Health & Consumer Protection
Directorate-General

European guidelines for quality assurance in breast cancer screening and diagnosis

Fourth Edition

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Jan H.C.L. Hendriks | 1941-2004 |

This edition is dedicated to the memory of our colleague and friend Jan Hendriks who pioneered the quality assurance of breast radiology in The Netherlands and throughout Europe

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Preface

Markos Kyprianou*

The completion of the fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis exemplifies the unique role the European Union can play in cooperation with national governments, professional organisations and civil society to maintain and improve the health of Europe's citizens.

Breast cancer is the most frequent cancer and accounts for the largest number of cancer-related deaths in women in Europe. Due to demographic trends, significantly more women will be confronted with this disease in the future. Systematic screening of the female population based on mammography offers the perspective of saving many lives while reducing the negative side-effects of treatment by detecting cancer at earlier stages, when it is more responsive to less aggressive treatment.

These benefits can only be achieved, however, if the quality of services offered to women is optimal – not only with regard to the screening examination, but also the further diagnostic procedures, and the treatment of women for whom the screening examination yields abnormal results. Quality assurance of population-based breast screening programmes is therefore a challenging and complex management endeavour encompassing the entire screening process. This is only one of the key lessons learned in the European Breast Cancer Network in which scientists, clinicians and paramedical staff as well as advocates, health care planners and administrators across Europe have shared experiences. By working together to develop and implement comprehensive guidelines, women throughout the Union will receive the same high level services for breast screening.

The financial support of the European Union for this multidisciplinary, pan-European forum has not only helped to establish Europe as the world leader in implementing population-based breast cancer screening programmes. It has also helped to reveal that implementation of high quality standards in regional and national population-based screening programmes naturally leads to further innovation and improvement in the quality of breast services provided outside of screening programmes. The potential benefit to women of extending the improvements in quality assurance of screening to the full range of breast cancer care is enormous, because many women seek medical assistance for breast problems outside of screening programmes. The editors and contributors to this edition are therefore to be applauded for extending the scope of the guidelines so as to include quality assurance of multidisciplinary diagnosis of breast cancer, standards for specialist breast units and a certification protocol for diagnostic and screening services.

This Publication of the fourth edition of the guidelines by the European Union will ensure that any interested organisation, programme or authority in the Member States can obtain the recommended standards and procedures and appoint appropriate persons, organisations and institutions for the implementation of those.

Let me finally thank the editors and contributors for their efforts in compiling this volume which I am confident will be useful to guide work on breast cancer screening and diagnosis for the years to come.

Brussels, January 2006

* European Commissioner for Health and Consumer Protection

Preface

Maurice Tubiana*

It is a great honour for me to have been asked to write a preface to this fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis. My purpose will be to put them into perspective. At their meeting in Milan in June 1985, the heads of state of the Member States of the European Community (EC) decided to launch a European action against cancer. This decision was taken within the framework of the so-called 'Citizen' programme, the aim of which was to illustrate the practical advantages that a European cooperation could bring to the citizens of the Member States, in particular regarding health. Each of the 12 Member States appointed an expert in oncology, or in public health, in order to constitute the Committee of Cancer Experts. Sweden, which was not yet a member of the European Union (EU), was invited as an observer and also appointed an expert. The committee met for the first time in Brussels in November 1985, where the objectives of the action programme were discussed.

From the outset, reduction in the number of cancer deaths was the primary purpose of the European action. A reduction of 15% in the number of cancer deaths that would have occurred in the absence of such action appeared to be a difficult but realistic goal and was adopted by the committee. In fact, the Europe against Cancer programme achieved a reduction of 9% from 1985 to 2000 a result which is still appreciable. To move forward, the programme had to coordinate the efforts of various health professions as well as, political decision makers, governmental offices, and nongovernmental organisations in a common drive to achieve this goal. A further ambition was to show that actions on a European scale could enhance national strategies against cancer in each of the Member States.

It appeared immediately that prevention and screening were the two main areas in which a European action could be more effective than uncoordinated national efforts. Other areas of lesser priority were: clinical research, information for the general public, and education of health professionals in oncology. The budget was modest (11 million euros per year) but, nevertheless, it enabled the expert committee to propose and to carry out an ambitious strategy in a few well defined areas.

The decision to include systematic population based screening for specific sites of cancer was taken by the Committee of Cancer Experts at the first meeting in Brussels in November 1985. It was at the second meeting in February 1986 in Paris that breast, cervical and colorectal cancers were considered. At that time evidence was growing that screening for breast cancer by means of mammography could reduce mortality from this disease, at least in women aged 50 years and over. Experience had been accumulating in Europe, notably in Sweden, the UK, the Netherlands, and Italy, that population screening was feasible, with participation rates varying between 70 and 90%. A plan was made to enable each of the 12 EC Member States to propose pilot projects within its borders. The benefits of a European pilot network co-funded by the European Community would result from the pooling and dissemination of knowledge and expertise. A European action could also provide a practical basis for a decision, in the event that governments consider the implementation of a national breast cancer screening programme.

A subcommittee on screening was appointed by the Committee of the European Cancer Experts in order to select and fund pilot studies in the Member States after full consent of the national authorities. Another aim of the subcommittee was to monitor the results obtained in each pilot study and to promote cooperation among all persons involved in this action: project leaders of the pilot studies, expert consultants, and members of the staff of the Europe against Cancer

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programme. A network of individuals involved in the program was set up and meetings were held every six months in order to discuss problems encountered by the pilot studies. During the meetings the need for common rules concerning quality assurance and data collection became apparent.

The existence of false negatives (undetected cancers) reduces the number of detected cancers. On the other hand, a high rate of false positives increases the anxiety of women because they provoke unnecessary examinations. Screening is worthwhile only if the increase in human life outweighs the economic and social costs (anxiety, unnecessary examinations) that it may produce. Thus it is mandatory to find a balance between sensitivity and specificity in order to reach an acceptable ratio between true positives and false positives. Improvement of benefits (fewer false negatives) and a decrease in the social and psychological burden (fewer false positives) can be achieved by the implementation of rigorous quality assurance, systematic training of health care personnel, follow-up of women who have been screened, and an annual evaluation of screening results.

We knew that modern medical undertakings require specific training, accreditation, quality assurance and evaluation, including audits by outside teams. In 1988-1990, many observers were sceptical; they felt that in many EU countries physicians accustomed to substantial professional freedom would not accept the standardization of diagnostic procedures and protocols inherent to population-based screening programmes, such as double reading of mammograms. Within the Screening Subcommittee, we were much more optimistic but realised that it was a difficult challenge. In 1990, the subcommittee decided that guidelines should be prepared in order to assist health professionals and project leaders. These draft guidelines were circulated among network members for comment and the final version of the first edition was adopted in 1992.

The first edition of the document 'European Guidelines for Quality Assurance in Mammography Screening' (Kirkpatrick et al, 1993) was available in each of the official languages of the European Community on request. It was extremely well accepted and deeply appreciated because it provided a basic tool for all those interested in breast screening. These guidelines contributed immensely to the success of the breast screening projects of the Europe against Cancer programme and had a great impact in all Member States. In France, for example, the national guidelines were based on the European guidelines which set the standards. A few years later the evolution of techniques and practices rendered necessary the publication of a second edition which was followed by a third four years later, both of which were very successful. Thus, the standards and recommendations in the third edition provided the regulatory framework for the population-based breast screening programme recently introduced in Germany. Without any doubt the current fourth edition will also become the basic reference for quality assurance of breast cancer screening.

The European guidelines, besides their contribution to the accomplishments of the breast screening projects, have had two beneficial consequences. First, they not only improved the quality of breast screening but also that of diagnosis and treatment of breast cancer, and they have greatly reduced the differences among EU countries in the quality of care of breast disease. The second favourable outcome has been the demonstration that, contrary to some preconceptions, the basic requirements of modern medicine are well accepted when efforts are made in EU countries. Training can be improved; accreditation, rigorous quality assessment and evaluation by outside experts can be implemented. Ultimately, progress depends not only on the dedication of practitioners, but also on the courage of politicians and administrators. Breast cancer screening and efforts in prevention, such as the fight against smoking, clearly show that European cooperation in public health can be fruitful.

Paris, September 2005

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Summary document

Introduction

In presenting this fourth edition to you, we pay tribute to the success of its predecessor, published in 2001, which has been one of the most requested European Commission publications and used as the basis for the formation of several national guidelines. European Parliament subsequently requested the European Breast Cancer Network (EBCN) to produce a further edition. EUREF, as the guidelines co-ordinating organisation of the Network, and the guidelines Editors welcomed the opportunity to broaden the screening focus of previous editions, introducing further aspects of diagnosis and breast care, by collaborating with EUSOMA. The title of these guidelines has accordingly been altered to reflect this, with the addition of EUSOMA chapters on specialised breast units, quality assurance in diagnosis and loco-regional treatment of breast cancer. Important new chapters have been added on communication and the physico-technical aspects of digital mammography, while other chapters have been revised and updated. There is an executive summary for quick reference including a summary table of key performance indicators. Variations in style and emphasis have been unavoidable given the diverse sources of the contributions. However, the Editors have attempted to maintain conformity of approach.

Since the third edition, the European Union has gained 10 new Member States having varying levels of experience and infrastructure for breast screening and diagnosis. While this presents a new challenge for the EBCN, it is a pleasure to welcome our new colleagues and revisit the original concept of the Europe against Cancer Pilot Programmes, founded in 1988, the success of which led to the production of the first edition of the European Guidelines in 1993. This concept was to share multidisciplinary experience, disseminate best practice and provide a mechanism whereby support for the less experienced could be provided to ensure a more uniform standard of service delivery with the ability to progress as one with continuing advances in technical and professional knowledge.

Certain principles remain just as important in diagnosis as they are in screening. Training, multi-disciplinary teamwork, monitoring and evaluation, cost-effectiveness, minimising adverse effects and timeliness of further investigations are referred to constantly throughout subsequent chapters, reflecting their crucial place in any breast unit. A multidisciplinary team should include radiographers, pathologists, surgeons and nurses with additional input from oncologists, physicists and epidemiologists as appropriate. It is recognised that different team compositions will be suitable according to various stages of the screening, diagnostic and treatment processes.
Mammography is still the cornerstone of screening and much diagnostic work, so that a substantial part of these guidelines remain dedicated to those necessary processes and procedures which will optimise benefits, reduce morbidity and provide an adequate balance of sensitivity and specificity. It is essential that these guidelines be used to support and enhance local guidelines and not to conflict with them.

As pointed out in the third edition, there must be political support in order to achieve high quality screening, diagnostic and breast care services. Mechanisms for a meaningful quality-assured programme rely on sufficient infrastructure, financing and supervision, all of which require political goodwill to implement and maintain.
These guidelines have relied significantly upon knowledge and experience gained by the European Breast Cancer Network and its associated professionals. Over 200 professionals and client and patient advocates from 18 Member States of the European Union as well as Norway, Switzerland, Israel, Canada and the United States contributed to the current revised edition of the European guidelines. The new chapters and the major changes in the previous chapters were discussed and approved by the members of the European Breast Cancer Network (EBCN) at its annual meeting held 23-25 September 2004 in Budapest. The United Kingdom National Guidelines have formed the basis of some sections.

The Editors are conscious of the importance of raising and maintaining standards across all the Member States. While never abandoning those standards crucial for mortality reduction, we have as far as possible attempted to set out an equitable balance of best practice and performance indicators which can be used across a wide spectrum of cultural and economic healthcare settings. As with any targets, these can be constantly reviewed in the light of future experience. It is not the purpose of these guidelines to promote recent (and often costly) research findings

until they have been demonstrated to be of proven benefit in clinical practice, neither should this edition be regarded as a text book or in any way a substitute for practical clinical training and experience.

The third edition correctly forecast an increase in the use of digital mammographic techniques, although the logistical use of these in screening is still being evaluated. This edition therefore includes a section on physico-technical guidelines for digital mammography – the production of which was eagerly awaited by equipment manufacturers and professionals alike. Over the next five years we are likely to see an increase in three-dimensional imaging techniques – using ultrasound, digital mammography with tomosynthesis, and even computed tomography.

We believe that a major change will occur with more widespread use of accreditation/ certification of clinics and hospitals providing breast services. A process of voluntary accreditation is seen as central in the drive towards the provision of reliable services. Women, as well as purchasers and planners of healthcare services, should be able to identify those units where they will receive a guaranteed level of service, and one obvious way to provide this knowledge is through a mechanism of external inspection of processes and outcomes resulting in the granting of a certificate. Even highly centralised and quality assured national screening programmes require each unit to undergo full external multi-disciplinary review on a regular basis. We believe that Europa Donna could play an important role in encouraging women to recognise the importance of such an enterprise.

As nominated representatives of EUREF and EUSOMA we are proud to introduce this fourth edition of the European Guidelines to you. Although the largest version yet, we trust that it remains manageable and will be of continued benefit to those colleagues striving to improve their services, and to those many women in need of them.

Dr Nick Perry,
Chairman of the European
Reference Organisation for
Quality Assured Breast Screening
and Diagnostic Services

Professor Luigi Cataliotti,
President of the European
Society of Mastology

Executive Summary

Breast cancer is currently the most frequent cancer and the most frequent cause of cancer-induced deaths in women in Europe. Demographic trends indicate a continuing increase in this substantial public health problem. Systematic early detection through screening, effective diagnostic pathways and optimal treatment have the ability to substantially lower current breast cancer mortality rates and reduce the burden of this disease in the population.

In order that these benefits may be obtained, high quality services are essential. These may be achieved through the underlying basic principles of training, specialisation, volume levels, multidisciplinary team working, the use of set targets and performance indicators and audit. Ethically these principles should be regarded as applying equally to symptomatic diagnostic services and screening.

The editors of the fourth edition have maintained focus on screening for breast cancer while at the same time supporting the provision of highly effective diagnostic services and the setting up of specialist breast units for treatment of women, irrespective of whether a breast lesion has been diagnosed within a screening programme or not. By so doing we support the resolution of the European Parliament in June 2003 (OJ C 68 E, 2004), calling on the EU member states to make the fight against breast cancer a health policy priority and to develop and implement effective strategies for improved preventive health care encompassing screening, diagnosis and treatment throughout Europe.

The primary aim of a breast screening programme is to reduce mortality from breast cancer through early detection. Unnecessary workup of lesions which show clearly benign features should be avoided in order to minimise anxiety and maintain a streamlined cost-effective service. Women attending a symptomatic breast service have different needs and anxieties and therefore mixing of screening and symptomatic women in clinics should be avoided.

Our incorporation of additional text and sections on diagnostic activity has resulted in an expanded fourth edition. We have prepared this Executive Summary in an attempt to underline what we feel to be the key principles that should support any quality screening or diagnostic service. However the choice of content is to some extent arbitrary and cannot in any way be regarded as an alternative to the requirement for reading each chapter as a whole, within the context of the complete guidelines.

Fundamental points and principles

- In June 2003 the European Parliament called for establishment of a programme by 2008 which should lead to a future 25% reduction in breast cancer mortality rates in the EU and also a reduction to 5% in the disparity in the survival rates between member states (OJ C 68 E, 2004).

- Implementation of population-based breast screening programmes, prioritisation of quality assurance activities such as training and audit, together with the setting up of specialist breast units for management of breast lesions detected inside or outside screening programmes are regarded as essential to achieving these aims.

- Results of randomised trials have lead to the implementation of regional and national population based screening programmes for breast cancer in at least 22 countries within the past 20 years (Shapiro et al. 1998).

- An international agency for research on cancer (IARC) expert working group, has reviewed the evidence and confirmed that service screening should be offered as a public health policy directed to women age 50-69 employing two-yearly mammography (IARC Working Group on the Evaluation of Cancer Preventive Strategies 2002). This is consistent with the European Council Recommendation Recommendation of 2 December 2003 on Cancer Screening (OJ L 327/34-38).

- Breast cancer screening is a complex multidisciplinary undertaking, the objective of which is to reduce mortality and morbidity from the disease without adversely affecting the health status of participants. It requires trained and experienced professionals using up-to-date and specialised equipment.

- Screening usually involves a healthy and asymptomatic population which requires adequate information presented in an appropriate and unbiased manner in order to allow a fully informed choice as to whether to attend. Information provided must be balanced, honest, adequate, truthful, evidence-based, accessible, respectful and tailored to individual needs where possible.

- Mammography remains the cornerstone of population-based breast cancer screening. Due attention must be paid to the requisite quality required for its performance and interpretation, in order to optimise benefits, lower mortality and provide an adequate balance of sensitivity and specificity.

- Physico-technical quality control must ascertain that the equipment used performs at a constant high quality level providing sufficient diagnostic information to be able to detect breast cancer using as low a radiation dose as is reasonably achievable. Routine performance of basic test procedures and dose measurements is essential for assuring high quality mammography and comparison between centres.

- Full-field digital mammography can achieve high image quality and is likely to become established due to multiple advantages such as image manipulation and transmission, data display and future technological developments. Extensive clinical, comparative and logistical evaluations are underway.

- The role of the radiographer is central to producing high quality mammograms which, in turn, are crucial for the early diagnosis of breast cancer. Correct positioning of the breast on the standard lateral oblique and cranio-caudal views is necessary to allow maximum visualisation of the breast tissue, reduce recalls for technical inadequacies and maximise the cancer detection rate.

- Radiologists take prime responsibility for mammographic image quality and diagnostic interpretation. They must understand the risks and benefits of breast cancer screening and the dangers of inadequately trained staff and sub-optimal equipment. For quality loop purposes the radiologist performing the screen reading should also be involved at assessment of screen detected abnormalities.

- All units carrying out screening, diagnosis or assessment must work to agreed protocols forming part of a local quality assurance (QA) manual, based on national or European documents containing accepted clinical standards and published values. They should work within a specialist framework, adhering to set performance indicators and targets. Variations of practices and healthcare environments throughout the member states must not interfere with the achievement of these.

- A robust and reliable system of accreditation is required for screening and symptomatic units, so that women, purchasers and planners of healthcare services can identify those breast clinics and units which are operating to a satisfactory standard. Any accreditation system should only recognise centres that employ sufficiently skilled and trained personnel.

- The provision of rapid diagnostic clinics where skilled multidisciplinary advice and investigation can be provided is advantageous for women with significant breast problems in order to avoid unnecessary delay in outline of management planning or to permit immediate discharge of women with normal/benign disease.

- Population breast screening programmes should ideally be based within or closely associated with a specialised breast unit and share the services of trained expert personnel.

- All staff in a screening programme should:
  - Hold professional qualifications as required in each member state
  - Undertake specialist training
  - Participate in continuing medical education and updates
  - Take part in any recognised external quality assessment schemes
  - Hold any necessary certificate of competence

- Each screening unit should have a nominated lead professional in charge of overall performance, with the authority to suspend elements of the service if necessary in order to maintain standards and outcomes.

- All units involved in screening, diagnostic or therapeutic activities must ensure the formation of proper multidisciplinary teamwork involving a full range of specially trained professionals including a radiologist, radiographer, pathologist, surgeon, nurse counsellor and medical oncologist/radiotherapist.

- All women requiring breast surgery or other treatment should have their clinical, imaging and pathology findings discussed and documented in regular pre-operative and post-operative meetings of the full multi-disciplinary team.

- The surgeon must ensure that women receive information on treatment options and be aware that breast conserving surgery is the treatment of choice for the majority of small screen-detected cancers. Where appropriate, patients should be offered a choice of treatment including immediate or delayed breast reconstruction should mastectomy be required.

- The pathologist is a key member of the multidisciplinary team and must participate fully in pre-operative and post-operative case discussions. Accurate pathological diagnosis and the provision of prognostically significant information are vital to ensure appropriate patient management as well as accurate programme monitoring and evaluation.

- Patient support must be provided by specialist breast care nurses or appropriately psychologically professionally trained persons with expertise in breast cancer. They must be available to counsel, offer practical advice and emotional support.

- Quality assurance programmes should be mandatory for breast cancer services in order to qualify for funding from healthcare providers.

- Evaluation of the impact of screening requires the complete and accurate recording of all individual data pertaining to the target population, the screening test, its result, decisions made and the eventual outcome in terms of diagnosis and treatment.

- The protection of individual data is a basic right of every citizen in the EU – however, if appropriate precautions are taken, personal data may be used for promotion of public health.

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Summary table of key performance indicators

Introduction

For ease of reference we have included a summary table of key performance indicators from these guidelines. Please note that the numbering of the indicators is not indicative of importance. For more complete information regarding definition and context, further reference should be made to the source of each parameter within the text as listed. On occasions we have had to accept that different disciplines and different Member States show some variation of priorities and target levels. In all cases we have attempted to list what we regard as the most widely used and generally appropriate professionally agreed levels for usage in a Pan-European setting. In any case, all targets should be constantly reviewed in the light of experience and revised accordingly with regard to results achieved and best clinical practice. As far as possible, targets given refer to women over 50 years of age attending a screening programme.

Abbreviations used for reference to the chapters, e.g.:
3T1 Chapter 3, table 1
4.7 Chapter 4, paragraph 7

Performance indicator	Acceptable level	Desirable level
1. Target optical density[2AT4.1]	1.4 - 1.9 OD	1.4 - 1.9 OD
2. Spatial resolution[2AT4.1]	> 12 lp/mm	> 15 lp/mm
3. Glandular dose – PMMA thickness at 4.5 cm[2AT4.1]	< 2.5 mGy	< 2.0 mGy
4. Threshold contrast visibility[2AT4.1]	< 1.5%	< 1.5%
5. Proportion of women invited that attend for screening[1T32]	> 70%	> 75%
6. Proportion of eligible women reinvited within the specified screening interval[1T32]	> 95%	100%
7. Proportion of eligible women reinvited within the specified screening interval + 6 months[1T32]	> 98%	100%
8. Proportion of women with a radiographically acceptable screening examination[3.8, 5.4.3.1]	97%	> 97%
9. Proportion of women informed of procedure and time scale of receiving results[3.8, 5.4.3.1]	100%	100%
10. Proportion of women undergoing a technical repeat screening examination[1T32, 3.8, 4T2, 5.4.3.1]	< 3%	< 1%
11. Proportion of women undergoing additional imaging at the time of the screening examination in order to further clarify the mammographic appearances[1T32]	< 5%	< 1%
12. Proportion of women recalled for further assessment[1T32, 4T2]		
• initial screening examinations	< 7%	< 5%
• subsequent screening examinations	< 5%	< 3%

Performance indicator	Acceptable level	Desirable level
13. Proportion of screened women subjected to early recall following diagnostic assessment[4T2]	< 1%	0%
14. Breast cancer detection rate, expressed as a multiple of the underlying, expected, breast cancer incidence rate in the absence of screening (IR)[1T33, 4T1]		
• initial screening examinations	3 x IR	> 3 x IR
• subsequent-regular screening examinations	1.5 x IR	> 1.5 x IR
15. Interval cancer rate as a proportion of the underlying, expected, breast cancer incidence rate in the absence of screening[1T33]		
• within the first year (0-11 months)	30%	< 30%
• within the second year (12-23 months)	50%	< 50%
16. Proportion of screen-detected cancers that are invasive[1T33, 4T1]	90%	80-90%
17. Proportion of screen-detected cancers that are stage II+[1T33]		
• initial screening examinations	NA	< 30%
• subsequent-regular screening examinations	25%	< 25%
18. Proportion of invasive screen-detected cancers that are node-negative[1T33]		
• initial screening examinations	NA	> 70%
• subsequent-regular screening examinations	75%	> 75%
19. Proportion of invasive screen-detected cancers that are ≤ 10 mm in size[1T33, 4T1]		
• initial screening examinations	NA	≥ 25%
• subsequent-regular screening examinations	≥ 25%	≥ 30%
20. Proportion of invasive screen-detected cancers that are < 15 mm in size[7A.2]	50%	> 50%
21. Proportion of invasive screen-detected cancers < 10 mm in size for which there was no frozen section[5.8.2, 9T1]	95%	> 95%
22. Absolute sensitivity of FNAC[5.5.3, 6A A1.3]	> 60%	> 70%
23. Complete sensitivity of FNAC[5.5.3, 6A A1.3]	> 80%	> 90%
24. Specificity of FNAC[5.5.3, 6A A1.3]	> 55%	> 65%
25. Absolute sensitivity of core biopsy [5.5.3, 6A A1.3]	> 70%	> 80%
26. Complete sensitivity of core biopsy[5.5.3, 6A A1.3]	> 80%	> 90%
27. Specificity of core biopsy[5.5.3, 6A A1.3]	> 75%	> 85%
28. Proportion of localised impalpable lesions successfully excised at the first operation[4T2, 5.8.2, 7A.3]	> 90%	> 95%

Performance indicator	Acceptable level	Desirable level
29. Proportion of image-guided FNAC procedures with insufficient result[4T2, 5.5.2]	< 25%	< 15%
30. Proportion of image-guided FNAC procedures from lesions subsequently proven to be malignant, with an insufficient result[4T2, 5.5.2]	< 10%	< 5%
31. Proportion of patients subsequently proven to have breast cancer with a pre-operative FNAC or core biopsy at the diagnosis of cancer[7B.2]	90%	> 90%
32. Proportion of patients subsequently proven to have clinically occult breast cancer with a pre-operative FNAC or core biopsy that is diagnostic for cancer[7B.2]	70%	> 70%
33. Proportion of image-guided core/vacuum procedures with an insufficient result[4T2]	< 20%	< 10%
34. Benign to malignant open surgical biopsy ratio in women at initial and subsequent examinations[1T32, 4T2, 5.8.2, 7A.3]	≤ 1 : 2	≤ 1 : 4
35. Proportion of wires placed within 1 cm of an impalpable lesion prior to excision[4T2, 5.8.2, 7A.3]	90%	> 90%
36. Proportion of benign diagnostic biopsies on impalpable lesions weighing less than 30 grams[5.8.2, 7A.3]	90%	> 90%
37. Proportion of patients where a repeat operation is needed after incomplete excision[7A.4]	10%	< 10%
38. Time (in working days) between:		
• screening mammography and result[4T2]	15 wd	10 wd
• symptomatic mammography and result[5.9]	5 wd	
• result of screening mammography and offered assessment[4T2]	5 wd	3 wd
• result of diagnostic mammography and offered assessment[5.9]	5 wd	
• assessment and issuing of results[5.9]	5 wd	
• decision to operate and date offered for surgery[5.9]	15 wd	10 wd
39. Time (in working days) between:		
• screening mammography and result [1)]		
≤ 15 wd	95%	> 95%
≤ 10 wd	90%	> 90%
• symptomatic mammography and result [1)]		
≤ 5 wd	90%	> 90%
• result of screening mammography and offered assessment [1)]		
≤ 5 wd	90%	> 90%
≤ 3 wd	70%	> 70%

Performance indicator	Acceptable level	Desirable level
• result of symptomatic mammography and offered assessment [1)]		
≤ 5 wd	90%	> 90%
• assessment and issuing of results [1)]		
≤ 5 wd	90%	> 90%
• decision to operate and date offered for surgery [1)]		
≤ 15 wd	90%	> 90%
≤ 10 wd	70%	> 70%

[1)] To assist in monitoring and comparing performance between and within screening programmes, this summary table of indicators includes recommendations on the minimum proportion of women who should observe acceptable and recommended time periods.

1

Epidemiological guidelines for quality assurance in breast cancer screening

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This chapter is the revision of:

- Chapter 2 'Epidemiological guidelines for quality assurance in breast cancer screening' in the third edition of the 'European guidelines for quality assurance in mammography screening', published in 2001 (ISBN 92-894-1145-7). Authors: M. Broeders, M. Codd, L. Nyström, N. Ascunce, E. Riza;
- Protocol II-A 'Quality Assurance in the Epidemiology of Breast Cancer Screening' in the second edition of the 'European Guidelines for Quality Assurance in Mammography Screening', published in 1996 (ISBN 92-827-7430-9). Authors: M. Broeders, M. Codd, N. Ascunce, A. Linos, A. Verbeek.

1.1 Introduction

That a breast cancer screening programme can reduce breast cancer mortality in the age group 40-74 years has been shown in several randomised controlled trials and in the overview of the Swedish randomised trials.[1,2] The level of reduction has varied from a few percent up to 40% (HIP trial). The reason for this variation has not been analysed but can be due to the type of intervention i.e. mammography alone (Swedish trials) or including palpation (HIP, Edinburgh and Canadian trial). It can also be affected by the intensity of the intervention i.e. the time period from the start of the screening programme until the control group was also invited to screening, length of the screening interval, awareness of the disease, screening outside the programme, and the quality of screening.

The favourable results of the randomised trials have led to the implementation of regional and national population-based screening programmes for breast cancer in at least 22 countries since the end of the 1980s.[3] This type of screening is usually referred to as service screening, since mammography is offered as a public health policy on a routine basis, as opposed to mammography offered in the context of a randomised controlled trial. So far, studies on the effectiveness of service screening suggest similar or slightly smaller effects than the summary estimate for the randomised controlled trials.[4-10]

An International Agency for Research on Cancer (IARC) expert working group[11] has reached consensus, based on a review of published evidence, on the recommendation that service screening offered as a public health policy should be directed to women 50-69 employing two-yearly mammography. This is consistent with the European Council recommendation on cancer screening (2 December 2003). The IARC panel also encouraged cost effectiveness studies on screening younger and older age groups.

A breast cancer screening programme is a complex multidisciplinary undertaking. The objective of screening for breast cancer is to reduce morbidity and mortality from the disease without adversely affecting the health status of those who participate in screening. The effectiveness of a programme is a function of the quality of the individual components. Success is judged, not only by the outcome of the programme and its impact on public health, but also by the organisation, implementation, execution and acceptability of the programme. Epidemiology is the fundamental guiding and unifying discipline throughout the entire process of a screening programme, from the organisational and administrative aspects, up to the evaluation and assessment of impact.

Organisation
Fundamental epidemiological concerns at this phase of the programme include:
a) the availability and accuracy of the necessary epidemiological data upon which the decision to begin screening is based,
b) the availability and accessibility of essential demographic data to identify the target population and set up an invitation system,
c) the availability and accessibility of quality assured services for diagnosis and treatment of breast cancer,
d) promotional efforts to encourage participation in the programme,
e) a working relation with the local Cancer Registry, if available, and
f) maintenance of population and screening registers to include adjustments to the target population as required.

Evaluation of outcomes and interpretation of results from the entire screening programme is affected by these organisational aspects. The opportunity to describe them is provided in paragraphs 1.2 and 1.3 of these guidelines. It is recognised that the context and logistics of screening programmes will differ by country and even by region. For example the prior existence of a population register facilitates the issuing of personalised invitations, whereas the absence of a population register may lead to recruitment by open invitation. Many of these contextual differences will explain the outcomes.

Implementation
From an epidemiological perspective implementation entails more than simply carrying out the screening process and onward referral for assessment whenever required. The particular epidemiological concerns at this phase focus on the complete and accurate recording of all individual data pertaining to every participant, the screening test, its result, the decisions made as a consequence and their eventual outcome in terms of diagnosis and treatment. A fundamental concern at each step is the quality of the data collected. To this end paragraphs 1.4, 1.5, 1.6 and 1.7 provide detailed guidelines as to the type of data, which should be recorded.

Evaluation
Evaluating a breast screening programme is an epidemiological undertaking of paramount importance, the components of which are outlined in paragraphs 1.8 and 1.9. A key component in the evaluation of screening is the ascertainment of interval cancers, a process that requires forward planning and links with population-based cancer registries. Parameters of performance relevant to the process of screening and its early outcomes are measures of programme quality, which become available early in the lifetime of a screening programme. To determine whether a programme has been effective with regard to its impact on morbidity and mortality demands continuous follow up of the target population over an extended period of time, ascertainment and recording of vital and disease-free status at defined intervals, and determination of programme impact based on established epidemiological methods. However, it will not be possible to calculate these endpoints unless adequate provision has been made in the planning process for the complete and accurate recording of the necessary data.

Therefore, the epidemiological function in a screening programme is dependent on the development of comprehensive systems for documentation of the screening processes, monitoring of data acquisition and quality, and accurate compilation and reporting of results. The aim of these epidemiological guidelines is to propose a unified methodology for collecting and reporting screening programme data using commonly agreed terminology, definitions and classifications. This allows each programme to monitor and evaluate outcomes of its own screening process. Although detailed comparison may not be possible, outcomes of programmes reporting data using these guidelines can be related to each other. These guidelines may also prove to be of value for new breast screening programmes and regional programmes in the process of extending to national programmes.

Data protection
Following the EU directive 95/46/EC to control data collection and its usage, the protection of individual data is a basic right of every citizen in the European Union. This directive came into force in 1997, Member States being required to implement this as national law by the year 2000. There are however exceptions where rigorous data protection may interfere with the promotion of public health. The organisation of an effective (breast) cancer screening programme requires accurate identification of the eligible target population. This information is available from population registers but protected by the above-mentioned directive. In certain circumstances therefore, exemptions may be made for public health reasons (e.g. article 8, paragraph 3).
For the authoritative text of the Directive, reference should be made to the Official Journal of the European Communities of 23 November 1995 No. L. 281 p. 31.

Specific instructions for completion of tables in the epidemiological guidelines
- For completion of the tables in the epidemiological guidelines, the database supporting the production of results should consist of individual records (one record per woman for each screening episode). It is essential to keep all information on each screening episode, including invitation history, preferably as calendar dates referring to an event during the screening episode. This ensures maximal flexibility of the database for future evaluation efforts and participation in multi-centre studies (see also Chapter 8).
- Data on the screening episode should always refer to absolute numbers in the first instance. Some tables also allow for the calculation of certain performance indicators.

- Data should be reported separately for three groups of women, i.e. those attending for:
  - initial screening, i.e. the first screening examination of individual women within the screening programme, regardless of the organisational screening round (INITIAL);
  - subsequent screening at the regular interval, i.e. in accordance with the routine interval defined by the screening policy (SUBS-R);
  - subsequent screening at irregular intervals, i.e. those who miss an invitation to routine screening and return in a subsequent organisational screening round or attend a subsequent screening more than a defined period of time after the previous test (SUBS-IRR).

  Only the first organised screening round will consist entirely of women invited and attending for the first time; all additional rounds will be comprised of women falling into each of the categories described above. The cut-off point for separating 'subsequent regular' from 'subsequent irregular' screening should be established in line with the routine screening interval, taking into consideration that most programmes do not succeed in keeping the routine screening interval for each individual participant (e.g. a cut-off point at 30 months for a programme with a 2-year screening interval).
- For reasons of comparability and in accordance with European policy, data should be reported separately for the 50-69 age group. Screening programmes inviting younger or older women can expand the tables in the protocol to incorporate additional age groups.
- Age should be determined as the age of the woman at the time of the screening examination for that particular screening round. For non-participants, age should be determined as the age of the woman at the time of invitation (not the age at reminder). The outcome of the screening examination for a woman should thus be recorded in the same age category throughout a particular screening episode. Women aged 70 at the time of screening should be excluded from analysis for the 50-69 age group.
- Numbers in the tables should reflect women, not breasts or lesions. In the event of detecting more than one lesion in a woman, the lesion with the worst prognosis should be recorded. The following algorithm should be used for recording data: distant metastases > positive axillary lymph nodes > size of the invasive tumour > ductal carcinoma in situ (DCIS), where > indicates 'worse than'. In the event of more than one lesion in a woman where it is not possible to determine difference in prognosis, then the lesion requiring the most invasive procedure should be recorded.

1.2 Local conditions governing the screening process at the beginning of a breast screening programme

The aim of this paragraph is to describe the situation at the beginning of a breast screening programme, i.e. the context within which it is to be or has been established.

Table 1 documents baseline requirements for a screening programme. The availability and reliability of target population data will depend on the existence and accessibility of registers in the region to be screened. Demographic data on the target population can come from various sources, e.g. census data, population registers, electoral registers, population surveys, health care data or health insurance data. For a screening programme to be population-based, every member of the target population who is eligible to attend (on the basis of pre-decided criteria) must be known to the programme. The target population of the programme can be a fixed or a dynamic cohort, which will influence the denominator used in calculating screening outcomes. In some areas, opportunistic screening may be widespread and diluting the effect of a breast screening programme. Please provide the best estimate of the percentage of the target population undergoing screening mammography (coverage) outside the programme.

Table 1: Baseline conditions at the beginning of a breast screening programme

Name of region/country
Year that the programme started
Age group targeted
Size of target population*
Sources of demographic data*
Population-based (yes/no)*
Type of cohort (fixed/dynamic)*
Proportion of target population covered by opportunistic screening* (%)
Source of data for the above estimate

* cf Glossary of terms

Table 2 specifies which of the registers listed are available in the screening region or country and to what extent they overlap with the screening area. Further details of relevance are whether they are population-based and whether they are accessible to members of screening programme staff. Data on the occurrence of breast cancer may come from vital statistics registers, cancer registers, review of death certificates, etc. In this respect, it is of interest to specify whether ductal carcinomas in situ (DCIS) or lobular carcinomas in situ (LCIS) are included in breast cancer incidence (BCI) rates (see paragraph on background incidence rate below).

Table 2: Cancer registration in the target population

Details of the register	**Cancer register**	**Breast cancer register***
Year that the register started		
National (N)/Regional (R)		
Overlap with screening area (%)		
Population based* (yes/no)		
Accessible (yes/no)		
DCIS included in BCI rate* (yes/no)		
LCIS included in BCI rate* (yes/no)		

* cf Glossary of terms

Background incidence rate

The background incidence rate is the breast cancer incidence rate that would be expected in the targeted population in the absence of screening. There are several reasons why it is not always easy to obtain a valid estimate of the background incidence rate.

When a country is not (yet) fully covered by an organised screening programme, it may be possible to get a background incidence rate from a (regional) cancer registry covering a neighbouring region.[12] If there are no regional registries that have this information, a database like EUCAN[13]

may provide a reference as long as screening covers only a small part of the country. Using EUCAN as the source for background incidence rate has the disadvantage that variations in incidence within a country are not acknowledged.
The aforementioned approach will be inaccurate when opportunistic screening is prevalent in a country. Depending on the extent and quality of opportunistic screening, breast cancer incidence will most likely have increased and thus it will be no valid estimate for the background incidence rate.

If organised screening covers the whole country, the background incidence rate becomes an unknown entity and should be extrapolated from the historical background incidence rate. The historical background incidence rate is usually taken as the rate in the calendar year (or e.g. a 3-year average of the calendar years) before screening was introduced in the population. Extrapolation of the background incidence rate should take into account, at least in Northwestern Europe, the annual increase (of about 2-3%) in breast cancer incidence over time.[14] Again though, if opportunistic screening was already prevalent in the years before organised screening started, it may be impossible to get a valid estimate of the real background incidence rate.

Since the proportion of DCIS in an unscreened population is largely dependent on the extent of opportunistic screening and how effective it was in detecting DCIS, inclusion of DCIS may cause considerable regional variation of the background incidence rate.
It is therefore recommended that for computing background incidence rates only invasive breast cancer data should be used whenever the data is available. This will also allow for an easier comparison with published incidence rates, since most cancer registries currently interpret 'breast cancer' as invasive cancer (coded by ICD-9 174) and do not include DCIS (coded by ICD-9 233.0 and unfortunately rarely consistently recorded and routinely published as a separate incidence rate).

Table 3 outlines the background information on breast cancer occurrence in the target population required to interpret outcome measures of a screening programme. Breast cancer incidence and mortality rates are requested for women aged 50-69 in five-year age categories. For purposes of comparability, world standardised mortality and incidence rates for the age category 50-69 should also be provided as well as the calendar year to which these rates refer.

Table 3: Breast cancer occurrence, rates/100,000 women per year

	Age group				
	50-54	**55-59**	**60-64**	**65-69**	**Total**
Breast cancer incidence*					
• Absolute number of cases					
• Rate per 100,000					
• World ASR* in the year _____	NA	NA	NA	NA	
Invasive breast cancer incidence*					
• Absolute number of cases					
• Rate per 100,000					
• World ASR* in the year _____	NA	NA	NA	NA	
Advanced breast cancer incidence*					
• Absolute number of cases					
• Rate per 100,000					
• World ASR* in the year _____	NA	NA	NA	NA	
Breast cancer mortality*					
• Absolute number of cases					
• Rate per 100,000					
• World ASR* in the year _____	NA	NA	NA	NA	

* cf Glossary of terms NA = not applicable

Table 4 A potential determinant of participation in a breast screening programme is whether the participating woman is required to pay for the screening examination. When a consultation with a family practitioner is required to gain access to the screening examination, the costs of this consultation should be included in the fee paid. In some screening programmes, the fee for the screening examination will be paid, partly or completely, by a third party. Third party payment may be either through vouchers available to the woman before screening or through a system in which the woman pays in advance and gets reimbursed after the screening. Alternatively, a third party may pay the fee directly to the screening unit or organisation.

Table 4: Fees paid for the screening examination

Fees paid by the woman herself (in Euros): • For the screening examination • To receive the results
Third party payment (% of costs covered): • Through vouchers • Through reimbursement system • Directly to screening unit*

* cf Glossary of terms

Table 5 Several factors can be identified which encourage or impede the setting up of a breast screening programme. Such potential factors are: cost, fear, lack of interest or conflict of interest, political support, accessibility, integration into the existing health care system, data protection legislation. These can also include reasons for not responding to the invitation to be screened, and women's attitudes about and knowledge of screening guidelines.

Table 5: Potential conditions for/against screening

Please specify any conditions that may have worked for or against screening in your screening programme:

1.3 Invitation scheme

The aim of this paragraph is to describe the invitation scheme used by the screening programme, i.e. the methodology used to identify and invite members of the target population. A number of data sources can be used. For each source, information on its accuracy is requested.

Table 6 lists the sources of demographic data potentially used and the contribution of each to the identification of the target population in preparation for the first screening round. It is recognised that relative contributions of these sources will vary and may be difficult to estimate.

Table 6: Sources and accuracy of target population data (first round)

Data source	Target population* identified (%)	Best estimate of register accuracy (%)	Computer (C)/ Manual (M)
Population register			
Electoral register			
Other registers			
Self-registration*			
Other, please specify which:			

* cf Glossary of terms

Table 7 After the creation of a screening register which identifies the target population at the start of the screening programme with maximal accuracy and completeness, every effort should be made to ensure that this information remains up-to-date. Ideally, a permanent link with a population register should be established, offering the possibility of daily updates of the screening register. In this way, women who move into or out of the screening area or who have died, can be identified and included or excluded from the invitation scheme. Potential access to other sources allowing for adjustments of the screening register are also listed.
Please also indicate the frequency with which this information is used to update the screening register.

Table 7: Maintenance of the screening register

Estimate of screening register: • Completeness (%) • Accuracy (%)
Sources of screening register updates (yes/no): • Census data/population register • Cancer registration • Death registration • Health care data/health insurance data • Social insurance/tax records • Data on population migration • Returned invitations • Other:
Frequency with which screening register is updated

Table 8 Depending on the programme several combinations of call systems may be used. Invitations may be by personalised letter, by personal oral invitation or by open non-personal invitation, or by a combination of all three. Women who do not respond to the initial invitation may be issued a reminder, again by any available means listed below. The time interval (column 4 and 7) between invitation and reminder usually varies by programme. Some programmes may issue more than one reminder, or reminders by multiple methods. It may not be possible to ascertain the success of individual types of reminders.

