and non-operative diagnostic techniques.

Breast assessment units which are not functioning as part of a specialist breast unit must have written protocols available for triple assessment techniques. Additional mammographic techniques must include the ability to perform paddle compression and microfocus magnification views. Image guided sampling techniques must be available with the ability to perform these either under ultrasound or stereotactic control. If abnormalities are visible sonographically, it is more suitable for sampling to be performed under ultrasound control. It is generally advisable for image guided sampling to be performed for any solid sonographically detected lesion. If required, microcalcification may occasionally be sampled under ultrasound control, but more usually stereotactic procedures will be required. For audit and documentation purposes, any image-guided sampling procedure should have at least one recorded image showing accuracy of needle placement.

Sampling techniques may include fine needle aspiration cytology, core biopsy or vacuum-assisted biopsy techniques, the use of which will depend upon the local radiological and cytological expertise, and audit of results obtained. In expert hands, FNAC still has a role and can allow immediate cytology reporting or checking for adequacy of cellularity.

Core biopsy can provide increased sensitivity and specificity compared to fine needle aspiration cytology. Core biopsy is preferred for lesions of architectural distortion and microcalcifications, and may also allow definitive diagnosis of a benign lesion which will then not require surgical excision

biopsy. If core biopsy is performed for microcalcification it is essential that specimen radiography of the cores be obtained to demonstrate the presence of calcification.

Sampling techniques should be carried out with due regard to the imaging or clinical modality carrying the most suspicious features. Where there is a possibility of discordant clinical and imaging findings with regard to any lesion, it is advisable to carry out sampling under both imaging and clinical guidance. Very occasionally there may remain a significant discordance between suspicious radiological features and benign sampling where no reasonable pathological correlation can be made, following case discussion between the radiologist and pathologist. Under these circumstances, open surgical excision is advisable.

It is regarded as good practice that lesions which are predominantly architectural distortion should be subject to excision biopsy following pre-operative diagnostic workup due to a significant risk of associated malignancy which may not be demonstrated even under ideal sampling conditions. Recent work however has shown that it may be safe to leave radial scars in place providing sufficient material has been obtained – at least 12 core samples (6). Also lesions that are proven to contain atypical ductal hyperplasia should be subject to excision due to the risk of associated malignancy.

Where resources allow, vacuum-assisted biopsy techniques offer significant advantages for biopsy in a proportion of patients in achieving definitive pre-operative diagnosis and reducing the need for surgical intervention. This technique can provide greater tissue volume for histological analysis with less risk of epithelial displacement or underestimation of disease such as DCIS or invasive tumours. It can also be used for excision of benign lesions. Where resources are scarce, it should be borne in mind that the disposable elements of FNAC are approximately 1 Euro compared to core biopsy, 20 Euros, and vacuum-assisted biopsy technique, 300 Euros. Costs of time and number of staff involved in performance of the procedure, and non-disposable equipment costs must also be considered and balanced with the true benefit of the procedure in relation to subsequent patient management.

Radiographic, radiological and histo/cytopathological staff must be fully conversant with the accurate carrying out and interpretation of all these procedures. Specific standards of performance in sampling procedures must be adhered to, particularly with regard to insufficiency of results and non-operative diagnosis (see Targets).

### 5.1 Diagnostic classification

A simple five-points classification system should be used as described below to convey an overall impression (which is auditable) in addition to the normal descriptive methods.

#### Radiology

R1 Normal/benign

R2 A lesion having benign characteristics

R3 An abnormality present of indeterminate significance

R4 Features suspicious of malignancy

R5 Malignant features

While this system is sufficient for most working purposes, if desired, use can be made of the ACR BIRADS system which is a more complex but precise classification in terms of percentage likelihood (7)

#### Ultrasound

U1 Normal/benign

- U2 A lesion having benign characteristics
- U3 An abnormality present of indeterminate significance
- U4 Features suspicious of malignancy
- U5 Malignant features

Fine Needle Aspiration Cytology

- C1 Inadequate for diagnosis
- C2 Benign epithelial cells
- C3 Atypia probably benign
- C4 Suspicious of malignancy
- C5 Malignant

Core Biopsy/Histology

- B1 Unsatisfactory/Normal breast tissue
- B2 Benign
- B3 Benign but of uncertain malignant potential
- B4 Suspicious of malignancy
- B5 Malignant

A negative or benign clinical examination must not be allowed to downgrade the importance of suspicious imaging or cyto/histological findings unless the radiologist or pathologist has been fully consulted.