Table 8: Mode of invitation

Mode of invitation	**Initial screening***			**Subsequent screening***		
	Invitation (yes/no)	Reminder (yes/no)	Interval* (weeks)	Invitation (yes/no)	Reminder (yes/no)	Interval* (weeks)
Personal letter • By mail • Other • Fixed date						
Personal oral invitation • By screening unit* • Other • Fixed date						
Non-personal invitation • Letter • Public announcement						

* cf Glossary of terms

Table 9 The target population for the breast screening programme includes all women eligible to attend screening on the basis of age and geographic location. However, each programme may apply additional inclusion/exclusion criteria to identify the 'eligible population' for screening. In addition, screening programmes may apply their own criteria to exclude certain women from screening outcomes. Potential exclusions from both the target population and screening outcomes for initial and subsequent screening examinations are listed in table 9. If the screening policy allows for exclusions, please specify the exact definition of the respective criteria in a footnote. The ease with which such individuals can be identified and excluded from the target population will vary by screening programme; for some programmes it may not be possible to identify any category of potential exclusion prior to invitation.

Table 9: Potential adjustments to identify the 'eligible' population

	Initial screening*		**Subsequent screening***	
Target population* (n)				
Eligible population* (n)				
Reason for exclusion	**Excluded from**		**Excluded from**	
	Target (yes/no, n)	Outcomes (yes/no, n)	Target (yes/no, n)	Outcomes (yes/no, n)
Previous breast cancer				
Previous mastectomy • Unilateral • Bilateral				
Recent mammogram*				
Symptomatic women*				

Incapacitated • Physical • Mental • Other
Death
Other:

* cf Glossary of terms
n = number

1.4 Screening process and further assessment

This paragraph describes the entire screening and assessment process, from mammographic detection of breast abnormalities through further investigation of those abnormalities, to diagnosis and further management of a malignant lesion.

Table 10 describes the screening facilities available and whether they are dedicated completely to breast cancer screening. It also requires information on the availability of assessment centres, where women might go for further assessment of a perceived abnormality detected at the screening examination.

Table 10: Screening facilities

Screening facilities	Number	Dedicated*
Mammography machines		
Static units		
Semi-mobile units		
Mobile units		
Other units		
Assessment centres		

* cf Glossary of terms

In **table 11** further details on the screening policy of the programme are requested such as: the age group targeted, the screening test used (whether single or two-view mammography, with or without clinical examination), the interval between screening examinations, the possibility of an intermediate mammogram (which however is not recommended after screening – see Chapter 4 on Radiology) and the assessment facilities for invasive investigations (centralised or not). If the majority of screening mammograms are double read, please also specify the policy to resolve discrepancies between the interpretations of the two readers, e.g. the woman is always recalled, discussion between readers, review by third reader, review by consensus panel or committee. In case the screening programme changed its policy after the introduction, please complete table 11 a second time, highlight any changes made and indicate the year of change.

Table 11: Screening policy*

Age group targeted
Screening test* • Initial screening* • Subsequent screening*
Screening interval* (months)
Intermediate mammogram* (yes/no) • After screening (not recommended) • After assessment
Double reading (%)
Policy to resolve discrepancies
Centralised assessment (yes/no)

* cf Glossary of terms

Tables 12, 13 and 14 describe the outcomes of screening invitations and examinations, as well as the additional investigations, which may be undertaken prior to, and including surgery. The order of investigations as listed does not necessarily imply that each participant will go through all stages before surgical excision and final diagnosis. Tables 13 and 14 should be reported separately for the three groups of women described in the introduction ('specific instructions for completion of tables'):
- initial screening (INITIAL);
- subsequent screening at the regular interval (SUBS-R);
- subsequent screening at irregular interval (SUBS-IRR).

The group of women that attend for initial screening will change over time. In the implementation phase of the programme, the age distribution in this group will reflect the age group targeted for screening. However, once the programme is fully implemented, women attending their first screening examination within the programme will be mostly 50-51 years old in a programme starting at 50.

The cut-off point for separating 'subsequent regular' from 'subsequent irregular' screening should be established in line with the routine screening interval, taking into consideration that most programmes do not succeed in keeping the routine screening interval for each individual participant (e.g. a cut-off point at 30 months for a programme with a 2-year screening interval).

Table 12 lists the number of women that are targeted, eligible, invited and finally screened with the aim to calculate the participation rate (total and by subgroups). Participation rate should be tabulated by first invitation and subsequent invitations, the latter being subdivided between those not having attended at the previous invitation and those having attended. The latter parameter reflects satisfaction towards service received at screening and adherence to the programme.Participation rates are usually reported by screening round or by calendar year.

Table 12: Invitation outcomes (FIRST/SUBSEQUENT INVITATIONS)

	Age group 50-54	55-59	60-64	65-69	Total
Target population* (n)					
Eligible population* (n)					
Women invited* (n)					
Women screened* (n)					
Participation rate (%)*					

n = number

Table 13 lists possible screening outcomes. The result of the screening examination can be recorded in various categories, that may not all be available in the screening programme, e.g. a screening programme may not have the option of intermediate mammography directly following the screening examination. Further assessment includes non-invasive and invasive investigations for medical reasons.

Table 13: Screening outcomes (INITIAL/SUBS-R/SUBS-IRR)

	Age group 50-54	55-59	60-64	65-69	Total
Women screened* (n)					
Outcome of the screening test:** (n) • Negative • Intermediate mammogram following screening* • Repeat screening test* - recommended - performed • Further assessment* - recommended - performed • Unknown/not available					

* cf Glossary of terms

** after repeat screening test if necessary

n = number

Table 14 describes the outcomes of non-invasive and invasive investigations following the results of screening (not as part of the screening examination!). These investigations can be performed at the time of screening when facilities are available in the screening unit or they can be performed on recall, i.e. the woman will have to come back to the screening unit for further investigation. As a result of non-invasive assessment, further clarification of the perceived abnormality may be required using invasive investigations (normally performed only on recall). However, a woman may also undergo further assessment by invasive investigations directly following the screening examination.

It is further recognised that open excisional biopsies for purely diagnostic purposes may be difficult to measure and to differentiate from tumorectomy which is performed for therapeutic reasons.

Table 14: Screening outcomes: further investigations (INITIAL/SUBS-R/SUBS-IRR)

Investigations after screening	Age group 50-54	55-59	60-64	65-69	Total
Repeat screening test* (n) • At screening • On recall*					
Additional imaging* (n) • At screening • On recall*					
Types of additional imaging* (n) • Repeat views (medical) • Cranio-caudal view • Other views • Ultrasound • MRI					
Clinical examination* (n) • At screening • On recall*					
Cytology* (n) • Recommended • Performed Core biopsy* (n) • Recommended • Performed Open biopsy* (n) • Recommended • Performed					
Repeat screening test rate* (%)					
Additional imaging rate* (%)					
Recall rate* (%)					
Further assessment rate* (%)					

* cf Glossary of terms

n = number

Table 15 classifies the results of the overall screening process in four categories, partly overlapping with the results of the screening test in table 13.

An overall breast cancer detection rate represents the performance of a screening programme but also reflects the age structure of the population being screened. To provide a more sensitive measure of performance, table 15 also allows for the calculation of age-specific detection ratios per 5-year age groups. The cancer detection rate should include cancers detected at intermediate mammography, since these are considered screen-detected cancers. However, they also represent a delayed diagnosis and should be subject to separate analysis and review.

The incidence rate for breast cancer in the denominator of the formula should reflect the background incidence rate, i.e. the underlying (expected) incidence rate in the absence of screening. As outlined earlier, it is recommended that for computing the background incidence rate only invasive breast cancers should be considered whenever the data is available. It should further be noted that the expected rates will increase marginally with each screening year because of the annual increase in the estimated background incidence.

$$\textbf{Age-specific detection ratio} = \frac{\text{Cancer detection rate in a 5-year age group}}{\text{Background (invasive) breast cancer incidence in that age group}}$$

Table 15: Outcome of screening process after assessment (INITIAL/SUBS-R/SUBS-IRR)

	Age group 50-54	55-59	60-64	65-69	Total
Outcome of screening process (n): • Negative • Intermediate mammogram following assessment* • Breast cancers detected: - DCIS - invasive cancers • Unknown/not available					
Breast cancers detected (n): • At routine screen • At intermediate mammography*					
Breast cancer detection rate*					
Background breast cancer incidence rate*					
Age-specific detection ratio*					

* cf Glossary of terms n = number

Table 16 summarises the results of screening in terms of positive predictive values (PPV) of specific interventions that take place in the course of mammographic screening and in further assessment of abnormal lesions. Results can be expected to vary between initial and subsequent screening examinations. PPV is expressed as a proportion. Please refer to the Glossary of terms (paragraph 1.11) for definition of the individual PPVs listed in table 16.

Table 16: Positive predictive value of specific interventions in screening for breast cancer, age group 50-69 (INITIAL/SUBS-R/SUBS-IRR)

Outcome of the intervention		Breast cancer detected Yes	No	PPV*
Screening test*	Positive			
Recall*	Positive			
Cytology*	Positive (C5**)			
Core biopsy*	Positive (B5**)			
Open biopsy*	NA			NA

* cf Glossary of terms

** C5 and B5: for definitions please refer to Chapter 6A and 6B respectively

NA = not applicable

1.5 Primary treatment of screen-detected cancers

It is recognised that collecting data on treatment on a regular basis may be a difficult and time consuming activity, especially in those screening programmes where treatment is not considered to be part of the screening process. On the other hand, it should be realised that the long-term effect of screening will be heavily influenced by the way screen-detected cases are treated. A high-quality screening programme will only lead to a long-term mortality reduction if the treatment of women detected at screening is of equally high quality. Thus it is strongly recommended to designate this task to a nominated person, either within or outside the screening programme, who takes responsibility for collecting this type of data and linking it with the screening data (see Chapter 8 on Data collection and monitoring).
Detailed guidance on the management of screen-detected lesions and appropriate quality indicators can be found in the surgical chapters in this document (Chapter 7).
Screening programmes are also encouraged to design surveys on quality of treatment on all cases arising in their target population, in co-operation with cancer registries and clinicians, This includes cancers diagnosed outside screening (interval cancers, cancers in non attenders, cancers in women not invited).

All women with breast cancer detected at screening, with or without signs of distant metastases, will be offered surgical treatment. Surgery may be preceded by neo-adjuvant therapy to reduce the size of the tumour. It should be noted that in that case, the pTNM classification is no longer relevant. For ductal carcinoma in situ (DCIS) and invasive cancers nodal status may be assessed either by axillary dissection or, more recently, a sentinel lymph node procedure. These options are categorised in **tables 17 and 18.** The primary treatment options according to disease stage of screen-detected breast cancers and breast cancer diagnosed outside screening (interval cancer as well as other 'control' cancers - optional) can be registered in **tables 19 and 20.**

Table 17: Primary treatment* of screen-detected *ductal carcinoma in situ*

	Age group				
	50-54	**55-59**	**60-64**	**65-69**	**Total**
Breast conserving surgery[1] (n) • Sentinel node procedure • Axillary dissection performed					
Mastectomy (n) • Sentinel node procedure • Axillary dissection performed					
Treatment refusal/unknown (n)					
TOTAL (n)					

[1] less than mastectomy; n = number * cf Glossary of terms

Table 18: Primary treatment* of screen-detected *invasive* breast cancers

	Age group				
	50-54	**55-59**	**60-64**	**65-69**	**Total**
Neo-adjuvant therapy* (n)					
Breast conserving surgery[1] (n) • Sentinel node procedure • Axillary dissection performed					

Mastectomy (n) • Sentinel node procedure • Axillary dissection performed
Treatment refusal/unknown (n)
TOTAL (n)

[1] less than mastectomy; n = number * cf Glossary of terms

Table 19: Primary treatment* of screen-detected breast cancers according to stage at diagnosis

	Stage at diagnosis							
	0	**I**	**IIA**	**IIB**	**IIIA**	**IIIB**	**IV**	**Unk[2]**
Neo-adjuvant therapy* (n)								
Breast conserving surgery[1] (n) • Sentinel node procedure • Axillary dissection performed								
Mastectomy (n) • Sentinel node procedure • Axillary dissection performed								
Treatment refusal/unknown (n)								
TOTAL (n)								

[1] less than mastectomy; n = number * cf Glossary of terms

Table 20: Primary treatment* of breast cancers diagnosed outside screening according to stage at diagnosis (OPTIONAL)

	Stage at diagnosis							
	0	**I**	**IIA**	**IIB**	**IIIA**	**IIIB**	**IV**	**Unk[2]**
Neo-adjuvant therapy* (n)								
Breast conserving surgery[1] (n) • Sentinel node procedure • Axillary dissection performed								
Mastectomy (n) • Sentinel node procedure • Axillary dissection performed								
Treatment refusal/unknown (n)								
TOTAL (n)								

[1] less than mastectomy; n = number * cf Glossary of terms

1.6 Disease stage of screen-detected cancers

The aim of this paragraph is to describe the disease stage of screen-detected cancer cases. The classification of primary tumour (T), regional lymph node involvement (N) and distant metastasis (M) follows the pTNM classification[15] for reasons of comparison and is listed in chapter 6B, Appendix 5 of this document. More detailed guidance on the pathological service in a breast screening programme can also be found in the pathology chapters 6A en 6B.
A prerequisite for a reduction in breast cancer mortality is a more favourable stage distribution in screen-detected cancers compared with clinically diagnosed cancers. Tumour size and axillary lymph node involvement for invasive cancers are of central importance here, and are assessed preferably after surgery (pT and pN). Age categories in **tables 21 and 22** refer to the age of a woman at the preceding screening examination.
The categorisation of size according to pathological diameter, as described above, is based on the pTNM-classification. However, it is recommended to also register the size of the tumour on a continuous scale. This will facilitate recategorisation in the event that consensus is reached on a different prognostic threshold (e.g. 15 mm).

Stage grouping

Stage 0	pTis	pN0	M0
Stage I	pT1	pN0	M0
Stage IIA	pT0	pN1	M0
	pT1	pN1	M0
	pT2	pN0	M0
Stage IIB	pT2	pN1	M0
	pT3	pN0	M0
Stage IIIA	pT0	pN2	M0
	pT1	pN2	M0
	pT2	pN2	M0
	pT3	pN1	M0
	pT3	pN2	M0
Stage IIIB	pT4	any pN	M0
Stage IIIC	any pT	pN3	M0
Stage IV	any pT	any pN	M1

Table 21: Size and nodal status of screen-detected cancers (INITIAL/SUBS-R/SUBS-IRR)

	Age group				
	50-54	**55-59**	**60-64**	**65-69**	**Total**
pTis					
• pN–					
• pN+					
• pNx					
pT1micab					
• pN–					
• pN+					
• pNx					
pT1c					
• pN–					
• pN+					
• pNx					

pT2
- pN–
- pN+
- pNx

pT3
- pN–
- pN+
- pNx

pT4
- pN–
- pN+
- pNx

pTx
- pN–
- pN+
- pNx

pN– = axillary node negative (pN0) pN+ = axillary node positive (any node positive; pN1-3)
pNx = nodal status cannot be assessed (e.g. previously removed, not done)

Table 22: Disease stage of screen-detected cancers (INITIAL/SUBS-R/SUBS-IRR)

	Age group 50-54	55-59	60-64	65-69	Total
Stage 0 • pTispN0M0					
Stage I • pT1pN0M0					
Stage IIA • pT0pN1M0 • pT1pN1M0 • pT2pN0M0					
Stage IIB • pT2pN1M0 • pT3pN0M0					
Stage IIIA • pT0pN2M0 • pT1pN2M0 • pT2pN2M0 • pT3pN1M0 • pT3pN2M0					
Stage IIIB • pT4anypNM0 • AnypTpN3M0					
Stage IV • AnypTanypNM1					
Unknown					

1.7 Post-surgical treatment of screen-detected cancers

All women with breast cancer detected at screening, with or without signs of distant metastases, will be offered some form of surgical treatment (primary treatment). In addition, most women will receive some form of post-surgical treatment (adjuvant treatment). For ductal carcinoma in situ (DCIS) and invasive cancers several types of treatment are categorised in **table 23.** The post-surgical treatment options according to disease stage of screen-detected breast cancers and breast cancer diagnosed outside screening (interval cancer as well as other 'control' cancers - optional) can be registered in **tables 24 and 25.**

Table 23: Post-surgical treatment* of screen-detected breast cancers

	Age group				
	50-54	55-59	60-64	65-69	Total
Ductal carcinoma in situ					
• Radiotherapy					
• Treatment refusal/unknown					
Invasive cancers					
• Chemotherapy					
• Radiotherapy					
• to the breast					
• to the chest wall					
• to the lymph stations					
• Hormonal therapy					
• Other treatments					
• Treatment refusal/unknown					

* cf Glossary of terms

Table 24: Post-surgical treatment* of screen-detected breast cancers according to stage at diagnosis

	Stage at diagnosis							
	0	I	IIA	IIB	IIIA	IIIB	IV	Unk[1]
Chemotherapy								
Radiotherapy								
• to the breast								
• to the chest wall								
• to the lymph stations								
Hormonal therapy								
Other treatments								
Treatment refusal/unknown								

[1] unk = unknown

* cf Glossary of terms

Table 25: Post-surgical treatment* of breast cancers diagnosed outside screening according to stage at diagnosis (OPTIONAL)

	Stage at diagnosis							
	0	I	IIA	IIB	IIIA	IIIB	IV	Unk[1]
Chemotherapy								
Radiotherapy • to the breast • to the chest wall • to the lymph stations								
Hormonal therapy								
Other treatments								
Treatment refusal/unknown								

[1] unk = unknown * cf Glossary of terms

Table 26 reflects the distribution of the number of days between the day of screening and the initial day of assessment. To estimate the total waiting time, the number of days between day of screening and the day of surgery for those women undergoing surgery as a result of the screening examination is registered. For those women not undergoing surgery, the interval between the day of screening and the day of final assessment should be registered.
In case a cancer is detected at intermediate mammography, which is by definition a screen-detected cancer, the day of screening should be replaced by the day that the intermediate mammogram was performed.

Table 26: Number of days between screening and surgery or screening and final assessment (age group 50 - 69 years) for screen-detected cancers

	Percentiles				
	5%	25%	50%	75%	95%
Day of screening - initial day of offered assessment					
Day of screening - day of offered surgery					
Day of screening - day of final offered assessment					

1.8 Follow up of the target population and ascertainment of interval cancers

Introduction
This paragraph will describe objectives for monitoring interval cancers and document the processes of follow up of the target population of a mammography screening programme.
The purpose of monitoring interval cancers is two fold. Radiological review of interval cancers is crucial since it serves both quality assurance and training (see Chapter 4 on Radiology). For

evaluation purposes, monitoring interval cancers allows for the calculation of parameters providing an early estimate of the impact of the screening programme in modifying the appearance of the disease, and thereby its effects, in the population. Therefore, data collection and reporting should be directed to all cancers appearing in the target population. Completeness of data collection and the use of different inclusion and exclusion criteria may limit the comparability of interval cancer rates in different populations. Parameters presented in this section aim at reducing these sources of variation and assist in the estimation of the effect of screening within each programme. Background incidence, breast awareness, the availability of timely diagnosis and the diffusion of spontaneous screening can also affect comparisons. For this reason it is recommended that numerical targets, not provided here, be set at a national or regional level.

Comprehensive follow up of a target population necessitates ascertainment and reporting of all breast cancers:
a. women who were invited for screening and who attended
b. women who were invited for screening but who did not attend
c. women who were not invited for screening

Group c includes women not yet invited for screening at the time of follow up as well as women in the target population who were never invited because of inadequate or incomplete population registers. The size and complexity of this group may differ between health care environments and may be determined in part by the frequency of update of population registers.

Methods of follow up for cancer occurrence
Methods of follow up for cancer occurrence may differ by country, by region or by screening programme, depending on the availability and accessibility of data and data sources. **Table 27** outlines the methods by which the target population may be followed to ascertain breast cancer occurrence, for each of the groups as defined above. It is sufficient to mark the boxes with a √. In the last row of the table, please provide details on the method for record linkage that you use to identify interval cancers.

Table 27: Methods of follow up for cancer occurrence

Data source	Participants	Non-participants	Persons not invited
Screening programme register			
Cancer / pathology register			
Breast care / clinical records			
Death register / certificate review			
Other, specify:			
Specify method of record linkage:			

Categories of cancer in the target population
Combining data on cancer occurrence from whatever source, with information on individual screening histories, including date of invitation, response to invitation, attendance for and outcome of screening with/without further assessment, permits classification of cancers that occur in members of the target population into the following categories:
a. Screen-detected cancer:
A primary breast cancer that is identified by the screening test, with/without further assessment, in a member of the target population, who was invited for and attended for screening.

b. Interval cancer:
A primary breast cancer which is diagnosed in a woman who had a screening test, with/without further assessment, which was negative for malignancy, either:
- before the next invitation to screening, or
- within a time period equal to the screening interval in case the woman has reached the upper age limit for screening.

c. Cancer in non-participant:
A primary breast cancer that occurs in a member of the target population who was invited for screening but did not attend.

d. Cancer in women not invited:
A primary breast cancer that occurs in a member of the target population who was not, or not yet, invited for screening.

Typically, a mammographic screening programme is organised into 'rounds' of screening, i.e. first, second, etc. at a defined interval, e.g. 24 months, depending on the programme's screening policy. Follow up begins at the start of a screening round and extends to the time of the next routine screening examination for those who attend screening as scheduled. For those who do not attend regularly, and for those women who, during the follow up period, exceed the upper age limit for screening, follow up should be continued for a period at least commensurate with the usual screening interval. This applies to all categories of women, i.e. participants, non-participants and those not invited for screening, in so far as this is possible.

In follow up of the target population it is relevant to examine *separately* those cancers (of all categories) identified during, or occurring after, the first round of screening, and those identified during, or occurring after, a subsequent round of screening. This is because the first round of screening is comprised entirely of women being screened for the first time (initial screenees); subsequent rounds of screening are comprised of women being screened for the first time, as well as those who have previously been screened. To capture this information, breast cancers in the target population should be cross-classified for first and subsequent rounds of screening as well as for initial and subsequent screening examinations. In this classification, it is also important to retain details on both the screening period (mth/yr –mth/yr) and the follow up period (mth/yr – mth/yr).

It is important to monitor all relevant dates so one can distinguish e.g. within the group of cancers in non-participants those who never participate in any round (permanent non-participants) from those non-participants who did not attend after the most recent invitation but who have previously attended at least one screening occasion (temporary non-participants).

Date of diagnosis of breast cancers in the target population
An important consideration in classifying breast cancers that occur in the target population is the date used as the date of diagnosis. The category to which a cancer will be assigned may depend on which one of several possible dates of diagnosis is used. It is strongly recommended to use always the same data for classifying cancers with different modes of detection in the population. This date should be the same date as used by major cancer registries, i.e. the date of the first morphological (cytological or histological) confirmation of the cancer diagnosis.

Relationship of breast cancers in the target population to selected programme performance indicators
Examination of the relationship between breast cancer occurrence in the target population and programme performance indicators, e.g. participation rate, recall rate, assessment rate, is an important component of the evaluation of a mammography screening programme. Of particular interest is the relation of an indicator of sensitivity of the screening programme, such as the interval cancer rate, with indicators of specificity, such as additional imaging rate, recall rate, assessment rate and benign biopsy rate (see Glossary of terms for definitions).
International comparisons of these relationships are currently under way to define the direction of the relationships and programme factors most strongly associated with the occurrence of interval cancers.

Relationship of breast cancers in the target population to tumour size and stage at diagnosis
Tumour size and stage at diagnosis of breast cancer differ according to the category of cancer, i.e. whether screen-detected, interval or non-participant cancer. While such detailed data may not be available from all data sources, it is recommended that these data are collected on all categories of cancer in so far as it is possible. This would permit comparison between the categories of cancer with respect to tumour size and stage at diagnosis as outlined in **table 28.** The classification used is defined in Chapter 6B, Appendix 5 of this document and paragraph 1.6 and follows the 6th edition of the TNM classification of malignant tumours.[15] As stated before, it is recommended to record tumour size in mm to allow for flexibility in categorisation.

Table 28: Relationship of breast cancers in the target population to tumour size, regional lymph node involvement and stage at diagnosis

Size of primary tumour	**SD**	**IC**	**NP**	**NI**
pTis				
pT1mic				
pT1a				
pT1b				
pT1c				
pT2				
pT3				
pT4				
pTx				
TOTAL				

Regional lymph node	**SD**	**IC**	**NP**	**NI**
pN–				
pN+				
pNx				
TOTAL				

Stage at diagnosis	**SD**	**IC**	**NP**	**NI**
Stage 0				
Stage I				
Stage II				
Stage III				
Stage IV				

Stage unknown
TOTAL

SD= screen-detected cancer IC = interval cancer
NP = cancer in non-participant NI = cancer in not invited

Classification of interval cancers

This section concentrates specifically on interval cancers of a mammography screening programme. A prerequisite for a breast cancer mortality reduction by screening is a reduction of the rate of advanced stages of breast cancer in the screened population, i.e. of screen-detected plus interval cancers, compared to the respective rates without screening. Precise information on tumour size and axillary lymph node involvement are thus of central importance also for interval cancers. Table 29 corresponds to some extent to table 19, but takes the time course of occurrence into account.

Interval cancers by stage and lymph node involvement in defined time periods following screening

While the aspiration in a screening programme is to have a fixed interval between screening examinations, e.g. 24 months, in practice it may not be possible to have the exact interval for every woman. This 'round slippage' may be due to several factors, including administrative factors, changes to scheduled invitations, etc. In a screening programme with a screening interval of 24 months, it is customary to group interval cancers which occur:
a. in the first 12 months after a negative screening examination;
b. in the second 12 months after a negative screening examination;
c. after 24 months.
This highlights the need to define the date of diagnosis of the interval cancer.

Table 29 provides the opportunity to record interval cancers by size and lymph node involvement in defined time periods following screening, separately for initial and subsequent screening examinations.

Table 29: Classification of interval cancers by size and lymph node involvement in defined time periods following initial and subsequent screening examinations.

	Time since screening examination (mths)			
	0-11	12-23	24+	Total
pTis				
• pN–				
• pN+				
• pNx				
pT1micab				
• pN–				
• pN+				
• pNx				
pT1c				
• pN–				
• pN+				
• pNx				
pT2				
• pN–				
• pN+				
• pNx				

pT3 • pN– • pN+ • pNx
pT4 • pN– • pN+ • pNx
pTx • pN– • pN+ • pNx

pN– = axillary node negative (pN0)
pN+ = axillary node positive (any node positive; pN1-3)
pNx = nodal status cannot be assessed (e.g. previously removed, not done)

Correspondingly, **table 30** provides the opportunity to record interval cancers by size, nodal status and age group in five year age intervals for the above defined time periods (0-11 months, 12-23 months and 24+ months) combined. This table can be reproduced for initial and subsequent screening examinations or for first and subsequent rounds of screening as desired.

Table 30: Classification of interval cancers by size, lymph node and age group following initial and subsequent screening examinations.

	Age group				
	50-54	**55-59**	**60-64**	**65-69**	**Total**
pTis • pN– • pN+ • pNx					
pT1micab • pN– • pN+ • pNx					
pT1c • pN– • pN+ • pNx					
pT2 • pN– • pN+ • pNx					
pT3 • pN– • pN+ • pNx					
pT4 • pN– • pN+ • pNx					

pTx
- pN–
- pN+
- pNx

pN– = axillary node negative (pN0)
pN+ = axillary node positive (any node positive; pN1-3)
pNx = nodal status cannot be assessed (e.g. previously removed, not done)

Interval cases for estimating sensitivity of the screening programme and its impact
Sensitivity of the screening test is defined as the ability of identifying a case during its detectable phase. However, the impact of screening depends not only on the sensitivity of the screening test but also on the length of the screening interval. Therefore it is recommended that the following more general expression is computed:

$$\textbf{Sensitivity of the screening programme} = \frac{\text{Screen-detected cases}}{\text{screen-detected cases + all interval cancer cases}}$$

This proportion includes interval cancer cases whose preclinical detectable phase was not initiated at the time of the screening test, and therefore reflects sensitivity of the screening test, lead time, and length of the screening interval. This easy to calculate measure is useful in assessing the overall impact of a screening programme in detecting cancers in the screened population and does not require radiological classification of interval cancers. It is strongly suggested that size or stage categories are taken into account, as the benefit of the screening programme diminishes if interval cancers tend to be advanced. Survival of ductal carcinoma in situ and of invasive cancers up to 10 mm in size has been shown to be very good, irrespective of grade and (for invasive cancers) nodal status. Therefore, interval cancers diagnosed at these stages, as opposed to detecting the same lesions at screening, is likely to affect breast cancer mortality only marginally. The proportion of cases with unknown pathological size (pTx) should also be carefully noted. Although these cases are not included in stage-specific calculations, it is obvious that results would be meaningless if cases with pTx are numerous.
Calculation of screening programme sensitivity, as defined above, excludes potentially detectable cases being diagnosed after the screening interval or at the subsequent screening examination. Since the probability of diagnosing a case during the screening interval varies according to local diagnostic delay and the occurrence of spontaneous screening, comparisons across programmes should be made with caution. However, the proportion calculated for 'advanced cases' (pT2 or more) only is less likely to be affected by these factors.

It is important to calculate sensitivity of the screening programme separately for initial and subsequent screening examinations as the rate and stage distribution of screen-detected cancers are quite different. If numbers allow, these estimates should also be computed for 5-year age categories.

The occurrence of interval cancers can also be related to the background population incidence of cancer in the absence of screening **(table 31).** Several limitations arise in this respect:
a. The population incidence of breast cancer is altered by screening. Population incidence of breast cancer in the absence of screening can be used in the early stages of a screening programme, provided that the prevalence of opportunistic screening is low. However, the longer a screening programme proceeds, the more difficult it becomes to determine what the incidence of breast cancer would be in the absence of screening.
b. Thus far, the focus of this paragraph has been entirely on the 'individual interval', i.e. the interval between the date of the screening mammogram and development of the interval cancer. In the evolution of a screening programme, individual intervals begin and end at different times. It is therefore of some concern to select the appropriate background incidence rate and detection rate for a time period which compares appropriately to the time period covered by the combined individual data for a particular round of screening or period of interest.

If background incidence does not include in situ cancers, these should also be excluded from interval cancers for the calculation of this outcome measure. If numbers allow, the table should also be computed for 5-year age categories. In calculating the observed rates of interval cancers, the denominator should be the number of 'negative' screening tests (with/without further assessment). If available, the number of 'woman-years of follow up' after a negative test should be used instead, taking into account women 'lost to follow up'.

Table 31: Relationship of observed interval cancer rate, by time since last negative screening examination, to background incidence rate

	Initial screening examinations			**Subsequent screening examinations**		
Time since last negative screening examination	Background incidence/ 10,000 (E) Year	Interval cancers 10,000 (O) Year	O/E	Background incidence/ 10,000 (E) Year	Interval cancers 10,000 (O) Year	O/E
0-11 mths						
12-23 mths						
24+ mths						
TOTAL All ICs						

IC = interval cancer

1.9 Evaluation and interpretation of screening outcomes

Screening outcomes become available throughout the screening process and afterwards. It is important to define the audience for the evaluation results, since the responsibilities and expertise of the decision-makers will affect what questions should be asked. In general, a distinction can be made between evaluating the performance of the screening programme and its impact on health indicators such as mortality. Monitoring performance indicators is an organisational responsibility to be carried out by the project leader or relevant professional and administrative disciplines. Evaluating the impact on mortality and cost-effectiveness of a screening programme requires the application of complex epidemiological and statistical methodologies.

1.9.1 Performance indicators

Performance indicators reflect the provision and quality of the activities constituting the screening process without contributing directly to reduction in mortality. It is essential however that data elements are recorded and that indicators are produced and monitored at regular intervals. This is the basis of quality assurance activities within and across specialties.

There is an infinite number of possible process indicators reflecting specific parts of the screening programme. This outline is confined to those that are of importance epidemiologically.

The performance indicators to be evaluated include:
- Coverage (by invitation or by examination)
- Participation rate
- Technical repeat rate
- Additional imaging rate at the time of screening
- Recall rate
- Further assessment rate
- Rate of invasive investigations (cytology, core biopsy, open biopsy for diagnostic purposes)
- Proportion of malignant lesions with a pre-treatment diagnosis of malignancy
- Proportion of image-guided cytological procedures with an insufficient result from lesions subsequently found to be cancer
- Proportion of image-guided core biopsy procedures with an insufficient result or benign result from lesions subsequently found to be cancer
- Positive predictive value of screening test, recall, cytology and core biopsy
- Benign to malignant biopsy ratio
- Specificity of the screening test
- Surgical procedures performed
- Interval between screening test and issue of test result
- Interval between screening test and initial day of assessment
- Interval between screening test and final assessment/surgery
- Proportion of eligible women reinvited within the specified screening interval (± 2 months)
- Proportion of eligible women reinvited within the specified screening interval plus 6 months

Table 32 lists those performance indicators for which acceptable and desirable levels could reasonably be specified in a European context. Each screening programme could decide to expand this table to include other performance indicators.

Table 32: Indicators by which the performance of a breast screening programme is assessed

Performance indicator	Acceptable level	Desirable level	Screening programme 50-69
Participation rate*	> 70%	> 75%	
Technical repeat rate*	< 3%	< 1%	
Recall rate* • Initial screening • Subsequent-regular screening	 < 7% < 5%	 < 5% < 3%	
Additional imaging rate at the time of screening*	< 5%	< 1%	
Benign to malignant biopsy ratio*	≤1:2	≤1:4	
Eligible women reinvited within the specified screening interval (%)	> 95%	100%	
Eligible women reinvited within the specified screening interval + 6 months (%)	> 98%	100%	

* cf Glossary of terms

1.9.2 Impact indicators

Achievement of the objective of screening for breast cancer, i.e. mortality reduction, is inevitably long-term. Ascertainment of impact on mortality demands (a) that follow up of the screened cohorts continues over extended periods of time, (b) that data on vital status and disease-free interval be vigorously sought and recorded despite the problems of follow up, and (c) that adequate links exist between programme data and other relevant data sources, e.g. medical records, pathology registers, death certificate information. Models for evaluating the impact of screening on mortality have not yet been fully developed. Given that this area of analysis is still evolving, a frequently used alternative is to identify and monitor early surrogate measures that can possibly predict outcome.

Analysis of breast cancer mortality
The objective of a breast cancer screening programme is to detect the tumour as early as possible to facilitate effective treatment and thereby reduce the mortality due to the disease. Continuous evaluation of the programme is necessary to ensure that it is as effective as expected. Difficulties in determining the impact of population screening for breast cancer entail the application of observational research designs, the absence of readily available control groups or control areas and the lack of individual data.

In the past decades, breast cancer incidence rates have steadily risen in many countries while breast cancer mortality rates have remained stable. Recently though, in several countries, mortality rates have been shown to level off or decline[16,17] especially in countries where population-based screening programmes for breast cancer have been introduced in the late 1980s or early 1990s. An important question now is the relative contribution of screening to the reported declines in mortality.[18] Establishing a relationship with screening is not straightforward since in some countries with screening programmes, declines in mortality started already before screening was introduced, and declines also occurred in non-screened age groups and in some countries without a national screening programme.[14] This observation gives rise to questions about the potential contribution of other determinants of breast cancer mortality, in particular treatment advances.[19,20] Thus, the challenge for researchers in this area is to tease out the relative contributions of screening and nonscreening factors to the reported declines in mortality.[21]

A first step in the evaluation of screening is to look at trends in breast cancer mortality. However, especially when data come from population statistics, the potential impact of service screening on breast cancer mortality will take many years to emerge, starting from a few years after the introduction of a programme but taking decades to show a full effect.[11] The delay is caused by the fact that it usually takes a number of years before a screening programme is fully implemented and most screening programmes are not able to correct national or regional mortality statistics for breast cancers diagnosed in women before the start of the screening programme.[22,23] Further delays are due to the lack of information on the screening history of individual women. No corrections at the individual level can be made for the phased implementation of the screening programme and the varying participation behaviour of women invited when individual data are not available.[4]

To estimate the effect of the screening programme based on a comparison of the trend in the breast cancer mortality in areas with and without a programme additional questions should be considered. The most complicated is how the control area should be selected? What aspects should be prioritised with respect to comparability of the areas – risk factor pattern for breast cancer (often unknown), treatment programmes for breast cancer, accessibility to health care, etc.

So far, the majority of studies on the impact of service screening have compared trends in breast cancer mortality, either between geographical regions or over time.[4,5,9,24] The estimates for the observed reductions from these studies vary from 12%[25] to as much as 50%[26], with differing periods after the introduction of screening. However, ultimate proof that a service-based screening programme is effective can never be based solely on the analysis of trends, since factors other than screening may also be (partially or wholly) responsible for the changes in

breast cancer mortality. A few studies were able to identify a temporary group of contemporaneous controls that were not (yet) invited for screening but experienced similar exposure to breast cancer risk factors and treatment.[7,10,27,28] The effects estimated in these studies, in the order of a 15 to 25% breast cancer mortality reduction, can therefore be directly attributed to the screening programme. Unfortunately, this advantage is time-limited since the control groups were also invited eventually and these studies will therefore not be able to assess the long-term impact of the service screening programme. Lastly, several studies have used modelling to estimate the expected breast cancer mortality in the absence of screening.[23,28,31] By comparing the observed versus the expected numbers of breast cancer deaths, the models yielded estimates of the potential impact of the screening programme in the long-term in the order of 13 to 29%.

The number of studies on service screening efficacy, comparing breast cancer mortality in women actually screened to unscreened women, is limited so far. As expected, the results from these studies generally show higher effect estimates, even though the range is wide and varies from a 19%[6] to 63%[26] reduction in breast cancer mortality.

The disadvantage of using breast cancer mortality as the endpoint in evaluation of a screening programme is that it takes many years before an effect can be expected. It takes years until the study population is screened for the first round and many more years until it is possible to see an effect of the intervention. It is recommended to try to estimate the proportion of the study population exposed to the intervention from the start of the screening programme to be able to estimate when it is realistic to expect an effect.

Analysis of surrogate indicators

An attractive alternative to analysing breast cancer mortality is to identify early surrogate indicators and follow their development over time. Several characteristics have been indicated to predict a reduction in the breast cancer mortality e.g.

- Interval cancer rate*
- Breast cancer detection rate*
- Stage at diagnosis of screen-detected cancers
- Proportion of screen-detected invasive cancers ≤ 10 mm
- Proportion of screen-detected cancers that are invasive
- Proportion of screen-detected cancers with lymph node metastases

* cf Glossary of terms

After ascertainment, confirmation and classification of interval cancer cases identified, the following additional measures can be calculated, as outlined in paragraph 1.8:

- Number of interval cancers per 10,000 women screened negative by time since last screening examination
- The interval cancer rate in a defined period after screening expressed as a proportion of the background (expected) breast cancer incidence rate in the absence of screening. Please note that proportions for e.g. the first and second year after screening should not be considered cumulative.
- Age-specific interval cancer rates
- Round-specific interval cancer rates
- Association of interval cancer rates with other performance indicators of screening such as participation rate, recall/additional imaging rate and positive predictive value of screening mammography and of each investigation undertaken as further assessment of screen-detected lesions
- Sensitivity and impact of the screening programme

Table 33 lists those early surrogate indicators for which acceptable and desirable levels could reasonably be specified in a European context. Each screening programme could decide to expand this table to include other surrogate indicators.

The acceptable and desirable levels suggested for initial screening are limited to the implementation phase of the screening programme. As a screening programme progresses over

time, an increasing proportion of the initial screening examinations will come from women entering the programme at the lower age limit (e.g. 50-51 year old). This shift in age distribution will affect the outcome of the surrogate indicators for initial screens.

Most indicators are calculated as a proportion of 'total cancers screen-detected' or 'total invasive cancers screen-detected'. Cancers with unknown size or nodal status should be included in the denominator, even though the proportions calculated will seem too low if numbers unknown are high.

Table 33: Early surrogate indicators by which the impact of a breast screening programme is assessed

Surrogate indicator	Acceptable level	Desirable level	Screening programme 50-69
Interval cancer rate* / Background incidence rate* (%)			
• 0-11 months	30%	< 30%	
• 12-23 months	50%	< 50%	
Breast cancer detection rate*			
• Initial screening	3xIR	> 3xIR	
• Subsequent-regular screening	1.5xIR	> 1.5xIR	
Stage II+/Total cancers screen-detected (%)			
• Initial screening	NA	< 30%	
• Subsequent-regular screening	25%	< 25%	
Invasive cancers ≤10 mm/ Total invasive cancers screen-detected (%)			
• Initial screening	NA	≥ 25%	
• Subsequent-regular screening	≥ 25%	≥ 30%	
Invasive cancers/ Total cancers screen-detected (%)	90%	80-90%	
Node-negative cancers/ Total invasive cancers screen-detected (%)			
• Initial screening	NA	> 70%	
• Subsequent-regular screening	75%	> 75%	

IR = background incidence

NA = not applicable

* cf Glossary of terms

Proportions versus rates

Ideally, comparison of prognostic factors (size, stage) should be presented as rates per population screened, as opposed to proportions. Rates allow consideration of changes in the characteristics of cancers detected by screening.

In the early phase of a screening programme, when most examinations are prevalence screens, a high proportion of small or early-stages cancers will be detected (and, in consequence, a decreased percentage of advanced cancers). Similarly, significant 'overdiagnosis' of small lesions would lead to a decreased percentage of advanced cancers, although the absolute rates

may be unchanged. Expression of results as the percentage reduction in the incidence of advanced cancers requires an estimate of the incidence of advanced cancers that would have been observed in the absence of a screening programme.[11]

In principle, the calculation of the overall reduction of advanced cancers is straightforward: the aim of mammography screening is to detect breast cancers in an early localised stage in order to remove them and to prevent progression into an advanced potentially lethal stage.[32] Thus, effective screening should lead to a decline of advanced tumours among the screened women already in the time after the first screening round. Day et al.[33] and IARC[11] request a reduction of at least 30 %.
For the assessment of the reduction, the advanced interval cancers from the interval after the first screening round and the advanced screen-detected cancers of the second screening round have to be summed up and compared with the background incidence rate of advanced tumours; correspondingly, the advanced interval cancers from the interval after the second screening round and the advanced screen-detected cancers of the third screening round have to be considered and so on. This type of combining the data is somewhat unfamiliar, since interval cancers are usually related to the screening round before the respective interval (e.g., for sensitivity assessment).

Formally, the relative reduction may be computed by:

$$(2 \times b - (v + s)) / 2 \times b = 1 - (v + s) / 2 \times b$$

where
v denotes the rate of advanced *interval* breast cancers per 1000 screened women;
s denotes the rate of advanced *screen-detected* breast cancers per 1000 screened women in the screening round subsequent to the respective interval;
b denotes the *background* incidence rate of advanced breast cancers per 1000 women.

Twice the background rate b arises from the fact that one accumulates the advanced stages within the screening over a two-year period (if the screening interval is two years).

Even though it is rather simple to translate the suggested levels for surrogate indicators (in proportions) to rates, setting acceptable and desirable levels always involves estimating the background incidence. The problems in obtaining a valid estimate for background incidence have been outlined before (paragraph 1.2).
Determining a target for the reduction of the rate of advanced tumours by screening has the same problem. In addition to the screening-internal quantities s and v, the external quantity b enters into the formula. This quantity may be different from country to country and is dependent upon prevalence and effectiveness of opportunistic screening.

1.9.3 Cost-effectiveness

Prior to inception, a screening programme should be advised to carry out cost-effectiveness analyses to demonstrate the cost of achieving its proposed objectives, in comparison with alternative prevention strategies or no intervention at all. Studies have shown that the cost-effectiveness of mammography screening generally favours the organised centralised programmes, mainly because of better organisation, high attendance rate, extended invitation scheme covering a large part of the eligible population and comprehensive quality assurance procedures.[34] Comparison of cost-effectiveness among different programmes can only be made with caution as this is a complex procedure.
A computer simulation package (MISCAN) has been developed by the Erasmus University in Rotterdam (The Netherlands) for analysing and reproducing the observed results of screening projects and for predicting the future effects of alternative screening programmes.[35-37] In the present MISCAN model, breast cancer has four invasive, screen-detectable, pre-clinical states (<0.5 cm, 0.5-1 cm, 1-2 cm and >2 cm) and one non-invasive state, ductal carcinoma in situ. By generating individual life histories a dynamic population is simulated, representing the demography, mortality of all causes and incidence and mortality from breast cancer. In the

disease part of the programme the relevant stages of breast cancer are discerned and the natural history is simulated as a progression through these stages. Key parameters in the model of the performance of screening are mean duration of screen-detectable preclinical disease, sensitivity and improvement of prognosis for screen-detected cancers. The MISCAN model has been tested in several screening programmes throughout Europe. Other cost-effectiveness analyses, based on Markov and Monte Carlo computer models, have also been employed in studying the cost-effectiveness of breast cancer screening, in particular of women aged 40 to 49 years.

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1.11 Glossary of terms

Additional imaging: additional imaging required for medical reasons, after evaluation of the screening mammogram. This may take the form of repeat mammography, specialised views (e.g. magnification, extended craniocaudal, paddle views), ultrasound or magnetic resonance imaging (MRI). Additional radiology includes additional views taken at the time of the screening mammogram, as well as those carried out on recall. It does not include repeat mammograms for technical reasons. It also does not include intermediate mammograms. On the basis of additional imaging, a

woman may be dismissed, or may be recommended to have cytology or biopsy. Please note the difference between additional imaging and an intermediate mammogram.

Additional imaging rate: the number of women who have an additional imaging investigation as a proportion of all women who have a screening test. This includes additional images taken at the time of the screening test, as well as imaging for which women are recalled. The additional imaging rate does not include repeat mammography for technical reasons. It also does not include intermediate mammograms. Within the group with additional imaging, the rates of individual imaging procedures may be derived.

Adjuvant therapy: additional treatment after primary treatment in order to prevent recurrent disease.

Advanced breast cancer: breast cancers with more than 2 cm in greatest dimension (i.e. pT2 or more) or positive lymph node status (i.e. pN1 or more).

Age-specific detection ratio: the breast cancer detection rate in a specified age group divided by the background (invasive) incidence of breast cancer in that same age group.

Benign to malignant biopsy ratio: the ratio of pathologically-proven benign lesions to malignant lesions surgically removed in any round of screening. This ratio may vary between initial and subsequent screening examinations.

Background incidence rate: the incidence rate of invasive breast cancer that would be expected in the screened population in the absence of screening.

Breast cancer: a pathologically-proven malignant lesion which is classified as ductal carcinoma in situ or invasive breast cancer.

Breast cancer detection rate: the number of pathologically-proven malignant lesions of the breast (both in situ and invasive) detected in a screening round per 1000 women screened in that round. This rate will differ for initial versus subsequent screening examinations. Cancers detected at intermediate mammography should be regarded as screen-detected cancers and thus be included in the cancer detection rate. Recurrent breast cancers, detected for the first time at mammographic screening, should also be regarded as screen-detected cancers since they will be identified and diagnosed in the same way as a primary breast cancer. Cancer metastases diagnosed in the breast as a consequence of a primary cancer outside the breast should not be included in the cancer detection rate.

Breast cancer incidence rate: the rate at which new cases of breast cancer occur in a population. The numerator is the number of newly diagnosed cases of breast cancer (both in situ and invasive) that occur in a defined time period. The denominator is the population at risk of being diagnosed with breast cancer during this defined period, sometimes expressed in person-time.

Breast cancer mortality rate: the rate at which deaths of breast cancer occur in a population. The numerator is the number of breast cancer deaths that occur in a defined time period. The denominator is the population at risk of dying from breast cancer during this defined period, sometimes expressed in person-time.

Breast cancer register: a register of breast cancer cases specifically created for a screening programme, when a country or region does not have or can not access a pathology register and/or cancer register.

Clinical examination: inspection of the breast and palpation of the breast and regional lymph nodes.

Core biopsy: a percutaneous biopsy using a cutting needle to provide a core of tissue for histological assessment without the need for an operation. Vacuum-assisted biopsies are also included in this category. See Chapter 6B for further details and classification of results.

Coverage by examination: the extent to which the screening programme covers the eligible population by examination. It can be calculated as the ratio between the number of examinations during a period equal to the screening interval and the number of women in the eligible population.

Coverage by invitation: the extent to which the screening programme covers the eligible population by invitation. It can be calculated as the ratio between the number of invitations during a period equal to the screening interval and the number of women in the eligible population. Self registrations should be counted in the calculation of the extension of screening, but their number should be also reported separately. Self registrations in fact cause an underestimation of coverage by invitation.

Cytology: a procedure where cells are aspirated from a breast lesion using a simple blood taking needle, usually under negative pressure. Cysts can also be aspirated. Cytological preparations are examined for evidence of malignancy. See Chapter 6A for further details and classification of results.

Dedicated screening facility: a facility with specialised equipment and trained staff that is used solely for screening examinations and/or further assessment of women where a perceived abnormality was detected at the screening examination.

Dynamic cohort: a cohort for which membership is determined by eligibility for breast cancer screening and therefore gains and loses members. The composition of the cohort is continuously changing allowing for the addition of new members for screening and follow up, and cessation of screening for those who become older than the maximum screening age. In order for estimates of screening efficacy to be accurately derived it is essential to know the denominator of the dynamic cohort at all times.

Eligible population: the adjusted target population, i.e. the target population minus those women that are to be excluded according to screening policy on the basis of eligibility criteria other than age, gender and geographic location.

Fixed cohort: a cohort for which membership is determined by being present at some defining event. Thus, there are no entries during the study period, including the follow up period. In a screening programme this means that a specific birth cohort is selected for screening and follow up. Women entering the age category in subsequent years of the screening programme are not included in the study cohort.

Further assessment: additional diagnostic techniques (either non-invasive or invasive) that are performed for medical reasons in order to clarify the nature of a perceived abnormality detected at the screening examination. Further assessment can take place at the time of the screening test or on recall. It includes breast clinical examination, additional imaging and invasive investigations (cytology, core biopsy and open biopsies for diagnostic purposes).

Further assessment Rate: the number of women undergoing further assessment (either at screening or on recall) as a proportion of all women who had a screening examination.

Initial screening: first screening examination of individual women within the screening programme, regardless of the organisational screening round in which women are screened.

Intermediate mammogram following screening: a mammogram performed out of sequence with the screening interval (say at 6 or 12 months), as a result of the screening test, Cancers detected at intermediate mammography should be regarded as screen-detected cancers (not interval cancers). However they also represent a delayed diagnosis and should be subject to separate analysis and review. It is recommended that the screening policy does not allow the opportunity for an intermediate mammogram following screening.

Intermediate mammogram following further assessment a mammogram performed out of sequence with the screening interval (say at 6 or 12 months), as a result of the screening test and further assessment. Cancers detected at intermediate mammography following further assessment should be regarded as screen-detected cancers (not interval cancers). However they also represent a delayed diagnosis and should be subject to separate analysis and review. In the radiology chapter the term 'early recall' is used to refer to an intermediate mammogram following further assessment.

Interval cancer: a primary breast cancer, which is diagnosed in a woman who had a screening, test, with/without further assessment, which was negative for malignancy, either:
- before the next invitation to screening, or
- within a time period equal to a screening interval for a woman who has reached the upper age limit for screening.

Interval cancer rate: the number of interval cancers diagnosed within a defined time period since the last negative screening examination per 10,000 women screened negative. The rate of interval cancers can also be expressed as a proportion of the background (expected) breast cancer incidence rate in the screened group.

Neo-adjuvant therapy: systemic treatment before primary treatment.

Open biopsy: surgical removal of (part of) a breast lesion. This is also referred to as excisional biopsy.

Open biopsy rate: the number of women undergoing open biopsy as a proportion of all women who have a screening examination. This rate may differ for initial versus subsequent screening examinations.

Opportunistic screening: screening that takes place outside an organised or population-based screening programme. This type of screening may be the result of e.g. a recommendation made during a routine medical consultation, consultation for an unrelated condition, on the basis of a possible

increased risk of developing breast cancer (family history or other known risk factor).

Participation rate: the number of women who have a screening test as a proportion of all women who are invited to attend for screening. Self-registrations should be excluded from both the numerator and the denominator in the calculation of participation rate.

Primary treatment: initial treatment offered to women with breast cancer. Most women will be offered surgical treatment. Surgery may be preceded by neo-adjuvant therapy to reduce the size of the tumour. Women with large inoperable primary tumours and women with distant metastases usually receive medical systemic treatment as primary treatment.

Population-based: pertains to a population defined by geographical boundaries. For a screening programme to be population-based every member of the target population who is eligible to attend on the basis of predecided criteria must be known to the programme. This emphasises the need for accurate information on the population at risk, constituting the denominator of most rates.

Positive predictive value (PPV): the ratio of lesions that are truly positive to those test positive. It is intimately affected by the prevalence of the condition under study. Thus, with a prevalence of < 1%, as with breast cancer, one can expect a low positive predictive and a very high negative predictive value for screening mammography.

Post-surgical treatment: treatment in addition to primary treatment. Most women will receive some form of post-surgical treatment (adjuvant treatment), e.g. chemotherapy, radiotherapy, hormonal therapy.

PPV of cytology: the number of cancers detected as a proportion of the women with positive cytology (C5), i.e. suspicion of malignancy. In practice, the denominator corresponds to those women who undergo biopsy after cytology (see Chapter 6A).

PPV of recall: the number of cancers detected as a proportion of the women who were positive as a final result of further assessment after recall (but excluding those for technical recall) and therefore had a surgical referral.

PPV of screening test: the number of cancers detected as a proportion of the women with a positive screening test. In practice, the denominator corresponds to women undergoing further assessment either at the time of screening or on recall. Further assessment does not include additional mammograms for technical reasons (repeat screening tests).

Recall: refers to women who have to come back to the screening unit, i.e. who are physically recalled, as a consequence of the screening examination for:

a) a repeat mammogram because of a technical inadequacy of the screening mammogram (technical recall); or
b) clarification of a perceived abnormality detected at the screening examination, by performance of an additional procedure (recall for further assessment).

This group is different from those who may have additional investigations performed at the time of the screening examination, but who were not physically recalled for that extra procedure.

Recall rate: the number of women recalled for further assessment as a proportion of all women who had a screening examination.

Recent mammogram: a mammogram performed at a shorter time interval than the regular screening interval. Women who had a recent mammogram (either diagnostic or screening) may potentially be excluded from the target population and/or the results dependent on screening policy.

Repeat screening test: a screening test repeated for technical reasons, either at the time of the screening examination or on recall. The most common reasons for a repeat screening test are:
a) processing error;
b) inadequate positioning of the breast; or
c) machine or operator errors.
Technical recalls will be reduced considerably, though not necessarily completely eliminated, by onsite processing taking place before a woman is dismissed.

Screening interval: the fixed interval between routine screens decided upon in each screening programme dependent on screening policy.

Screening policy: the specific policy of a screening programme which dictates the targeted age and gender group, the geographic area to target, the screening test, the screening interval (usually two or three years), etcetera.

Screening test: the test that is applied to all women in the programme. This may be a single or two-view mammogram with or without clinical examination. The screening test does not include additional imaging tests carried out at the time of the initial screening examination.

Screening unit: a facility where screening examinations take place. It does not refer to the exact number of e.g. mammography machines within the unit.

Self-registration: women who are not invited, but present themselves for screening and are included in the screening roster. It is the responsibility of the screening staff to decide whether self-registered women qualify to become members of the screening roster or not. It would be expected that only women who are members of the target population and thus eligible to attend would be allowed to self-refer.

Sensitivity: the proportion of truly diseased persons in the screened population who are identified as diseased by the screening test. The more general expression for 'sensitivity of the screening programme' refers to the ratio of breast cancers correctly identified at the screening examination to breast cancers identified and not identified at the screening examination (i.e. true positives/true positives + false negatives). It is clear that to establish the sensitivity of the screening test in a particular programme there must be a flawless system for identification and classification of all interval cancers (false negatives).

Sources of demographic data: demographic data for the purpose of issuing invitations to screening may come from a population register, an electoral register, other registers, population survey, or census data.

Specificity: the proportion of truly non-diseased persons in the screened population who are identified as non-diseased by the screening test. Here it refers to the ratio of truly negative screening examinations to

those that are truly negative and falsely positive (i.e. true negatives/true negatives + false positive). To derive an absolutely accurate estimate of specificity would require that each person dismissed as having a negative screening test is followed for ascertainment of subsequent negativity, and that those who are recalled for additional investigation following the screening test are regarded as potentially all having a malignancy. The false positives are those who have a histologically-proven benign lesion.
A note of caution is warranted here, however, in that, not infrequently, it is known beforehand, on the basis of radiological investigation, that the offending lesion is benign. The reason for surgery on a benign lesion may be surgeon or patient preference for excision. In practice ascertainment of specificity is frequently made on the basis of the results of initial mammograms.

Subsequent screening: all screening examinations of individual women within the screening programme following an initial screening examination, regardless of the organisational screening round in which women are screened. There are two types of subsequent screening examinations:
- subsequent screening at the regular screening interval, i.e. in accordance with the routine interval defined by the screening policy (SUBS-R);
- subsequent screening at irregular intervals, i.e. those who miss an invitation to routine screening and return in a subsequent organisational screening round (SUBS-IRR).

Symptomatic women: women reporting breast complaints or symptoms at the screening examination may potentially be excluded from the target population and/or results according to screening policy.

Target population: the group of persons for whom the intervention is planned. In screening for breast cancer, it refers to all women eligible to attend for screening on the basis of age and geographic location (dictated by screening policy). This includes special groups such as institutionalised or minority groups.

Women invited: all women invited in the period to which data refer, even if they have yet to receive a reminder.

Women screened: all women screened in the period to which data refer, even if results of mammograms are not yet available.

World age-standardised rate: the rate that would have occurred if the observed age-specific rates had operated in the standard world population (please turn over):

Standard world population used for the computation of age-standardised mortality and incidence rates*:

Age (yrs)	World
0	2 400
1	9 600
5	10 000
10	9 000
15	9 000
20	8 000
25	8 000
30	6 000
35	6 000
40	6 000
45	6 000
50	5 000
55	4 000
60	4 000
65	3 000
70	2 000
75	1 000
80	500
85 +	500
TOTAL	100 000

*Smith PG (1992) Comparison between registries: age-standardized rates. In: Parkin DM, Muir CS, Whelan SL, Gao Y-T, Ferlay J, Powell J (eds) Cancer Incidence in Five Continents, Volume VI. IARC Scientific Publications No 120, Lyon, p 865-870

2

European protocol for the quality control of the physical and technical aspects of mammography screening

2a ***Screen-film mammography***

2b ***Digital mammography***

Executive summary

A prerequisite for a successful screening project is that the mammograms contain sufficient diagnostic information to be able to detect breast cancer, using as low a radiation dose as is reasonably achievable (ALARA). This quality demand holds for every single mammogram. **Quality Control (QC)** therefore must ascertain that the equipment performs at a constant high quality level.

In the framework of 'Europe Against Cancer' (EAC), a European approach for mammography screening is chosen to achieve comparable high quality results for all centres participating in the mammography screening programme. Within this programme, **Quality Assurance (QA)** takes into account the medical, organisational and technical aspects. This section is specifically concerned with the quality control of physical and technical aspects of medical imaging in mammography and the dosimetry.

The intention of this part of the guidelines is to indicate the basic test procedures, dose measurements and their frequencies. The use of these tests and procedures is essential for ensuring high quality mammography and enables comparison between centres. This document is intended as a minimum standard for implementation throughout the EC Member States and does not reduce more comprehensive and refined requirements for QC that are specified in local or national QA Programmes. Therefore some screening programmes may implement additional procedures.

Quality Control (QC)

Mammography screening should only be performed using modern dedicated X-ray equipment and appropriate image receptors.

QC of the physical and technical aspects in mammography screening starts with specification and purchase of the appropriate equipment, meeting accepted standards of performance. Before the system is put into clinical use, it must undergo acceptance testing to ensure that the performance meets these standards. This holds for the mammography X-ray equipment, image receptor, film processor, viewing device and QC test equipment. After acceptance, the performance of all equipment must be maintained above the minimum level and at the highest level possible.

The QC of the physical and technical aspects must guarantee that the following objectives are met:

1. The radiologist is provided with images that have the best possible diagnostic information obtainable when the appropriate radiographic technique is employed. The images should at least contain the defined acceptable level of information, necessary to detect the smaller lesions (see CEC Document EUR 16260).
2. The image quality is stable with respect to information content and optical density and consistent with that obtained by other participating screening centres.
3. The breast dose is As Low As Reasonably Achievable (ALARA) for the mammographic information required.

QC Measurements and Frequencies

To attain these objectives, QC measurements should be carried out. Each measurement should follow a written QC protocol that is adapted to the specific requirements of local or national QA programmes. **The European Protocol for the Quality Control of the Physical and Technical Aspects of Mammography Screening** gives guidance on individual physical, technical and dose measurements, and their frequencies, that should be performed as part of mammography screening programmes.

Several measurements can be performed by the local staff. The more elaborate measurements should be undertaken by medical physicists who are trained and experienced in diagnostic radiology and specifically trained in mammography QC. Comparability and consistency of the results from different centres is best achieved if data from all measurements, including those performed by local technicians or radiographers are collected and analysed centrally.

Image quality and breast dose depend on the equipment used and the radiographic technique employed. QC should be carried out by monitoring the physical and technical parameters of the mammographic system and its components. The following components and system parameters should be monitored:

- X-ray generator and exposure control system
- Bucky and image receptor
- Film processing (for screen-film systems)
- Image processing (for digital systems)
- System properties (including dose)
- Monitors and printers (for digital systems)
- Viewing conditions

The probability of change and the impact of a change on image quality and on breast dose determine the frequencies at which the parameters should be measured. The protocol gives also the acceptable and achievable limiting values for some QC parameters. The acceptable values indicate the minimal performance limits. The achievable values indicate the limits that are achievable. Limiting values are only indicated when consensus on the measurement method and parameter values has been obtained. The equipment required for conducting QC tests are listed together with the appropriate tolerances in Table II.
Methods of dosimetry are described in the 'European Protocol on Dosimetry in Mammography' (EUR16263). It provides accepted indicators for breast dose, from both measurements on a group of women and test objects.

The first (1992) version of this document (REF: EUR 14821) was produced by a Study Group, selected from the contractors of the CEC Radiation Protection Actions. In the second (1996) and third (1999) version the test procedures and limiting values have been reviewed critically based on literature, the experience gained by users of the document and comments from manufacturers of equipment and screen-film systems. Due to the introduction of digital mammography an addendum on digital mammography was made in 2003. The current version incorporates both screen-film and digital mammography and is based on further practical experience with the protocol, comments from manufacturers and the need to adapt to new developments in equipment and in the literature.

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2a European protocol for the quality control of the physical and technical aspects of mammography screening

Screen-film mammography

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2a.1 Introduction to the measurements

This protocol describes the basic techniques for the quality control (QC) of the physical and technical aspects of mammography screening. It has been developed from existing protocols (see section 5, bibliography) and the experience of groups performing QC of mammography equipment. Since the technique of mammographic imaging and the equipment used are constantly improving, the protocol is subject to regular updates.

Many measurements are performed using an exposure of a test object. All measurements are performed under normal working conditions: no special adjustments of the equipment are necessary.
Two standard types of exposures are specified:

- The **reference exposure-** which is intended to provide information on the system under **defined** conditions, independent of the clinical settings
- The **routine exposure-** which is intended to provide information on the system under **clinical** settings

For the production of the reference or routine exposure, an object is exposed using the machine settings as follows (unless otherwise mentioned):

	Reference exposure:	**Routine exposure:**
test object thickness	45 mm[1]	45 mm
test object material	PMMA	PMMA
tube voltage	28 kV	as used clinically
target material	molybdenum	as used clinically
filter material	molybdenum	as used clinically
compression device	in contact with test object	in contact with test object
anti scatter grid	present	present
source-to-image distance	matching with focused grid	matching with focused grid
phototimer detector	in position closest to chest wall	in position closest to chest wall
automatic exposure control	on	as used clinically
optical density control	as leading to the reference optical density	as leading to the target optical density

The optical density (OD) of the processed image is measured at the **reference ROI,** which lies 60 mm from the chest wall side and laterally centred. The **reference optical density** is preferably 1.60 ± 0.15 OD.

All measurements should be performed with the same cassette to rule out differences between screens and cassettes except when testing individual cassettes (as in section 2a.2.2.2).

Limits of acceptable performance are given, but often a better result would be achievable. Both the acceptable and achievable limits are summarised in section 2a.4, table 1. Occasionally no limiting value is given, but only a typical value as an indication of what may normally be expected. The measurement frequencies indicated in the protocol (summarised in section 2a.4) are the

minimum required. When the acceptable limiting value is exceeded the measurement should be repeated. If necessary, additional measurements should be performed to determine the origin of the observed problem and appropriate actions should be taken to solve the problem.
For guidance on the specific design and operating criteria of suitable test objects; see the Proceedings of the CEC Workshop on Test Phantoms (see section 2a.5, Bibliography). Definition of terms, such as the 'reference ROI' and the 'reference density' are given in section 2a.1.2. The evaluation of the results of the QC measurements can be simplified by using the forms for QC reporting provided in section 2a.6.

2a1.1 Staff and equipment

Several measurements can be performed by the local staff. The more elaborate measurements should be undertaken by medical physicists who are trained and experienced in diagnostic radiology and specifically trained in mammography QC. Comparability and consistency of the results from different centres is best achieved if data from all measurements, including those performed by local technicians or radiographers are collected and analysed centrally.

The staff conducting the daily/weekly QC-tests will need the following equipment[2] at the screening site:

- Sensitometer
- Densitometer
- Thermometer
- PMMA plates[4,5]
- Standard test block[3] (45 mm PMMA)
- QC test object
- Reference cassette

The medical physics staff conducting the other QC-tests will need the following additional equipment and may need duplicates of many of the above:

- Dosemeter
- kVp-meter
- Exposure time meter
- Light meter
- QC test objects
- Aluminium sheets
- Focal spot test device + stand
- Stopwatch
- Film/screen contact test device
- Tape measure
- Compression force test device
- Rubber foam
- Lead sheet
- Aluminium stepwedge

2a.1.2 Definition of terms

Accuracy — Gives how close the measured value of a quantity is to the true value. In this document accuracy is used to check the correspondence between nominal and measured values of high voltage applied to an x-ray tube. The nominal value is taken as true value. The accuracy is calculated as relative difference between measured (m) and true (t) value, according to (m/t - 1), or as percentage, (m/t -1) x 100%.

Air kerma — Quotient of d_{Etr} by dm where d_{Etr} is the sum of initial kinetic energies of all the charged ionising particles liberated by uncharged ionising particles in a mass of air dm (adapted from ICRU 1980). The common unit for air kerma is milliGray (mGy).
Air kerma measures, employing a ionization chamber or another dose detector calibrated in mammography energy range, can be used to evaluate the entrance dose (Entrance Surface Air Kerma – ESAK).

Antiscatter grid — Device positioned close to the entrance surface of an image receptor for reducing the amount of scattered radiation reaching the receptor.

Automatic Exposure Control (AEC) — Operation mode of an X-ray machine by which the tube loading is automatically controlled and terminated when a preset radiation exposure to a dose detector located under the image receptor is reached. Some more sophisticated equipment also allow the automatic selection of tube potential (kV), target and filter materials.

Average glandular dose (AGD) — Reference term (ICRP 1987) for radiation dose estimation from X-ray mammography i.e. the average absorbed dose in the glandular tissue in a uniformly compressed breast. AGD value depends on X-ray beam quality (HVL), breast thickness and composition. If breast thickness and composition are not known, AGD can be referred to a standard breast.

Baseline value — Value of a parameter defined on basis of many repeated measurements (at least 10), that can be considered typical for a system. Generally, the baseline value is used when absolute limits for a parameter do not exist.

Breast compression — Application of a compression force to the breast during image acquisition. This immobilises the breast, which limits motion artifacts, and reduces breast thickness, which limits scatter effects and makes breast thickness approximately uniform.

Compression paddle — Thin device (few millimetres) rectangular shaped, made of plastic material (typical PMMA or polycarbonate) that can be positioned parallel to and above the breast table of a mammography apparatus.

Contrast threshold — Contrast level that produces a just visible difference between an object and the background.

D_{min} — Optical density obtained after processing of a non-exposed film. D_{min} is not zero due to the absorption of light in the film support and emulsion itself. In practice, for QC measurements, the density of the first step of a sensitometric strip is taken as D_{min}. It is taken as a measure of the 'base+fog' value.

D_{max} — Maximum optical density achievable with an exposed film; usually the density of the darkest step of a sensitometric strip. It corresponds to the saturation zone of a film response curve.

Film gradient — Index used to evaluate the film contrast.

Grad — See Film gradient.

Heel effect — Decreasing optical density measurable on a film in the cathode-anode direction, caused by the non-uniform intensity distribution of the X-ray beam. It is due to the geometric setup of the X-ray tube.

Half Value Layer (HVL) — Thickness of absorber which attenuates the air kerma of non-monochromatic X-ray beams by half. The absorber normally used to evaluate HVL of low energy X-ray beams, such as mammography beams, is high purity aluminium (≥ 99.9%). It should be noticed

that a correct measurement of HVL requires 'good geometry' conditions (proper distances among source, attenuator and image receptor, collimation and perpendicular incidence at image receptor entrance), rather far from geometry imposed by mammography equipment. Thereby, the HVL measurement is a sort of verification about the compatibility of radiation spectra with standard values measured with calibrated beams.

Image quality

There is not a definition of image quality univocally accepted. Commonly, it is possible to define quality indices representing the information content of the image; this is often done by test objects including details whose visibility can be quantified by means of proper scoring criteria.

Limiting value

Maximum or minimum limit of a possible range, considered acceptable for a given parameter.

Mean gradient (MGrad)

Parameter describing the film contrast in the exposure range, which contains most diagnostic information. MGrad is calculated as the slope of the line through the points $D_{0.25}$ = (D_{min} + 0.25) OD and D_2 = (D_{min} + 2.00) OD. Since the film curve is constructed from a limited number of points, $D_{0.25}$ and D_2 must be obtained by interpolation. Linear interpolation will result in sufficient accuracy.

Measurement error

Standard deviation if the number of repeated measurements is large enough (at least 5); maximum error [(max-min)/2] for few measures.

Middle gradient ($Grad_{1,2}$)

Parameter describing the film contrast in the middle of the diagnostic range. $Grad_{1,2}$ is calculated as the slope of the line through the points D_1 = (D_{min}+ 1.00) OD and D_2 = (D_{min}+ 2.00) OD. Since the film curve is constructed from a limited number of points, D_1 and D_2 must be obtained by interpolation. Linear interpolation will result in sufficient accuracy.

Net optical density

Optical density excluding base and fog. Base+fog value is determined measuring the optical density into a non-exposed area of film (see D_{min}).

Optical density (OD)

Logarithm (base 10) of the ratio between light intensity produced by a visible light source and perpendicularly incident on a film (Io), and light intensity transmitted by the film (I): OD = $\log_{10}$ (Io/I)
Optical density is measured by an instrument named densitometer, that measures transmitted light intensity into an area of the order of mm^2.
Variations in optical density should be measured along a direction parallel to the major axis of image receptor (perpendicular to cathode-anode direction), to avoid influences by the angular distribution of X-ray intensity (heel-effect).

Patient dose

Generic term for a variety of radiation dose quantities applied to a (group of) patient(s).

PMMA

The synthetic material polymethylmethacrylate. Trade names include Lucite, Perspex and Plexiglas.

Precision

See Reproducibility.

Quality assurance — As defined by the WHO (1982): 'All those planned and systematic actions necessary to provide adequate confidence that a structure, system or component will perform satisfactorily in service (ISO 6215-1980). Satisfactory performance in service implies the optimum quality of the entire diagnostic process i.e., the consistent production of adequate diagnostic information with minimum exposure of both patients and personnel.'

Quality control — As defined by the WHO (1982): 'The set of operations (programming, coordinating, carrying out) intended to maintain or to improve [. . .] (ISO 3534-1977). As applied to a diagnostic procedure, it covers monitoring, evaluation, and maintenance at optimum levels of all characteristics of performance that can be defined, measured, and controlled.'

QC test object — Object made of tissue simulating material (typically PMMA) for image quality evaluation; it generally includes objects simulating mammographic lesions (microcalcifications, fibers, masses) and/or resolution patterns and step wedges to measure parameters such as spatial resolution or contrast, related to image quality.

Radiation quality — See HVL.

Reference cassette — Cassette, properly identified, used for QC tests. Using a single cassette permits to exclude variations in optical density caused by changes in absorption from different cassettes or individual screen efficiencies.

Reference exposure — Exposure of the standard test object with predetermined values of parameters to provide an image at reference conditions.

Reference optical density — Optical density of (1.6 ± 0.1) OD, measured in the reference ROI.

Reference ROI — Considering an image obtained by the standard test block, the reference ROI is centred 60 mm perpendicular from the chest wall in the middle of the major film axis.

Relative error — Ratio between measurement error and mean value.

Reproducibility — Indicates the measurement precision or the reliability of tested equipment.

Region Of Interest (ROI) — Measurement area of optical density whose boundaries can be virtually defined on an image. ROI size can be around 1 cm^2.

Routine exposure — Exposure of the standard test block under the conditions that would normally be used to produce a mammogram having the routine optical density into the reference ROI. The routine exposure is used to check optical density and dose stability under clinical conditions.

Routine optical density — Optical density measured in the reference ROI of a standard block image obtained by a routine exposure. This value is chosen by the site personnel as optimal value for mean clinical mammograms provided by a specific imaging chain. The routine net optical density should be included into the interval [1.4-1.9] OD.

Spatial resolution (at high or low contrast)

Describes the smallest detectable detail at a defined contrast level to a given background. It is commonly evaluated by means of bar patterns, i.e. test objects constituted by groups of absorbing lines (typically Pb or Au) alternated to transparent lines of the same size. Line groups have increasing spatial frequency (typically expressed in 'line pairs/mm'); the frequency at which line paires remain distinguishable is taken as the limiting spatial resolution. In conditions of 'high contrast', that can be obtained by exposing the bar pattern only, this evaluation provides an estimation of the limiting spatial resolution of the whole mammography unit. The spatial resolution test can also be performed for 'low contrast' conditions, in order to simulate the degradation of both spatial resolution and contrast typical of clinical images. Image quality test objects including among the details one ore more bar patterns are available on the market.

Speed

Synonym of film sensitivity, is a parameter inversely proportional to dose. Speed is defined as the reciprocal of dose necessary to produce on a film an optical density equal to 1.00 + D_{min}; conventionally, it has been established that speed 100 means the film needs 10 μGy to produce 1.00 OD above base+fog, while speed 400 means the film requires 2.5 μGy to obtain the same result. If film Speed is higher, the dose necessary to obtain a same value of optical density is lower. Since in practice the sensitometric curve is constructed from a limited number of points, the film speed must be obtained by interpolation. Linear interpolation will result in sufficient accuracy.

Standard breast

Mathematical model generally used for calculations of glandular dose in Monte Carlo simulations. It consists of a 40 mm thick central region comprising a certain mixture by weight of adipose tissue and glandular tissue (dependent on compressed breast thickness and age) surrounded by a 5 mm thick superficial layer of adipose tissue (simulating skin absorption). The standard breast is semicircular with a radius ≥ 80 mm and has a total thickness of 50 mm (40+5+5). It is commonly assumed that a uniform PMMA block 45 mm thick is equivalent in absorption to a standard breast. (Note that other definitions of a standard breast have been used in other protocols. As an example, in the UK the standard breast has a total thickness of 45 mm with a 35 mm thick central region.)

Standard test block

PMMA test object to simulate the absorption of a standard breast. Its thickness is (45.0 ± 0.5) mm and the remaining dimensions can be either rectangular ≥ 150 mm x 100 mm or semi-circular with a radius of ≥ 100 mm. The standard test block can be used to check the AEC behaviour or to evaluate a mean value of AGD.

Typical value

Value of a parameter found in most facilities in comparable measurements. The statement of typical value is an indication about values that could be expected, without imposing any limits to obtainable results.

Tube loading

Product of the X-ray tube current (milliampere, mA) and the exposure time (seconds, s). It is quantified in units of mAs.

Tube potential

The potential difference in units of kilovolt (kV) applied across the anode and cathode of an X-ray tube during a radiographic exposure.

Tube yield Ratio between air kerma (mGy) measured without any test object and the tube loading (mAs), for a known distance between the X-ray source and the dosimeter and for preset exposure parameters.

X-ray spectrum Distribution of photon energies in an X-ray beam. It depends on anode and filter material and tube potential, as well on all attenuators (tube output window, compression device, air gap) between anode and breast.

2a.2 Description of the measurements

Generally when absolute measurements of dose are performed, make sure that the proper corrections for temperature and air pressure are applied to the raw values. Use one and the same box of (fresh) film throughout the tests described in this protocol.

Local basic safety tests should be followed. If no local basic safety tests are available, an example of such tests can be found in appendix 1.

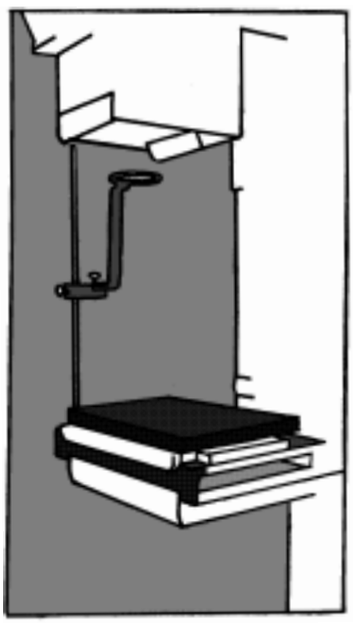
2a.2.1 X-ray generation

2a.2.1.1 X-ray source

The measurements to determine the focal spot size, source-to-image distance, alignment of X-ray field and image receptor, radiation leakage and tube output, are described in this section.

2a.2.1.1.1 Focal spot size

The measurement of the focal spot size is intended to determine its physical dimensions at installation or when resolution has markedly decreased. The focal spot size must be determined for all available targets of the mammography unit. For routine quality control the evaluation of spatial resolution is considered adequate.



The focal spot dimensions can be obtained by using one of the following methods.

- Star pattern method; a convenient method (routine testing)
- Slit camera; a complex, but accurate method for exact dimensions (acceptance testing)
- Pinhole camera; a complex, but accurate method to determine the shape (acceptance testing)
- Multi-pinhole test tool, a simple method to determine the size across the field (routine/acceptance testing)

Some fully automated digital devices to measure focal spot size are available. If validated they may be used.
When doing focal spot size measurements, it is advised to use one of the above mentioned methods consistently.

A magnified X-ray image of the test device is produced using a non-screen cassette. This can be achieved by placing a black film (OD ≥ 3) between screen and film. Select the focal spot size required, 28 kV tube voltage and a focal spot charge (mAs)

Fig. 2.1 Focal spot size measurement using the star pattern method

to obtain an optical density between 0.8 and 1.4 OD base and fog excluded (measured in the central area of the image). The device should be imaged at the reference ROI of the image plane, which is located at 60 mm from the chest wall side and laterally centred. Remove the compression device and use the test stand to support the test device. Select about the same focal spot charge (mAs) that is used to produce the standard image of 45 mm PMMA, which will result in an optical density of the star pattern image in the range 0.8 to 1.4.
According the IEC/NEMA norm, an 0.3 nominal focal spot is limited to a width of 0.45 mm and a length of 0.65 mm. A 0.4 nominal focal spot is limited to 0.60 and 0.85 mm respectively. No specific limiting value is given here, since the measurement of imaging performance of the focal spot is incorporated in the limits for spatial resolution at high contrast. (see 2a.2.5.2)

Focal spot size: star pattern method
The focal spot dimensions can be estimated from the 'blurring diameter' on the image (magnification 2.5 to 3 times) of the star pattern. The distance between the outermost blurred regions is measured in two directions: perpendicular and parallel to the tube axis. Position the cassette on top of the bucky (no grid).
The focal spot is calculated by applying formula 2.1, which can also be found in the completion form.

$$f = \frac{\pi\theta}{180} \frac{d_{blur}}{(m_{star} - 1)} \qquad (2.1)$$

where q is the angle of the radiopaque spokes, and d_{blur} is the diameter of the blur.
The magnification factor (m_{star}) is determined by measuring the diameter of the star pattern on the acquired image (d_{image}) and the diameter of the device itself (d_{star}), directly on the star, and is calculated by:

$$m_{star} = d_{image} / d_{star} \qquad (2.2)$$

Limiting value	None.
Frequency	At acceptance and when resolution has changed.
Equipment	Star resolution pattern (spoke angle 1° or 0.5°) and appropriate test stand.

Focal spot size: slit camera method
To determine the focal spot dimensions (f) with a slit camera, a 10 mm slit is used. Remove the compression device and use a test stand to support the slit. Produce two magnified images (magnification 2.5 to 3 times) of the slit, perpendicular and parallel to the tube axis.
The dimensions of the focal spot are derived by examining and measuring the pair of images through the magnifying glass. Make a correction for the magnification factor according to $f=F/m_{slit}$, where F is the width of the slit image. The magnification factor (m_{slit}) is determined by measuring the distance from the slit to the plane of the film ($d_{slit\text{-}to\text{-}film}$) and the distance from the focal spot to the plane of the slit ($d_{focal\ spot\text{-}to\text{-}slit}$). m_{slit} is calculated by:

$$m_{slit} = d_{slit\text{-}to\text{-}film} / d_{focal\ spot\text{-}to\text{-}slit} \qquad (2.3)$$

Note: $m_{slit} = m_{image} - 1$, and the method requires a higher exposure than the star pattern method.

Limiting value	None.
Frequency	At acceptance and when resolution has changed.
Equipment	Slit camera (10 µm slit) with appropriate test stand and magnifying glass (5-10x), having a built-in graticule with 0.1 mm divisions.

Focal spot size: pinhole method

To determine the focal spot dimensions (f) with a pinhole, a µ30 m gold/platinum alloy pinhole is used. Produce a magnified image (magnification 2.5 to 3 times) of the pinhole.
The dimensions of the focal spot are derived by examining the images through the magnifying glass and correcting for the magnification factor according to $f = F/m_{pinhole}$, where F is the size of the imaged focal spot. The magnification factor ($m_{pinhole}$) is determined by measuring the distance from the pinhole to the plane of the film ($d_{pinhole\text{-}to\text{-}film}$) and the distance from the focal spot to the plane of the pinhole ($d_{focal\ spot\text{-}to\text{-}pinhole}$). $m_{pinhole}$ is calculated by:

$$m_{pinhole} = d_{pinhole\text{-}to\text{-}film} / d_{focal\ spot\text{-}to\text{-}pinhole} \qquad (2.4)$$

Note: The method requires a higher exposure than the star pattern method.

Limiting value	None.
Frequency	At acceptance and when resolution has changed.
Equipment	Pinhole (diameter 30 µm) with appropriate test stand and magnifying glass (5-10x), having a built-in graticule with 0.1 mm divisions.

The multi-pinhole device is used similarly. It allows an estimate of the focal spot size at any position in the x-ray field. This method is not suitable for measuring the dimension of fine focus because of the relatively large size of the pin-holes.

2a.2.1.1.2 Source-to-image distance

Measure the distance between the focal spot indication mark on the tube housing and the top surface of the bucky. Add distance between bucky surface and the top of the image receptor.
The source-to-image distance can be determined more accurately by imaging an object with known dimensions a (≥ 10 cm) positioned on the breast support table and positioned at a distance d (≥ 20 cm) above the breast support table. Measure the dimensions of the imaged object on image 1 (object on breast support table) and image 2 (object at distance d above the breast support table). Using formula 2.5 the source-to-image distance can be calculated.

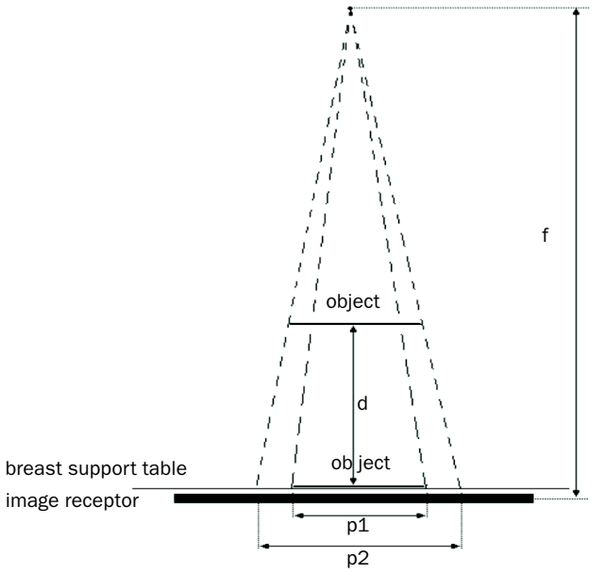


Fig. 2.2 Source-to-image distance measurement

$$f = \frac{d}{a * \left(\frac{1}{p1} - \frac{1}{p2} \right)} \qquad (2.5)$$

f = source-to-image distance
d = distance between the object in position 1 and 2
a = size of the imaged object
p1 = size of the object on image 1 (object on the breast support table)
p2 = size of the object on image 2 (object at a distance d above the breast support table)

Limiting value Manufacturers specification, typical 600-650 mm.
Frequency At acceptance, if the source-to-image distance is adjustable: every six months.
Equipment Tape measure, arbitrary test object.

2a.2.1.1.3 Alignment of X-ray field/image receptor

The alignment of the X-ray field and image receptor at the chest wall side can be determined with two loaded cassettes and two X-ray absorbers, e.g. coins.
Place one cassette in the bucky tray and the other on top of the breast support table. Make sure the second cassette has a film loaded with the emulsion side away from the screen. It must extend beyond the chest wall side about 30 mm. Mark the chest wall side of the bucky by placing the absorbers on top of the cassette. Automatic exposure will result in sufficient optical densities. Reposition the films on a light box using the imaged absorbers as a reference. The alignment between the film, X-ray field and chest wall edge of the bucky should be measured.

Fig. 2.3 Alignment of X-ray field/image receptor measurement

Note 1: The lateral edges of the X-ray field should at least expose the image receptor. A slight extension beyond any edge of the image receptor is acceptable.
Note 2: If more than one field size or target is used, the measurement should be repeated for each.

Limiting value For all focal spots:
All sides: X-rays must cover the film by no more than 5 mm outside the film.
On chest wall edge: distance between film edge and edge of the bucky must be ≤ 5 mm.
Frequency Yearly.
Equipment X-ray absorbers - e.g. coins, rulers, iron balls, tape measure.

2a.2.1.1.4 Radiation leakage

The measurement of leakage radiation comprises two parts; firstly the location of leakage and secondly, the measurement of its intensity.
Position a beam stopper (e.g. lead sheet) over the end of the diaphragm assembly such that no primary radiation is emitted. Enclose the tube housing with loaded cassettes and expose to the maximum tube voltage and a high tube current (several exposures). Process the films and pin-point any excessive leakage. Next, quantify the amount of radiation at the 'hot-spots' at a distance of 50 mm of the tube with a suitable detector. Correct the readings to air kerma rate in mGy/h (free in air) at the distance of 1 m from the focal spot at the maximum rating of the tube.

Limiting value Not more than 1 mGy in 1 hour at 1 m from the focus at the maximum rating of the tube averaged over an area not exceeding 100 cm^2, and according to local regulations.
Frequency At acceptance and after intervention on the tube housing.
Equipment Dose meter and appropriate detector.