5.2 Targets

% of image guided FNAC procedures with an insufficient result

Minimum standard <25%    Expected <15%

% of image guided FNAC procedures from lesions subsequently proven to be malignant having an insufficient result

Minimum standard <10%    Expected <5%

% of women with breast cancer having a non-operative diagnosis of malignancy (FNAC/CB reported as definitely malignant)

Minimum standard >70%    Expected >90%

5.3 Cytology/histology quality assurance

Suggested thresholds for FNAC performance

	Minimum	Preferred
Absolute sensitivity	>60%	>70%
Complete sensitivity	>80%	>90%
Specificity	>55%	>65%
Positive predictive value C5	>98%	>99%
False negative rate	<6%	<4%
False positive rate	<1%	<0.5%

#### Suggested thresholds for core biopsy performance

	Minimum	Preferred
Absolute sensitivity	>70%	>80%
Complete sensitivity	>80%	>90%
Specificity	>75%	>85%
Positive predictive value C5	>99%	>99.5%
False positive rate	<0.5%	<0.1%
Miss rate (B1+B2 from cancer)	<15%	<10%

#### 5.4 Audit

For audit purposes it is proposed that the standard assessment data set be used as recommended in the QT audit document approved by EUSOMA and available on the following sites: [www.eusoma.org](http://www.eusoma.org) and [www.cpo.it/qt](http://www.cpo.it/qt)

#### 5.5 Cytology/core biopsy reporting standards

Standard reporting forms should be used. These are usually individual to each member state, but otherwise reference can be made to the sites above

#### 5.6 Basic requirements for a Breast Assessment Unit

In addition to the standards achieved by the Diagnostic Mammography Unit, a centralised system of diagnostic assessment for mammographically or clinically detected lesions must be available. There should be a full range of assessment facilities provided in order to allow complete and adequate work up by the Unit without necessarily having to refer the woman on for further investigation elsewhere.

The Breast Assessment Unit should:

- A. Perform at least 2,000 mammograms a year.
- B. Be able to perform physical examinations and ultrasound examinations as well as the full range of radiographic procedures. Provide cytological examination and/or core biopsy sampling under radiological or sonographic guidance.
- C. Employ a trained radiologist reading at least 1,000 mammograms a year.
- D. Have organised and specialist cytological and histopathological support services.
- E. Participate in multidisciplinary communication and review meetings with others responsible for diagnostic and treatment services.
- F. Monitor data and feedback of results.
- G. Keep a formal record of the assessment process and outcomes.

The requirements placed upon a breast assessment centre as part of a specialist breast unit may be even more rigorous than these (see chapter 9 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis) .

## **6. Multidisciplinary Activity**

All breast units engaged in diagnostic or therapeutic surgical excision biopsy must ensure the formation of proper multidisciplinary teamwork involving the following personnel: Radiographer, radiologist, histo/cytopathologist, surgeon nurse counsellor. If treatment is involved, the team should include a radiotherapist/medical oncologist. In view of the importance of the management decisions taken in such meetings, it is crucial that the meetings is attended by senior professionals and that these issues are not delegated to junior members of the team.

Before a woman is considered for surgical excision biopsy her case and results should have been discussed in the setting of a full multidisciplinary meeting. By so doing the surgeon will be best appraised of the likelihood of malignancy, the extent of abnormality on imaging and any discordant results which may have been obtained upon review of the case, which might lead to an alteration of surgical planning or management. Similarly all biopsy results should be discussed in a multidisciplinary audit setting to establish the nature of disease, its extent, completeness of excision and the appropriateness of the histology compared to the pre-operative diagnosis. Unexpected results should be discussed in this setting to establish their veracity, to confirm that the correct lesion has been excised and to provide a source of learning and experience.

The results of discussions that have taken place during formal multi-disciplinary meetings should be recorded and documented for audit purposes.

## **7. Staging and Follow-up**

Bone scanning, liver ultrasonography and chest radiography are commonly used in patients with newly diagnosed breast cancer as part of baseline staging. However in the absence of symptomatic disease, this routine diagnostic work-up may not be cost-effective, or justified. Multiple studies of this strategy have shown early detection of asymptomatic metastases, but such early detection does not affect quality of life or survival. Most recurrences are detected in cases with an advanced stage at diagnosis. These findings indicate that a complete diagnostic work-up to detect metastases is unnecessary in the majority of patients with newly diagnosed breast cancer, whereas it may be indicated for patients with advanced disease (stage III-IV).

Imaging should be used to diagnose women with symptoms suggestive of metastatic disease. Women with pain suggestive of bone metastases should have plain films initially. If such films are normal and symptoms persist, bone scintigraphy and/or MRI can be used. MRI can be very useful in differentiating osteoporotic vertebral collapse from metastases. Solitary bone lesions in the absence of visceral metastases will often require bone biopsy to confirm metastatic disease, especially in patients with a primary tumour having good prognostic features. Symptoms suggestive of lung metastases should be

investigated using a chest x-ray initially and CT if required. Abnormal liver function and/or abdominal pain can be investigated using ultrasound or CT.

Patients with confirmed metastases at one site will require radiological staging of their disease for two reasons. Firstly, to assess the burden and sites of metastases as this will affect both prognosis and therapeutic options. Secondly, assessable lesions need to be identified to allow assessment of response to systemic therapy. This will allow cessation of expensive and toxic therapies which are not working and make possible timely institution of second line therapies.

Periodic diagnostic assessment, currently referred to as follow-up, is a common practice in breast cancer patients after the completion of primary treatment.

Follow-up may have different aims:

- Early detection and early treatment of recurrent disease, either local or metastatic. Recurrences are concentrated in the first three years and then having a stable 1-2% yearly incidence. Breast cancer is a systemic chronic disease: the risk of dying from it remains higher as compared to healthy subjects up to 30 years after primary treatment. About 50% will recur during their lifetime.
- surveillance of the contralateral breast with a 5 times higher risk of developing a metachronous cancer which may have an independent impact on prognosis
- improvement of quality of life by reassuring the patient
- to monitor the status of the disease
- to monitor and prevent negative side effects of treatment (e.g. endometrial cancer in Tamoxifen users, or osteoporosis in premenopausal women undergoing hormone deprivation)

Each of these aims has been the object of discussion over time, based on several conflicting experiences.

No definitive evidence is available thus far that early detection and treatment of recurrence may have a favourable impact on prognosis. It is well known that earlier detection is associated with less extensive recurrence and that limited recurrent tumour burden is associated with prolonged survival, but this is not sufficient to demonstrate a real benefit as improved survival might be simply due to diagnostic anticipation (lead time) with no real postponement of death. In a Randomised Controlled Trial published in 1994 (8), intensive follow up [Chest X ray, liver echography, radionuclide bone scan, mammography(MX)and physical examinations (PE)every 6 or 12 months] showed no effect on mortality at 5 and 10 years, when compared with minimal follow-up( PE and MX only ).

The evidence of long term cure of limited as compared to extensive local recurrences suggest a possible favourable prognostic impact of early detection of these events, particularly as regards recurrences in the axilla and in the surgical scar or conserved breast. Such events are likely to become more frequent with the adoption of conservative therapeutic options as tumorectomy and sentinel node technique. Although no definitive evidence of a favourable prognostic impact of early detection of local recurrences is available, the presumed benefit and the fact that early detection in the asymptomatic

phase is achieved by palpation and mammography, which are included in a 'minimalist' follow-up approach, justifies such a current practice.

Early detection of primary breast cancer may reduce breast cancer mortality, as shown by several controlled studies of screening by mammography. There is no reason why this should not occur also for contralateral metachronous breast cancer, although the magnitude of such an impact is certainly reduced for the concurrent prognostic effect of first breast cancer. A recent report has shown a higher risk of breast cancer death for subjects developing a symptomatic, rather than an asymptomatic metachronous contralateral breast cancer detected by periodic mammography (9). Periodic mammography (often with a higher frequency as compared to screening of healthy subjects) is currently performed even in a 'minimalist' follow-up approach.