2a.2.1.1.5 Tube output

The specific tube output (µGy/mAs) and the output rate (mGy/s) should both be measured using a Molybdenum-Molybdenum target-filter combination at 28 kVp on a line passing through the

focal spot and the reference ROI, in the absence of scatter material and attenuation (e.g. due to the compression plate). A tube load (mAs) similar to that required for the reference exposure should be used for the measurement. Correct for the distance from the focal spot to the detector and calculate the specific output at 1 metre and the output rate at a distance equal to the focus-to-film distance (FFD).
If the measurements are used for dosimetry, tube output measurements should be performed at all relevant spectra with the compression plate in position.

Limiting values	Acceptable: > 30 µGy/mAs at 1 metre, achievable > 40 µGy/ mAs at 1 metre > 70% of value at acceptance for all target-filter combinations.
Frequency	Every six months and when problems occur.
Equipment	Dose-meter, exposure timer.

Note: A high output is desirable for a number of reasons e.g. it results in shorter exposure times, minimising the effects of patient movement and ensures adequate penetration of large/dense breasts within the setting of the guard timer. In addition any marked changes in output require investigation.

2a.2.1.2 Tube voltage and beam quality

The radiation quality of the emitted X-ray beam is determined by tube voltage, anode material and filtration. Tube voltage and Half Value Layer (i.e. beam quality assessment) can be assessed by the measurements described below.

2a.2.1.2.1 Reproducibility and accuracy

A number of tube voltages should be checked, which cover the range of clinically used settings. The reproducibility is measured by repeated exposures at one fixed tube voltage that is normally used clinically (e.g. 28 kVp).

Note: Consult the instruction manual of the kVp-meter for the correct positioning.

Limiting value	Accuracy for the range of clinically used tube voltages: < ± 1 kV, reproducibility < ± 0.5 kV.
Frequency	Every six months.
Equipment	kVp-meter.

2a.2.1.2.2 Half Value Layer (HVL)

The Half Value Layer can be assessed by adding thin aluminium (Al) filters to the X-ray beam and measuring the attenuation.
Position the exposure detector at the reference ROI (since the HVL is position dependent) on top of the bucky. Place the compression device halfway between focal spot and detector. Select a molybdenum/molybdenum target/filter combination, 28 kV tube voltage and an adequate tube loading (mAs-setting), and expose the detector directly. The filters can be positioned on the compression device and must intercept the whole radiation field. Use the same tube load (mAs) setting and expose the detector through each filter. For higher accuracy (about 2%) a diaphragm, positioned on the compression paddle, limiting the exposure to the area of the detector may be used (see European Protocol on Dosimetry in Mammography, ISBN 92-827-7289-6). At acceptance the measurements should be repeated for all relevant spectra for average glandular dose calculations. The HVL is calculated by applying formula 2.5.

$$HVL = \frac{X_1 \ln\left(\frac{2Y_2}{Y_0}\right) - X_2 \ln\left(\frac{2Y_1}{Y_0}\right)}{\ln\left(\frac{Y_2}{Y_1}\right)} \qquad (2.6)$$

The direct exposure reading is denoted as Y_0; Y_1 and Y_2 are the exposure readings with added aluminium thickness of X_1 and X_2 respectively.

Note 1: The purity of the aluminium ≥ 99.9% is required. The thickness of the aluminium sheets should be measured with an accuracy of 1%.
Note 2: For this measurement the output of the X-ray machine needs to be stable.
Note 3: The HVL for other (clinical) tube voltages and other target materials and filters may also be measured for assessment of the average glandular dose (see appendix 5 and the European Protocol on Dosimetry in Mammography, ISBN 92-827-7289-6).
Note 4: Alternatively a digital HVL-meter can be used, but correct these readings under extra filtration following the manufacturers' manual.

Limiting value	For 28 kV Mo/Mo the HVL must be over 0.30 mm Al equivalent, and is typically < 0.40 mm Al. Typical values of HVL for relevant target-filter combinations and tube voltages, are shown in appendix 5, table A5.3.
Frequency	Yearly.
Equipment	Dosemeter, aluminium sheets: 0.30, 0.40, 0.50, 0.60 mm.

2a.2.1.3 AEC-system

The performance of the Automatic Exposure Control (AEC) system can be described by the reproducibility and accuracy of the automatic optical density control under varying conditions, like different object thickness and tube voltages. Essential prerequisites for these measurements are a stable operating film-processor and the use of the reference cassette. If more than one breast support table, with a different AEC detector attached, is used then each system must be assessed separately.

2a.2.1.3.1 Optical density control setting: central value and difference per step

To compensate for the long term variations in mean density due to system variations the central optical density setting and the difference per step of the selector are assessed. To verify the adjustment of the optical density control, produce exposures in the clinically used AEC mode of the standard test object with varying settings of the optical density control selector.
A target value for the mean optical density at the reference ROI should be established according to local preference, in the range: 1.4 – 1.9 OD, base and fog included.

Limiting value	The optical density (base and fog included) of the step used clinically at the reference ROI should remain within ± 0.15 OD of the target value. The change produced by each step in the optical density control should be about 0.10 OD. Step-sizes within the range 0.05 to 0.20 OD are acceptable. The acceptable value for the range covered by full adjustment of the density control is > 1.0 OD.
Frequency	Step-size and adjustable range: every six months. Density and mAs-value for clinically used AEC setting: daily.
Equipment	Standard test block, densitometer.

2a.2.1.3.2 Back-up timer and security cut-off

The AEC system should also be equipped with a back-up timer or security cut-off which will terminate the exposure in case of malfunctioning of the AEC system or when the required exposure is not possible. Record the mAs-value at which the system terminates the exposure e.g. when using increasing thickness of PMMA plates.

Warning: An incorrect functioning of the back-up timer or security cut-off could damage the tube. To avoid excessive tube load consult the manual for maximum permitted exposure time.

Limiting value	The back-up timer and/or security cut-off should function properly.
Frequency	Yearly.
Equipment	PMMA plates or sheet of lead covering the detector.

2a.2.1.3.3 Short term reproducibility

Position the dosemeter in the x-ray beam but without covering the AEC-detector. The short term reproducibility of the AEC system is calculated by the deviation of the exposure meter reading of ten routine exposures (45 mm PMMA).
If it is noticed that the system switches between two spectra, release the compression paddle and compress again or use another PMMA thickness (add for example 0.5 cm PMMA) to force the choice of one single spectrum and repeat the measurement.

Limiting value	Deviations from the mean value of exposures < ± 5%, achievable < ± 2%.
Frequency	Every six months.
Equipment	Standard test block, dosemeter.

Note: For the assessment of the reproducibility, also compare these results from the short term reproducibility with the results from the thickness and tube voltage compensation and from the optical density control setting at 45 mm PMMA at identical settings. Any problem will be indicated by a mismatch between those figures.

2a.2.1.3.4 Long term reproducibility

The long term reproducibility can be assessed from the measurement of optical density and tube load (mAs) resulting from the exposures of a PMMA-block or the QC test object in the daily quality control. Causes of deviations can be found by comparison of the daily sensitometry data and tube load (mAs) recordings (see 2a.2.3.2).

Limiting value	The variation from the target value must be within < ± 0.20 OD; achievable < ± 0.15 OD.
Frequency	Daily.
Equipment	Standard test block or QC test object, densitometer.

2a.2.1.3.5 Object thickness and tube voltage compensation

Compensation for object thickness and tube voltage should be measured by exposures of PMMA plates in the thickness range 20 to 70 mm in the clinically used AEC mode. If the system only incorporates a semi-automatic exposure control, spectrum should be manually increased with thickness, see appendix 4. At acceptance all AEC modes should be checked. Record the spectrum, which is chosen by the AEC at all thicknesses. Record the value of the thickness indicator at all thicknesses. Measure the optical density in the reference ROI.

Limiting value	All optical density variations from the chosen target optical density must be within ± 0.15 OD. Achievable: ± 0.10 OD. Typical spectra for each PMMA thickness can be found in appendix 4. The value of the thickness indicator must be within ± 0.5 cm of the thickness of the PMMA plates.
Frequency	Every six months: full test. Weekly: 20, 45, 65 mm PMMA exposed as for clinical setting.
Equipment	PMMA: plates 10x180x240 mm^3, densitometer.

2a.2.1.3.6 Correspondence between AEC sensors

Some mammography systems incorporate several independent AEC sensors. For these systems it should be checked whether the optical density of images made with different sensors correspond and if the correct sensor is chosen by the system.
To test correspondence, images of a homogeneous PMMA plate (45 mm thick) should be made

with each AEC sensor. Choose the sensors manually. The optical density at the position of the AEC sensor, which was used for that particular image, should be measured.
To test whether the correct AEC sensor is chosen, extra attenuation material (for example: 2 or 3 aluminium sheets used for HVL measurements) should be positioned above one AEC sensor position. The markers on the compression paddle can be used as guidance. The whole sensor should be covered and adjacent sensors should not be covered. The sensor, above which the extra attenuation has been placed, must be chosen automatically by the system. If another sensor is chosen, increase the amount of attenuating material until the correct sensor is chosen or until it is beyond any doubt that the sensor does not work properly. This procedure must be repeated for all sensor positions.

Note: If the Heel effect is large, it may be necessary to add extra attenuating material for sensor positions near nipple side. The marker on the compression paddle may not always completely coincide with the real position of the sensor.

Limiting value	The variation in optical density between all AEC sensors should be within 0.20 OD. The correct AEC sensor must be chosen.
Frequency	Every six months: full test.
Equipment	Standard test block, densitometer.

2a.2.1.4 Compression

The compression of the breast tissue should be firm but tolerable. There is no optimal value known for the force, but attention should be given to the applied compression and the accuracy of the indication. All units must have motorised compression.

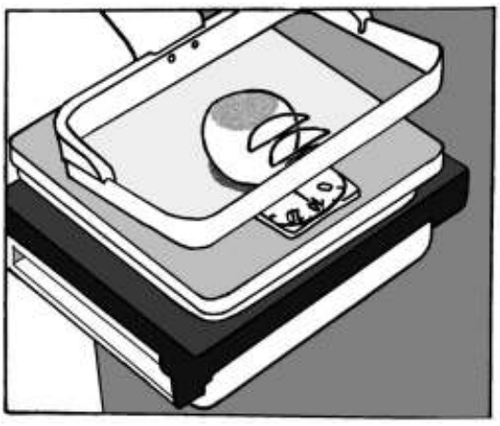


Fig. 2.4 Compression force measurement

2a.2.1.4.1 Compression force
The compression force can be adequately measured with a compression force test device or a bathroom scale (use compressible material e.g. a tennis ball to protect the bucky and compression device). The compression device should be examined for possible cracks (which might only be clearly visible under compression) and sharp edges.

When compression force is indicated on the console, it should be verified whether the figure corresponds with the measured value. It should also be verified whether the applied compression force is maintained over a period of 1 minute. A loss of force over this time may be explained, for example, by a leakage in the pneumatic system.

Limiting value	Maximum automatically applied force: 130 - 200 N. (~ 13-20 kg), and must be maintained unchanged for at least 1 minute. The indicated compression force should be within ± 20 N of the measured value. The compression device should not contain any cracks or sharp edges.
Frequency	Yearly.
Equipment	Compression force test device.

2a.2.1.4.2 Compression plate alignment

The alignment of the compression device at maximum force can be visualised and measured when a piece of foam-rubber is compressed. Measure the distance between bucky surface and compression device on each corner. Normally, those four distances are equal. Misalignment normal to the chest wall side is less disturbing than in the parallel direction, as it compensates for the heel effect. The upright edge of the device must be projected outside the receptor area and optimally within the chest wall side of the bucky.

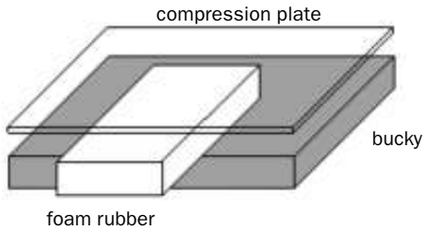


Fig. 2.5 Compression plate alignment measurement, symmetrical load

Limiting value	Minimal misalignment is allowed, the difference between the measured distances at the left and the right side of the compression paddle should be ≤ 5 mm for symmetrical load.
Frequency	Yearly.
Equipment	Foam rubber (specific mass: about 30 mg/cm^3), tape measure.

2a.2.2 Bucky and image receptor

If more than one bucky and image receptor system is attached to the imaging chain than each system must be assessed separately.

2a.2.2.1 Anti scatter grid

The anti scatter grid is composed of strips of lead and low density interspace material and is designed to absorb scattered photons. The grid system is composed of the grid, a cassette holder, a breast support table and a mechanism for moving the grid.

2a.2.2.1.1 Grid system factor

The grid system factor can be determined by dose measurements. Produce two images, one with and one without the grid system. Use manual exposure control to obtain images of about reference optical density. The first image is made with the cassette in the bucky tray (imaged using the grid system) and PMMA on top of the bucky. The second with the cassette on top of the bucky (imaging not using the grid system) and PMMA on top of the cassette. The grid system factor is calculated by dividing the dose meter readings, corrected for the inverse square law and optical density differences.

Note: Not correcting the doses for the inverse square law will result in an over estimation of 5%.

Typical value	< 3.
Frequency	At acceptance and when dose or exposure time increases suddenly.
Equipment	Dosemeter, standard test block and densitometer.

2a.2.2.1.2 Grid imaging

To assess the homogeneity of the grid in case of suspected damage or looking for the origin of artefacts, the grid may be imaged by automatic exposure of the bucky at the lowest position of the AEC-selector, without any added PMMA. This in general gives a good image of the gridlines.

Remark: For some systems it is not possible to image the grid due to the minimum required exposure time.

Limiting value	No significant non uniformity.
Frequency	Yearly.
Equipment	None.

2a.2.2.2 Screen-film

The current image receptor in screen-film mammography consists of a cassette with one intensifying screen in close contact with a single emulsion film. The performance of the stock of cassettes is described by the inter cassette sensitivity variation and screen-film contact.

2a.2.2.2.1 Inter cassette sensitivity and attenuation variation and optical density range

The differences between cassettes can be assessed with the reference exposure (section 2a.1). Select an AEC setting (should be the normal position and using a fixed tube voltage, target and filter) to produce an image having about the clinically used mean optical density on the processed film. Repeat for each cassette using films from the same box or batch. Make sure the cassettes are identified properly. Measure the exposure (in terms of mGy or mAs) and the corresponding optical densities on each film at the reference ROI. To ensure that the cassette tests are valid the AEC system in the mammography unit needs to be sufficiently stable. It will be sufficient if the variation in repeated exposures selected by the AEC for a single cassette is (in terms of mGy and mAs) $< \pm 2\%$.

Limiting value	The exposure, in terms of mGy (or mAs), must be within ± 5% of the mean for all cassettes. The maximum difference in optical density between all cassettes: ± 0.10 OD is acceptable, ± 0.08 OD is achievable.
Frequency	Yearly, and after introducing new screens.
Equipment	Standard test object, dosemeter, densitometer.

2a.2.2.2.2 Screen-film contact

Clean the inside of the cassette and the screen. Wait for at least 5 minutes to allow air between the screen and film to escape. Place the mammography contact test device (about 40 metal wires/inch, 1.5 wires/mm) on top of the cassette and make a non grid exposure to produce a film with an average optical density of about 2 OD at the reference ROI. Regions of poor contact will be blurred and appear as dark spots in the image. Reject cassettes only when they show the same spots when the test is repeated after cleaning. View at a distance of 1 meter. Additionally the screen resolution may be measured by imaging a resolution pattern placed directly on top of a cassette.

Limiting value	No significant areas (i.e. > 1 cm^2) of poor contact are allowed in the diagnostically relevant part of the film.
Frequency	Every six months and after introducing new screens.
Equipment	Mammography screen-film contact test device, densitometer and viewbox.

2a.2.3 Film processing

The performance of the film processing greatly affects image quality. The best way to measure the performance is by sensitometry. Measurements of temperature and processing time are performed to establish the baseline performance.

2a.2.3.1 Baseline performance of the processor

2a.2.3.1.1 Temperature verification and baseline

To establish a baseline performance of the automatic processor, the temperature of developer and fixer are measured. Take care that the temperature is measured at a fixed point, as recommended by the manufacturers. The measured values can be used as background information when malfunction is suspected. Do not use a glass thermometer because of the contamination risk in the event of breakage.

Limiting value	Compliance with the manufacturer's recommendations.
Frequency	Every six months.
Equipment	Electronic thermometer.

2a.2.3.1.2 Processing time

The total processing time can be measured with a stopwatch. Insert the film into the processor and start the timer when the signal is given by the processor. When the processed film is available, stop the timer. When malfunction of the processor is suspected, measure this processing time exactly the same way again and check to see if there is any difference.

Limiting value	Compliance with the manufacturer's recommendations.
Frequency	At acceptance and when problems occur.
Equipment	Stopwatch.

2a.2.3.2 Film and processor

The films used in mammography should be specially designed for that purpose. Light sensitometry is a suitable method to measure the performance of the processor. Disturbing processor artefacts should not be present on the processed image.

2a.2.3.2.1 Sensitometry

Use a sensitometer to expose a film with light and insert the exposed side into the processor first. Before measuring the optical densities of the step-wedge, a visual comparison can be made with a reference strip to rule out a procedure fault, like exposure with a different colour of light or exposure of the base instead of the emulsion side.
From the characteristic curve (the graph of measured optical density against the logarithm of exposure by light) the values of base and fog, maximum density, speed and film gradients can be derived. These parameters characterise the processing performance. A detailed description of these ANSI-parameters and their clinical relevance can be found in appendix 2, film parameters.

Typical values:	base and fog: 0.15 – 0.25 OD	
	contrast:	MGrad: 3.0 - 4.0 [see note]
		$Grad_{1\text{-}2}$: 3.5 – 5.0
Frequency	Daily.	
Equipment	Sensitometer, densitometer.	

Note: There is no clear evidence for the optimal value of film gradient; the ranges quoted are based on what is typical of current practice and are dependent on the film, which is used. At the top end of these ranges the high film gradient may lead to under- and over exposure of parts of the image for some types of breast, thereby reducing the information content.

A further complication of using a very high film contrast is that stable conditions with very low variability of the parameters are required to achieve any benefit in terms of overall image quality (See appendix 3).

2a.2.3.2.2 Daily performance

The daily performance of the processor is assessed by sensitometry. After the processor has been used for about one hour each morning, perform the sensitometry as described above. The variability of the parameters can be calculated over a period of time e.g. one month (see calculation of film parameters in appendix 2).

Limiting value	See table below.
Frequency	Daily and more often when problems occur.
Equipment	Sensitometer, densitometer.

The assessment of variations can be found in the use of the following table, where the values are expressed as a **range** (Max value - Min value). Acceptable and achievable ranges are quoted in the table below. For centres where computer facilities for calculating speed and film gradient (Mgrad and $Grad_{1,2}$) are not available, speed and contrast indices are given. However, this approach is less satisfactory as these indices are not pure measures of speed and contrast.

Assessment of variations	**acceptable**	**achievable**
base and fog	< 0.03	< 0.02 OD
speed	< 0.05	< 0.03
mean gradient (Mgrad)	< 10% of baseline value	< 5% of baseline value
mid gradient ($Grad_{1,2}$)	< 0.40	< 0.20
speed index	< 0.30	< 0.20 OD
contrast index	< 0.30	< 0.20 OD

2a.2.3.2.3 Artefacts

An image of the standard test block obtained daily, using a routine exposure, should be inspected. This should show a homogeneous density, without significant scratches, shades or other marks indicating artefacts.

Limiting value	No artefacts.
Frequency	Daily.
Equipment	Standard test block or PMMA plates 40-60 mm and area 18X24 cm, viewing box.

2a.2.3.3 Darkroom

Light tightness of the darkroom should be verified. It is reported, that about half of darkrooms are found to be unacceptable. Extra fogging by the safelights must be within given limits.

2a.2.3.3.1 Light leakage

Remain in the darkroom for a minimum of five minutes with all the lights, including the safelights, turned off. Ensure that adjacent rooms are fully illuminated. Inspect all those areas likely to be a source of light leakage. To measure the extra fog as a result of any light leakage or other light sources, a pre-exposed film of about 1.2 OD is needed. This film can be obtained by a reference

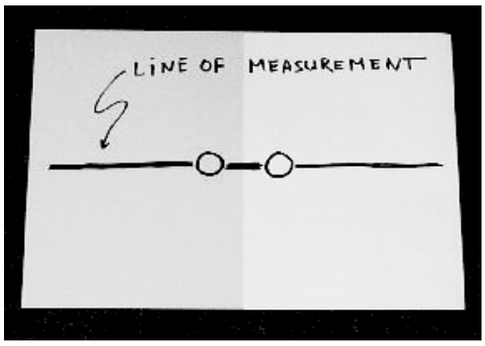


Fig. 2.6 Line of measurement when performing the light leakage measurement

exposure of a uniform PMMA block. Always measure the optical density differences in a line perpendicular to the tube axis to avoid influence of the heel effect.

Open the cassette with pre-exposed film and position the film (emulsion up) on the (appropriate part of the) workbench. Cover half the film and expose for two minutes. Position the cover parallel to the tube axis to avoid the influence of the heel effect in the measurements. Measure the optical density difference of the background (D_{bg}) and the fogged area (D_{fogged}). The extra fog (ΔD) equals:

$$\Delta D = D_{fogged} - D_{bg} \quad (2.7)$$

Limiting value	Extra fog: $\Delta D \leq 0.02$ OD in 2 minutes.
Frequency	Yearly and when light leakage is suspected.
Equipment	Film cover, densitometer.

2a.2.3.3.2 Safelights

Perform a visual check that all safelights are in good working order (filters not cracked). To measure the extra fog as a result of the safelights, repeat the procedure for light leakage but with the safelights on. Make sure that the safelights were on for more than 5 minutes to avoid start-up effects.

Limiting value	Extra fog: $\Delta D \leq 0.10$ OD in 2 minutes.
Frequency	Yearly and every time the darkroom environment has changed.
Equipment	Film cover, densitometer.

2a.2.4 Viewing conditions

Since good viewing conditions are important for the correct interpretation of the diagnostic images, they must be optimised. Although the need for relatively bright light boxes is generally appreciated, the level of ambient lighting is also very important and should be kept low. In addition it is imperative that glare is minimised by masking the film.

The procedures for photometric measurements and the values required for optimum mammographic viewing are not well established. However there is general agreement on the parameters that are important. The two main measurements in photometry are luminance and illuminance. The luminance of viewing boxes is the amount of light emitted from a surface measured in candela/m^2. Illuminance is the amount of light falling on a surface and is measured in lux (lumen/m^2). The illuminance that is of concern here is the light falling on the viewing box, i.e. the ambient light level. (An alternative approach is to measure the light falling on the film reader's eye by pointing the light detector at the viewing box from a suitable distance with the viewing box off.) Whether one is measuring luminance or illuminance one requires a detector and a photometric filter. This combination is designed to provide a spectral sensitivity similar to the human eye. The collection geometry and calibration of the instrument is different for luminance

and illuminance. To measure luminance a lens or fibre-optic probe is used, whereas a cosine diffuser is fitted when measuring illuminance. Where the only instrument available is an illuminance meter calibrated in lux it is common practice to measure luminance by placing the light detector in contact facing the surface of the viewing box and converting from lux to cd/m^2 by dividing by π. Since this approach makes assumptions about the collection geometry, a correctly calibrated luminance detector is preferred.
There is no clear consensus on what luminance is required for viewing boxes. It is generally thought that viewing boxes for mammography need to be higher than for general radiography. In a review of 20 viewing boxes used in mammographic screening in the UK, luminance averaged 4500 cd/m^2 and ranged from 2300 to 6700 cd/m^2. In the USA the ACR recommend a minimum of 3500 cd/m^2 for mammography. However some experts have suggested that the viewing box luminance need not be very high provided the ambient light is sufficiently low and that the level of ambient light is the most critical factor. The limiting values suggested here represent a compromise position until clearer evidence is available.

2a.2.4.1 Viewing box

2a.2.4.1.1 Luminance

The tendency to use a high optical density for mammography means that one must ensure that the luminance of the viewbox is adequate. Measure the luminance in the centre of each viewing panel using a luminance meter calibrated in cd/m^2. An upper limit is included to minimise glare where films are imperfectly masked.

Limiting value	Luminance should be in the range 3000-6000 cd/m^2. The deviation of the luminance between the centres of all panels of a viewing box < ± 15% from the mean value of all panels.
Frequency	Yearly.
Equipment	Luminance meter.

2a.2.4.1.2 Homogeneity

The homogeneity of a single viewing box is measured by multiple readings of luminance over the surface of the illuminator, compared with the luminance in the middle of the viewing panel. Readings very near the edges (e.g. within 5 cm) of the viewing box should be avoided. Gross mismatch between viewing boxes or between viewing conditions used by the radiologist and those used by the radiographer should be avoided. If a colour mismatch exists, check to see that all lamps are of the same brand, type and age. The local personnel has to make sure that all tubes are changed at the same time. To avoid inhomogeneities as a result of dust, clean the light boxes should be regularly cleaned inside and outside.

Limiting value	The luminance across each panel should be within 30% of the luminance in the centre of the panel.
Frequency	Yearly.
Equipment	Luminance meter.

2a.2.4.2 Ambient light

When measuring the ambient light level (illuminance), the viewing box should be switched off. Place the detector against the viewing area and rotate away from the surface to obtain a maximal reading. This value is denoted as the ambient light level.

Limiting value	Ambient light level < 50 lux.
Frequency	Yearly.
Equipment	Illuminance meter.

2a.2.5 System properties

The success of a screening programme is dependent on the proper information transfer and therefore on the image quality of the mammogram. Decreasing the dose per image for reasons of radiation protection is only justified when the information content of the image remains sufficient to achieve the aims of the breast cancer screening programme.

2a.2.5.1 Dosimetry

Image PMMA plates of 20 mm thickness in clinical settings. Record the entrance surface air kerma and the exposure factors chosen by the AEC. Repeat this measurement for 30, 40, 45, 50, 60 and 70 mm PMMA thickness. Calculate the average glandular dose for a breast equivalent to each PMMA thickness. A detailed description of the calculation of the average glandular dose can be found in appendix 5.

Limiting value

A maximum average glandular dose is set per PMMA thickness:

Thickness of PMMA	**Equivalent breast thickness**	**Maximum average glandular dose to equivalent breasts**	
		acceptable level	achievable level
[cm]	[cm]	[mGy]	[mGy]
2.0	2.1	< 1.0	< 0.6
3.0	3.2	< 1.5	< 1.0
4.0	4.5	< 2.0	< 1.6
4.5	5.3	< 2.5	< 2.0
5.0	6.0	< 3.0	< 2.4
6.0	7.5	< 4.5	< 3.6
7.0	9.0	< 6.5	< 5.1

Frequency
Every six months.

Equipment
Dose meter, standard test block, densitometer.

2a.2.5.2 Image Quality

The information content of an image may best be defined in terms of just visible contrasts and details, characterised by its contrast-detail curve. The basic conditions for good performance and the constancy of a system can be assessed by measurement of the following: resolution, contrast visibility, threshold contrast and exposure time.

2a.2.5.2.1 Spatial resolution

One of the parameters which determine image quality is the system spatial resolution. It can be adequately measured by imaging two resolution lead bar patterns, up to 20 line pairs per mm (lp/mm) each. They should be placed on top of PMMA plates with a total thickness of 45 mm. Image the patterns at the reference ROI both parallel and perpendicular to the tube axis, and determine these resolutions.

Note: If the resolution is measured at different heights between 25 and 50 mm from the tabletop it can differ by as much as 4 lp/mm. The distance from the chest wall edge is critical, but the position parallel to the chest wall side is not critical within ± 5 cm from the reference ROI. Resolution is generally worse parallel to the tube axis due to the asymmetrical shape of the focal spot.

Limiting value	Acceptable: > 12 lp/mm, achievable: > 15 lp/mm at the reference ROI in both directions.
Frequency	Weekly.
Equipment	PMMA plates 180x240 mm, resolution pattern(s) up to 20 lp/mm, densitometer.

2a.2.5.2.2 Image contrast

Since image contrast is affected by various parameters (like tube voltage, film contrast etc.) this measurement is an effective method to detect a range of system faults. Make a reference exposure of an aluminium or PMMA stepwedge and measure the optical density of each step in the stepwedge. Draw a graph of the readings at each step against the stepnumber. The graph gives an impression of the contrast. Since this graph includes the processing conditions, the film curve has to be excluded to find the radiation contrast, see Appendix 3.

Remark: The value for image contrast is dependent on the whole imaging chain, therefore no absolute limits are given. Ideally the object is part of, or placed on top of, the daily quality control test object.

Limiting value	Acceptable: ± 10%, achievable: ± 5%.
Frequency	Weekly, and when problems occur.
Equipment	PMMA or aluminium stepwedge, densitometer.

2a.2.5.2.3 Threshold contrast visibility

Extensive test: Threshold contrast visibility is determined for circular details with diameters in the range from 0.1 to 2 mm. The details are imaged on a background object with a thickness equivalent (in terms of attenuation) to 50 mm of PMMA. The details must be positioned at a height of 20 to 25 mm above the breast support table[6]. Use the exposure factors that would be selected clinically. Make two images. Three experienced observers should determine the minimal contrast visible on both images. The detail diameter must cover the range from 0.1 to 2 mm. In this range minimal contrast visible for a large number of detail diameter must be determined at acceptance and at least 5 detail diameters in subsequent tests.
The threshold contrast performance specified here relates to the nominal contrast calculated for the details for a 28 kV tube voltage with a molybdenum target and filter materials as explained in appendix 6. This nominal contrast depends on the thickness and materials used to manufacture the test object, and is independent of the actual spectrum used to form the image, which should be that used clinically. It does not include the effects of scatter. The average nominal threshold contrasts should be compared with the limiting values below.
Weekly a simple test should give an indication of the lowest detectable contrast of 'large' objects (diameter > 5 mm). Therefore a selection of low contrast objects have to be embedded in a PMMA test object to mimic clinical exposures. There should be at least two visible and two non-visible objects. Note, that the result is dependent on the mean OD of the image and on noise.
Produce a routine exposure and let two or three observers examine the low contrast objects. The number of visible objects is recorded. Ideally the object is part of, or placed on top of, the daily quality control test object.

Limiting value	Extensive test: results at acceptance are used as reference. Weekly test: minimum detectable contrast for a 5-6 mm detail < 1.5%.
Frequency	Yearly (extensive test), weekly (simple test).
Equipment	Test object with low contrast details plus PMMA plates, to a thickness of 45 mm, densitometer.

2a.2.5.2.4 Exposure time

Long exposure times can give rise to motion unsharpness. Exposure time may be measured by some designs of kVp- and output meters. Otherwise a dedicated exposure timer has to be used. The time for a routine exposure is measured.

Limiting value	Acceptable: < 2 sec.; achievable: < 1.5 sec.
Frequency	Yearly and when problems occur.
Equipment	Exposure time meter, standard test block.

2a.3 Daily and weekly QC tests

There are a number of tests that should be conducted daily or weekly. For this purpose, a dedicated QC-test object or set of test objects are convenient. The actual frequencies recommended for each measurement are specified in section 2a.2.3.2.2 and summarised in Table 2a.4.1. The procedure must facilitate the measurement of some essential physical quantities, and it should be designed to evaluate:

- AEC reproducibility
- Tube output stability
- Reference optical density
- Spatial resolution
- Image contrast
- Threshold contrast visibility
- Homogeneity, artefacts
- Sensitometry (speed, contrast, fog)

Practical considerations:

- Ideally the sensitometric stepwedge should be on the same film as the image of the test object, to be able to correct optimally for the processing conditions.
- To improve the accuracy of the daily measurement, the test object should be designed in such a way that it can be positioned reproducibly on the bucky.
- The shape of the test object does not have to be breast-like. To be able to perform a good homogeneity check, the test object should cover the normally imaged area on the image receptor (180x240 mm).
- For testing the AEC reproducibility, the PMMA test object may comprise several layers of PMMA, 10 or 20 mm thick. It is important to use the same PMMA blocks since variations in thickness of the PMMA plates will influence the tube load (mAs) read-out. Sufficient blocks are required to make up a thickness in the range 20-70 mm to adequately simulate the range of breast thickness found clinically.

2a.4 Tables

Table 2a.4.1 Frequency of quality control, measured and limiting values

2a.2.1 X-ray generation and control	frequency	typical value	limiting value acceptable	limiting value achievable	unit
X-ray source					
- focal spot size	i	0.3	IEC/NEMA	-	-
- source-to-image distance	i	≥ 600	-	-	mm
- alignment of x-ray field/ image receptor	12	-	< 5	< 5	mm
- film/bucky edge	12	-	≤ 5	≤ 5	mm
- radiation leakage	i	-	< 1	< 1	mGy/hr
* output	6	-	> 30% > 70% of baseline	> 40	µGy/mAs
tube voltage					
- reproducibility	6	-	< ± 0.5	< ± 0.5	kV
- accuracy (25 – 31 kV)	6	-	< ± 1.0	< ± 1.0	kV
- HVL	12	-	See appendix 5 table A5.3	See appendix 5 table A5.3	
AEC					
* central opt. dens control setting	6	-	< ± 0.15 of target value	-	OD
- target opt. dens. control setting	6	-	1.4 -1.9		OD
- opt. dens. control step	6	-	0.05 - 0.20	0.05 - 0.10	OD
- adjustable range	6	-	> 1.0	> 1.0	OD
* short term reproducibility	6	-	< ± 5%	< ± 2%	mGy
* long term reproducibility	d	-	< ± 0.20	< ± 0.15	OD
- object thickness	w	-	< ± 0.15	< ± 0.10	OD
and tube voltage compensation	6	-	< ± 0.15	< ± 0.10	OD
- spectra	6	See appendix 4			
- correspondence between AEC sensors	6	-	< 0.20		OD
compression					
- compression force	12	-	130 - 200	-	N
- maintain force for 1 minute	12	-	1	1	min
- compression force indicator	12	-	< ± 20	< ± 20	N
- compression plate alignment, symmetric	12	-	≤ 5	≤ 5	mm

2a.2.2 Bucky and image receptor	frequency	typical value	limiting value acceptable	limiting value achievable	unit
anti scatter grid					
* grid system factor	i	< 3	-	-	-
screen-film					
* inter cassette sensitivity variation (mAs)	12	-	< ± 5%	< ± 5%	mGy
* inter cassette sensitivity variation (OD range)	12	-	< ± 0.10	< ± 0.08	OD
- screen-film contact	12	-	No significant areas of poor contact	-	-

Table 2a.4.1 continued

2a.2.3 Film processing	**frequency**	**typical value**	**limiting value** acceptable	achievable	**unit**
processor					
- temperature	i	34 - 36	-	-	°C
- processing time	i	90 - 120	-	-	s
film					
- sensitometry: base and fog	d	0.15 - 0.25[1]	-	-	OD
speed	d	-	-	-	-
Contrast Mgrad:	d	3.0 - 4.0[2]	-	-	-
$Grad_{1,2}$	d	3.5 - 5.0	-	-	-
- daily performance	d	-	See 2a.2.3.2	See 2a.2.3.2	-
- artefacts	d	-	No disturbing artefacts	-	-
darkroom					
- light leakage (extra fog in 2 minutes)	12	-	≤ + 0.02	≤ + 0.02	OD
- safelights (extra fog in 2 minutes)	12	-	≤ + 0.10	≤ + 0.10	OD

2a.2.4 Viewing conditions	**frequency**	**typical value**	**limiting value** acceptable	achievable	**unit**
viewing box					
- luminance	12	-	3000 - 6000	3000 - 6000	cd/m^2
- homogeneity	12	-	< ± 30%	< ± 30%	cd/m^2
- luminance difference between panels	12	-	< ± 15%	< ± 15%	cd/m^2
environment					
- ambient light level	12	-	< 50	< 50	lux

2a.2.5 System properties	**frequency**	**typical value**	**limiting value** acceptable	achievable	**unit**
dosimetry					
* Glandular dose	6				
- PMMA thickness (cm)					
2.0			< 1.0	< 0.6	mGy
3.0			< 1.5	< 1.0	mGy
4.0			< 2.0	< 1.6	mGy
4.5			< 2.5	< 2.0	mGy
5.0			< 3.0	< 2.4	mGy
6.0			< 4.5	< 3.6	mGy
7.0			< 6.5	< 5.1	mGy
image quality					
* spatial resolution, reference ROI	w	-	> 12	> 15	lp/mm
* threshold contrast visibility	w	-	< 1.5%	< 1.5%	-
* exposure time	12	-	< 2	< 1.5	s

End of table 2a.4.1 i = At acceptance; d = daily; w = weekly; 6 = every 6 months; 12 = every 12 months * standard measurement conditions
1. For standard blue based films only 2. Depend on the film which is used

Table 2a4.2 QC equipment specifications

QC equipment	accuracy	reproducibility	unit
sensitometer	-	± 2%	OD
densitometer	± 2% at 1.0	± 1%	OD
dosemeter	± 5%	± 1%	mGy
thermometer	± 0.3	± 0.1	°C
kVp-meter for mammographic use	± 2%	± 1%	kV
exposure time meter	± 5%	± 1%	s
luminance meter	± 10%	± 5%	$Cd.m^{-2}$
illuminance meter	± 10%	± 5%	klux
test objects, PMMA	± 2%	-	mm
compression force test device	± 10%	± 5%	N

aluminium filters (purity ≥ 99.9%)
aluminium stepwedge
resolution pattern
focal spot test device
stopwatch
film/screen contact test tool
tape measure
rubber foam for compression plate alignment
lead sheet

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2a.6 Completion forms for QC reporting

QC report

based on

The European protocol for the quality control of the physical and technical aspects of mammography screening

Fourth edition

Date: _____

Contact: _____

Institute: _____

Address: _____

Telephone: _____

Conducted by: _____

2a.2.1 X-ray generation and control

2a.2.1.1 X-ray source

2a.2.1.1.1 Focal spot size

Class (large) focal spot: _____ (IEC)

* *star pattern method*

diameter star pattern	d_{star}	____ mm
spoke angle θ	θ	____ °
diameter magnified star image	d_{mag}	____ mm
diameter first MTF zero ⊥ AC axis	$d_{blur,\perp}$	____ mm
diameter first MTF zero // AC axis	$d_{blur,//}$	____ mm

$$m_{star} = \frac{d_{mag}}{d_{star}} \; ; \; f = \frac{\pi \times \theta}{180} \times \frac{d_{blur}}{(m-1)}$$

* *slit camera method*

width slit		____ mm
distance slit-to-film	$d_{slit\text{-}film}$	____ mm
distance focus-to-slit	$d_{focus\text{-}slit}$	____ mm
width slit image ⊥ AC axis	F⊥	____ mm
width slit image // AC axis	F //	____ mm

$$m_{slit} = \frac{d_{slit-film}}{d_{focus-slit}} \; ; \; f = \frac{F}{m_{slit}}$$

* *pinhole method*

diameter pinhole		____ µm
distance pinhole-to-film	$d_{pinhole\text{-}film}$	____ mm
distance focus-to-pinhole	$d_{focus\text{-}pinhole}$	____ mm
diameter pinhole ⊥ AC axis	f⊥	____ mm
diameter pinhole // AC axis	f //	____ mm

$$m_{pinhole} = \frac{d_{pinhole-film}}{d_{focus-pinhole}} \; ; \; f = \frac{F}{m_{pinhole}}$$

Focal spot size f⊥ = _____ mm

f// = _____ mm

Accepted: yes / no

2a.2.1.1.2 Source-to-image distance

Nominal value:	____ mm
Measured value :	
- Focus indication to bucky:	____ mm
- Bucky to cassette:	____ mm
Source-to-image distance:	____ mm

2a.2.1.1.3 Alignment of X-ray field / image receptor

Distance at chest wall side film:	inside/outside image receptor:
position	
- left:	____ mm, in / out
- nipple:	____ mm, in / out
- right :	____ mm, in / out
- chest :	____ mm, in / out
Distance between film edge and bucky edge:	____ mm

Accepted: yes / no

2a.2.1.1.4 Radiation leakage

Description of position of 'hot spots'
1 _____
2 _____
3 _____

detector surface area: ____ mm^2

	measured:	calculated for
distance from tube:	50 mm	1000 mm,
surface area:	____ mm^2	100 cm^2:
nr:		
1. _____	____	____ mGy/hr
2. _____	____	____ mGy/hr
3. _____	____	____ mGy/hr

Accepted: yes / no

2a.2.1.1.5 Tube output

Focus to detector distance:	____ mm
Surface air kerma:	____ mGy
Focal spot charge:	____ mAs
Specific tube output at 1 m	____ µGy/mAs
Output rate at FFD	____ mGy/s

Accepted: yes / no

2a.2.1.2 Tube voltage

2a.2.1.2.1 Reproducibility and accuracy

Pre-set tube load:	____ mAs
Clinically most relevant kV:	____ kV

Accuracy at clinical tube voltage settings

Setting	____	____	____	28	____	____	____	kV
Measured	____	____	____	____	____	____	____	kV
Deviation	____	____	____	____	____	____	____	kV

Accepted: yes / no

Reproducibility at the clinically most relevant tube voltage setting

Set tube voltage ____ kV
Measured value: 1.____ 2.____ 3.____ 4.____ 5.____ kV
Reproducibility (max difference from the mean): ____ kV

Accepted: yes / no

2a.2.1.2.2 Half Value Layer

Target/filter:	Mo/Mo				
Measured tube voltage:	28 kV				
Pre-set tube load:	____ mAs				
Filtration:		0.0	0.30	0.40	mm Al
Exposure:		Y_0	Y_1	Y_2	
	1.	____	____	____	mGy
	2.	____	____	____	mGy
	3.	____	____	____	mGy
Average exposure:		____	____	____	mGy

$$HVL = \frac{X_1 \ln(\frac{2Y_2}{Y_0}) - X_2 \ln(\frac{2Y_1}{Y_0})}{\ln(\frac{Y_2}{Y_1})} = \text{____ mm Al}$$

Deviation exposure at 0 mm Al: ____ %

Accepted: yes / no

Half Value Layer for average Glandular Dose calculations

Target/filter:	___ / ___				
Measured tube voltage:	____ kV				
Pre-set tube load:	____mAs				
Filtration:		0.0	____	____	mm Al
Exposure:		Y_0	Y_1	Y_2	
	1.	____	____	____	mGy
	2.	____	____	____	mGy
	3.	____	____	____	mGy
Average exposure:		____	____	____	mGy

HVL: ____ mm Al

Deviation exposure at 0 mm Al : ____ %

2a.2.1.3 AEC-system

2a.2.1.3.1 Optical density control setting: central value and difference per step

Target density value: ____ OD

Setting	Exposure mGy	Tube load mAs	Density OD	Density incr. OD
-3	____	____	____	____
-2	____	____	____	____
-1	____	____	____	____
0	____	____	____	____
1	____	____	____	____
2	____	____	____	____
3	____	____	____	____

Accepted: yes / no

Adjustable range: ____ OD

Accepted: yes / no

Optical density control setting for reference density: ____
Optical density control setting for target density: ____

2a.2.1.3.2 Back-up timer and security cut-off

Exposure terminates by exposure limit : yes/no
Alarm or error code: yes/no
Exposure: ____ mGy
Tube load: ____ mAs

2a.2.1.3.3 Short term reproducibility

Optical density control setting: ____

Exp. #	Exposure (mGy)	Tube load (mAs)
1	____	____
2	____	____
3	____	____
4	____	____
5	____	____
6	____	____
7	____	____
8	____	____
9	____	____
10	____	____

Deviation in tube load: ____ % (= 100 x (max-min)/mean)

Accepted: yes / no

2a.2.1.3.4 Long term reproducibility: Forms should be made to suit the local preferences.