Several circulating markers have been tested to detect breast cancer, and generally have been abandoned for routine testing. Two arguments argue against the use of markers in clinical practice. First the imperfect sensitivity and specificity, second the current lack of curative therapy for metastatic breast cancer.

At the moment most of the International Societies do not recommend the use of routine tumour markers in the surveillance of breast cancer as there is good evidence not to include blood work (as well as diagnostic imaging) as part of screening for distant disease

In conclusion follow-up of breast cancer patients is standard practice all over the world. The investigation of distant metastases aimed at early detection and treatment seem to have no prognostic impact, for the present state of art of diagnosis and treatment, but minimalist follow-up, based on periodic physical examination and mammography (conserved and/or contralateral breast), seems a reasonable option as its possible advantages in terms of prognosis and psychological impact have never been denied.

New prospective studies of follow-up efficacy should concentrate on new protocols suggesting higher sensitivity and/or specific subgroups promising higher therapeutic and cost-effectiveness potential.

## **8. Surgical Aspects**

The surgeon is a member of the multidisciplinary team and should participate in regular multidisciplinary review for case management and audit purposes. The surgeon should be fully involved in the assessment of women and should always see and examine the patient before accepting her for surgery.

It should be agreed surgical policy that mammography is carried out prior to breast surgery providing the woman is in an appropriate age group. Firstly as a matter of good practice to demonstrate the nature and extent of any disease that is identifiable, secondly to ensure that full imaging information is available for interval cancer review should the women have previously attended a breast screening programme.

The surgeon should be discouraged from cutting specimens open after removal in theatre before sending them to pathology. All specimens should be marked and orientated according to recognised local protocols. The surgeon should ensure completeness of excision, which may be assisted by the use of two plane specimen radiography. At operation, the use of frozen sectioning is generally

inappropriate, particularly in the assessment of clinically impalpable lesions. It may occasionally be justified to enable a firm diagnosis of invasive malignancy to be made in order to allow definitive surgery to be carried out in one operative procedure. In general terms surgeons should adhere to the principles laid out in chapter 7, and in particular the monitoring of surgical outcome measures as defined in chapter 8 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis. The surgeon should ensure that all data necessary for subsequent patient management and audit should be recorded including the size of any tumour, its grade, type, lymph node status and biological characterisation. A suitably agreed minimum data set reporting form should be used.

### 8.1 Pre-operative localisation

Lesions that are either impalpable or difficult to locate with certainty on clinical examination will require some form of pre-operative localisation marking procedure provided by the radiologist .

In order to limit the number of unnecessary biopsy procedures performed, it is recommended that the ratio of benign to malignant surgical excision biopsies performed for diagnostic purposes should not exceed 0.5:1. Already diagnosed benign lesions and lesions removed due to patient choice are excluded. For cosmetic reasons it is important to minimise the extent of benign biopsy for impalpable lesions, and at present the most suitable discriminatory factor used is the weight of the specimen. Over 90% of diagnostic biopsies for impalpable lesions which subsequently prove benign should weigh less than 30 grams.

When breast cancer has been diagnosed and the patient agrees to conservative surgery, localisation procedures are mandatory. The target is the full excision of the tumour with uniform margins. In the past, the standard approach to tumour localisation has been hook wire or dye localisation. An ultrasound or mammographic - guided hook wire is inserted in the breast and placed by the radiologist within one centimetre of the lesion, if possible in at least 90% of cases, or a second wire should be inserted. In cases of segmental microcalcification it may be advantageous for the radiologist to bracket the extent of the calcification with guide wires to allow complete surgical excision. The surgeon must be provided with a full and accurate description of the procedure performed and a precise report of the relative placement of the wire compared to the lesion. Relevant images correctly marked should also be provided.

The hook-wire method is particularly useful for deep lesions mainly in dense breasts where it can be anchored more securely. The disadvantage is that this procedure must be carried out shortly before surgery and it requires accurate planning. The hook wire may move from its original position, this happens more frequently in fatty breasts. For dye localisation, it is important to use a sterile charcoal suspension that does not diffuse into the surrounding tissue and that stays in for a long time. The injection of the charcoal is guided by mammographic, stereotactic or ultrasound examination. The trace goes from the lesion to the skin where a small spot is evident.

The indications for this method are the same as for the hook-wire but the advantage is that it can be carried out at the time of cytological or micro histological pre-operative diagnosis.

A more recent method for localisation of non-palpable tumours is called ROLL (radio-guided occult lesion localisation) (10). Before the operation, the patient is injected with 0.2 - 0.3 ml of 99 mTc - labelled colloid particles of human serum albumin into the centre of the suspicious lesion under stereotactic or ultrasound control. The excision biopsy is performed using a gamma detecting probe. The site of the lesion shows the maximum radioactivity. Margins of resection are defined where radioactivity falls sharply. After excision, the probe is used to check the resection

bed. ROLL is particularly recommended in micro calcification clusters, in parenchymal distortion and in single opacities. A technique of intra-operative ultrasound guided excision of non-palpable breast cancer is also feasible for patients with ultrasound detectable lesions, with results that are comparable to those reported with other methods.

When the lesion is visible on x-ray, specimen radiographs must be available in, or in very close proximity to the operating theatre so that confirmation of excision of the lesion can be confirmed without delay and prior to skin closure. Surgical clips should be used for orientation. Successful excision of impalpable lesions is therefore a combination of surgical as well as radiological skill and the proportion of impalpable lesions successfully excised at the first operation and not requiring a second operation should be in excess of 90%. Specimen radiographs must also be made available to the pathology department. It is accepted that the only true reflection of excision adequacy is the subsequent rate of local recurrence.

## 8.2 Targets

Proportion of wires placed within 1cm of an impalpable lesion prior to excision

Minimum Standard >90%

Proportion of impalpable lesions successfully excised without recourse to second operation

Minimum Standard >90%

Proportion of benign diagnostic biopsies on impalpable lesions weighing less than 30 grams

Minimum Standard >90%

The rate of benign to malignant operations performed for diagnostic biopsy purposes

Minimum Standard 0.5:1

No frozen section performed if tumour diameter <10mm

Minimum Standard 95%

## 9. Anxiety and Delays

Delays at any stage of the diagnostic process may result in anxiety for the woman, which sometimes may be considerable. Targets should be set in terms of working days (w.d.) at every stage where delay may arise.

Delay between mammography and result

Minimum standard - <5 w.d.

Delay between result of imaging and offered assessment

Minimum standard - <5 w.d.

Delay between assessment and issuing of results

Minimum standard - <5 w.d.

Delay between decision to operate and date offered for surgery

Minimum standard - <15 w.d. Ideally <10 w.d.

95% of women should receive full and adequate assessment in three appointments or less.

90% of women with symptoms and signs strongly suggesting the presence of breast cancer should be seen within two weeks of referral, and agreed protocols should be in place to facilitate this.

Unnecessary distress may be caused not only by delays as listed above but also by failure of efficient communication between the diagnostic team and the woman. Failure to reach a definitive diagnosis due to imprecise methods of assessment also results in anxiety.

If possible the radiologist should be present in the clinic at the time when a woman has her mammogram so that any necessary further investigation e.g. ultrasound examination, can be performed without delay. It is also important that full verbal information on the status of her investigations and diagnosis be given to the woman at suitably relevant stages throughout the diagnostic process. As far as possible the woman should be informed of the result of her examination before she leaves the clinic and of the need for any necessary further investigation to be performed.

The failure of the assessment process to make a definitive diagnosis of either a benign or a malignant condition is an undesirable outcome of assessment and further increases anxiety. For this reason the use of early recall for a repeat examination at a time shorter than that normally specified for a routine follow up is to be avoided. Women must be informed of when to expect results and should be provided with written information at appropriate stages in the diagnostic procedure. However women should not be informed by letter or telephone of the likelihood of malignancy being present. Such information should be given verbally to her in the presence of a nurse counsellor.

#### 9.1 Rapid diagnostic / one stop clinics

There is considerable advantage to the formation of rapid diagnostic clinics, set up in breast units, where the diagnostic team may work together in a multidisciplinary setting. Women may receive a diagnosis and management plan in the quickest time possible, either during the same clinic, or having all necessary investigations at the same time and returning for results within 24 – 48 hours. Complex investigations such as MRI, if required, may take longer to organise. The main advantages of this system are to reduce anxiety, and to provide a certain level of skill and teamwork not otherwise available. For this reason as previously recommended all women with discrete masses or significant signs or symptoms must be referred directly to a specialist breast unit, and not to a basic diagnostic unit.