2a.2.1.3.5 Object thickness and tube voltage compensation

Optical density control setting: ____
Mode name: ____

PMMA thickness	Target/ filter	Tube voltage (kV)	Optical Density (OD)	Thickness Indication (mm)
10 mm	____	____	____	____
20 mm	____	____	____	____
30 mm	____	____	____	____
40 mm	____	____	____	____
50 mm	____	____	____	____
60 mm	____	____	____	____
70 mm	____	____	____	____

Variation in optical density: ____ OD

Accepted: yes / no

2a.2.1.3.6 Correspondence between AEC sensors

AEC sensor position	Tube load (mAs)	Optical Density
____	____	____ OD
____	____	____ OD
____	____	____ OD
____	____	____ OD
____	____	____ OD
____	____	____ OD
Difference in Optical Density		____ OD

AEC sensor position	Position extra attenuation	Tube load (mAs)	Chosen AEC sensor position
____	____	____	____
____	____	____	____
____	____	____	____
____	____	____	____
____	____	____	____
____	____	____	____

Accepted: yes / no

2a.2.1.4 Compression

2a.2.1.4.1 Compression force

Force indication: ____ N
Measured compression force: ____ N
Compression force after 1 min: ____ N

Accepted: yes / no

2a.2.1.4.2 Compression plate alignment

Attachment compression plate: in order/out of order

Symmetric load
Thickness indication: ____ cm

Height of compression plate above the bucky at full compression:

	left	right	difference(l/r)	
Rear :	____	____	____	cm
Front :	____	____	____	cm
Difference(r/f)	____	____		cm

Accepted: yes / no

2a.2.2 Bucky and image receptor

2a.2.2.1 Anti scatter grid

2a.2.2.1.1 Grid system factor

	Exposure [mGy]	Tube load [mAs]	Density [OD]
Present:	____	____	____
Absent:	____	____	____
Grid system factor:	____		

Accepted: yes / no

2a.2.2.1.2 Grid imaging

Additional grid images made:

#	Added PMMA	Description of artefacts
1.	yes/no	_____
2.	yes/no	_____
3.	yes/no	_____

Accepted: yes / no

2a.2.2.2 Screen-film

2a.2.2.2.1 Inter cassette sensitivity and attenuation variation and optical density range

AEC setting: ____

Cassette id	Exposure [mGy]	Tube load [mAs]	Density [OD]
1	____	____	____
2	____	____	____
3	____	____	____
4	____	____	____
5	____	____	____
6	____	____	____
7	____	____	____
8	____	____	____
9	____	____	____
10	____	____	____
11	____	____	____
12	____	____	____
Average values:	____	____ mAs	____ OD
Max. deviation:	____ %	____ mAs	____ OD
Reference cassette:	____		

Accepted: yes / no

2a.2.2.2.2 Screen-film contact

Cassette id:	Description of artefacts:
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____
____	_____

Accepted: yes / no

2a.2.3 Film processing

2a.2.3.1 Baseline performance of the processor

2a.2.3.1.1 Temperature

Point of measurement in bath: _____

	Developer	Fixer
Reference/nominal:	____	____
Thermometer		
Reference:	____	____
Local:	____	____
Console:	____	____

2a.2.3.1.2 Process time

Time from processor signal to film available: ____ s

2a.2.3.2 Film and processor

2a.2.3.2.1 Sensitometry, daily performance, artefacts:

Forms should be made to suit the local preferences

2a.2.3.3 Darkroom

2a.2.3.3.1 Light leakage

Fog (after 2 min.) of a pre-exposed film on the workbench:

point:	1	2	3	4	5	
D(fogged):	____	____	____	____	____	OD
D(background):	____	____	____	____	____	OD
Difference:	____	____	____	____	____	OD

Average difference: ____ OD

Accepted: yes / no

Positions of light sources and leaks in the darkroom:

- _____
- _____

2a.2.3.3.2 Safelights

Type of lighting: direct/indirect
Height : ± ____ meter above workbench
Setting: ____
Filter condition : good / insufficient / absent / not checked

Fog (after 2 min.) of a pre-exposed film on the workbench:

point:	1	2	3	4	5	
D(fogged)	____	____	____	____	____	OD
D(background):	____	____	____	____	____	OD
Difference:	____	____	____	____	____	OD

Average difference: ____ OD

Accepted: yes / no

2a.2.4 Viewing conditions

2a.2.4.1 Viewing box

2a.2.4.1.1 Viewing box luminance and 2a.2.4.1.2 Homogeneity

Viewing panel Luminance (cd/m^2)	1	2	3	4	5
Centre	____	____	____	____	____
Top left	____	____	____	____	____
Top right	____	____	____	____	____
Bottom left	____	____	____	____	____
Bottom right	____	____	____	____	____
Difference in luminance between the centres (%)	____	____	____	____	____
Maximum deviation in luminance compared to the luminance in the centre (%)	____	____	____	____	____

Accepted: yes / no

2a.2.4.2 Ambient light level

Reading from the illuminance meter (detector at the image plane, box is off): ____ lux

Accepted: yes / no

2a.2.5 System properties

2a.2.5.1 Dosimetry

PMMA thickness (mm)	Average glandular dose (mGy)
20	____
30	____
40	____
50	____
60	____
70	____

Accepted: yes / no

2a.2.5.2 Image quality

2a.2.5.2.1 Spatial resolution

Position of the centre of the pattern:

Height above the bucky surface: ____ mm
Distance from thorax side of the bucky: ____ mm
Distance from AC axis: ____ mm

Resolution	R⊥ AC-axis	R//AC-axis
image 1	____	____
image 2	____	____
image 3	____	____
image 4	____	____

Accepted: yes / no

2a.2.5.2.2 Image contrast

image	mAs	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10
1	____	____	____	____	____	____	____	____	____	____	____
2	____	____	____	____	____	____	____	____	____	____	____
3	____	____	____	____	____	____	____	____	____	____	____
4	____	____	____	____	____	____	____	____	____	____	____
5	____	____	____	____	____	____	____	____	____	____	____

Graph(s) attached

2a.2.5.2.3 Threshold contrast visibility

Observer	# objects identified
1	____
2	____
3	____

Accepted: yes / no

Diameter disc (mm)	Threshold contrast (%)
0,1	____
0,2	____
0,5	____
1,0	____
2,0	____

2a.2.5.2.4 Exposure time

AEC setting for a routine image: ____
Tube load obtained: ____ mAs
Exposure time: ____ s

Accepted: yes / no

2b

European protocol for the quality control of the physical and technical aspects of mammography screening

Digital mammography

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- the Digital Mammography Project of the Leuven Universitary Center of Cancer Prevention (LUCK).

Both projects are partners of the European Breast Cancer Network (EBCN).

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Foreword

The 'European guidelines for quality assurance in mammography screening' (European Guidelines, 2001) include as chapter 3 the 'European protocol for the quality control of the physical and technical aspects of mammography screening'. In this protocol the requirements for an adequate screen-film imaging system are defined. In recent years, the image detection technology used in mammography has extended to include the use of digital detector systems. This technology is different in so many ways, that it is necessary to set new quality standards and test procedures specifically for digital systems.

This document is based on the addendum to chapter 3 of the European guidelines (3rd edition), which was released in November 2003 (Addendum, 2003). The approach to quality assessment and control in this protocol is comparable in the sense, that the measurement and evaluation of performance are in principle independent of the type and brand of the system used. The measurements are generally based on parameters that are extracted from the images that are produced when a phantom with known physical properties is exposed under defined conditions. The limiting values are based upon the quality that is achieved by screen-film systems, which fulfil the demands of the European guidelines.
To fulfil the European guidelines in mammography screening, the digital x-ray system must pass all relevant tests at the acceptable level. The achievable level reflects the state of the art for the individual parameter.

This protocol for digital mammography is work-in-progress and subject to improvements as more experience in digital mammography is obtained and new types of digital mammography equipment are developed. Changes in measuring techniques or limiting values will lead to a new version number, changes in wording or added comments will change the sub-number. Updates on the current version will be made available on the EUREF website (www.euref.org). It is recommended that users check the website for updates before testing digital mammography equipment.

In the text some lines are printed in parentheses [like these]. This text is a remark.

Text in a box like this needs further evaluation.

2b.1 Introduction to the measurements

To produce images with adequate quality, each part of the imaging chain must function within the limits of performance given. Experience with some digital systems shows, that non-compliance results in a seriously diminished information transfer to the observer. This can be expected to result in a lower detection rate for microcalcifications and/or for low contrast lesions.
To facilitate the relevant quality control, the user must be able to evaluate the status of the acquisition system including detector, the processing system and the display system (see fig. 1). This protocol follows recommendations according to the DICOM standard (NEMA, Digital Imaging and Communications in Medicine). The equipment therefore must be able to transmit and receive digital mammogram images as IOD's (Information Object Definitions) of modality 'MG' (mammography) or 'CR' (computed radiography), in compliance with parts 3 (IOD definition), 5 (data structures and encoding), 6 (data dictionary) and 7 (message exchange) of the DICOM standard. Modality MG is preferred over modality CR (for example because MG includes exposure parameters and the terms 'for processing' and 'for presentation' are used to distinguish unprocessed and processed images).

The general principles for testing the three main parts of the imaging chain, illustrated in figure 1, are discussed below.

Acquisition system including image receptor
The acquisition system (fig. 1, A) can be evaluated:
- By inspection of a recent 'bad pixel map'. This map (either an image or a table) defines the position of all pixels of which the pixel value is not based on its own del reading (see 2b.2.2.3.2). It must be accessible to the user at any time and be usable independently of a given equipment and manufacturers permission.
- By the assessment of the relation between X-ray exposure parameters, dose to the image receptor and pixel values. An 'unprocessed image' (DICOM defines such an image as 'for processing'), presenting a linear or other known mathematical relationship between del dose and pixel value, must be accessible. This image type must also be available for CAD (computer aided detection) or other processing software.
- By an indication of the nominal sensitivity setting of the system in every image.
  Since image quality increases with dose, the preference for higher system dose can be expected. This leads to a higher mean glandular dose and consequent higher radiation risk to the women screened. In screen-film systems the dose to the image receptor is linked to the mean optical density of each film, given the speed class of the system (speed class 100 corresponds roughly to an air kerma of 10 μGy at the place of the image receptor). An indication, comparable to speed class, must be provided for digital systems to keep the radiologist informed on the average doses delivered. It is recommended that manufacturers provide sufficient information in the header of the file to allow calculation of the average glandular dose for each individual patient. A working group of DICOM is drafting the definitions.
- For the evaluation of the acquisition system this protocol follows some draft procedures of the American Association of Physicists in Medicine (AAPM) Task Group 10 (Samei, 2001) and of preliminary results of the American College of Radiology Imaging Network Dmist trial (ACRIN Dmist).

Processing system
- In future the processing system (fig 1, B) may be evaluated by the inspection and scoring of a test set of images (either mammograms or phantom images), which have been processed in the available standard processing algorithm.
  - These images are to be inserted by the user as 'unprocessed images' (DICOM: 'for processing') and processed by the software of the manufacturer before displaying.
  - The manufacturer must provide information in general terms on the processing applied.
- The processing algorithms are built to enhance the visibility of specific image details. At this moment little experience and literature on the effects is available. These algorithms therefore are not addressed in the present protocol. The observer is urged to convince himself of the value of the algorithms provided.

- Evaluation of processing algorithms and CAD (computer aided detection) will be addressed in a future version of this protocol.

Display system

- The display system (fig 1, C) can be evaluated by the inspection on the display system (printer or monitor) of synthetic test images, produced in DICOM format and independent of the phantom images delivered by the manufacturer. The user must be able to insert these images as 'processed images' (DICOM: 'for presentation'). They are not processed further before displaying. Evaluation of such images is necessary to confirm compliance to quality standards other than those of the manufacturer. It must be possible to load and display these phantom images using the imaging system under evaluation.
- For the evaluation of the display system this protocol follows the advice of AAPM Task Group 18 (Samei, 2004) and of preliminary results of the ACRIN Dmist trial.

The measurements in the protocol are in principle chosen and described to be generally applicable. Where the tests are similar to those required for screen-film mammography, a reference to the relevant part of the European guidelines is given. When necessary, different test procedures are given for CR (computed radiology, i.e. photo-stimulable phosphor type) systems and DR (direct radiology, i.e. solid state type, including scanning slot) systems separately.

Many measurements are performed by an exposure of a test object. All measurements are performed under normal working conditions: no special adjustment of the equipment is necessary. Since the available settings in the different systems vary in spectrum and X-ray quantity for the different breast thicknesses, no common standard exposure can be indicated. Therefore dose calculations for the comparison of systems are based on the AGD (average glandular dose) to the breast (or simulated breast) rather than on entrance surface air kerma.
To evaluate the clinical use of a system, a standard type of exposure is specified: the routine exposure, which is intended to provide information on the system under clinical settings.

For the production of the routine exposure, a test object is exposed using the machine settings as follows (unless stated otherwise):

	Routine exposure:
test object thickness:	45 mm
test object material:	PMMA
tube voltage:	as used clinically
target material:	as used clinically
filter material:	as used clinically
compression device:	in contact with test object
anti scatter grid:	as used clinically
source-to-image distance:	as used clinically
photo timer detector (for CR):	in position closest to chest wall
automatic exposure control:	as used clinically
exposure control step:	as used clinically
exposure-to-read-time (for CR):	1 minute[7]
image processing:	off

Mean pixel values and their standard deviation are measured in a standard region of interest (ROI), which has an area of 4 cm^2 and is positioned 60 mm from the chest wall side and laterally centred.

Limits of acceptable performance for image quality and dose are based on the limits of acceptable performance of screen-film mammography systems. The relation between dose and limits of visibility of details for a certain contrast are based on the performance of a large number of screen-film systems in the UK, the Netherlands, Germany, Belgium and France. These acceptable limits are given, but often a better result is achievable. When applicable the achievable values are also given. Both the acceptable and achievable values are summarised in Appendix 7. Occasionally no limiting value is given, but only a typical value as an indication of what may normally be expected. The measurement frequencies indicated in the protocol (appendix 6) are the minimum required. When the acceptable limiting value is exceeded the measurement should be repeated. If necessary, additional measurements should be performed to determine the origin of the observed problem and appropriate actions that should be taken to solve the problem.
For some tests the limiting values are **provisional,** this means that the limiting value needs further evaluation and may be changed in the future. Check the EUREF website for updates. In some cases further remarks about the limiting values can be found in a box.

Guidance on the specific design and operating criteria of suitable test objects will be given by a separate project group of the European Breast Cancer Network (EBCN). Definition of terms, such as the reference ROI and signal-to-noise-ratio are given in section 2b.1.5. The evaluation of the results of the QC measurements can be simplified by using the forms for QC reporting that are provided on the EUREF homepage (www.euref.org).

2b.1.1 Staff and equipment

The local staff can perform several measurements. The more elaborate measurements should be undertaken by medical physicists who are trained and experienced in diagnostic radiology and specifically trained in mammography QC. Comparability and consistency of the results from different centres is best achieved if data from all measurements, including those performed by local technicians or radiographers, are collected and analysed centrally.

The staff conducting the daily/weekly QC-tests will need the following equipment[8] at the screening site:

- Standard test block[9] (45 mm PMMA[10])
- Reference cassette (CR systems)
- Digital QC test images
- PMMA plates[11]

The medical physics staff conducting the other QC-tests will need the following additional equipment and may need duplicates of some of the above[3]:

- Dose meter
- Tube voltage meter
- Exposure time meter
- Telescopic luminance meter
- Illuminance meter
- QC test objects
- Digital QC test images
- Contrast-detail test object
- Densitometer
- Aluminium sheets
- Focal spot test device + stand
- Screen-film contact test device
- Tape ruler
- Compression force test device
- Rubber foam
- Lead sheet
- Expanded polymer spacers

2b.1.2 System demands

Accessibility
It must be possible to access and insert DICOM images as 'for processing' and 'for presentation' to allow evaluation of the image receptor, image processing and image presentation separately.

AEC
The As Low As Reasonably Achievable (ALARA) principle on dose administered to the patient necessitates the use of an automated exposure control (AEC) system to ensure the optimal exposure of the image receptor compensating for breast thickness and composition. The use of a look up table, only based on the measured thickness of the compressed breast, increases the mean dose to the patients. This is due to the necessary margin in exposure to avoid increased noise by underexposure in dense breasts and to compensate for the incorrect reading of the thickness.

Image receptor
The required physical size of the image receptor and the amount of missed tissue at the short sides and especially at the chest wall side are important for an optimal imaging of the breast tissues. An upper limit is given for the amount of missed tissue at chest wall side, but the acceptance of other margins remains the responsibility of the radiologist.

Display system
Optimal transfer of the information in digital mammograms will be reached, when every pixel in the matrix is projected to at least one pixel on the display system and when the pixel size on the display system is sufficiently small to show details that coincide with the maximum sensitivity of the eye of the observer (1-3 lp/mm at a viewing distance of 30 cm). In screening the monitor should allow for the inspection of the image at full size in full resolution, since the number of images read does not allow time consuming procedures like roaming or zooming. Normally two images are viewed at the same time, and with the current technology it is therefore recommended that diagnostic workstations with two large (45-50 cm diagonal (19-21^{II})) high quality, 5 megapixel monitors are used.
On the acquisition unit it may be acceptable to use a monitor with lower specification, depending on the tasks of the radiographer.
Further research is needed to demonstrate whether cheaper solutions (e.g. 3 megapixel monitors) may be sufficient in clinical situations.

Viewing conditions
Since the maximum intensity on the monitor (300-800 cd/m^2) is much lower than that of a viewing box with unexposed and developed film (3000-6000 cd/m^2) and due to the reflection characteristics of the monitor, the amount of ambient light might seriously diminish the visible dynamic range and the visibility of low contrast lesions. The ambient light level therefore should be low (less than 10 lux) to allow maximal extension to the lower part of the range. Although this level has proven to be acceptable, a short time to adapt to this level might be necessary.

Computed Radiography (CR) system
Measurements should be performed with the same phosphor screen to rule out differences between screens except when testing individual screens as in section 2b.2.2.4 and when testing contrast threshold visibility as in section 2b.2.4.1. The exposure-to-read-time is standardised to minimize differences caused by varying time delays (i.e. fading of the latent image).
The DICOM standard allows both IOD's of 'CR' and 'MG' to be used for CR images. This may lead to improper hanging of the images by different display systems.

Direct Radiography (DR) detector
When measurements are performed for which no image is required (e.g. HVL or tube voltage), the detector should be covered sufficiently to prevent ghost images appearing on subsequent use of the system.
When the absorbers in the QC test object lead to automatic exposure values other than those that would be obtained with homogeneous PMMA, set the system manually to these values.

Printer
The pixel size of the printer should be in the same order of magnitude as (or less than) the pixel size of the image and should be < 100 micron.

2b.1.3 Order of the measurements

It is advisable to perform measurements such as homogeneity, NPS, linearity, MTF first and ghosting last to prevent the influence of possible ghost images. After the ghosting measurement it is advised to make some additional images with a homogeneous block of PMMA covering the whole detector to make sure that ghosts do not appear on clinical images.

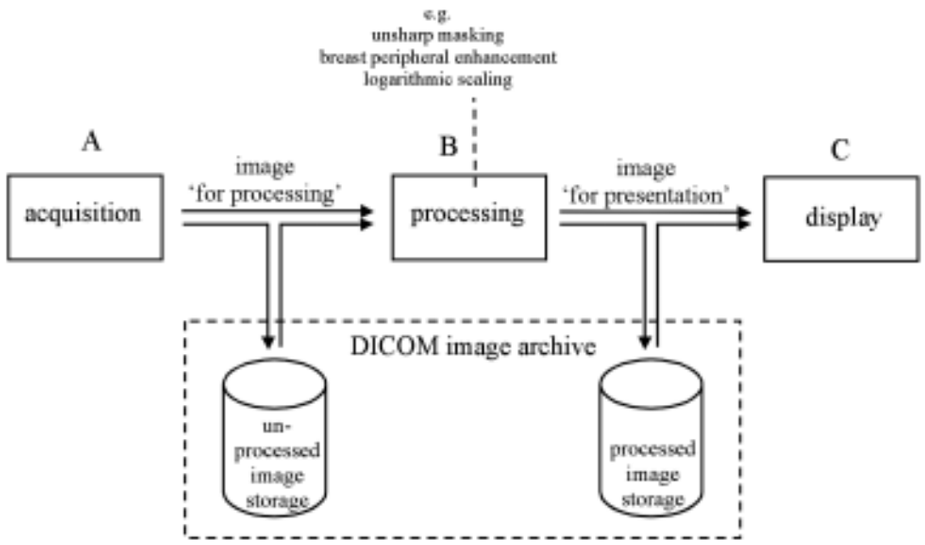


Fig.1

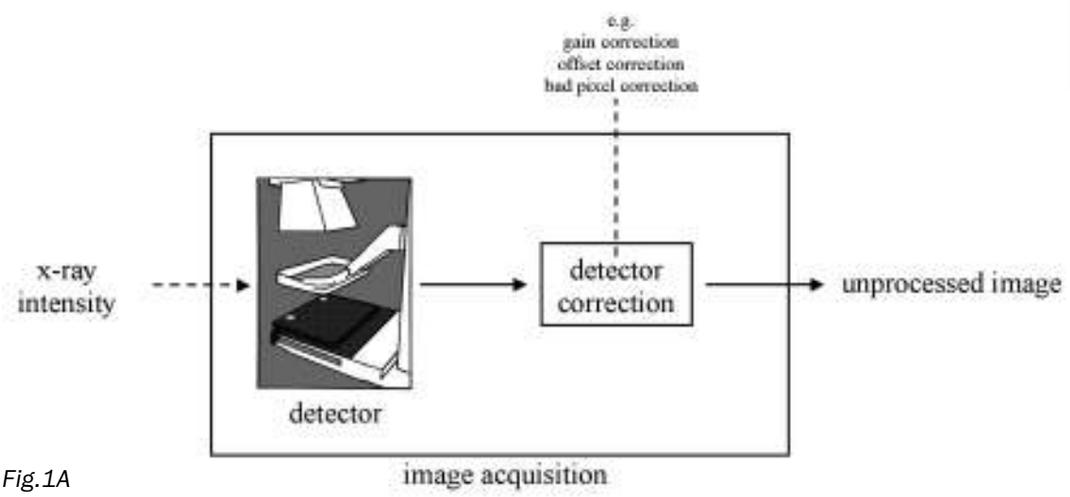


Fig.1A

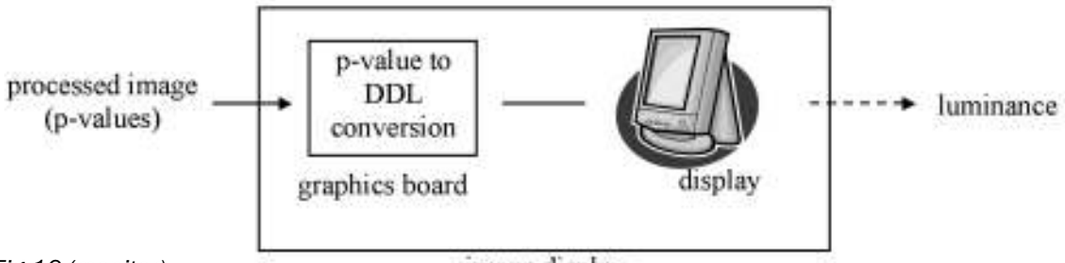


Fig.1C (monitor)

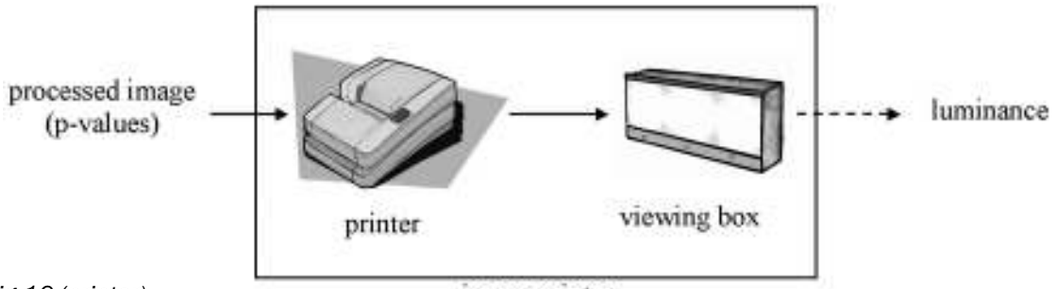


Fig.1C (printer)

2b.1.4 Philosophy

Introduction
The primary scope of this document is setting standards for mammography screening, however similar standards are expected for diagnostic mammography.

The imaging chain in digital mammography can be divided into three independent parts:
1. Image acquisition, which includes the X-ray generation, the image receptor and (for some systems) image receptor corrections.
2. Image processing, which includes the image processing software.
3. Image presentation, including monitor, image presentation software, printer and viewing box.

In the European protocol for the quality control of the physical and technical aspects of mammography screening these parts of the imaging chain are evaluated separately. This is a practical approach because each requires very different evaluation techniques and it allows the use of equipment and software from different vendors. In the present version of the protocol (version 4) only image acquisition and image presentation are considered. Due to the large number of processing techniques and the shortcomings of classical test objects with regard to the evaluation of post processing as histogram and texture based processing, evaluation of the image processing part of the imaging chain has not been addressed (yet). However, manufacturers have to specify in general terms, which image processing techniques are applied and it is advised to evaluate image processing by comparing mammograms to images from the previous screening round by experienced readers.

The digital section of this chapter of the European guidelines should not be considered as a guide for the optimal working point of a particular system or as a guide to optimise image quality. Different research groups are studying these issues and manufacturers are still working on the optimizing of current systems and the development of new techniques. We urge the reader of this document to keep track of all new developments in this rapidly changing technology. Updates of this protocol will be available at www.euref.org.

2b.1.4.1 Methods of testing

The tests as described in the present text on image acquisition are based on the expertise of the different European groups in digital mammography, the American College of Radiology Imaging Network Dmist trial (ACRIN Dmist) QC protocol (and experiences with this protocol which were shared generously by the QC team of the trial), manufacturers QC tests and the publication from American Association of Physicists in Medicine (AAPM) Task Group 10 concerning CR systems.
The tests in the image presentation section are based on the testing methods and test images of AAPM Task Group 18. This includes conformation to the DICOM standard for presentations.

Before publication the test methods have been evaluated using a number of different types of digital systems. For some types of systems only a small number of evaluation tests have been performed due to limited accessibility. Due to the rapidly changing technologies, new methods of testing may be necessary in the future. Check for updates on the EUREF website.

2b.1.4.2 Limiting values

Limiting values have been derived as much as possible from practice using screen-film mammography: it is assumed to be a requirement that digital mammography should perform at least as well as screen-film mammography.
For some test items the limiting values need more evaluation. In these cases, the limiting values have been made provisional. For some requirements, we depend on the provision of additional features by the manufacturers. In these cases, a date is given by which the items should be made available.

To remain up-to-date with the latest insights, the protocol will be updated continuously. Latest versions will be made available on the EUREF website (www.euref.org).
The philosophy of important QC tests and remarks are explained in the following paragraphs.

2b.1.4.3 Image acquisition

The X-ray generation part of the protocol is essentially identical to that of screen-film mammography. Therefore it will not be discussed in this section.

Automatic exposure control
Some digital mammography equipment on the market, are still 'in development'. One of the features not yet incorporated in some systems, is an automatic exposure control device. This has a number of disadvantages:

1. In the case of completely manual settings, mistakes in exposure settings may occur and lead to under- or overexposure and leading to insufficient image quality or unnecessary patient dose. Contrary to screen-film mammography, in which underexposure is immediately recognized from a change in the optical density of the film, underexposure in digital mammography is not easily recognized by the radiographer or the radiologist. This may lead to insufficient image quality.
2. The system might not be able to handle the high throughput necessary in mammography screening.
3. Due to the unknown breast content, exposure factors must be tuned to dense breasts to guarantee a sufficiently high image quality. This leads, however, to unnecessarily high exposures for other women and does not comply with the As Low As Reasonably Achievable (ALARA) principle. Some manufacturers try to compensate for this by providing exposure tables for several types of breast composition. However, it is not always clear how these tables were set-up and how the categories of breast content are defined or anticipated. The problem comes down to the user who has to choose the right exposure table. This is difficult since breast content may not be known until the breast is imaged.

Therefore, the authors have stated that systems used for mammography screening should incorporate an AEC. Manufacturers of equipment without Automatic Exposure Control (AEC), are

urged to implement such a device in their systems before January 2006. For the time being systems which incorporate an exposure table in the software that account only for compressed breast thickness, will be allowed. We advise against systems in which both spectrum and dose have to be set completely manually.

2b.1.4.4 Image quality evaluation

Image quality is evaluated in terms of threshold contrast visibility at a standard simulated breast thickness. This provides a measure of image quality for an average breast. As this test is rather time consuming, the evaluation is restricted to this standard thickness. The image quality of other thicknesses is related to the image quality at the standard thickness using simpler parameters, which describe the image quality relative to the image quality at the standard thickness.

2b.1.4.4.1 Image quality at standard thickness

Image quality is expressed in terms of threshold contrast visibility using clinical exposure settings. This allows evaluation of the image quality of a digital image receptor in relationship to the spectrum and dose levels, which are used clinically on that particular system.
For the evaluation of threshold contrast visibility 'unprocessed' phantom images must be used. In this way, only the image acquisition part of the system is included and the image quality evaluation cannot be considered as a 'whole-system' test.
It is acknowledged that it is not possible to get 'unprocessed' images from all systems yet. For these systems threshold contrast visibility has to be determined on images with the least possible image processing. This processing may introduce artefacts due to histogram or texture based processing techniques. Therefore care needs to be taken in interpretation of these processed contrast-detail (CD) images.

To increase reliability at least six phantom images are required. To reduce the (in-) visibility of small disks due to the accidental relative position of the disks and the dels of the detector the phantom has to be repositioned slightly after acquisition of each image. Extensive window levelling and zooming must be performed to optimize the visibility of the dots in each section of the phantom image. This prevents the monitor from being the limiting factor for the threshold contrast evaluation instead of the quality of the unprocessed image. At least three readers should score two different images each.
A problem with scoring CD images is the inter- and intra-reader variability. Therefore CDMAM images with scores are available on the EUREF website for reference purposes. In future, the threshold contrast visibility test may be performed using computer readout of the phantom images. This will solve problems with inter- and intra-observer variability Allowance may need to be made for differences between human and machine measurements of threshold contrast.
At this moment image quality is evaluated using a total attenuation equivalent to 50 mm PMMA thickness. This has been chosen because image quality information was available for this thickness. In the future, the image quality evaluation may be performed at the thickness of 45 mm PMMA, which has been chosen as the standard thickness for other tests in the European Guidelines.

Two kinds of limiting values have been set: acceptable and achievable limiting values. The acceptable limiting values have been derived from screen-film mammography, the achievable limiting values have been derived from current full-field digital mammography systems.
The acceptable limiting values have been derived by stating that image quality of digital mammography must be (at least) comparable to screen-film mammography (Young, 2004). For this purpose the image quality of a large number of screen-film mammography systems in different screening programmes has been determined using CD analysis. The CDMAM phantom has been used for these measurements. It was chosen that the image quality limiting values for digital mammography should be such that 97.5% of the screen-film systems in the UK would comply. This means that the image quality limits are not very demanding and it must be realized that a system just complying to the acceptable limits would probably not be considered equivalent to top quality screen-film systems.

The resulting limiting values have been checked with the image quality levels found in the Dutch screening and in some of the German screening projects (of which data was available) and were found to be realistic.
Furthermore the limiting values have been checked with the CD curves from some hospitals in which it was established (by radiologists) that image quality of the digital system was too low for mammography. (The visibility of microcalcifications was regarded insufficient). Threshold contrast visibility for small diameters did not meet the acceptable limiting values in these hospitals. The image quality of a system is only acceptable if contrast threshold values for all diameters comply with the limiting values.
The achievable limiting values have been derived as averages from a number of established digital mammography systems. At the EUREF website CDMAM images with scores can be found for reference purposes.

2b.1.4.4.2 Image quality at other PMMA thicknesses

In version 1.0 of the protocol for digital mammography image quality at thicknesses other than standard thickness is related to the image quality at the standard thickness using Signal-to-Noise Ratio (SNR) and Contrast-to-Noise Ratio (CNR) requirements. The absolute values of SNR and CNR are system dependent (they are dependent on for example pixel size), therefore limiting values need to be expressed in terms of variation in SNR over the whole range of simulated breast thicknesses and percentage of CNR at standard thickness respectively.
However there are difficulties with this measurement. At this moment three kinds of parameters are used by manufacturers to control image quality in AEC systems: dose to the detector (pixel value), SNR and CNR.
Screen-film mammography systems and some digital systems keep dose to the AEC detector constant over the whole range of breast thicknesses (for digital systems this means that pixel value is kept constant), some other systems keep SNR constant and recently a system has been introduced which tries to keep CNR constant.

In the view of the authors CNR would be the right measure to quantify image quality at thicknesses other than standard thickness. CNR should not necessarily be equal across the whole range of breast thicknesses. However, problems arise when setting the CNR value at standard thickness as reference for other thicknesses using the method described in version 1.0 of the Protocol for digital mammography. If the CNR at standard thickness is high, CNR at other thicknesses may fail, not because image quality is too low, but because image quality at standard thickness is relatively high. So the method of testing and limiting values needed to be revised.
In this fourth edition of the guidelines the value of CNR at standard thickness is estimated which would be obtained on a system if this system just complied with the acceptable limiting values of threshold contrast visibility. In the calculation of this minimum CNR level it is assumed that quantum noise is the main source of noise in the system. The calculation is based on the Rose theory, from which can be derived that threshold contrast visibility is inversely related to CNR. The calculated CNR at the acceptable limiting value of threshold contrast is the lower limit of CNR at standard thickness. Lower limits of CNR at other thickness are related to this value providing sufficient CNR for the whole range of breast thickness.

2b.1.4.5 Glandular dose

It is assumed that average glandular dose levels in digital mammography systems should be no more than for screen-film systems. To ensure this, the limiting dose values have been changed compared to the third edition of the European guidelines for quality assurance in mammography screening in three aspects:
In the present version of the protocol the clinical spectrum is used for dose measurements instead of a standard spectrum, the dose limits have been made independent of optical density and a limiting dose value per PMMA thickness is introduced. The reasons for these changes will be explained in the next paragraphs.

In the third edition of the protocol for screen-film systems, limiting dose values were measured using a standard spectrum. This requirement of the third edition cannot be fulfilled by some digital mammography systems due to the available spectra. For example: scanning slot systems use tungsten instead of molybdenum targets due to the required tube loading. Furthermore using clinical spectra in dose measurements is closer to clinical practice.
In the third edition, Entrance Surface Air Kerma (ESAK) limits at standard thickness have to be measured for a given optical density. Practical ESAK values are found to be far below the limiting value, even at the clinically used optical density. In digital mammography the link between limiting dose values and OD is non-existent. Therefore a choice had to be made what limiting dose value would be appropriate for digital mammography. In the view of the authors, inspired by the ALARA principle, dose should not increase substantially when changing to digital mammography. Data from the Dutch (Beckers 2003), Swedish (Leitz 2001), Norwegian (Pedersen 2000) and UK (NHSBSP 2000, 2003) screening programmes show that average glandular dose levels in screen-film mammography systems are between 0.8 and 2.5 mGy for 4.5 cm PMMA in clinical settings (corrected for difference in standard PMMA thickness in the UK and the Netherlands). Therefore an average glandular dose limit of 2.5 mGy at standard thickness in clinical settings has been chosen to ensure that dose levels in digital mammography will not exceed those of screen-film mammography. This limiting value is comparable to the objective of the NHSBSP in the UK to have average glandular dose levels of 2 mGy or less (for 4.0 cm PMMA) and the limiting average glandular dose value for the Dutch screening programme (3 mGy for 5.0 cm PMMA). In the present version of the protocol limiting dose values for a range of PMMA thickness have been introduced. This has been done because in some non-AEC systems it was noticed that manufacturers decreased dose at standard thicknesses to comply with the limiting value at standard thickness while dose levels at other thickness were found to be (much) higher than found in screen-film mammography. Besides this it has been found that some systems did use much lower tube voltages than in screen-film mammography (thus increasing patient dose substantially). In measurements performed by some of the authors, these very low values proved unnecessary for image quality, therefore the use of these tube voltages does not comply with the ALARA principle. Setting limiting dose levels per PMMA thickness prevents this situation. The limiting values for PMMA thicknesses other than standard thickness have been obtained by averaging all measured glandular dose levels per PMMA thickness from all X-ray units of the Dutch screening programme and some German screening trials. The resulting average glandular dose against PMMA thickness curve has been scaled to the limiting value at standard thickness. The results have been compared with the dose values per PMMA thickness found in the UK and some of the German screening projects (screen-film mammography). The limiting values were found to be reasonable.

2b.1.4.6 Exposure time

The exposure time should be sufficiently short to avoid motion unsharpness. For scanning slot systems a distinction has to be made between the time in which each individual part of the breast is exposed and the total scanning time. The first is important for motion unsharpness, the latter for the time during which the breast of a woman is compressed.
For most systems exposure time increases rapidly with breast thickness and content. Depending on the screen-film combination and the clinically used spectra this range may vary from 0.2 to 3 seconds. For some scanning slot systems however, scanning time and exposure time are fairly constant for the whole range of breast thickness and content. Due to this design, these systems may not comply with the limiting value of 2 seconds at standard thickness. Ideally exposure time should be below a certain limiting value even for very thick and dense breasts, so the limiting value at standard thickness may not be the right measure to prevent motion unsharpness for all breasts. Because this worst case liming value has not been determined yet, the value of 2 seconds at standard thickness is maintained, with the exception that scanning slot systems for which exposure time is only slightly dependent on breast thickness and content do not have to comply. For these systems clinical results will have to show that motion unsharpness is not a problem.

2b.1.4.7 Image receptor

2b.1.4.7.1 Response function

The response function should comply with a specification. The response function may be linear or logarithmic or fulfil some other mathematical relationship. The response function should be monotonous increasing (or decreasing). In some systems manufacturers certain value is added to the pixel value of all pixels to prevent negative values. When calculating SNR this offset must be taken into account. The response function of current CR systems is not linear but may be logarithmic. For these systems the response function needs to be linearised before SNR and CNR calculations are performed.

2b.1.4.7.2 Noise evaluation

Noise is evaluated by plotting SNR squared against entrance surface air kerma (ESAK) for systems with a linear response (such as current DR systems) and Standard Deviation squared against one over ESAK for systems with a logarithmic response (such as current CR systems). The non-linearity and the offset of the curve are indications of the presence of additional noise. At acceptance a reference curve is measured. At subsequent QC tests the results should be compared to the reference curve.

2b.1.4.7.3 Missed tissue at chest wall side

The limiting value on the amount of missed tissue at chest wall side is based on characteristic values found in screen-film mammography systems. In November 2003 (date of publication of version 1.0 of the protocol for digital mammography), some specific designs of digital mammography system did not comply with the limiting value of 5 mm. Because it is stated that digital mammography should be at least equal to screen-film mammography, the manufacturers of systems, that do not comply with the limiting value, have been urged to reduce the amount of missed tissue at chest wall side for their system(s). A number of responding manufacturers have stated that they will comply.

2b.1.4.7.4 Detector element failure (DR)

It is very important to check the number and position of defective detector elements (dels). At this moment manufacturers are reluctant to provide this kind of information to users, but buyers of equipment have the right to know the extent to which the images on their systems are reconstructed. Therefore this information should be made available to the user.
It is demanded that a bad pixel map (either an image or a table with the position of all pixels of which the pixel value is not based on its own del reading) is incorporated and that this map is accessible to the user at any time and in such a format that it can be used independent of the equipment of the manufacturer.
Limiting values on detector element failure should firstly (and most importantly) be based on clinical relevance. At this moment there is not much information available on this subject. It is expected that the loss of individual microcalcifications will not influence diagnostic decisions, so (reconstructed) individual defective dels can be allowed. If a large number of dels are defective within a certain area, this might influence diagnostic decisions. The difficulty is where to draw the line.
Secondly, the correction algorithm, which is used on a particular X-ray unit, must be considered. If an algorithm cannot handle the reconstruction of certain defective del values, this might lead to unwanted artefacts on the image, even if the area is sufficiently small not to influence diagnostics. For both reasons it is currently advisable to refer to the specifications of the manufacturer for the number of defective detector elements, which can be allowed on a particular detector.

2b.1.4.7.5 Image receptor homogeneity

For DR detectors, detector corrections are applied. In this correction the pixel value of defective dels is reconstructed from the readout of neighbouring dels and corrections for differences in electronic gain of the read-out and individual detector element sensitivity variations are

performed. For some systems, the latter correction has to be performed by the user. If the user has to perform this calibration, sufficient time must have passed since the last images were made to prevent the influence of possible ghost images on the calibration. These corrections can be checked in a homogeneity test.
Strictly speaking the correction for differences in sensitivity is only valid at the spectrum and simulated breast thickness at which calibration is performed. Therefore it is advised to perform the homogeneity test at several clinically relevant spectra and thickness at acceptance. At acceptance, a baseline is established for the homogeneity test. For some types of DR detectors homogeneity changes relatively quickly over time. Therefore it is advised to check image homogeneity regularly (weekly) and check the results with the baseline. The frequency may change in future and may be dependent on the type of digital system. For CR systems the usefulness of the homogeneity test needs to be established. For the moment it is also recommended to perform this test on CR systems.
Problems may occur if the Heel effect and geometric effects are relatively large. These effects might influence the results of the image receptor homogeneity measurement. If a specific system does not comply with the provisional limiting values it is advised to check whether geometry or the Heel effect causes this deviation or any malfunction in the system. It is recommended that the images are checked visually for artefacts.

2b.1.4.7.6 Fading of latent image (CR)
At acceptance it is advised that the fading of the latent image on the phosphor screens is measured. With the results of this test the importance of using the same exposure-to-processing time (in clinical practice and during quality control tests) can be determined.

2b.1.4.7.7 Ghosting
Several reports on ghosting in DR systems have been published (for example: Siewerdsen, 1999). In CR systems ghosts may occur if the erasure of the screens is not performed optimally. This ghosting is quantified by comparing the pixel value of an induced ghost image to a known contrast in the image (contrast of an aluminium sheet). After the ghosting measurement it is advised to make some additional images with a homogeneous block of PMMA covering the whole detector to make sure that ghosts will not appear on clinical images.
For scanning slot systems ghosts will not show with the proposed method of testing, but any ghosting is included in MTF measurements.

2b.1.4.8 Image presentation

The whole image presentation section of this protocol is based on the work of AAPM Task Group 18. Only measurements which differ from the recommendations of Task Group 18 and limiting values for which systems do not comply are mentioned below.

2b.1.4.8.1 Monitors

2b.1.4.8.1.1 Ambient light
AAPM Task Group 18 does not have specific limiting values on ambient light. In fact maximum ambient light levels are dependent on the minimum luminance and reflection characteristics of the monitor. For reasons of simplicity a single ambient light limiting value has been set.

2b.1.4.8.1.2 Grayscale display function
The grayscale display function of the monitor is checked against the DICOM Greyscale Standard Display Function (GSDF). It is noticed that a number of display systems do not comply to the GSDF. Manufacturers are urged to comply with this part of the DICOM standard. Test image TG18-QC seems to be a good and quick (daily) test for the display on the monitor.