## **10. Pathology QA Aspects**

Accurate pathological diagnoses and the provision of prognostically relevant information are essential to ensure proper patient management, programme monitoring and evaluation. Each Specialist Breast Unit including a Diagnostic Breast Assessment Unit should have access to high quality pathology services provided by pathologists with special expertise in breast pathology.

Pathologists providing a breast histopathology and/or cytopathology service should have had specialist training (see Chapter 10, Guidelines for Training in the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis) and participate in a continuing educational

programme. They should follow recommended reporting guidelines and diagnostic protocols and should participate in relevant External Quality Assessment schemes.

The pathologist is a key member of the specialist multidisciplinary team and has a primary role in the pre- and postoperative conferences. Patient management is largely based on the pathological findings. They should be sufficiently detailed and accurate.

The pathologist should have a general knowledge of:

- The principles of breast cancer treatment: surgery, radiotherapy and medical treatment
- The principles of imaging of breast lesions,
- The basic epidemiological aspects of breast cancer

The pathologist should have special expertise in:

- The classification of malignant non-invasive and invasive lesions, and the assessment of relevant immuno-histochemical tests e.g. hormone receptor- and HER2-status,
- The radiological and pathological correlation of benign and malignant lesions,
- The optimal handling of surgical biopsy specimens, the use of specimen radiography and the assessment of the surgical margins,
- The interpretation of needle core biopsy and fine needle aspiration cytology,
- The interpretation of sentinel node biopsy samples.

Specialist Breast Units and Diagnostic Breast Assessment Units deal with patients having palpable as well as non-palpable breast lesions. Requirements for histopathological assessment, reporting protocols and quality assurance for both types of lesions are practically the same, and are laid out in chapter 6 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis.

All pathology laboratories should be accredited according to national standards.

## **11. The Place of Magnetic Resonance Imaging in Breast Diagnosis**

As previously stated MRI is not yet part of the initial diagnostic workup. The full role and place of MRI in breast diagnosis is still being evaluated, however the procedure is becoming more established and widely used. It already has an established role in the evaluation of breast implants and in the differentiation of recurrent disease from post surgical scarring, where it has a very high negative predictive value. There is however no evidence at present for its usefulness or cost effectiveness as routine follow-up after breast cancer surgery.

MRI is of proven value in helping to establish the degree of disease present where malignancy is already established or highly likely in dense breasts or tumours having a likelihood of multi-focality, multicentricity or bilaterality. It has also been shown to have a high sensitivity in the detection of malignancy in younger women of high risk groups. MRI is of value in assessing the extent of residual disease following induction chemotherapy prior to surgical treatment. Other indications may include looking for the site of an occult primary tumour, or establishing whether a residual tumour is present in the breast following an apparent failure to surgically excise a tumour. The assessment of axillary lymph node recurrence, also clinical or mammographic abnormalities difficult to assess by conventional means are other potential uses.

It is recommended that MRI of the breast is best carried out in units with sufficient experience, having the necessary equipment and expertise to proceed to MR guided biopsy for lesions that are occult on conventional imaging following second look ultrasound.

## **12. Sentinel Lymph Node Biopsy Procedures**

Sentinel lymph node biopsy has become an established technique, with sensitivity in excess of 90%. The technique can be used to allow avoidance of axillary clearance and possible associated morbidity in a number of women. Pre-operative axillary ultrasound may detect abnormal lymph nodes which can further be investigated by ultrasound-guided FNAC. If this confirms involvement, the surgeon can immediately proceed to an axillary dissection. Identification can be made using an injection of a blue dye or radioisotope, either alone or in combination, which improves the identification rate. The technique requires close co-operation between the surgeon, radiologist, nuclear physicist and pathologist.

The European Working Group for Breast Screening Pathology has described the formulation of guidelines for this procedure (11). Further reference should be made to the pathology and surgery sections in chapters 6 and 7 of the 4<sup>th</sup> edition of the European guidelines for quality assurance in breast cancer screening and diagnosis.

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