2b.1.4.3.2 Printers

2b.1.4.3.2.1 Greyscale display function

The suggestions for QC made by AAPM Task Group 18 have been adapted slightly. Task Group 18 measurements are based on measuring luminances of a printed test pattern on a viewing box. These measurements should be performed for all combinations of printers and viewing boxes. From a quality control point of view this is impractical, therefore a standard viewing box has been defined (luminance of the viewing box without film: 4000 cd/m^2, luminance contribution due to ambient illuminance reflecting of the printout: 1 cd/m^2. The optical densities of the test pattern should be such that the printout in combination with this virtual viewing box would comply with the GSDF. The luminance of the viewing boxes is controlled by the tests described in the screen-film section of the European guidelines.

2b.1.4.3.2.2 Pixel size

To be able to print images with sufficient resolution, the pixel size of the printer should be in the same order of magnitude as (or less than) the pixel size of the image and should always be < 100 micron.

2b.1.5 Definition of terms

The definitions given here specify the meaning of the terms used in this document.

Active display area — The part of the display used for displaying images, applications and the desktop.

Bad pixel map — A map (either an image or a table) which defines the position of all pixels of which the pixel value is not based on its own del reading.

Bit-depth — Number of values which can be assigned to a pixel in a certain digital system, expressed in bits.

Computer Aided Detection (CAD) — Software to aid the radiologists' detection of suspect areas in the breast image.

Computed Radiography (CR) — Digital radiology technology using photostimulable phosphor plates.

Contrast to Noise Ratio (CNR) — The CNR is calculated as follows for a specific test object (e.g. 0.2 mm Al thickness on 45 mm PMMA).

$$CNR = \frac{\text{mean pixel value (signal)} - \text{mean pixel value (background)}}{\sqrt{\frac{\text{Standard deviation (signal)}^2 + \text{Standard deviation (background)}^2}{2}}}$$

Del — Discrete element in a DR detector.

Detective Quantum Efficiency (DQE) — Function which describes the transfer of SNR as function of spatial frequency when recording an X-ray image. The DQE gives the efficiency with which the device uses the available quanta.

Detector corrections — Correction in DR systems whereby the pixel value of defective detector elements are reconstructed and pixel values are corrected for individual detector element sensitivity variations and electronic gain of the read-out.

Direct Radiography (DR)	Digital radiology technology using sealed units mounted on a radiography system, which captures X-rays and produces a digital image by sampling the X-ray image.
Digital Driving Level (DDL)	Digital value which is the input for a display system.
Exposure indicator	Number ascribed to an image related to the exposure.
Exposure time	The time between the first and last moment that primary X-rays reach an individual part of an imaged object.
Ghost image	Residuals of previous images visible on the current image.
Modulation Transfer Function (MTF)	Function, which describes how the contrast of image components is transmitted as a function of their spatial frequency content.
Noise	Fluctuations in pixel values which are unrelated to the imaged object. The standard deviation in a ROI in the output image is taken as measure of noise.
Noise power spectrum (NPS)	Function which describes image noise as a function of spatial frequency.
P-value	See presentation value.
Pixel	Picture element, the smallest unit in the image.
Pixel pitch	Physical distance between the centres of adjacent pixels. In the DICOM tags pixel pitch is called imager pixel spacing and is generally equal to detector element spacing.
Pixel value	Discrete value assigned to a pixel, in mammography systems the number of pixel values range from 1024 (10-bits) to 16384 (14 bits), depending on the detector.
Pixel value offset	Constant value that is added to the values of all pixels.
Presentation value	Pixel value after Value Of Interest Look-Up-Table (VOI LUT) or window width and window level settings have been applied.
Primary class display device	A display device used for the interpretation of medical images (also referred to in the text as 'diagnostic display device').
Processed image	The image after image processing, ready for presentation on the monitor or print-out. In the DICOM file the value of tag Pixel Intensity Relationship (0028,1040) is 'for presentation'.
Raw image	See unprocessed image.
Reference region-of-interest (ROI)	The region-of-interest (≈ 4 cm^2, either circular or square) in which mean pixel values and standard deviation are measured. The centre of the region-of-interest is positioned 60 mm perpendicular to the chest wall edge of the table and centred laterally.
Secondary class display device	A display device used for viewing the images, but not for diagnosis.

(Nominal) sensitivity setting

Indication of the sensitivity setting of the system, comparable to the speed class in screen-film systems. The practical method to implement a (nominal) sensitivity setting will be discussed with manufacturers.

Screen processing

Image processing applied in a CR system during read-out of the imaging plate.

Signal to Noise Ratio (SNR)

The SNR is calculated as follows for a specific ROI:

$$SNR = \frac{\text{mean pixel value - pixel value offset}}{\text{standard deviation in pixel value}}$$

Standard test block

PMMA test object to represent approximately the average breast (although not an exact tissue-substitute) so that the X-ray machine operates correctly under automatic exposure control and the dose meter readings may be converted into dose to glandular tissue. The thickness is 45 ± 0.5 mm. The standard test block covers the whole detector.

Threshold contrast

The smallest detectable contrast for a given detail size that can be shown by the imaging system with different intensity (density) over the whole dynamic range. The threshold contrast is a measure for imaging of low-contrast structures.

Uncorrected image

The image in a DR system before any image processing, including detector corrections and flat-fielding, is performed.

Unprocessed image

The image of a DR system after flat-fielding and detector corrections but before other image processing has been applied. In the unprocessed image the pixel value is in general linear to pixel exposure. In the DICOM file the value of tag Pixel Intensity Relationship (0028,1040) is 'for processing'. International Electrotechnical Commission (IEC) Maintenance Team (MT) 31 refers to the unprocessed image as 'raw data'.

Variation

$$\text{Variation} = \frac{\text{maximum value - minmum value}}{\text{mean value}} \times 100\%$$

VOI LUT

Value of interest lookup table, defines the (non-linear) transformation of pixel values into values meaningful for presentation (presentation values).

Window centre

Setting defining (together with window width) a linear relationship between modality pixel values and pixel values meaningful for presentation (presentation values).

Window width

Setting defining (together with window centre) a linear relationship between modality pixel values and pixel values meaningful for presentation (presentation values).

2b.2 Image acquisition

2b.2.1 X-ray generation

2b.2.1.1 X-ray source

The measurements to determine the focal spot size, source-to-image distance, alignment of X-ray field and image receptor, radiation leakage and tube output are described in this section.

> To prevent ghosting artefacts, it is advised to cover the detector with a lead sheet during all tests for which no image is required and use the non-imaging mode (if available) on the X-ray unit.

2b.2.1.1.1 Focal spot size

Use the methods and limiting values described in section 2a.2.1.1.1 of the screen-film part of the European guidelines. Either film or the digital detector may be used, but beware of detector saturation.

2b.2.1.1.2 Source-to-image distance

Use the method and limiting values described in section 2a.2.1.1.2 of the screen-film part of the European guidelines. The distance on the digital images may be obtained by multiplying distance in number of pixels with the pixel pitch.

2b.2.1.1.3 Alignment of X-ray field/image area

For CR systems use the method and limiting values described in section 2a.2.1.1.3 of the screen-film part of the European guidelines. (Currently the most convenient method for DR systems is with screen-film cassettes or CR cassettes. In future these facilities might not be available. If cassettes and film processor are unavailable at the test site, use cassettes that can be read-out or processed elsewhere or use self developing such as Polaroid Type 57 or Gafchromic XR Type T film[12]).

2b.2.1.1.4 Radiation leakage

For CR systems use the method and limiting values described in section 2a.2.1.1.4 of the screen-film part of the European guidelines. (Currently the most convenient method for DR systems is with screen-film or CR cassettes. In future this might be a problem. If cassettes and film processor are unavailable at the test site, use cassettes that can be read-out or processed elsewhere or use self developing such as Polaroid Type 57 or Gafchromic XR Type T film[12]).

2b.2.1.1.5 Tube output

Use the measurement method described in section 2a.2.1.1.5 of the screen-film part of the European guidelines. Tube output measurements should be performed at all clinically used target-filter combinations for dose calculations (if necessary). Measurements should be performed with compression paddle in place. To calculate the transmission factor of the compression paddle, which may be needed for glandular dose estimates, tube output measurements should also be performed without compression paddle. The transmission factor should be calculated as the measured air kerma in presence of the compression paddle, divided by the measured air kerma in absence of the compression paddle.

2b.2.1.2 Tube voltage and beam quality

The beam quality of the emitted X-ray beam is determined by tube voltage, anode material and filtration. Tube voltage and beam quality can be assessed by the measurements described below.

2b.2.1.2.1 Tube voltage

Both the accuracy and reproducibility of the tube voltage are measured. Use the method and limiting values described in section 2a.2.1.2.1 of the screen-film part of the European guidelines.

2b.2.1.2.2 Half Value Layer (HVL)

Use the method described in section 2a.2.1.2.2 of the screen-film part of the European guidelines.

2b.2.1.3 AEC-system

It is generally recommended that systems used for mammography screening incorporate an AEC. The performance of the AEC system should be tested in terms of reproducibility and accuracy under varying conditions (object thickness and beam quality). The AEC system should adjust target, filter and tube voltage such that image quality is sufficient and dose is within an acceptable range. Semi-automated systems that start from a user defined target, filter and tube voltage but adapt dose according to breast transparency, are also acceptable.
The use of a look-up-table (LUT) for the determination of target, filter, tube voltage and dose based on compressed breast thickness can only be allowed if this LUT is programmed into the X-ray unit. However, it must be realized that these systems do not take breast composition into account and therefore cannot be fully optimized with respect to image quality and dose. For this kind of system some guidance for QC measurements is given in appendix 8.
For dose measurements it is essential that the dosimeter is positioned outside the region in which the exposure settings are determined. Alternatively, dose can be calculated using tube loading (mAs) and tube output.

> Manufacturers of equipment, which do not incorporate an AEC, are urged to implement an AEC in their mammography X-ray units before January 2006.
> The authors advise against the use of mammography X-ray units on which the exposure settings have to be set completely manually.

2b.2.1.3.1 Exposure control steps: central value and difference per step (if applicable)

This test item only applies to mammography units with exposure control steps. Image the standard test block at the different exposure control steps (or a relevant subset). Record entrance dose (or tube loading). Calculate exposure steps in entrance dose (or tube loading).

Remark: If it is noticed that the system switches between two spectra, release the compression paddle and compress again or use another PMMA thickness (add for example 0.5 cm PMMA) to force the choice of one single spectrum and repeat the measurement.

The central setting is the standard setting. In this setting image quality must be sufficient, this is determined by contrast threshold visibility measurements, see section 2b.2.4.1.

Typical value	5 - 15% increase in exposure per step[13].
Frequency	Every six months.
Equipment	Standard test block, dose meter.

2b.2.1.3.2 Back-up timer and security cut-off

Use the method and limiting values described in section 2a.2.1.3.2 of the screen-film part of the European guidelines. Make sure that the detector is completely covered, or tape some lead plates to the tube window.

Warning: An incorrect functioning of the back-up timer could damage the tube. To avoid excessive tube load, consult the manual for maximum permitted exposure time.

2b.2.1.3.3 Short term reproducibility

Use the method and limiting values described in section 2a.2.1.3.3 of the screen-film section of the European guidelines.

Remark: If it is noticed that the system switches between two spectra, release the compression paddle and compress again or use another PMMA thickness (add for example 0.5 cm PMMA) to force the choice of one single spectrum and repeat the measurement.

2b.2.1.3.4 Long term reproducibility

Use the weekly homogeneity check (see section 2b.2.2.3.1) for long term reproducibility.

Limiting value	The variation of SNR in the reference ROI and dose < ± 10%.
Frequency	Weekly.
Equipment	Standard test block.

2b.2.1.3.5 Object thickness and tube voltage compensation

Compensation for object thickness should be measured by exposures of PMMA plates in the thickness range from 20 to 70 mm (steps of 10 mm), using the clinical AEC settings (tube voltage, target, filter and mode). The compression paddle must be in contact with the PMMA plates.

Image PMMA plates of 20 mm thickness, with an aluminium object of 0.2 mm thickness on top, if necessary in manual mode and with settings as close as possible to the clinical AEC settings (if manual mode is used, substract the pre-exposure from the settings). Position the aluminium object as shown in figure 2.1. Measure the mean pixel value and standard deviation in a ROI (4 cm^2) with (position 2) and without (position 1) aluminium object. Calculate CNR. Repeat this measurement for 30, 40, 45, 50, 60 and 70 mm PMMA thickness.

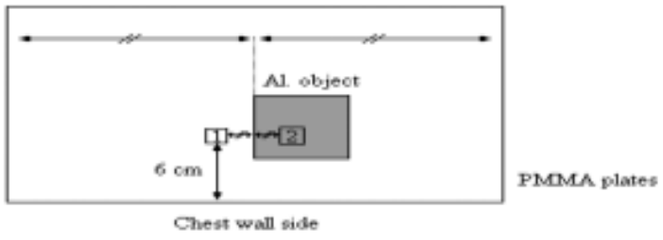


Fig. 2.1 Position of the aluminium filter for the CNR measurement

Image quality is evaluated for one thickness (at the equivalent of 5.0 cm PMMA) using contrast threshold measurements (section 2.4.1). At other PMMA thicknesses $CNR_{limiting\ value}$ is related to the $CNR_{limiting\ value}$ at 5.0 cm PMMA to ensure image quality at other thicknesses[14].

The following formula is used to calculate the limiting value of CNR at standard thickness:

$$Threshold\ contrast_{measured} * CNR_{measured} = Threshold\ contrast_{limiting\ value} * CNR_{limiting\ value}$$

The value of CNR at 5.0 cm thickness is related to the measured threshold contrast visibility in section 2b.2.4.1. Using the formula above the limiting value of CNR at standard thickness can be estimated using the measured threshold contrast in section 2b.2.4.1 and the (acceptable) limiting value of value of the 0.1 mm diameter disc. The calculated $CNR_{limiting\ value}$ should be used as the 100% level mentioned in the limiting values below.

Limiting value CNR per PMMA thickness, see table for **provisional** limiting values; Compare CNR values with results at acceptance

PMMA Thickness	CNR[15] (relative to 5.0 cm PMMA)
[cm]	[%]
2.0	> 115
3.0	> 110
4.0	> 105
4.5	> 103
5.0	> 100
6.0	> 95
7.0	> 90

Frequency Every six months.
Equipment PMMA: a set of 10 mm thick PMMA plates covering the complete detector area, 0.2 mm thick Al object (for example: the filters which are used for the HVL measurement).

2b.2.1.4 Compression

Use the method and limiting values described in section 2a.2.1.4 of the screen-film part of the European guidelines.

2b.2.1.5 Anti scatter grid

The anti scatter grid is designed to absorb scattered photons. The tests in this section only apply to mammography units with (removable) grid. Some digital mammography systems do not incorporate anti scatter grids (e.g. scanning systems).

2b.2.1.5.1 Grid system factor

Image the standard test block in clinical setting with grid. Record entrance dose and measure the mean pixel value in the reference ROI. Expose two images without grid with mean pixel values respectively below and above the value of the image with grid. Interpolate the pixel values to obtain the entrance dose for which the pixel value is similar to the image with grid. Calculate the grid system factor by dividing the entrance dose with grid by the entrance dose without grid.

Limiting value Manufacturers specification, typical value < 3.
Frequency At acceptance.
Equipment Standard test block, dose meter.

2b.2.1.5.2 Grid imaging

Use the method and limiting values described in section 2a.2.2.1.2 of the screen-film part of the European guidelines. The imaging of the grid is not possible for some grids due to minimum required exposure times.

2b.2.2 Image receptor

This section describes measurements applicable to both DR and CR systems i.e. the image receptor response and missed tissue at chest wall side. Other measurements apply to DR or CR systems only. For a DR system detector element failure is determined. The performance of the imaging plates of a CR system can be described by the CR plate sensitivity and the sensitivity to other sources of radiation.

2b.2.2.1 Image receptor response

The measurement of the response is performed to check compliance with manufacturers specifications, pixel value offset and the presence of additional noise sources beside quantum noise.

2b.2.2.1.1 Response function

The response function of the detector can be assessed by imaging a standard test block with different entrance doses (tube loading) at the clinically used beam quality. Use the manual mode for this measurement. Use at least 10 different tube loadings (mAs values). The range of mAs values should be chosen such that the linearity measurement includes a wide range of entrance surface air kerma (for example: 1/10 to 5 times[16] the entrance surface air kerma for a routine exposure).
For systems with a linear response, such as currently available DR systems, measure the mean pixel value and standard deviation in the reference ROI on the unprocessed image. Plot the mean pixel value against entrance surface air kerma. Determine linearity by plotting a best fit through all measured points and determine the zero crossing to check presence of a pixel value offset. Calculate the square of the correlation coefficient (R^2). Compare the results to previous measurements.

For systems with a non-linear response, such as currently available CR systems, plot mean pixel value against . log relative entrance surface air kerma. Refer to the information provided by the manufacturer whether pixel value should be linear or logarithmic versus entrance surface air kerma at the applied screen processing. Post processing should be turned off. The screen processing should be turned off as much as possible (see appendix 7). Determine linearity by plotting a best fit through all measured points. Calculate the square of the correlation coefficient (R^2). Compare the results to previous measurements.

Appendix 7 provides information about the relation between entrance surface air kerma and exposure indicator for some CR systems and screen processing modes.

Limiting value	R^2 > 0.99, results at acceptance are used as reference.
Frequency	Every six months. At acceptance: additional measurements at minimum and maximum tube voltage used in clinical practice at every target-filter combination.
Equipment	Standard test block, dose meter.

2b.2.2.1.2 Noise evaluation

Measure the mean pixel value and standard deviation in the reference ROI on the unprocessed images of the response function measurement (2b.2.2.1.1). For systems with a linear response, calculate the SNR and plot SNR^2 against entrance surface air kerma. Determine linearity by plotting a best fit through all measured points. Calculate the square of the correlation coefficient (R^2). Repeat this measurement for all available target-filter combinations used in clinical practice. Non-linearity is an indication for the presence of additional noise sources besides quantum noise. (At acceptance: additional measurements at minimum and maximum tube voltage used in clinical practice for each target-filter combination). Compare the results to previous measurements.
For systems with a logarithmic response plot standard deviation squared against 1/entrance surface air kerma. Determine linearity by plotting a best fit through all measured points. Calculate the square of the correlation coefficient (R^2). The offset is an indication for the presence of additional noise sources besides quantum noise. Compare the results to previous measurements.

For CR systems: No post processing should be applied, the screen processing should be turned off as much as possible (see appendix 7).

Limiting value	Results at acceptance are used as reference
Frequency	Every six months. At acceptance: additional measurements at minimum and maximum tube voltage used in clinical practice at every target-filter combination
Equipment	Standard test block, dose meter

2b.2.2.2 Missed tissue at chest wall side

Determine the width of tissue not imaged between the edge of the breast support table and the imaged area. This can be done by several methods. In some phantoms markers at a fixed distance from chest wall side are incorporated. The position of these markers on the image can be used to determine the missed tissue at chest wall side. For CR systems, this measurement should be repeated 5 times to check whether the insertion of the plate in the cassette is reproducible.

Limiting value	Width of missed tissue at chest wall side ≤ 5 mm.
Frequency	At acceptance.
Equipment	Phantom with markers positioned close to the bucky surface.

2b.2.2.3 Image receptor homogeneity and stability

2b.2.2.3.1 Image receptor homogeneity

The homogeneity of the image receptor can be obtained by exposing at clinical settings a standard test block covering the complete detector. Record the exposure settings and tube loading. Evaluate the unprocessed image by calculating the mean pixel value and standard deviation in a ROI (a square with an area of 1 cm^2). Move the ROI over the whole image. Determine the mean pixel value in the whole image and the mean SNR in all ROI's. Compare the mean pixel value and the SNR of each ROI to the overall mean pixel value and the mean SNR. Compare the SNR to previous homogeneity tests. Software for determining detector homogeneity is available on: www.euref.org.
To exclude failure due to inhomogeneities in the standard block, rotate the standard test block 180° and repeat the measurement.
Check the homogeneity visually. The window width should be set at 10% of the mean pixel value.

Perform this measurement at acceptance also at other PMMA thickness (for example with PMMA blocks of 20 and 70 mm thickness). For all measurements clinical settings should be used.

For CR systems: No post processing should be applied, the screen processing should be turned off as much as possible (see appendix 7).

It is acknowledged that the Heel effect and geometry effects influences the results of the homogeneity measurement. If a specific system does not comply with the provisional limiting values it is advised to check whether geometry or the Heel effect causes this deviation or some malfunction in the system. For CR systems an additional homogeneity image can be obtained by exposing a cassette using half dose under normal conditions and half dose with the cassette rotated 180° in the bucky to minimize the Heel effect and geometric effects.

Limiting value	**(provisional)** Maximum deviation in mean pixel value < ± 15% of mean pixel value in whole image, maximum deviation in SNR < ± 15% of mean SNR in all ROI's, maximum variation of the mean SNR between weekly images < ± 10%, entrance surface air kerma (or tube loading) between weekly images < ± 10%.
Frequency	Weekly and after maintenance, at acceptance also at 20 and 70 mm PMMA thickness.
Equipment	Standard test block covering the complete detector, at acceptance also PMMA blocks of 20 and 70 mm thickness covering the complete detector, software for determining detector homogeneity.

2b.2.2.3.2 Detector element failure (DR systems)

Inspect the most recent 'bad pixel map' of the manufacturer. This map (either an image or a table) defines the position of all pixels of which the pixel value is not based on its own del reading. This bad pixel map must be accessible by the user at any time and must be usable independent of the equipment of that manufacturer.
Evaluate the up to date information on bad columns and bad dels from the manufacturer and compare the position and number of defective dels to previous maps. Large clusters of defective dels and dels from which the reading is influenced by neighbouring defective dels may become visible in the image of a screen-film contact tool.

Limiting value	At this moment no limits have been established. In future versions of this protocol limits will be set and probably the number of defective dels/columns will (also) be limited by the percentage of a certain area, which is defective. At this moment it is advised to refer to the limits of the manufacturer.
Frequency	Every six months.
Equipment	Bad pixel map.

2b.2.2.3.3 Uncorrected defective detector elements (DR systems)

To determine the number and position of defective detector elements not corrected by the manufacturer, an image of the standard test block made at clinical settings should be evaluated by calculating the mean pixel value in ROIs (squares with an area of 1 cm^2). Move the ROI over the whole image. Determine the pixels deviating more than 20% from the mean pixel value in a ROI. To increase reliability deviating pixels can be determined on four images. Pixels, which deviate more than 20% on several images, are potentially bad pixels. If the deviating pixels are in one column, it is likely to be a bad column. Software for determining the number of uncorrected defective detector elements is available on: www.euref.org.

Limiting value	No limits have been set yet on the number of uncorrected defective detector elements.
Frequency	Weekly.
Equipment	Standard test block covering the complete detector, at acceptance also PMMA blocks of 20 and 70 mm thickness covering the complete detector.

2b.2.2.4 Inter plate sensitivity variations (CR systems)

Image the standard test block using the AEC exposure setting that is normally used clinically. Record the entrance surface air kerma (or tube loading). Process the plate. The screen processing should be turned off as much as possible (see appendix 7). No post processing should be applied. Measure the mean pixel value and standard deviation in the reference ROI. Calculate SNR. Repeat this measurement for all imaging plates. Evaluate the homogeneity of each image.

Limiting values	SNR variation in the reference ROI between all imaging plates < ± 15%, variation in entrance surface air kerma (or tube loading) < ± 10%, no major inhomogeneities on the images.
Frequency	Yearly and after introducing new imaging plates.
Equipment	Standard test block.

2b.2.2.5 Influence of other sources of radiation (CR systems)

Erase a single imaging plate. Tape two different coins, one on each side of the cassette. Store the imaging plate in the storage area during a maximal time period, for example during the complete acceptance test. Process the plate. The screen processing should be turned off as much as possible (see appendix 7). No post processing should be applied. Evaluate the visibility of the coins on the resulting image.

Limiting value	The coins should not be visible.
Frequency	At acceptance and when changes in storage of the cassettes have occurred.
Equipment	Two coins of different size (for example a one and a two Euro coin).

2b.2.2.6 Fading of latent image (CR systems)

Image the standard test block using one fixed exposure that is normally used clinically. Process the plate after 1 minute. Measure the mean pixel value in the reference ROI. Repeat the measurement with different time periods before read-out (2, 5, 10, 30 minutes).

Limiting value	Results at acceptance are used as reference.
Frequency	At acceptance and when image quality problems are suspected.
Equipment	Standard test block.

2b.2.3 Dosimetry

Use the method and limiting values described in paragraph 2.5.1 of the screen-film part of the European guidelines. The PMMA plates should cover the whole detector. For dose measurements it is essential that the dose probe is positioned outside the region in which the exposure settings are determined. Alternatively, dose can be calculated using tube loading (mAs) and tube output.

2b.2.4 Image Quality

2b.2.4.1 Threshold contrast visibility

Threshold contrast visibility is determined for circular details with diameters in the range from 0.1 to 2 mm. The details are imaged on a background object with a thickness equivalent (in terms of attenuation) to 50 mm of PMMA. The details must be positioned at a height of 20 to 25 mm above the breast support table[17]. Use the exposure factors that would be selected clinically. Make six images of the details and move the details slightly between the images to obtain

images with different relative position of the details and the detector elements. Three experienced observers should determine the minimal contrast visible on two images. Every observer must score two different images. The whole detail diameter range specified in the table below must be covered. In this range minimal contrast visible for a large number of detail diameter must be determined at acceptance and at least 5 detail diameters in subsequent tests. This evaluation should be done on unprocessed images. The window width and level and zoom facilities must be adjusted to maximise the visibility of the details on the displayed images.

It is acknowledged that at present it is not possible to get unprocessed images from some systems. For these systems threshold contrast visibility evaluation should be done on processed images. The image processing may introduce artefacts on phantom images and may be different from image processing for mammograms due to histogram or local texture based processing techniques. Therefore care needs to be taken in interpretation of these processed images.

The threshold contrast performance specified here relates to the nominal contrast calculated for the details for a 28 kV tube voltage with molybdenum target and filter materials as explained in appendix 6. This nominal contrast depends on the thickness and materials used to manufacture the test object, and is independent of the actual spectrum used to form the image, which should be that used clinically. It does not include the effects of scatter. The average nominal threshold contrasts should be compared with the limiting values below.
For CR systems: No post processing should be applied, the screen processing should be turned off as much as possible (see appendix 7). If the screens comply with the limiting values of section 2b.2.2.4 inter plate sensitivity variations, it is not necessary to use the same screen in the threshold contrast visibility measurement.

Limiting value See table

	Threshold contrast			
	Acceptable value		Achievable value	
Diameter of detail [mm]	Radiation contrast using Mo/Mo 28 kV [%]	Equivalent gold thickness[18] [µm]	Radiation contrast using Mo/Mo 28 kV [%]	Equivalent gold thickness[11] [µm]
5*	< 0.85	0.056	< 0.45	0.032
2	< 1.05	0.069	< 0.55	0.038
1	< 1.40	0.091	< 0.85	0.056
0.5	< 2.35	0.150	< 1.60	0.103
0.25	< 5.45	0.352	< 3.80	0.244
0.1	< 23.0	1.68	< 15.8	1.10

* This diameter size is optional

Frequency Yearly.
Equipment Contrast detail phantom.

The threshold contrast standards defined in the table above are chosen to ensure that digital mammography systems perform at least as well as screen-film systems (Young, 2004). They have been derived from measurements on screen-film and digital mammography systems using the Nijmegen CDMAM contrast detail phantom version 3.4 (see section 2b.1.4). However it is intended that they are sufficiently flexible to allow testing by other designs and makes of test

objects. The values quoted form a smooth curve and may be interpolated for other detail diameters. It is expected that a new design of test object will be developed that will simplify the testing against these standards on a routine basis.
On the EUREF website (www.euref.org) CDMAM images and scores are available for reference purposes.

2b.2.4.2 Modulation Transfer Function (MTF) and Noise Power Spectrum (NPS) [optional]

Image an MTF test tool. Determine the MTF of the detector by using appropriate software tools. Image a NPS phantom, or the standard test block. Determine the NPS of the detector by using appropriate software. Use the resulting MTF and NPS of the acceptance test as reference. The measurement can be repeated when in doubt about the quality of the detector.

Limiting value	Results at acceptance are used as reference.
Frequency	At acceptance and when image quality problems are suspected.
Equipment	MTF test tool, software to calculate MTF, NPS phantom [standard test block], software to calculate NPS.

2b.2.4.3 Exposure time

Long exposure times can give rise to motion unsharpness. Exposure time is defined as the time during which primary X-rays reach each individual part of an imaged object. Exposure time may be measured by some designs of tube voltage and output meters. Otherwise a dedicated exposure timer has to be used. The time for a routine exposure in all clinical AEC modes is measured at standard PMMA thickness. For scanning slot systems, also measure the scanning time.

Remark: For most systems exposure time increases rapidly with breast thickness and content. Depending on the screen-film combination and the clinically used spectra this range may vary from 0.2 to 3 seconds. For some scanning slot systems however, scanning time and exposure time are fairly constant for the whole range of breast thickness and content. Due to this design, these systems may not comply with the limiting value of 2 seconds at standard thickness. Ideally exposure time should be below a certain limiting value even for very thick and dense breasts, so the limiting value at standard thickness may not be the right measure to prevent motion unsharpness for all breasts. Because this worst case liming value has not been determined yet, the value of 2 seconds at standard thickness is maintained, with the exception that scanning slot systems for which exposure time is only slightly dependent on breast thickness and content do not have to comply. For these systems clinical results will have to show that motion unsharpness is not a problem.

Limiting value	Exposure time: acceptable: < 2 s[19]; achievable: <1.5 s; scanning time: values at acceptance are used as reference, typical value: 5 - 8 s.
Frequency	Yearly.
Equipment	Exposure time meter, standard test block.

2b.2.4.4 Geometric distortion and artefact evaluation

Evaluate geometric distortion by measuring distances (with digital distance measuring tools) on an image of a phantom with straight lines (CDMAM, Toronto geometric distortion phantom etc.). Image a wire mesh (e.g. mammography screen-film contact test device) at the standard AEC setting. For CR systems: process the plate. The screen processing should be turned off as much as possible (see appendix 7). No post processing should be applied. Evaluate the grid pattern on the resulting image.

For the different digital systems, different types of artefacts can occur. Inspect all test images for artefacts.

Limiting value	No disturbing artefacts, no visible distortion.
Frequency	Every six months.
Equipment	Test object with horizontal, vertical and diagonal lines, wire mesh.

2b.2.4.5 Ghost image/erasure thoroughness

A ghost image is the residue of a previous image on the present image. In this measurement an induced ghost image is related to the contrast of 0.1 mm Al at clinical setting.

In manual mode an image of the standard test block is made using clinical settings. The block is positioned such that half of the detector is covered and half of the detector is not covered. For the second image (at clinical settings) the standard test block covers the whole detector and the aluminium object is placed exactly centred on top of the standard block (see figure 2.2). The time between both images should be approximately one minute.

Repeat the ghost image measurement a number of times during testing.

For CR systems: No post processing should be applied, the screen processing should be turned off as much as possible (see appendix 7).

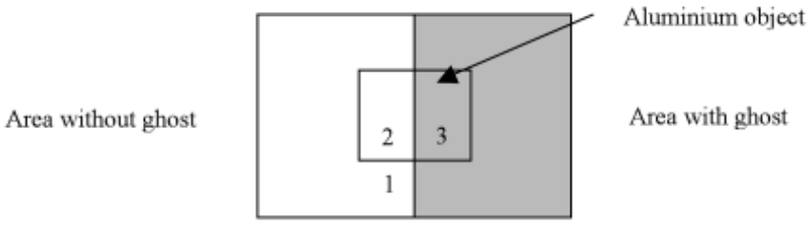


Fig. 2.2 Ghost image / erasure thoroughness measurement

Measure the mean pixel value (PV) in the ROI (area: 4 cm^2) on the locations shown in the figure above (on the second image) and calculate the 'ghost image'-factor.

$$\text{Ghost image factor} = \frac{\text{mean pixel value (region 3) - mean pixel value (region 2)}}{\text{mean pixel value (region 1) - mean pixel value (region 2)}}$$

If the system fails to meet the limiting value, check the homogeneity of the image. If the Heel effect is large regions 1 to 3 should be chosen on a line parallel to chest wall side.

> If the ghost image test is performed last, it is advised to make a number of images of a homogeneous block PMMA covering the whole detector afterwards to get rid of possible ghosts.

Limiting value	'Ghost image'-factor < 0.3 **(provisional)**.
Frequency	Yearly.
Equipment	Standard test block, aluminium object of 0.1 mm thickness (for example: the filters which are used for the HVL measurement).

2b.3 Image processing

Image processing will not be considered in this version of the protocol. Manufacturers have to specify in general terms which image processing is applied. It is advised that image processing is evaluated clinically by comparing the image quality of mammograms (for example: a set of 50 mammograms) to mammograms of previous screening rounds by experienced readers. Special attention should be given to the visualization of microcalcifications and subtle structures.

2b.4 Image presentation

The tests in this section are based upon the work of AAPM TG18 (American Association of Physicists in Medicine, Task Group 18). The TG18 test patterns described in this section should be obtained independently from the manufacturer, and can be downloaded from the TG18 website (2k versions should be used when available): http://deckard.mc.duke.edu/~samei/tg18. Some mammography display systems need adjusted versions of the test patterns, these will be available from the EUREF website.

Some general remarks:
- The test patterns have to be displayed at full resolution (exactly one display pixel for each pixel in the digital image) or printed at full size, contrast and brightness of the images may not be adjusted.
- For the tests in this chapter, the use of the display (primary class (diagnostic) or secondary class display device) often determines the limiting values.
- Some of the tests in this chapter are for Cathode Ray Tube (CRT) displays or Liquid Crystal Displays (LCDs) only.
- A magnifying glass may be used in the evaluation of printed images.
- The monitors should be tested as used clinically (e.g. third monitor on, viewing boxes on covered with films).

2b.4.1 Monitors

2b.4.1.1 Ambient light

Most of the quality tests in this chapter are highly sensitive to ambient light, therefore all of them should be performed under clinical conditions (room lights, light boxes and other display devices should be at the same luminance level as under clinical conditions). The ambient light should be measured at the centre of the display with the light detector facing outwards and the display switched off.

Limiting value	Ambient light should be less than 10 lux for primary display devices. [The maximum ambient light actually depends on the reflection characteristics and minimum luminance of the monitor, but for reasons of simplicity this is ignored here.]
Frequency	Every six months. (Every time the system is used, it has to be made sure that ambient light conditions have not changed.)
Equipment	Illuminance meter.

2b.4.1.2 Geometrical distortion (CRT displays)

Visually check whether the TG18-QC image (fig. 4.1) is displayed without geometrical distortion. To do so, inspect the lines and borders of the test pattern.

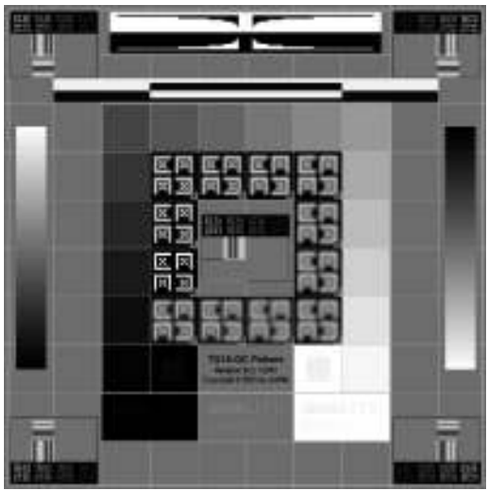


Fig. 4.1 TG18-QC test pattern

Limiting value Borders should be completely visible, lines should be straight, the active display area should be centred on the screen.
Frequency Daily.
Equipment TG18-QC test pattern.

2b.4.1.3 Contrast visibility

The TG18-QC test pattern contains several items for evaluating the contrast visibility of a display. Each of the sixteen luminance patches located approximately equidistant from the centre of the image, contains four corner squares at equal low contrast steps to the patch (fig 4.2). The two patches in the bottom with minimum and maximum pixel value, surrounding the test pattern name, contain a centre square with a pixel value of 5% and 95% of the maximal grey level respectively. The letters 'QUALITY CONTROL' in the three rectangles below these patches are displayed with decreasing contrast to the background. The visible part of the letters should be written down and checked with the visibility at acceptance, in order to keep track of contrast degradation. If contrast visibility is not sufficient, it may help to dim the room lights. If this is done however, the lights should also be dimmed while using the displaying system clinically. The appearance of the TG18-QC test pattern also depends on the mapping of pixel values to luminance. Therefore if this test has failed, the tests in sections 2b.4.1.6 and 2b.4.1.7 should be performed.

Remark: It should be kept in mind that the luminance of LCD monitors depends on the viewing angle. When large viewing angles are used, contrast visibility may not comply with the limiting values.

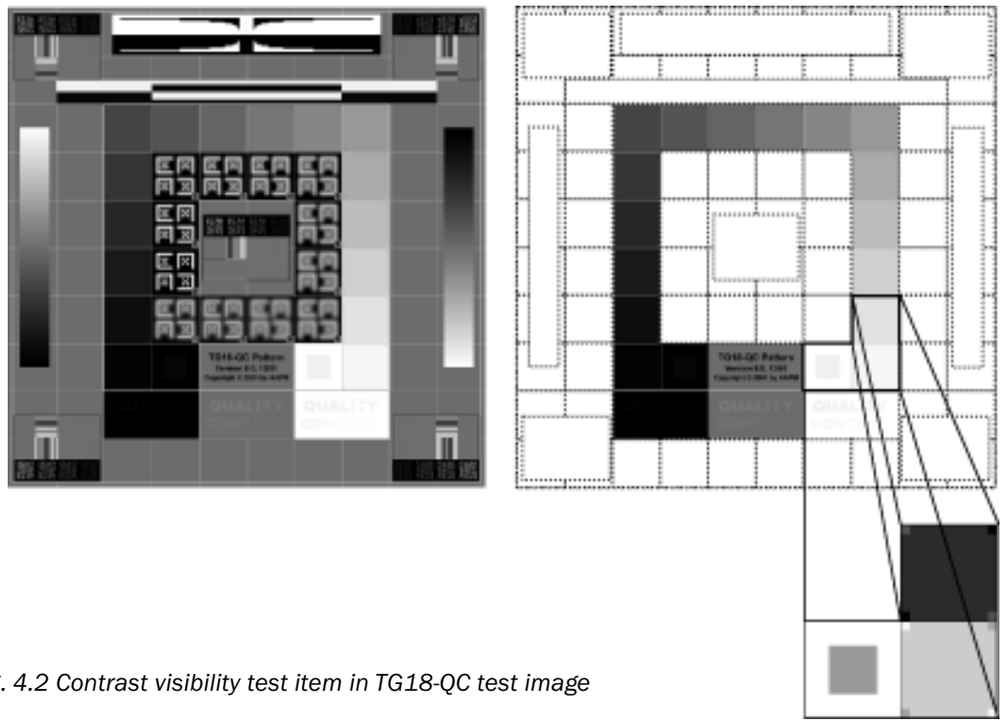


Fig. 4.2 Contrast visibility test item in TG18-QC test image

Limiting value	All corner patches should be visible, the 5% and 95% pixel value squares should be clearly visible.
Frequency	Daily.
Equipment	TG18-QC test pattern.

2b.4.1.4 Resolution

Evaluate horizontal and vertical line patterns to check display resolution visually.
AAPM Task Group 18 provides 6 line patterns at different background luminance levels. (Horizontal line patterns TG18-LPH10, -LPH50 and -LPH89; Vertical line patterns TG18-LPV10, -LPV50 and -LPV89.)

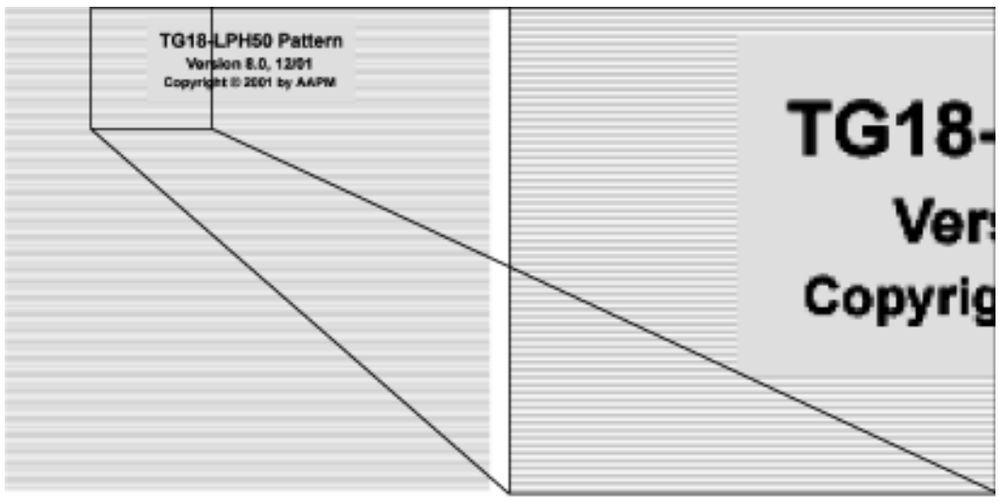


Fig. 4.3 Zoomed versions of the TG18-LPH50 pattern

Limiting value	All line patterns should be discernible.
Frequency	Every 6 months.
Equipment	2kx2k TG18-LPH10, TG18-LPH50, TG18-LPH89, TG18-LPV10, TG18-LPV50 and TG18-LPV89 test patterns.

2b.4.1.5 Display artefacts

The TG18-QC test pattern also contains some elements, which can be used for recognising display artefacts. The image should be carefully checked for defect pixels (LCD only), steps in the black-to-white and white-to-black ramp bars (this can reveal an insufficient bit depth), and artefacts near the black-to-white and white-to-black transitions (video card). Also pay attention to temporal instability (flicker) and spatial instability (jitter).

Limiting Values	No disturbing artefacts should be visible.
Frequency	Daily.
Equipment	2kx2k TG18-QC test pattern.

2b.4.1.6 Luminance range

Measure the maximum and minimum luminance of the display device. Test patterns TG18-LN12-01 and TG18-LN12-18 can be used.
The ratio of maximum and minimum display luminance, in the presence of ambient light, is an indicator of luminance contrast response capabilities of the monitor (under the current environmental conditions). Both luminances should be measured using a telescopic luminance meter, to include the influence of ambient light.
The ratio can be increased by reducing ambient light or by display adjustments. DICOM GSDF conformance (section 2b.4.1.7) makes sure the available contrast is spread out in an appropriate and standard manner over the full greyscale range of the monitor.

Remark: It should be kept in mind that the luminance of LCD monitors depends on the viewing angle. When large viewing angles are used, the luminance range may not comply with the limiting values.

Limiting Values	The maximum to minimum luminance ratio should be at least 250 for primary display devices, or 100 for secondary display devices. The difference of maximum luminances between displays belonging to one displaying station should not exceed 5% of the lowest.
Frequency	Every six months or when contrast visibility has changed.
Equipment	Telescopic luminance meter, TG18-LN12-01 and TG18-LN12-18 test patterns.

2b.4.1.7 Greyscale Display Function

To make sure a mammogram will appear similarly on different viewing stations and on printed film, the mapping of greyscale values to display luminance or optical density should be consistent. In this measurement it is determined whether a display conforms to the DICOM Greyscale Standard Display Function (GSDF).

The greyscale display function (GDF) can be determined by measuring the luminance of the 18 AAPM luminance test patterns (TG18-LN12-01 through TG18-LN12-18). The test patterns should be displayed full screen and the luminance has to be measured at the centre of the screen. The shape of the GDF depends on the ambient light in the room. Therefore room lights, light boxes and other display devices should be at the same luminance level as when the system is used clinically. A telescopic luminance meter should be used to include the influence of ambient light.

The measured values can be inserted into a spreadsheet (available on the EUREF website: www.euref.org) to automatically determine GSDF conformance.

After doing this measurement, the amount of ambient light may not be increased anymore, otherwise the contrast response has to be measured again!

Remark: This test only applies to primary and secondary display systems. The acquisition workstation monitor is excluded from this test. Due to the required ambient light levels in the mammography room the acquisition workstation monitor will not comply with the limiting values of primary and secondary displays. Therefore this monitor should only be used to check positioning techniques, not for diagnosis and image quality checks.

It is acknowledged that some displaying systems do not comply with the DICOM Greyscale Standard Function. Manufacturers are urged to comply with this standard.

Remark: It should be kept in mind that the luminance of LCD monitors depends on the viewing angle. When large viewing angles are used, the display on a monitor may not comply with the GSDF.

Limiting value	The calculated contrast response should fall within ± 10% of the GSDF contrast response for primary class displays (± 20% for secondary class displays).
Frequency	Every six months and when contrast visibility has changed.
Equipment	Telescopic luminance meter, TG18-LN12-01 through TG18-LN12-18 test patterns.

2b.4.1.8 Luminance uniformity

When the display has been tested for DICOM conformance at the centre of the monitor, this does not mean contrast visibility is optimal at every position on the monitor. One could test the GDF for several locations on the monitor, but it is more convenient to check display uniformity. Measure the display luminance at five locations for each monitor. The test patterns TG18-UNL10 and TG18-UNL80 can be used (fig. 4.4).

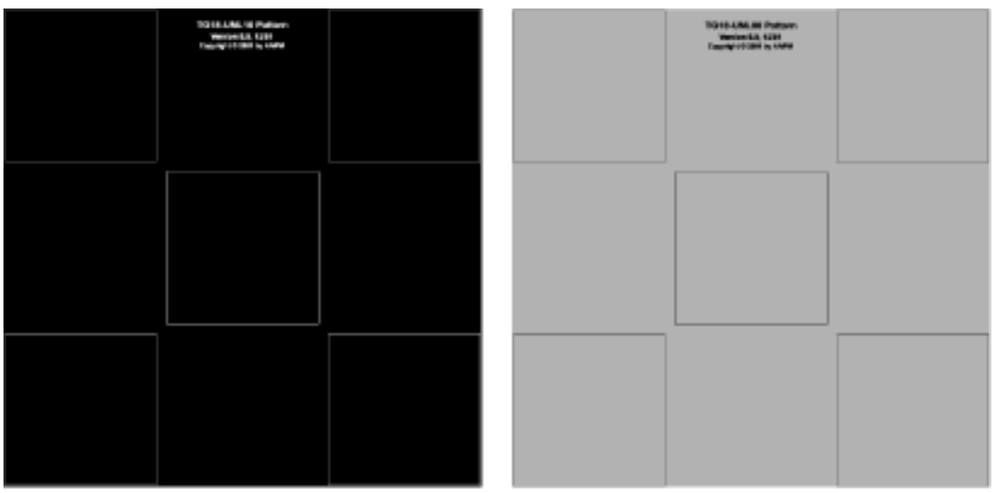


Fig. 4.4 TG18-UNL10 an TG18-UNL80 test pattern

Limiting value	Maximum luminance deviation of a display device should be less than 30% for CRT displays and LCD displays ((Lmax-Lmin)/ Lcentre < 0.3).
Frequency	Every six months and when contrast visibility has changed.
Equipment	Luminance meter (telescopic luminance meters should be equipped with a cone or baffle for this measurement), TG18-UNL10 and TG18-UNL80 test patterns.

2b.4.2 Printers

2b.4.2.1 Geometrical distortion

Print the TG18-QC test pattern (fig. 4.1) and check visually if the image is printed without geometrical distortion. Only the lines and borders of the test pattern are used to do this.

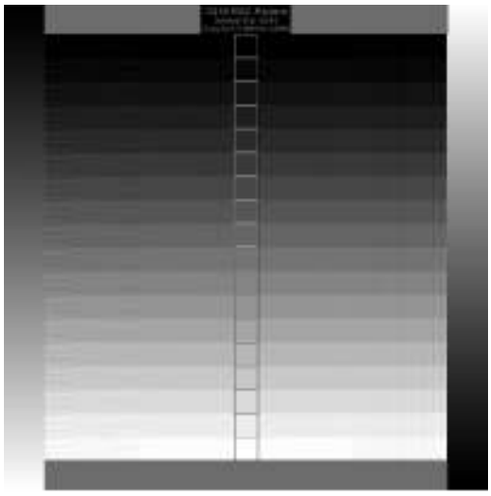
Limiting value	Borders should be completely visible, lines should be straight.
Frequency	Daily.
Equipment	TG18-QC test pattern.

2b.4.2.2 Contrast visibility

Print the TG18-QC test pattern (see fig. 4.1). Check the visibility of the several items for evaluating the contrast visibility (see fig. 4.2). Be sure that the viewing box, on which the test pattern is checked, has sufficient luminance.
If contrast visibility is not sufficient, it may help to use diaphragms (if clinically used) or dim the room lights. If this is done however, the lights should also be dimmed while using the displaying system clinically. The appearance of the TG18-QC test pattern also depends on the mapping of pixel values to densities. Therefore if this test has failed, the tests in sections 2b.4.2.5 and 2b.4.2.6 should be performed.

Limiting value	All corner patches should be visible, the 5% and 95% pixel value squares should be clearly visible.
Frequency	Daily.
Equipment	TG18-QC test pattern.

2b.4.2.3 Resolution



Evaluate horizontal and vertical line patterns to check the resolution of a print-out.
The fine detail horizontal and vertical line patterns in the TG18-PQC test pattern (fig 4.5) can be used.

Limiting value	All line patterns should be discernible[20].
Frequency	At acceptance and when decreased resolution is suspected.
Equipment	TG18-PQC test pattern.

Fig. 4.5 TG18-PQC test pattern

2b.4.2.4 Printer artefacts

Print the TG18-QC, -PQC, -UN80 and -UN10 test patterns. Check the image for printer artefacts, for example banding and streaking artefacts, pick-off artefacts, etc.

Limiting Values	No disturbing artefacts should be visible.
Frequency	Daily.
Equipment	TG18-QC, TG18-PQC, TG18-UN10 and TG18-UN80 test patterns.

2b.4.2.5 Optical Density Range (optional)

Print the TG18-QC test pattern. Measure D_{min} and D_{max} on this image.

Limiting value	D_{min} < 0.25 OD, D_{max} > 3.40 OD[21] (provisional).
Frequency	Every six months.
Equipment	Densitometer, TG18-QC test pattern.

2b.4.2.6 Greyscale Display Function

To make sure a mammogram will appear similarly on different viewing stations and on printed film, the mapping of greyscale values to display luminance or optical density should be consistent. In this measurement it is determined whether a printer conforms to the DICOM Greyscale Standard Display Function (GSDF).

The greyscale display function (GDF) can be determined by printing the TG18-PQC test pattern and measuring the optical density of marked regions of the 18 bars. The GDF is determined by the luminance corresponding with the optical density. The relationship between the luminance (L) and the optical density (D) of the printed bars is:

$L = L_a + L_0 * 10^{-D}$
where: L_a is the luminance contribution due to ambient illuminance reflected off the film, and
L_0 is the luminance of the light box with no film present

Printed mammograms may be viewed on different viewing boxes and under a variety of viewing conditions. It is not desirable to repeat this measurement for each viewing box. Assuming each viewing box, on which printed mammograms will be diagnosed, complies with the limiting values, a standard viewing box is defined. For this standard viewing box L_a is 1 cd/m^2 and L_0 is 4000 cd/m^2.

The measured values can be inserted into an spreadsheet (available on the EUREF website: www.euref.org) to automatically determine GSDF conformance.

Limiting value	The calculated contrast response should fall within ± 10% of the GSDF contrast response.
Frequency	Every six months and when contrast visibility has changed.
Equipment	Densitometer, TG18-PQC test pattern.

2b.4.2.7 Density uniformity

Print the test patterns TG18-UNL10 and TG18-UNL80. Measure the optical density at the five marked locations.

Limiting value	Maximum optical density deviation should be less than 10% ((Dmax-Dmin)/Dcentre < 0.1).
Frequency	Every six months and when contrast visibility has changed.
Equipment	Densitometer, TG18-UNL10 and TG18-UNL80 test patterns.

2b.4.3 Viewing boxes

If mammograms are read on printed images, check the viewing boxes using the method and limiting values described in the European guidelines for quality assurance in mammography screening, third edition (page 87).

2b.5 CAD software

May be considered in future versions of this protocol.

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Table 2b.1: Frequencies of Quality Control

This protocol is work-in-progress and subject to improvements as more experience in digital mammography is obtained and new types of digital mammography equipment are developed. Therefore the frequencies of quality control may change in future. Updates will be made available on the EUREF website (www.euref.org). It is recommended that users check the website for updates before testing digital mammography equipment.

Table 2b.1.1 Frequencies of Quality Control

2b.2	**Image acquisition**					
test-item		**acceptance and on indication**	**yearly**	**six monthly**	**weekly**	**daily**
2b.2.1	X-ray generation					
2b.1.1	X-ray source					
2b.1.1.1	Focal spot size	X				
2b.1.1.2	Source-to–image distance	X		if adjustable		
2b.2.1.1.3	Alignment of X-ray field/image area	X	X			
2b.2.1.1.4	Radiation leakage	X				
2b.2.1.1.5	Radiation output	X		X		
2b.2.1.2	Tube voltage and beam quality					
2b.2.1.2.1	Tube voltage	X		X		
2b.2.1.2.2	Half Value Layer	X				
2b.2.1.3	AEC-system					
2b.2.1.3.1	Exposure control steps	X		X		
2b.2.1.3.2	Back-up timer and security cut-off	X	X			
2b.2.1.3.3	Short term reproducibility	X		X		
2b.2.1.3.4	Long term reproducibility	X			X	
2b.2.1.3.5	Object thickness and tube voltage compensation	X		X		

O: optional test, X: required test

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Table 2b.1.1 continued

test-item		acceptance and on indication	yearly	six monthly	weekly	daily
2b.2.1.4	Compression	X	X			
2b.2.1.5	Anti scatter grid					
2b.2.1.5.1	Grid system factor (if present)	X				
2b.2.1.5.2	Grid imaging	O	O			
2b.2.2	Image receptor					
2b.2.2.1	Image receptor response					
2b.2.2.1.1	Response function	X		X		
2b.2.2.1.2	Noise evaluation	X		X		
2b.2.2.2	Missed tissue at chest wall side	X				
2b.2.2.3	Detector homogeneity and stability					
2b.2.2.3.1	Detector homogeneity	X			X	
2b.2.2.3.2	Detector element failure (DR)	X		X		
2b.2.2.3.3	Uncorrected defective DELs (DR)	X			X	
2b.2.2.4	Inter plate sensitivity variations (CR)	X	X			
2b.2.2.5	Influence of other sources of radiation (CR)	X				
2b.2.2.6	Fading of latent image (CR)	X				
2b.2.3	Dosimetry	X		X		
2b.2.4	Image quality					
2b.2.4.1	Threshold contrast visibility	X	X			
2b.2.4.2	MTF and NPS	O				
2b.2.4.3	Exposure time	X	X			

O: optional test, X: required test

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Table 2b.1.1 continued

test-item		acceptance and on indication	yearly	six monthly	weekly	daily
2b.2.4.4	Geometric distortion and artefact evaluation	X		X		
2b.2.4.5	Ghost image / erasure thoroughness	X	X			
2b.4	**Image presentation**					
2b.4.1	Monitors					
2b.4.1.1	Ambient light	X		X		
2b.4.1.2	Geometrical distortion (CRT)	X				X
2b.4.1.3	Contrast visibility	X				X
2b.4.1.4	Resolution	X		X		
2b.4.1.5	Displaying artefacts	X				X
2b.4.1.6	Luminance range	X		X		
2b.4.1.7	DICOM Greyscale Standard Display Function	X		X		
2b.4.1.8	Luminance uniformity	X		X		
2b.4.2	Printers					
2b.4.2.1	Geometrical distortion	X				X
2b.4.2.2	Contrast visibility	X				X
2b.4.2.3	Resolution	X				
2b.4.2.4	Printer artefacts	X				X
2b.4.2.5	Optical Density range	O		O		
2b.4.2.6	DICOM GSDF	X		X		
2b.4.2.7	Density uniformity	X		X		
2b.4.3	Viewing boxes	X	X			

O: optional test, X: required test

Table 2b.2 Limiting values

Table 2b.2.1 Limiting values

2b.2. Image acquisition	typical value	limiting value acceptable	limiting value achievable	unit
2b.2.1 X-ray generation				
X-ray source				
See European Guidelines, part A, table 4.1.				
tube voltage				
See European Guidelines, part A, table 4.1.				
AEC				
- exposure contol steps	5 - 15%			mGy or mAs
- back-up timer and security cut-off	-	function properly		
- short-term reproducibility	-	< ± 5%	< ± 2%	mGy
- long-term reproducibility				
variation in SNR	-	< ± 10%		mGy
variation in dose	-	< ± 10%		mGy
- object thickness and tube voltage compensation				
CNR per PMMA thickness				
2.0 cm	-	> 115%		
3.0 cm	-	> 110%		
4.0 cm	-	> 105%		
4.5 cm	-	> 103%		
5.0 cm	-	> 100%		
6.0 cm	-	> 95%		
7.0 cm	-	> 90%		
compression				
See European Guidelines, part A, table 4.1.				
anti scatter grid				
See European Guidelines, part A, table 4.1.				

2b.2.2 Image receptor	typical value	limiting value acceptable	limiting value achievable	unit
response function				
- linearity	-	$R^2 > 0.99$	-	-
- noise evaluation	-	-	-	-
missed tissue at chest wall side				
detector homogeneity	-	≤ 5	-	mm
- variation in mean pixel value (on image)	-	< ± 15%	-	-
- variation in SNR (on image)	-	< ± 15%	-	-
- variation in mean SNR (between images)	-	< ± 15%	-	-
- variation in dose (between images)	-	< ± 10%	-	mGy
detector element failure				
- number of defective dels	-	not yet established	not yet established	-
- position of defective dels	-	not yet established	not yet established	-

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Table 2b.2.1 continued

2b.2.2 Image receptor	**typical value**	**limiting value** acceptable	achievable	**unit**
uncorrected dels				
- number of uncorrected defective dels	-	not yet established	not yet established	-
- position of uncorrected defective dels	-	not yet established	not yet established	-
inter plate sensitivity variations				
- variation in SNR	-	< ± 15%	-	-
- variation in dose	-	< ± 10%	-	-
influence of other sources of radiation	-	coin not visible	-	-
fading of latent image	-	-	-	-

2b.2.3 Dosimetry	**typical value**	**limiting value** acceptable	achievable	**unit**
- glandular dose per PMMA thickness				
2.0 cm	-	< 1.0	< 0.6	mGy
3.0 cm	-	< 1.5	< 1.0	mGy
4.0 cm	-	< 2.0	< 1.6	mGy
4.5 cm	-	< 2.5	< 2.0	mGy
5.0 cm	-	< 3.0	< 2.4	mGy
6.0 cm	-	< 4.5	< 3.6	mGy
7.0 cm	-	< 6.5	< 5.1	mGy

2b.2.4 Image quality	**typical value**	**limiting value** acceptable	achievable	**unit**
threshold contrast visibility				
- detail				
5.0 mm (optional)	-	< 0.85%	< 0.45%	-
2.0 mm	-	< 1.05%	< 0.55%	-
1.0 mm	-	< 1.40%	< 0.85%	-
0.5 mm	-	< 2.35%	< 1.60%	-
0.25 mm	-	< 5.45%	< 3.80%	-
0.10 mm	-	< 23.0%	< 15.8%	-
MTF and NPS				
- MTF (optional)	-	-	-	-
- NPS (optional)	-	-	-	-
exposure time	-	< 2.0	< 1.5	s
scanning time	5 to 8			s
geometric distortion and artefact evaluation				
- geometric distortion	-	no distortions	-	-
- artefact evaluation	-	no disturbing artefacts	-	-
ghost image factor	-	0.3	-	-

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Table 2b.2.1 continued

2b.4 Image presentation	**typical value**	**limiting value** acceptable	achievable	**unit**
2b.4.1 monitors				
- ambient light	-	< 10	-	lux
- geometrical distortion	-	straight lines		
- contrast visibility	-	corner patches visible	-	
		squares visible	-	
- resolution	-	line pattern discernible	-	
- display artefacts	-	no disturbing artefacts	-	
- luminance range				
* ratio maximum/minimum luminance	-	250	-	
* difference in luminance left and right monitor	-	5%	-	Cd/m^2
- DICOM greyscale standard display function	-	± 10% of GSDF	-	
- luminance uniformity				
* deviation in luminance (CRT display)	-	30%	-	Cd/m^2
2b.4.2 printers				
- geometrical distortion	-	straight lines	-	
- contrast visibility	-	corner patches visible	-	
		squares visible		
- resolution	-	line pattern discernible	-	
- printer artefacts	-	no disturbing artefacts	-	
- optical density range (optional)	-	$D_{min} < 0.25$[1], $D_{max} > 3.4$[1]	-	OD
- DICOM greyscale standard display function	-	± 10% of GSDF	-	
- density uniformity				
* deviation in optical density	-	< 10%	-	OD
2b.4.3 viewing boxes				
See European Guidelines, part A, table 4.1.				

[1] Provisional limiting values

European protocol for the quality control of the physical and technical aspects of mammography screening

Appendices

Appendix 1: Mechanical and electrical safety checks

Introduction

Basic mechanical and electrical safety tests should be performed according to local regulations. If such regulations do not exist this appendix gives an example of such tests based on the UK protocol.

Mechanical Function and Safety checks

The following features of the equipment should be checked:

- All movements should operate smoothly and be free running. The force needed to move any part should be less than 30 N.
- All mechanical/electromechanical brakes should function properly.
- All scales/indications on linear/rotational movements and focus film distance (FFD) (if adjustable) should be clearly marked.
- All beam limiting diaphragms should be marked with their field sizes at the relevant FFD.
- Power driven vertical movement of the U-arm should be possible with the patient leaning against the breast support platform (without compression applied).
- Vertical and rotational movement of the U-arm should be prevented when compression is applied.
- All foot switches should operate correctly.
- All attachments should locate correctly and their locks should function properly.
- It should be possible to move the AEC detector properly into the pre-set positions.
- The bucky assembly should provide firm retention of the cassette (with the U-arm both vertical and horizontal) but allow easy insertion and removal.
- The interlock to prevent exposure when the cassette is not correctly positioned should operate correctly.
- The light intensity from the x-ray field light should be adequate.
- The movement of the compression device should be smooth.
- When compression is applied, it should not be possible to move the U-arm.
- The automatic release of the compression plate after an exposure should function correctly. The override of this automatic release should also function correctly.
- An emergency release of compression should be available and function properly.
- The compression paddle and breast support platform should be smooth and must not have any sharp edges or surfaces, etc. which may injure the patient.
- The edges of the radiation protection screen should be clearly defined so that the operator is aware of the outline.
- The restraining devices use (for X-ray unit, radiation protective screen, etc.) provided on mobile units should be effective in use.

Markings and labelling

The following should be clearly marked or indicated:

- The focal spot size and position.
- The amount of inherent, added and total filtration (usually in mm of aluminium) including that of alterable or removable filters.
- The position of AEC detectors.
- The function of all controls.

Radiation safety

The following checks relate to the safe operation of the x-ray unit:

- A mains isolator, accessible from the normal operating position should be provided.
- A visible indication must be provided on the control panel to show that the mains are switched on.
- The visible exposure warning indication must function correctly.
- The total filtration must be equivalent to at least 0.5 mm Al or 0.03 mm Mo.
- If the added filtration is removable or interchangeable, an interlock must be provided to prevent exposure if the filter is removed or incorrectly inserted.
- If the field-limiting diaphragm can be removed, an interlock should be provided to prevent exposure unless the diaphragm is properly aligned.
- The exposure must terminate if the exposure control is released prematurely.
- The location of the exposure control should confine the operator to the protected area during exposure.
- The exposure control should be designed to prevent inadvertent production of x-rays.
- The design of the exposure control should prevent further exposure unless pressure on the control is first released.

Integral radiation protection screen

A radiation protection screen should be provided to afford protection equivalent to at least 0.1 mm of lead at 50 kV and should allow good visibility of the patient by the operator and vice versa. The lead equivalence of the radiation protection screen should be marked (on both the glass and the panel where appropriate) at a specified voltage. If the lead equivalence is not marked and is not shown in the accompanying documentation, it will need to be measured.

X-ray room

- Room warning lights should be provided at all entrances to the x-ray room. These should indicate when x-rays are being or are about to be generated.
- A check on the room shielding, either visually, against the local requirements at the planning stage, or by transmission measurements, should be undertaken at or prior to installation.

Appendix 2: Film-parameters

The film curve can be characterised by a few parameters. Most important items are contrast, sensitivity and base and fog. There are different methods to calculate the film parameters. Existing normalisation's differ so much that the following method is suggested, derived from the Dutch protocol (1991), which is based on the ANSI (1983) norm.
Very high contrast can be a problem because of an associated reduction in dynamic range which may result in dense breast tissue being imaged in relatively low film densities where the film performance is relatively poor. To some extent this can be compensated for by setting relatively high average film densities, but even then a lower film contrast may better image local areas of dense tissue. Conversely a very low overall film contrast may indicate an inadequately processed film and subtle details may be missed by the radiologist.
Research has shown that film gradient measured by light sensitometry correlates well with film gradient measured by x-ray sensitometry using a fixed kV and target filter combination. One must bear in mind that film emulsions may respond slightly differently to the light from a sensitometer as opposed to the light from the screen used for imaging.

D_{min} Base and fog; the optical density of a non exposed film after developing. The minimum optical density can be visualised by fixation only of an unexposed film. The extra fog is a result of developing the (unexposed) emulsion.

D_{max} The maximum density achievable with an exposed film; i.e. the highest density step.

MGrad Mean Gradient; the property which expresses the filmcontrast in the diagnostic range. MGrad is calculated as the slope of the line through the points $D_1=D_{min}+0.25$ OD and $D_2=D_{min}+2.00$ OD. Since the film curve is constructed from a limited number of points, D_1 and D_2 must be interpolated. Linear interpolation of the construction points of the film curve will result in sufficient accuracy.

$Grad_{1,2}$ Middle Gradient; the property which expresses the filmcontrast in the diagnostic range. $Grad_{1,2}$ is calculated as the slope of the line through the points $D_1=D_{min}+1.00$ OD and $D_2=D_{min}+2.00$ OD. Since the film curve is constructed from a limited number of points, D_1 and D_2 must be interpolated. Linear interpolation of the construction points of the film curve will result in sufficient accuracy.

$Grad_{gland}$ The glandular tissue gradient can be defined as an alternatively. This is the gradient at glandular densities 0.8 – 1.2 OD. This gradient is used in combination with the $Grad_{fat}$.

$Grad_{fat}$ The alternative fat gradient is defined between densities of 2.0 and 2.4 OD. This gradient is used in combination with the $Grad_{fat}$.

Speed Sensitivity; the property of the film emulsion directly related to the dose. The Speed is calculated as the x-axis cut-off at optical density $1.00+D_{min}$, also called 'Speedpoint'. The higher the figure for Speed, the more dose is needed to obtain the right optical density. Since the film curve is constructed from a limited number of points, the Speed must be interpolated. Linear interpolation will result in sufficient accuracy.
Since these parameters are derived from the characteristic curve by interpolation they are not very practical if a computer is not available. A simpler procedure is to use the parameters below which are based on density measurements of particular sensitometric steps.

Speed Index The density of the step near to the speedpoint density 1.0 OD, base and fog excluded. Usually this is the density of step 11 of the sensitometric stepwedge.

Contrast Index 1 The difference in density found between the step nearest to the speedpoint density (1.0 OD, base and fog excluded) and the one with a 0.6 log E (factor 4) higher light exposure (normally 4 density steps) (ACR).

Contrast Index 2 The difference in density steps found between the step nearest to the speedpoint and the step nearest to a density at 2.0 OD, base and fog excluded (IPSM, see bibliography).

Appendix 3: A method to discriminate between processing and exposure variations by correction for the film-curve

The optical density of a film is the result of X-ray exposure and processing. The film is mainly exposed by light emitted by the intensifying screen. The light-emission of the screen is proportional with the incident X-ray exposure. Primary X-rays only contribute up to 5% of the total exposure. The developing process determines the optical density of the exposed area.
When an optical density in any given film is measured, the corresponding exposure is unknown. However, the film curve (measured with light-sensitometry) describes the relation between light-exposure and optical density. Any measured optical density can be converted into a relative log (light-exposure) or log (I') by interpolation of the film curve. This figure log (I') is a relative value and strongly depends on the sensitometer used. But still it is a useful value, closely related with the radiation dose applied and is therefore suitable to calculate the mass attenuation coefficient of an arbitrary X-ray step wedge.
Note that recently available films, using a different type of sensitizing and grains, in some cases show a discrepancy between the gradient as a result of light and by X-rays.

When the optical density of several images, taken under identical conditions, are measured, there will be a range of optical densities. This can either be the result of a change in exposure or a change in developing conditions. By calculating the relative figure log (I') we are able to distinguish between processor faults and tube malfunctions.

Approximation of X-ray contrast
To assess the X-ray contrast, correct the OD-readings of an Al-stepwedge for the processing conditions by converting the optical densities into a fictional 'exposure', log (I'), according the film curve. Now, a graph of the stepwedge number against 'exposure' will result in an almost straight line. The slope of this line is a measure for the X-ray contrast.

Appendix 4: Typical spectra per PMMA thickness in screen-film mammography

Changing X-ray spectrum influences both glandular dose and image quality. The choice of spectrum should be based on the optimization between both effects. In general the X-ray spectrum should be harder when (simulated) breast thickness is increased. In the table below some typical spectra, which are used in mammography, and which do not reduce contrast by more than 10% compared to an image made with Mo-Mo 28 kV are given. The results should be taken as typical values, not limiting values. When using the newly introduced high contrast films (like the Kodak EV film), the values in the table below may need adaptation.

A4.1: Typical spectra per PMMA thickness

	Spectrum			
PMMA thickness (cm)	Mo-Mo	Mo-Rh	Rh-Rh	W-Rh
2	25, 26 kV			
3	25-27 kV			
4	26-28 kV	26, 27 kV		
5	27-29 kV	26, 27 kV		
6	28-30 kV	27-30 kV	27-30 kV	
7	30, 31 kV	29-31 kV	29-31 kV	27-29 kV

Appendix 5: Procedure for determination of average glandular dose

A5.1 Dose to typical breasts simulated with PMMA

The doses to a range of typical breasts can be assessed using blocks of PMMA as breast substitutes. This method relies on the equivalence in attenuation between different thicknesses of PMMA and typical breasts [Dance et al, 2000] as listed in tables A5.1 and A5.2. It should be noted that since PMMA is generally denser than breast tissue any automatic selection of kV, target or filter may be slightly different from real breasts. This can be corrected by adding expanded polystyrene blocks to the PMMA as a spacer to make up a total thickness equal to the equivalent breast. On systems that determine the exposure factors primarily on attenuation such as the GE 2000D this should not be necessary. The average glandular dose (D) to a typical breast of thickness and composition equivalent to the thickness of PMMA tested is calculated by applying the following formula.

$$D = Kgcs \qquad (A5.1)$$

where K is the entrance surface air kerma (without backscatter) calculated at the upper surface of the PMMA. The factor g, corresponds to a glandularity of 50%, and is derived from the values calculated by Dance et al 2000 and is shown in table A5.1 for a range of HVL. The c-factor corrects for the difference in composition of typical breasts from 50% glandularity [Dance et al 2000] and is given here for typical breasts in the age range 50 to 64 in table A5.2. Note that the c and g-factors applied are those for the corresponding thickness of typical breast rather than the thickness of PMMA block used. Where necessary interpolation may be made for different values of HVL. Typical values of HVL for various spectra are given in table A5.3. The factor s shown in table A5.4 corrects for differences due to the choice of X-ray spectrum (Dance et al 2000).
The dose should be determined using the usual clinically selected exposure factors including any automatic selection of kV and target/filter combination.

A5.2 Clinical breast doses

It is also possible to measure the average glandular doses for a series of breast examinations on each mammography system. To do this, the breast thickness under compression is measured, and the tube voltage, and tube loading delivered are recorded.
From a knowledge of the output of the X-ray set for the kV and target and filter material used, this tube loading may be used to estimate average glandular dose using the following formula:

$$D = Kgcs \qquad (A5.2)$$

where K is the entrance surface air kerma calculated (in the absence of scatter) at the upper surface of the breast. The factor g, corresponds to a glandularity of 50%, and is shown in table A5.5 (Dance et al 2000). The factor c corrects for any difference in breast composition from 50% glandularity. C-factors for typical breast compositions in the age range 50 to 64 and 40 to 49 are shown in tables A5.6 and A5.7. The factor s corrects for differences due to the choice of X-ray spectrum as noted earlier. Measurement of compressed breast thickness for this purpose is performed by the radiographer, by reading the displayed compressed thickness on the X-ray set. The accuracy of the displayed thickness should be verified by applying a typical force (e.g. 100 N) to rigid material of known thickness. It may be necessary to apply correction factors if the displayed values are in error. An accuracy of better than ± 2 mm is required. Software for making such dose calculations has been published by the UK Breast Screening Programme (Young, 2001).

Table A5.1: g-factors for breasts simulated with PMMA

PMMA thickness (mm)	Equivalent breast thickness (mm)	g-factors (mGy/mGy) HVL (mm Al)							
		0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60
20	21	0.329	0.378	0.421	0.460	0.496	0.529	0.559	0.585
30	32	0.222	0.261	0.294	0.326	0.357	0.388	0.419	0.448
40	45	0.155	0.183	0.208	0.232	0.258	0.285	0.311	0.339
45	53	0.130	0.155	0.177	0.198	0.220	0.245	0.272	0.295
50	60	0.112	0.135	0.154	0.172	0.192	0.214	0.236	0.261
60	75	0.088	0.106	0.121	0.136	0.152	0.166	0.189	0.210
70	90		0.086	0.098	0.111	0.123	0.136	0.154	0.172
80	103		0.074	0.085	0.096	0.106	0.117	0.133	0.149

Table A5.2: c-factors for breasts simulated with PMMA

PMMA thickness (mm)	Equivalent breast thickness (mm)	Glandularity of equivalent breast	c-factors HVL (mm Al)						
			0.30	0.35	0.40	0.45	0.50	0.55	0.60
20	21	97	0.889	0.895	0.903	0.908	0.912	0.917	0.921
30	32	67	0.940	0.943	0.945	0.946	0.949	0.952	0.953
40	45	41	1.043	1.041	1.040	1.039	1.037	1.035	1.034
45	53	29	1.109	1.105	1.102	1.099	1.096	1.091	1.088
50	60	20	1.164	1.160	1.151	1.150	1.144	1.139	1.134
60	75	9	1.254	1.245	1.235	1.231	1.225	1.217	1.207
70	90	4	1.299	1.292	1.282	1.275	1.270	1.260	1.249
80	103	3	1.307	1.299	1.292	1.287	1.283	1.273	1.262

Table A5.3: Typical HVL measurements for different tube voltage and target filter combinations. (Data includes the effect on measured HVL of attenuation by a PMMA compression plate*.)

	HVL (mm Al) for target filter combination				
kV	Mo + 30 µm Mo	Mo +25 µm Rh	Rh +25 µm Rh	W +50 µm Rh	W +0.45 µm Al[22]
25	0.33 ± .02	0.40 ± .02	0.38 ± .02	0.52 ± .03	0.31 ± .03
28	0.36 ± .02	0.42 ± .02	0.43 ± .02	0.54 ± .03	0.37 ± .03
31	0.39 ± .02	0.44 ± .02	0.48 ± .02	0.56 ± .03	0.42 ± .03
34		0.47 ± .02		0.59 ± .03	0.47 ± .03
37		0.50 ± .02			0.51 ± .03

* Some compression paddles are made of Lexan, the HVL values with this type of compression plate are 0.01 mm Al lower compared with the values in the table.

Table A5.4: s-factors for clinically used spectra [Dance et al. 2000]

Spectrum	s-factor
Mo/Mo	1.000
Mo/Rh	1.017
Rh/Rh	1.061
Rh/Al	1.044
W/Rh	1.042
W/Al	1.05*

* This value is not given in the paper of Dance et al. The value in the table has been estimated using the S-values of other spectra.

Table A5.5: g-factors (mGy/mGy) for breast thicknesses of 2-11 cm and the HVL range 0.30-0.60 mm Al. The g-factors for breast thicknesses of 2-8 cm are taken from Dance (1990), and for 9-11 cm from Dance et al. (2000)

Breast Thickness (cm)	g-factors (mGy/mGy) HVL (mm Al)						
	0.30	0.35	0.40	0.45	0.50	0.55	0.60
2	0.390	0.433	0.473	0.509	0.543	0.573	0.587
3	0.274	0.309	0.342	0.374	0.406	0.437	0.466
4	0.207	0.235	0.261	0.289	0.318	0.346	0.374
4.5	0.183	0.208	0.232	0.258	0.285	0.311	0.339
5	0.164	0.187	0.209	0.232	0.258	0.287	0.310
6	0.135	0.154	0.172	0.192	0.214	0.236	0.261
7	0.114	0.130	0.145	0.163	0.177	0.202	0.224
8	0.098	0.112	0.126	0.140	0.154	0.175	0.195
9	0.0859	0.0981	0.1106	0.1233	0.1357	0.1543	0.1723
10	0.0763	0.0873	0.0986	0.1096	0.1207	0.1375	0.1540
11	0.0687	0.0786	0.0887	0.0988	0.1088	0.1240	0.1385

Table A5.6: c-factors for average breasts for women in age group 50 to 64 (Dance et al. 2000)

Breast Thickness (cm)	c-factors HVL (mm Al)						
	0.30	0.35	0.40	0.45	0.50	0.55	0.60
2	0.885	0.891	0.900	0.905	0.910	0.914	0.919
3	0.925	0.929	0.931	0.933	0.937	0.940	0.941
4	1.000	1.000	1.000	1.000	1.000	1.000	1.000
5	1.086	1.082	1.081	1.078	1.075	1.071	1.069
6	1.164	1.160	1.151	1.150	1.144	1.139	1.134
7	1.232	1.225	1.214	1.208	1.204	1.196	1.188
8	1.275	1.265	1.257	1.254	1.247	1.237	1.227
9	1.299	1.292	1.282	1.275	1.270	1.260	1.249
10	1.307	1.298	1.290	1.286	1.283	1.272	1.261
11	1.306	1.301	1.294	1.291	1.283	1.274	1.266

Table A5.7: c-factors for average breasts for women in age group 40 to 49 (Dance et al. 2000)

Breast Thickness (cm)	c-factors HVL (mm Al)						
	0.30	0.35	0.40	0.45	0.50	0.55	0.60
2	0.885	0.891	0.900	0.905	0.910	0.914	0.919
3	0.894	0.898	0.903	0.906	0.911	0.915	0.918
4	0.940	0.943	0.945	0.947	0.948	0.952	0.955
5	1.005	1.005	1.005	1.004	1.004	1.004	1.004
6	1.080	1.078	1.074	1.074	1.071	1.068	1.066
7	1.152	1.147	1.141	1.138	1.135	1.130	1.127
8	1.220	1.213	1.206	1.205	1.199	1.190	1.183
9	1.270	1.264	1.254	1.248	1.244	1.235	1.225
10	1.295	1.287	1.279	1.275	1.272	1.262	1.251
11	1.294	1.290	1.283	1.281	1.273	1.264	1.256

Appendix 6: Calculation of contrast for details in a contrast-detail test object

The minimum and achievable standards in section 2b.2.4.1 depend on the calculation of nominal contrast for the details involved. To allow different designs of test object the standard is specified in terms of radiation contrast for a typical spectrum using a tube voltage of 28 kV, a molybdenum target material and a 30 mm thick molybdenum filter. (The spectrum was derived from IPEM Report 78). The contrast of the discs and the threshold limiting values have been determined using the CDMAM phantom with a 2 cm thickness of PMMA above and 2 cm thickness below the test object. The CDMAM phantom includes an aluminium base which is approximately equivalent to 1cm of PMMA in terms of attenuation. In the European guidelines third edition however 4.5 cm has been chosen as the standard thickness of PMMA. Therefore in future threshold contrast might be determined at a total thickness equivalent to 4.5 cm PMMA. Calculated contrast for various thicknesses of gold are shown in Table A6.1. The corresponding contrast calculated for the use of a CDMAM phantom with 4 cm of PMMA and for gold details on 4.5 cm PMMA is shown. In both cases the effect of scatter is not included in the calculation.

Table A6.1: Calculated radiation contrast for various gold thickness on the standard test object

Thickness of gold (µm)	Radiation contrast (%) for gold disc on 4.5 cm PMMA	Radiation contrast (%) for CDMAM with 4 cm PMMA
0.1	1.63	1.57
0.5	7.83	7.60
1.0	15.02	14.55
1.5	21.57	20.92
2.0	27.56	26.76

Appendix 7: Computed Radiography screen processing modes

For all test-items the following screen processing settings must be chosen except for the test-items listed below. If a specific system or screen processing mode is not mentioned below, it is advised to refer to the manual of the manufacturer:

Fuji systems	Use FIXED EDR screen processing, suggested: S = 120, L = 2
Kodak systems	Use Pattern screen processing
Agfa systems	Use System diagnostics/flat field screen processing

Remark: For all measurements on the Fuji system an L-value of 2 is advised (which resembles the L-value in clinical practice). If clipping occurs with an S-value of 120, another S-value should be chosen.

2b.2.2.1.1 Response function

The following relations between pixel value (sensitivity/exposure index) and entrance surface air kerma should be linear (If a screen processing mode is not mentioned below, it is advised to refer to the manual of the manufacturer):

Fuji systems: Fixed EDR screen processingsuggested: S = 120, L = 2	Linear relations: Plot the mean pixel value in the reference ROI versus log entrance surface air kerma
Semi EDR screen processing	Plot sensitivity index versus inverse entrance surface air kerma
Kodak systems: Pattern screen processing	Plot the mean pixel value in the reference ROI versus log entrance surface air kerma
Agfa systems: System diagnostics/flat field screen processing	Plot the mean pixel value in the reference ROI versus log entrance surface air kerma

2b.2.2.1.2 Noise evaluation

Fuji systems	FIXED EDR screen processing, suggested: S = 120, L = 2
Kodak systems	Use Pattern screen processing
Agfa systems	Use System diagnostics/flat field screen processing

2b.2.4.1 Threshold contrast visibility

Fuji systems	Use FIXED EDR screen processing. The S and L value must be chosen such that they are typical for the clinical situation. These values may differ from site to site. Typical values (according to Fuji): S = 40 to 100, L = 1.8 to 2.6.
Kodak systems	Use Pattern screen processing
Agfa systems	Use System diagnostics/flat field screen processing

2b.2.4.5 Ghost image / erasure thoroughness

Fuji systems	Use FIXED EDR screen processing. The S and L value must be chosen such that they are typical for the clinical situation. These values may differ from site to site. Typical values (according to Fuji): S = 40 to 100, L = 1.8 to 2.6.
Kodak systems	Use Pattern screen processing
Agfa systems	Use System diagnostics/flat field screen processing

Notes

1. This is the PMMA thickness most commonly used, but others may be specified in parts of this protocol.
2. The specifications of the listed equipment are given, where appropriate, in section 4, table 2.
3. The standard test block may be composed of several PMMA plates.
4. PMMA (polymethylmethacrylate) is commercially available under several brandnames, e.g. Lucite, Plexiglas and perspex.
5. 150 X 100 mm or semi-circular with a radius of ≥µ100 mm, and covering a total thickness range from 20 to 70 mm PMMA.
6. In future the PMMA thickness may change to the 'standard thickness' of 45 mm with the details positioned at a height of 40 to 45 mm above the breast support table. This may mean that the limiting values need slight adjustment.
7. If the exposure-to-read-time other than one minute is more relevant for practical reasons, that other time should be chosen.
8. The specifications of the listed equipment are given, where appropriate, in chapter 3.5, table 2 of the European Guidelines, third edition.
9. The standard test block, covering the whole imaging area, may be composed of several PMMA plates.
10. PMMA (polymethylmethacrylate) is commercially available under several brand names, e.g. Lucite, Plexiglas and Perspex.
11. Covering the whole imaging area, and covering a total thickness range from 20 to 70 mm PMMA (Normally PMMA of 180 X 240mm is available).
12. These films have been reported as suitable for use in collimation assessment by Beideck and Gingold at the AAPM 2004 annual meeting.
13. These values are derived from screen-film mammography. At this moment no limiting values on exposure increase per step for digital mammography have been set, but they should be approximately uniform.
14. In future the contrast threshold visibility may be determined at the standard PMMA thickness of 45 mm, so CNR limits will also be relative to 45 mm in future.
15. These values are provisional, it is advised to check the EUREF website for alterations
16. For some scanning slot systems only a limited range of mA or mAs settings are available, for these systems images should be made at all settings.
17. In future the PMMA thickness may change to the 'standard thickness' of 45 mm with the details positioned at a height of 40 to 45 mm above the breast support table. This may mean that the limiting values need slight adjustment.
18. CDMAM phantom with a 4 cm thickness of PMMA, see appendix 6.
19. For some scanning slot systems, see the remark above.
20. Aliasing problems may occur due to the difference in pixel size of the printer and test pattern.
21. Further research is necessary to investigate whether the Dmin and Dmax limiting values are appropriate.
22. Data partly based on: Bengt Hemdal, Lars Herrnsdorf, Ingvar Andersson, Gert Bengtsson, Boel Heddson and Magnus Olsson, Average glandular dose in routine mammography screening with Sectra MicroDose Mammography, MDM, poster at: Medicinska Riksstämman, Göteborg, Sweden 2004.

3

Radiographical guidelines

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3.1 Introduction

Screening for breast cancer by means of mammography has been proven to reduce mortality from breast cancer. Mammography as a screening test has to meet stringent quality requirements. These requirements can only be met when a comprehensive quality assurance programme is in place.

High quality screening demands high quality mammography carried out in a manner which is acceptable to the women. The role of the radiographer is central to the success of the breast screening programme in producing high quality mammograms which are crucial for the early diagnosis of breast cancer.

The image quality can be affected by the following factors, which are of equal importance:
- the ambience
- the X-ray equipment
- the image production chain
- how the radiographer relates to the woman
- the training, experience and motivation of the radiographer

3.2 Technical quality control

Quality control as defined by the World Health Organisation (WHO) is the 'set of operations (programming, coordinating, carrying out) intended to maintain or to improve [...] (ISO 3534-1977). As applied to a diagnostic procedure, it covers monitoring, evaluation, and maintenance at optimum levels of all characteristics of performance that can be defined, measured and controlled.'

In mammography this is the technical part of the quality assurance programme and comprises the operational techniques and activities required to maintain the quality of the performance. Quality control is required in order to produce a technically optimum mammogram and is dependent on a number of factors within the image production chain. Image quality standards must be established in order to guarantee a high level of technical quality. It is the radiographers' duty to carry out quality control procedures, monitor, evaluate and take corrective action to maintain these standards. These are laid down in the European Protocol for the Quality Control of the Physical and Technical Aspects of Mammography Screening (see chapter 2).

In quality control the radiographers must be involved in:
- equipment specification and selection
- commissioning and acceptance tests
- in-service consistency testing
- image quality assessment - using a recognised phantom

Several measurements can be performed by the local staff. The more elaborate measurements should be undertaken by medical physicists who are trained and experienced in diagnostic radiology and specifically trained in mammography quality control. Comparability and consistency of the results from different centres is best achieved if data from all measurements, including those performed by local radiographers are collected and analysed centrally.

In a screening facility there will be more than one radiographer carrying out mammography and quality control. One nominated radiographer in each unit should be assigned the overall responsibility for quality control. One radiographer should also have responsibility for ensuring that essential servicing, maintenance and repairs are carried out satisfactorily by relevant equipment engineers. This may or may not be the same person. A further important duty is to provide notification of significant equipment problems, breakdown and unacceptable variances in performance to the appropriate persons.

In each unit a quality control reference document must contain acceptable tolerance limits and guidelines to be followed should these tolerances be exceeded.

Time must be set aside to allow all radiographic quality control procedures to be carried out and for data arising from these procedures to be analysed, evaluated and acted upon.

A suggested list of tests and frequencies

			paragraph no. European Protocol
Daily	X-ray machine	automatic exposure control reproducibility	2a.2.1.3
	film processor	sensitometry	2a.2.3.2
	cassettes	screen inspection and cleaning	
Daily or weekly	film-processor	cleaning	
	X-ray machine	automatic exposure control repeatability	2a.2.1.3
		AEC changing thickness	2a.2.1.3
		image quality	2a.2.5.2
Yearly	cassettes	film-screen contact	2a.2.2.2
		sensitivity and radiation absorption	2a.2.2.2
	illuminators	output	2a.2.4
Ongoing operator observations	all equipment	sharp edges	
		freedom of movement	
		brakes/locks	
		cassette robustness	
		foot switches	
		cables wear and tear	
		emergency compression	
		release	
		warning lights	

Individual centres should draw up their own specific list of tests and frequencies. Attention should also be paid to the appropriate regulations for the handling and disposal of chemicals.

3.3 Ergonomic design of the machine

The X-ray machine should be designed in such a way that it is easy to use by the radiographer and non-threatening to women.

The ergonomics of the X-ray machine play a role with respect to positioning. All radiographers, whatever their height, should find the X-ray machine easy to operate, knobs and buttons should be within easy reach. All movements should be quiet and smooth and the machine light in handling. It is essential that the X-ray machine is fitted with a foot-pedal operated compression plate in order to allow the radiographer to use both hands when positioning the breast. The breast support table should be easy to clean. It should not have any sharp edges, which may cause discomfort during positioning.

3.4 Mammographic examination

The colour, size and placement of the machine are important in order to create an atmosphere of calm and confidence in the mammography room. Ideally the room should be designated for breast imaging only.
The temperature and the lighting in the X-ray room should be conducive to a satisfactory examination.

3.4.1 Introduction to the examination

The radiographer greets the woman, introduces herself and establishes eye-contact. Wearing a name badge helps to create a more personal relationship with the woman.

The radiographer should determine the woman's previous mammographic experience and past breast problems. Any current breast symptoms or information, which may be of importance to the radiologist, should be recorded on the appropriate sheets.

In addition the radiographer should note any skin abrasions, skin tears or soreness particularly on the underside of the breast. If these are present, having the mammogram may aggravate the condition or make taking the mammogram more uncomfortable than might normally be expected. In that case the woman should be given the opportunity to make an informed decision regarding the possible consequences of undergoing mammography. (In some units local protocol may require the woman to sign a consent form before continuing with the examination.)

During the introductory talk, the information to the woman should include:
- the examination procedure, including the number of views to be taken and an outline of the positioning
- explanation of the importance of compression
- the procedure for notifying the results

3.4.2 Starting the examination

- select size of breast support table and compression paddle
- clean the X-ray machine
- decide which view to begin with and position X-ray machine accordingly
- select chamber position
- place cassette in cassette holder
- ensure correct identifications of the woman are in place
- position the breast
- ensure the woman is comfortable

- remove any overlying artefacts e.g. spectacles, shoulders and skin folds
- apply the compression slowly and carefully until the breast is firmly held
- make the exposure
- release the compression immediately
- remove and replace the cassette
- proceed to the next view

3.4.3 Compression

The radiographer should understand the need for compression in mammography. It is essential that the breast is properly compressed in order to achieve a good quality mammogram.

Compression is used for the following reasons:
- scattered radiation diminishes, thus improving the contrast of the images
- compression reduces the thickness of the breast, separates the various structures in the breast, thus reducing the overlapping of tissue shadows and giving better visualisation of the breast tissue
- radiation dose is reduced
- blurring due to movement is reduced

The importance of proper compression should be explained to the woman, before the breast is compressed. Most women find compression uncomfortable and for a few it might even be painful. The radiographer must emphasise that compression only lasts a few seconds but that it is necessary in order to obtain good images and does not harm the breast. The amount of compression women can tolerate varies. If a woman has extremely sensitive breasts it may be recommended that the examination is postponed and a suitable appointment can be made, when the breasts are less sensitive. The breast should be properly compressed, but no more than is necessary to achieve a good image quality. More compression will only cause the woman pain.

It has been shown that women will tolerate the compression better if they have a full understanding of the need. Experience has shown that compression is better accepted if the woman can feel in control and indicate when the pressure is starting to become unpleasant. Care should be taken to apply the compression slowly and carefully with encouragement throughout. During compression, the radiographer should constantly observe the woman.

The radiographer must never assume that the woman is putting on an act. Every woman is different and experiences mammography in a different way. Putting the woman and her feelings at the centre of the examination is conducive to a satisfactory experience.

3.4.4 Positioning

Breast positioning is an art. When evaluating a mammogram, incorrect positioning is the most common problem. The skills required to perform optimal mammographic positioning are high. It is important that the radiographer has sufficient time to carry out the investigation and pay sufficient attention to the woman in order to produce optimal images.

3.4.5 Standard views

- the cranio-caudal view
- the mediolateral oblique view

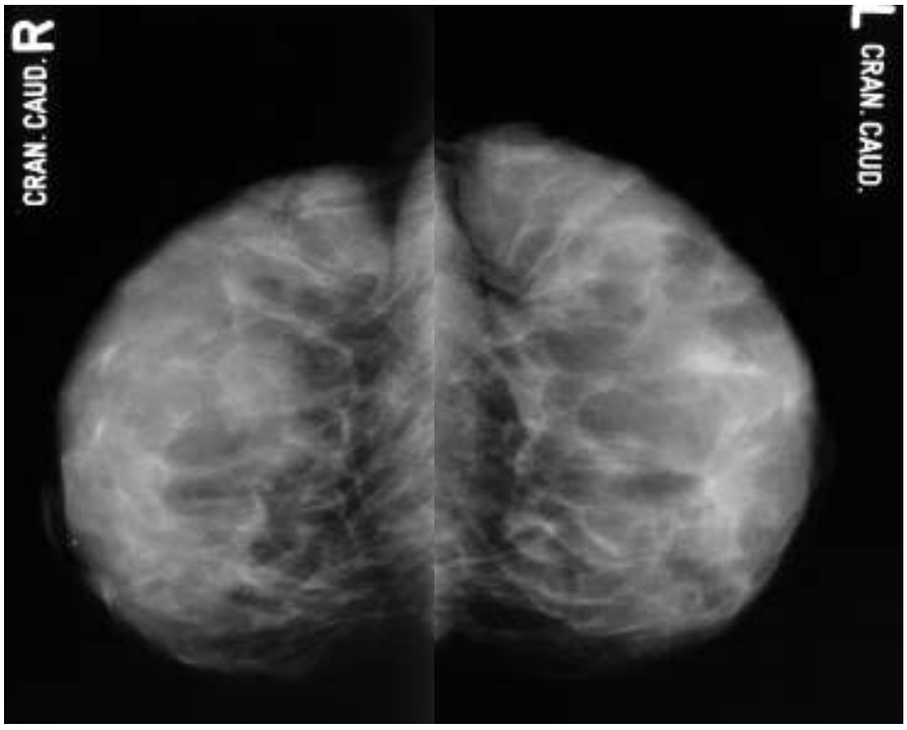
Common criteria for image quality assessment are:
- correct positioning of automatic exposure device
- appropriate compression

- absence of
  - skin folds
  - overlying artefacts such as shoulders, breast tissue
  - movement
  - post-development artefacts e.g. dust on the screens, pick-off from rollers
- correct identifications
- correct exposure
- correct development technique
- symmetrical images

3.4.5.1 Cranio-caudal view

The cranio-caudal (cc) view should show as much of the breast as possible. A correctly performed cc view will show virtually all the breast except the most lateral and axillary part.

The criteria for the image assessment of the cc view are:
- the medial border of the breast is shown
- as much as possible of the lateral aspect of the breast is shown
- if possible, the pectoral muscle shadow is shown on the posterior edge of the breast
- the nipple should be in profile
- symmetrical images



Cranio-caudal views, right and left.

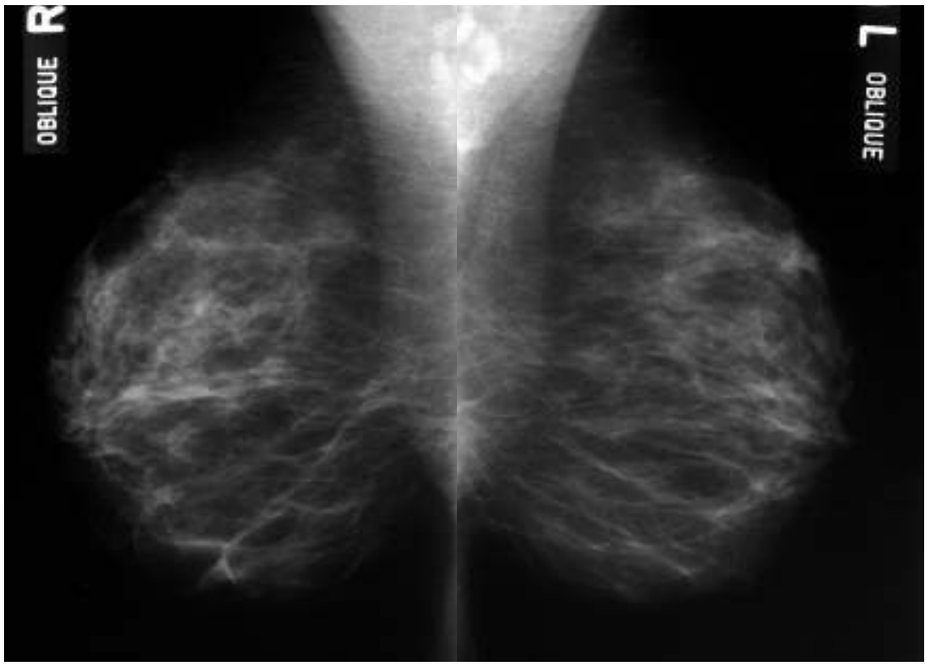
A key aspect to achieve a high quality cranio-caudal image is to adjust the film support table to the correct height for the woman. The height of the breast support table can be best determined when observed from the medial side of the breast. Once the height of the breast support table has been set, the radiographer lifts the breast and gently pulls the breast tissue forward away from the chest wall and places it on top of the breast support table. The breast should be in the centre of the breast support table. The breast should be held in place and the breast tissue smoothed out, while applying compression. It may occasionally be necessary to take an additional view in order to more fully visualise the lateral aspect of the breast.

To summarise:
- the breast is centrally positioned with the nipple in profile
- as much of the breast tissue as possible is visualised

Common errors leading to poor quality images:
- breast support table too low (this is also more uncomfortable for the woman)
- poor compression leading to pale images and movement blur
- skin folds in the lateral part of the breast
- breast tissue not pulled forward as much as possible
- nipple not in profile

3.4.5.2 Mediolateral oblique view

The criteria for the image assessment of the mediolateral oblique view:
- all the breast tissue clearly shown
- pectoral muscle to nipple level
- symmetrical images
- nipple in profile
- inframammary angle clearly demonstrated



Mediolateral oblique views, right and left.

Key aspects to achieve a high quality mediolateral oblique view are the height of the breast support table, the angle being used, the lift, spread and compression of the breast and the comfort of the woman.

To summarise:
- whole breast is imaged with the nipple in profile
- pectoral muscle shadow shown down the back of the breast at the correct angle
- the inframmary angle clearly demonstrated without overlying tissue

Common errors:
- breast support table too high or too low
- breast support table not correctly angled in order to follow the line of the woman's pectoral muscle
- inframammary angle not clearly shown
- insufficient lift and poor compression, resulting in a droopy breast

3.4.6 Other additional views

Other additional projections the radiographer should be aware of and should be able to perform include the lateral view (lateromedial/mediolateral) and the extended cranio-caudal view.

Techniques which are used in assessment include localised compression views and magnification views. Other specialised views may be required from time to time.

3.5 Social skills

In the context of a screening programme the radiographer is usually the only health professional the woman will meet. Communication between the radiographer and the woman is one of the most important aspects of the examination.

Radiographers play a key role in optimising the woman's experience, satisfaction and continued acceptance and uptake of the service. The acceptability of a breast screening programme is of the utmost importance to its success. The individual woman's needs and circumstances must be recognised in order to ensure a satisfactory and positive experience.

The radiographer must be friendly, caring and generate confidence in the woman, although she may have seen a great number of women on any day. When a pleasant, calm and informative atmosphere is created, the woman is more likely to relax. The radiographer should answer enquiries and explain the procedure carefully and emphasise the importance of proper compression in order to get understanding and cooperation from the woman. The woman should understand the process and timing for receiving her results. Women must feel at ease and feel they are being treated as important individuals. The radiographer should treat the woman the way she would like to be treated herself.

3.6 Consent

The woman should feel confident she has the ability to stop the procedure at any point. The radiographer should respect that right and recognise when consent is withdrawn.

3.7 Teamwork

It is recognised that good teamwork is required to produce optimal mammograms. Good communication including feedback is essential between radiographers, radiologists and physicists in setting, monitoring and evaluating standards for image quality.

The radiographers' responsibilities within the team are:
- to produce an optimum image with respect to positioning and technical aspects
- to produce the image in a manner which is acceptable to the woman to ensure a positive experience and therefore encourage future attendance
- to implement and carry out quality control procedures for equipment monitoring
- to assess the examinations she has performed

The radiographer should participate in multidisciplinary team meetings. Feedback is essential to maintain a high standard or to improve. In particular, regular communication with the radiologist is vital.

3.8 Radiographic quality standards

The radiographic quality objectives are:
- More than 97% of the women should have an acceptable examination, whether this is single view or double view mammography. A good diagnostic image meets the criteria laid down in the previous paragraphs.
- Less than 3% of the women should have a repeated examination, either a repeated mediolateral or cranio-caudal view. Audit must be carried out to monitor this.
- More than 97% of the women should be satisfied with their screening visit and feel the radiographer has met their needs.
- 100% of the women should be informed by the radiographer of the method and time scale for receiving their results.

Audit on client satisfaction should be carried out to monitor standards 3 and 4. Information on verbal and/or written complaints or compliments should be taken into account.

In addition:
- Radiographers should have their skills, expertise and time allocated appropriately to facilitate high quality mammography and enhance personal and client satisfaction.
- Radiographers should have allocated sessions for quality assurance in order to audit the quality standards and carry out comprehensive daily quality control.
- Radiographers should be involved in self appraisal, peer group discussions and discussions with the radiologists on the radiographic quality of the images produced in the department.
- Every effort should be made by the radiographers to constantly improve the quality of the images and the service to the women.

It is desirable that:
- Radiographers participate in the assessment clinics and are familiar with investigative procedures.
- Radiographers understand the concept and value of the multidisciplinar y approach to breast screening and are active members of the breast care multidisciplinary team.
- Radiographers should have up to date information and knowledge about issues on which the women may require further details relating to breast screening, for example, breast imaging and silicone breast implants, the impact of hormone replacement therapy on the breast and breast pain and tenderness.

3.9 Training

In order to achieve the radiographic standards required for high quality mammographic breast screening, all radiographers participating in the breast screening programme are expected to undergo a programme of training. This should be carried out by a recognised training centre.

The training programme should consist of two parts:

a. academic	3 days to one week
b. clinical	depending on the experience and existing skills of the radiographer two to six weeks

3.9.1 Academic component

A theoretical course to develop knowledge and understanding on all aspects of mammographic breast cancer screening and breast care that may include lectures, tutorials, demonstrations and reading.

Contents to include:
- anatomy and physiology
- pathology
- radiographic-pathologic correlation
- technical quality control
- communication and social skills
- organisation of the breast screening programme
- epidemiological aspects
- the management of breast cancer and treatment options
- health promotion

3.9.2 Clinical component

At the end of the clinical training the radiographer will be able to:
- make consistently good quality mediolateral oblique and cranio-caudal images
- decide if the images are acceptable from the positioning as well as the technical point of view
- carry out daily and/or weekly technical quality control procedures
- work with the woman in a satisfactory, friendly, caring way
- compare the mammogram with the previous one in order to achieve an optimum quality
- obtain satisfactory knowledge of X-ray equipment, film-screen combination and film processor
- carry out relevant administrative procedures

The radiographer will be familiar with:
- other imaging projections used to aid diagnosis e.g. magnification, stereotaxis
- other imaging techniques used to aid diagnosis e.g. ultrasound, MRI
- biopsy techniques e.g. fine needle aspiration cytology, needle core biopsy

3.9.3 Certification

It is recommended that the theoretical and practical knowledge, social skills, motivation and interest of the radiographer in training are tested. When the result is satisfactory the trainee should receive a certificate.

3.9.4 Continuing education

Every two to three years there should be at least a one-day refresher course in a recognised training centre for every radiographer involved in the screening programme. Subjects to be dealt with are positioning technique, physical quality control and the latest developments concerning equipment.

Radiographers are expected to update their knowledge and develop their skills in line with continuing professional development, for which participation in conferences and symposia can be a valuable contribution.

3.10 Staffing levels and working practices

Radiographic staffing levels are expected to reflect the workload. Working practices should not place undue pressure on the individual radiographer which may adversely effect quality.

Experience and research in the UK and the Netherlands have lead to recommended staffing levels for breast screening. When inviting the women it is important to take into account their expected participation rate. With 3 radiographers working together 10-12 women per hour can be examined. Each radiographer should be able to perform approximately 22 good quality sets of

mammograms during a six-hour screening day. One may choose to work with two or three radiographers, with or without involving an administrative worker as receptionist.
Adjustment needs to be made for women with special needs who may take longer to examine.

The minimum requirement with regard to participation for radiographers involved in a population based breast screening programme is two days per week. This is in order to maintain and develop the skills required to carry out optimum mammography and to be an active and useful member of the multidisciplinary team.

Similarly in a diagnostic breast care facility, for the same reasons as stated above, radiographers should carry out a minimum of 20 mammographic examinations per week.

3.11 Digital mammography

For a more comprehensive description of the physical and technical aspects of digital mammography we refer to Part b: 'Digital Mammography' of the European Protocol for the Quality Control of the Physical and Technical Aspects of Mammography Screening (Chapter 2).

The tasks of the radiographer in screening can be summarized as follows:
- communicate with the woman, attending the programme
- carry out quality control procedures, e.g. performing a phantom image
- performing the mammograms
- processing the mammograms
- assessing the mammograms

Below we briefly describe the changes (if any) concerning the above mentioned tasks.

The frequency and kind of tests concerning the technical quality control are summarized in Chapter 2a, Table 4.1: Frequency of quality control, measured and limiting values. Several measurements can be performed by the local staff, whereas the more comprehensive measurements are undertaken by medical physicists, specifically trained in mammography quality control.

When using a CR (computed radiography) system, using photostimulable phosphor plates the radiographer handles these plates as 'cassettes'. The other technology is a DR (direct radiography) system, using sealed units mounted on a radiography system which captures X-rays and produces a digital image by sampling the X-ray image. The CR system requires, as in screen-film mammography, the positioning of the AEC (automatic exposure control) system by the radiographer, whereas in the DR system the AEC should be incorporated in the equipment. Some digital mammography systems do not yet have an automatic exposure control device incorporated (see also Chapter 2b, paragraph 1.4 image acquisition). Manufacturers of equipment without AEC are urged to implement such a device in their systems.

The positioning of the mammograms is performed according to the guidelines. The size of the image receptor varies, e.g. 19x29 or 25x36 cm. The images are ready for presentation after image processing on the acquisition unit. For system demands see Chapter 2b, paragraph 1.2. The specification of the monitor of the acquisition unit depends on the task of the radiographer. It is recommended that for diagnostic purposes workstations with two large (45-50 cm diagonal (19-21^{II})) high quality 5 megapixel monitors are used. Positioning may be controlled on a monitor with lower specification.

Concerning the viewing conditions it is appropriate that the ambient light is low (less than 10 lux), since the maximum intensity on the monitor (300-800 cd/m^2) is much lower then that of a viewing box with unexposed and developed film (2000-4000 cd/m^2). Furthermore, due to the reflection characteristics of the monitor, the amount of ambient light might seriously diminish the visible dynamic range and the visibility of low contrast lesions.

Comparability of current and previous images is essential for the diagnostic assessment of the mammograms, both in film-screen as well as in digital mammography. Based on the review of interval cancers or late detected screening cancers we have learned that a developing or increasing density or microcalcifications is a significant sign for malignancy. In order to detect minor changes it is essential that radiologists are able to compare all images of at least the current and the previous screening examinations. Therefore, the positioning technique has to be as equal as possible.

3.12 Summary

3.12.1 Skills

- To achieve high quality mammograms radiographers need good technical skills to position the woman and her breasts.
- Radiographers should have an understanding of the anxieties and fears of women attending for breast screening and assessment. They need to have the skills to address those and meet the expectations of the women in order to obtain an optimum mammogram and a satisfactory screening experience.
- Radiographers need the knowledge to critically appraise the mammograms to determine if optimum images are achieved.

3.12.2 Technical quality control

Radiographers should have a clear understanding of the requirements of technical quality control on a day-to-day basis. They should be familiar with the techniques required to this end and have knowledge of the recording, monitoring, evaluation and corrective actions required.

3.12.3 Multidisciplinary teamwork

Radiographers should understand the concept and value of the multidisciplinary approach to breast cancer diagnosis.

They should have up-to-date information and knowledge on topics which the woman may inquire about in relation to her screening experience.

3.12.4 Training

Training in the various aspects of the radiographic standards related to high quality screening is required. Radiographers carrying out breast screening mammography should attend a recognised training facility and ensure they are participating in continuing professional development.

3.13 Conclusion

Radiographers play a key role in a high quality breast screening programme aiming for a significant reduction in mortality of breast cancer.

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4

Radiological guidelines

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4.1 Introduction

The purpose of a breast screening programme is to reduce mortality from breast cancer in the invited population. The key factors necessary to achieve this are a high acceptance by the target population, and a high level of quality of the entire screening process.

The radiologist has a role of primary importance, taking the greatest overall responsibility for mammographic image quality, and diagnostic interpretation. A thorough knowledge and understanding of the risks and benefits of breast cancer screening, and the dangers of the use of inadequately trained staff and sub-optimal equipment is necessary.

The radiologist must ensure that protocols are in place for satisfactory and complete assessment (work-up) of women with screen-detected abnormalities. Women referred for assessment must be examined in fully equipped centres, staffed by properly qualified personnel, in collaboration with a radiologist experienced in and involved with the screening process. This is to ensure that adequate imaging assessment is not denied on the basis of a negative clinical examination.

The lead programme radiologist must encourage the formation of a skilled multi-disciplinary professional team incorporating clinical and non-clinical specialists involved in the entire process of screening and diagnosis. This team should include radiographers, pathologists, surgeons and nurses with additional input from oncologists, physicists and epidemiologists as appropriate. All radiologists must be intimately associated with the organisation of the screening programme, and where possible the lead programme radiologist should act as Clinical Director.

The major responsibilities of the radiologist are to ensure that:
- a satisfactory quality assurance system is in place with sufficient quality control mechanisms to provide a high level of image quality
- radiological performance levels are sufficient to achieve the goals of the programme by effectively advancing the time of diagnosis of cancers arising in the screened population (and lowering the rate of advanced cancers)
- the adverse effects of screening are minimised

In order to reach these objectives it is necessary to accept the need for the setting of target standards and performance indicators, to comply with these wherever possible, and to take part in both internal and external audit procedures, with remedial action being undertaken where parameters are consistently breached. Standards in this document will frequently be defined at both minimum and desirable levels to acknowledge variation of expertise, but should never fall below those required to achieve mortality reduction, either in a centralised or decentralised setting. All standards should be regularly reviewed and if necessary revised in the light of experience and technological advances. It is accepted that certain standards may vary according to external factors such as geographical situation and background incidence of breast cancer.
As digital techniques become more sophisticated and widespread, it is likely they will have a significant impact on practice, analysis and performance of screening programmes.

These guidelines will outline some of the more important standards for radiologists and will describe methods to best achieve them. Essential prerequisites for screening units will be described in conjunction with other chapters, as will the importance of evaluating certain indicators (such as the interval cancer rate) and the organisation of optimal operating procedures.

The radiologist should constantly be aware of how the screening programme is performing and should encourage a process of continual quality improvement with performance feedback to team members.
In planning the screening programme and implementing its organisation, sufficient resources must be identified and allocated in order to facilitate the achievement of desired standards. Particular attention should be paid to adequate levels of staffing and equipment.

4.2 Image quality

It is the responsibility of the radiologist to ensure that all necessary physico-technical and professional quality control processes are continuously carried out so that the resultant image quality is high.

Knowledge of adequate positioning techniques used by the radiographer is necessary and the radiologist should assess these factors first before reporting on the mammogram. The key criteria are for the whole breast to be imaged, the outline of the pectoral muscle to be demonstrated down to nipple level, the nipple to be in profile and the inframammary angle shown (see Radiography Chapter). To visualise the skin is no longer a primary requirement – this may in any case be achieved using a bright light – as penetration of breast tissue is more important for the detection of small cancers.

The radiologist must also be conversant with the important aspects of processing techniques and exposure which play a vital role in final image quality in analogue setting. The basic inter-relationship of kV, film-screen type, contrast, resolution, processing time and temperature must be understood, likewise the importance of sufficiently high optical density for the detection of small invasive cancers. Adequate compression and lack of motion artefact are also important diagnostically. Film artefacts such as scratches and skin folds indicate sub-optimal technique, but may not be sufficient to interfere with diagnosis. Further details of these issues may be found in the physico-technical chapter.

Ultimately, having analysed the image quality with regard to all these features, the radiologist must be resolute in refusing to accept mammograms not meeting sufficient criteria for adequate diagnosis. These films should be repeated, and the numbers of women subject to technical recall must be recorded. All repeat examinations should be recorded whether at the time of screening, due to a technical problem being identified by the radiographer, or at a later date if the radiologist judges the films to be inadequate for diagnostic purposes.

In a decentralised screening programme it is the responsibility of the lead programme radiologist/ Clinical Director to suspend unsatisfactory clinics or offices where image quality in terms of radiographic positioning or adequate penetration of breast tissue remains unsatisfactory despite repeated attempts at quality improvement. It should be made clear to participating units at what point their continued breaches of guidelines will result in suspension. This may form part of a contractual agreement. It is the direct responsibility of the radiologist to ensure that individual films are not reported if they are of insufficient quality. Although this is not popular either with radiographers or with recalled women, it is a necessity in a small proportion of cases, acting as a safeguard for the quality of the screening process, and as a quality improvement feedback for radiographers.

Where there are problems with equipment or technique, the radiologist must discuss these matters with the relevant professional e.g. radiographer, physicist or equipment service engineer. High image quality is a key factor in the success of a screening programme, but the achievement of it is a complex issue and best managed with a multi-disciplinary input.

4.3 Full Field Digital Mammography (FFDM) with Soft Copy Reading

Digital technology has the potential to offer several advantages in future breast cancer screening programmes. The main advantage of digital mammography is that the processes of image acquisition, display, and storage are decoupled. Consequently, digital technology allows each step to be optimised individually. The true flexibility and the true benefit of digital technology are realized primarily in a soft-copy display of the images and consequently in soft-copy reading.

Optimal reading environments, high resolution monitors, and user-friendly image display are mandatory for the success of FFDM with soft-copy reading in a screening programme. The monitors used for radiologist reporting (work station) should be located in a quiet and darkened room. Ambient light interfering with the monitors must be avoided, as their light output is considerably less than that of a conventional viewing box. The work station must include two high resolution (2,5 x 2 K) monitors. Recent developments make the new flat panel monitors acceptable for FFDM soft-copy reading. It is absolutely necessary for screening that the image display is user-friendly. A dedicated pad which allows the reader to easily go through the reading protocol is strongly recommended. A systematic review of the images similar from case to case is important. Additional images taken by the radiographers should be kept at a minimum through feed-back from radiologists since these additional images ('mosaic') make the soft-copy reading more troublesome. Optional 'roam and zoom' must be kept at a minimum. Consequently, a default reading protocol used by all readers is recommended. The reading protocol used for image display on a user-friendly work station will most likely be crucial to the success of soft-copy reading.

4.4 Radiologist performance issues

Good team work will enhance the screening process and is likely to improve outcomes, so it is important that the radiologist should work closely with other professional colleagues as part of a multidisciplinary team. In order to maintain radiological performance standards it is vital that the radiologist has direct access to key performance indicators relating to screening and assessment, which of necessity, also includes full access to cytological and pathological records.

Feedback of results at all stages is an important learning and quality enhancing process and mechanisms should be in place to achieve this. Records must be kept of results and outcomes of all women in the programme. Regular multidisciplinary review meetings must be held to discuss cases both pre-operatively and postoperatively. This is beneficial for feedback purposes as well as providing an ideal mechanism for refining case management decisions. The review of interval cancers by radiologists, as part of an organised process, should be regarded as mandatory, being an excellent feedback and educational mechanism.

4.4.1 Advancement of the time of diagnosis

Table 1 lists the principal performance standards necessary to bring forward the time of diagnosis. The ratio of detection rates at initial and subsequent examinations to the expected incidence gives a good indication. The detection rate of cancers 'per se' is influenced by the wide variation in European regions of the underlying base incidence of breast cancer in the age group of the target population. The ratio between detection rate and expected incidence can be influenced by possible overdiagnosis.

The proportion of invasive cancers ≤ 10 mm in diameter detected at screening is an important indicator reflecting both radiological performance and image quality. A substantial proportion of cancers at this stage will provide a positive impact from screening. This parameter is also relatively easy to calculate if the pathological form includes pTNM staging and the criteria for measurement of small cancers are well established as described in the pathology chapter.

The proportion of screen-detected ductal carcinoma in situ (DCIS) is also a good parameter for evaluating performance. It is believed that removal of DCIS, particularly of the high grade type, contributes to long term mortality reduction. Its detection is also an indicator of image quality, radiologist prediction and assessment adequacy. Based on screening experience acquired mainly in national programmes from Northern Europe (UK, S, NL) we set the desirable standard value greater than 15% of cancers detected. Possible variation across Europe in incidence and pathological classification may be taken in account.

Table 1: Radiological performance: standards to advance the time of diagnosis in screened women age ≥ 50 years

Indicator	Minimum Standard	Desirable standard
Detection rate in women at initial examination/ expected incidence rate	3	> 3
Detection rate in women at subsequent examination/ expected incidence rate	1.5	> 1.5
Proportion of invasive cancers detected at initial screening ≤ 10 mm	20%	≥ 25%
Proportion of invasive cancers detected at subsequent screening ≤ 10 mm	25%	≥ 30%
DCIS as a proportion of all screen-detected cancers	10%	> 15%

4.4.2 Reduction of adverse effects

Any recall for a mammographic abnormality that turns out to be normal or benign must be regarded as unnecessary and represents a negative effect of screening. Unnecessary recalls are costly, cause psychological discomfort to the woman and, due to the limited specificity of assessment, may result in unnecessary open biopsies. This, in turn, may cause further expense, anxiety and diagnostic problems at subsequent screening. A low specificity in the screening programme is likely to lead to sub-optimal acceptance.

Recall rate
Unfortunately the specificity of mammography is limited, especially for small preclinical cancers, which are the main target of screening. The positive predictive value of mammography for preclinical cancer varies according to the radiological appearance of non-palpable lesions, but, with the exception of spiculate opacities and linear-branching microcalcifications, is usually below 50%. Asymmetries, well defined opacities and punctate microcalcifications have a predictive value for cancer of well below 10%. Knowing the limited specificity of mammography and concerned not to miss a cancer, radiologists will call for assessment even in the presence of radiological abnormalities of intermediate predictivity, and some unnecessary recalls are unavoidable.

Recalled cases should be reviewed and the positive predictive value for malignancy determined for each category of mammographic abnormality. This will allow the identification at each unit of poorly predictive patterns and the adoption of refined recall criteria in order to optimise sensitivity and specificity .

For audit purposes, it is suggested that radiological findings in women recalled for assessment are categorised as follows:
R1 - Normal/benign
R2 - A discrete lesion having benign characteristics
R3 - An abnormality present of indeterminate significance
R4 - Features suspicious of malignancy
R5 - Malignant features

This classification is widely used in European screening programmes for those women recalled for assessment. It is also useful for diagnostic mammography. The classification differs from the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADSTM) which is a more complex but precise classification in terms of percentage likelihood.

The recall rate will be influenced by the training and experience of the radiologist, by the image quality of the mammogram and by the use of the oblique view only as screening test. It is well known that many asymmetric densities or parenchymal distortions may be false images created by superimposition and can be easily recognised as such if the cranio-caudal view is available.

Provided that the reference standards referred to in table 1 are achieved, recall rates should be kept to the lowest possible level, and as shown in table 2, should be below 5% at initial screening. At subsequent screening, the availability of previous films for review will enable many questionable findings to be ruled out as negative or benign. Recall rates at subsequent screening should therefore be consistently lower, ideally below 3%. Recall rates lower than 1% are likely to be associated with a reduced cancer detection rate and an increase in interval cancers.

Repeated films for technical reasons should be kept to a minimum, ideally below 1 per 100 examined women

Early recall

Early recall may be defined as the recommendation for a woman to undergo a short term re-screen at an interval less than the routine round length of the programme. This practice creates anxiety and increases morbidity by promoting benign biopsies as well as having the potential to falsely reassure the woman. There is a low predictive value for malignancy with the use of early recall, and it should be avoided altogether or its use restricted to an absolute minimum (target < 1% of screened women). Early recall should never be used to mask insufficient or inadequate assessment procedures, or as a means of avoiding a skilled radiological decision.

It is not regarded as good practice to subject a woman to an early recall following the screening process alone. She should first have been completely assessed and the circumstances fully explained to her. Neither is it acceptable for a woman to undergo more than one early recall in a screening round, the only possible outcomes from this process being a decision to operate, or a return to routine screening.

Cancers detected in women placed on early recall are regarded by some programmes as interval cancers. As described in the Epidemiology Chapter, these are in fact screen-detected and must in all cases be separately counted from other screen-detected cancers as they represent a delayed diagnosis for women and a failure of the screening and assessment process.

Benign biopsy and non-operative diagnosis

The number of benign biopsies (open surgical excision) performed as a result of screening should be as low as possible. This can be achieved with adequate use of non-surgical interventions such as fine needle aspiration cytology (FNAC), core biopsy (CB) or vacuum assisted core biopsy (VACB). Some benign biopsies are inevitable due to patient choice or diagnostic difficulties with imaging, clinical and pathological features.

The benign to malignant ratio is a simple indicator to express the predictivity of a referral for open (surgical) biopsy The B/M ratio can be significantly lowered by accurate use of sampling techniques as described above. For this reason the proportion of such image-guided procedures with an inadequate or inconclusive result should be carefully monitored.

The proportion of women with a non-operative diagnosis of malignancy, i.e. with a result of FNAC and/or CB conclusive for malignancy (see Pathology Chapter) is a valid indicator of quality of assessment, related to a high predictive value for malignancy in referral for open biopsy. This facilitates treatment planning and allows more adequate and complete counselling for women, minimising delays and uncertainty.

Delay

Delay in communicating results, performing assessment or surgery is likely to cause distress and anxiety. It is bad practice, inconsiderate and must be avoided. Targets should be set for all stages as detailed in table 2.

Table 2: Standards to minimize adverse effects in screened women

Indicator	Minimum Standard	Desirable standard
Recall for assessment rate in women at initial examination	< 7%	< 5%
Recall for assessment rate in women at subsequent examination	< 5%	< 3%
Technical repeat rate	< 3%	< 1%
Benign to malignant biopsy ratio in women at initial and subsequent examination	≤ 1:2	≤ 1:4
Proportion of screen-detected breast cancer with a non-operative diagnosis of malignancy (FNAC or core biopsy reported as definitely malignant)	> 70%	> 90%
Proportion of image-guided FNAC procedures with an insufficient result	< 25%	< 15%
Proportion of image-guided FNAC procedures from lesions subsequently proven to be malignant, with an insufficient result	< 10%	
Proportion of image-guided core/vacuum procedures with an insufficient result (B1)	< 20%	< 10 %
Proportion of screened women subjected to early recall following diagnostic assessment	< 1 %	0
Proportion of localised impalpable lesions successfully excised at the first operation	> 90%	> 95%
Proportion of wires placed within 1 cm of an impalpable lesion prior to excision	90%	> 90%
Delay between screening and result	15 wd	10 wd
Delay between result and day of assessment appointment offered to the woman	5 wd	3 wd

wd= working days

4.5 Operating procedures

4.5.1 Viewing conditions

It is important to refer to the technical aspects of film viewing as outlined in the physico-technical chapter. Reading of screening mammograms requires a high degree of mental and visual concentration, and it is believed that performance may start to deteriorate after 30 - 40 minutes. It should only be done in a suitably undisturbed environment with control of background room light and care taken to reduce unnecessary light glare from the film viewer.

Removal of films from an individual light box will result in excessive light glare prior to replacement with the next set of mammograms. This is likely to result in a diminution of visual acuity. The use of a pre-loaded multiviewer/roller viewer is mandatory to avoid this problem, also to facilitate faster and more efficient film reading, allowing more prolonged maintenance of concentration. This technique also provides greater logistical ease and speed for double reading of screening mammograms.

Previous mammograms should be displayed at the time of screen reading if ever possible. This has the dual purpose of increasing cancer detection by the ability to perceive changes in appearance between examinations, and, more often, of reducing unnecessary recall to assessment for long standing benign lesions. Where previous films are displayed with the current screening examination, it is a matter of personal choice whether these films are from the immediately previous screening round, or a prior screening round in order to enable easier assessment of subtle changes that have occurred over a longer period of time than one round. However it is often the case that mammograms from earlier rounds are not of equivalent image quality to the current examination and this in itself may be counter productive for comparison purposes.

4.5.2 Single/double reading

Double reading increases sensitivity of the screening test by 5-15%, according to the methodology used and the skill of the reading radiologist. Even in centralised programmes with well trained radiologists fully dedicated to breast cancer screening and diagnosis, double reading is still recommended. Double reading should be carried out independently. In cases of discordant opinions, excellent results have been obtained using consensus discussion between the two radiologists or the practice of arbitration from a third screening radiologist. Double reading is recommended in centralised programmes for the first screening round and until the performance of the radiologists can be fully assessed.

In decentralised programmes, double reading is mandatory and should be performed at a centralised level. Second reading should be performed by radiologists who read a minimum 5,000 mammograms per year. In order to avoid an excessive decrease in specificity, cases recalled by one or both radiologists should be reviewed by an expert radiologist who can arbitrate. Overall recall rates should be kept to the standard values reported in table 2.

4.5.3 Assessment of screen-detected abnormalities

An abnormal finding on a screening mammogram requires recall to an assessment process where further investigations are undertaken, in order to confirm the presence of a malignant, benign or normal condition. Triple assessment i.e. the availability of clinical examination, further imaging (diagnostic mammography and ultrasound) and cell/tissue sampling should be available. This process should be led by a radiologist fully trained and experienced in breast screening. Assessment may also need to be provided to women who complain of significant symptoms at the time of screening or in those women where the radiographer feels a mass during mammographic positioning. Such symptoms should always be recorded by the radiographer and made available to the reporting radiologist. Adequate protocols must be in place either in a centralised or decentralised programme to ensure that assessment procedures are robust and complete. A decision on further management, or a return to routine rescreen may then be made. Radiologist sensitivity and specificity should be optimal so that women are not subjected to unnecessary anxiety from this process. The assessment facilities available should include further diagnostic mammography with special radiographic techniques such as microfocus magnification, ultrasound and a multidisciplinary input including clinical examination. Image guided cytological or core biopsy sampling must be available.

It is advisable that documented assessment protocols be devised and followed. For example it is not necessary to drain a cyst detected at assessment unless it is symptomatic, causing diagnostic problems, or if the woman requests it. Microfocus magnification techniques for

microcalcification should be performed in orthogonal planes, e.g. cranio-caudal and lateral. It is most effective to sample a lesion under ultrasound control if it can be demonstrated sonographically. Where there is doubt in the mind of the assessing radiologist, it is safest to sample under X-ray guidance. Unless the radiologist is very experienced, it is advisable that all solid lesions on ultrasound should be sampled as it is often not possible to reliably differentiate benign from malignant solid lesions on sonographic appearances alone.

For quality loop purposes, it is recommended that the radiologist performing the screen reading should also be involved at assessment. Where this is not possible it is vital to ensure that a complete feedback system is in place for exchange of follow up information and outcomes. All unnecessary intervention and creation of anxiety must be avoided. It is the radiologists' responsibility to ensure that all necessary investigations are carried out at assessment, preferably at the same visit, so that a decision is reached and information provided to the woman.

4.5.4 Quality assurance organisation

In any population based screening programme it is vital to balance the risks and benefits, ensuring the emphasis is placed firmly on the latter. This is best achieved with the formation of an extensive quality assurance organisation and programme. Preferably this should be introduced at or before the commencement of screening activities so that adequate working arrangements can be established at the outset of a programme and not require changing at a later and more difficult time.

Local quality assurance manuals should be in use, which should be based upon European or national documents. Regional and local organisations for QA should exist, working at individual discipline level as well in a multidisciplinary setting.

The organisation should ensure that all professionals participating in the screening programme are fully trained and comply with performance and working guidelines that should be approved by relevant national bodies and organisations. A central committee should decide policy. Results at local, regional and national levels must be produced in a complete and timely manner, available to political as well as professional groups, also being offered within the public domain.

Each screening unit should have a Quality Assurance Manager - one nominated person responsible for the overall quality of the programme who can be the focal point for all quality activities within that programme. Each programme must review its own results in order to understand its own performance and the Quality Assurance Manager must ensure that all results are collated for the programme and should act as a liaison between the local programme and the wider regional and national quality assurance organisations.

4.5.5 Number of views

Screening mammography using two views of each breast (medio lateral oblique plus cranio-caudal) has been proven to be more effective than single oblique view screening, particularly in the woman's first round. The use of two views provides a higher sensitivity and specificity as the second view may provide additional information by detecting abnormalities not seen on the oblique view only, and by avoiding unnecessary assessment for a woman with an apparent abnormality shown to be due to superimposition on the second view. The oblique projection gives the maximum possible visualisation of breast tissue. The cranio-caudal view does not demonstrate the axillary tail region so well, but provides a different projection of the breast tissue and the technique allows for better compression.

4.5.6 Localisation of non-palpable lesions

A substantial proportion of screen-detected abnormalities will be impalpable and therefore will require some form of localisation procedure prior to either diagnostic or therapeutic excision. It is the radiologist's responsibility to ensure that this process is carried out as effectively and accurately as possible so that lesions are satisfactorily excised in over 90% of cases at first operation (see EUSOMA Chapter on QA in diagnosis).

4.5.7 Multidisciplinary meetings

The outcome of assessment should be decided according to agreed multidisciplinary written protocols. A multidisciplinary clinical meeting should be organised at least weekly to discuss all cases which required tissue sampling, preferably before the patient receives her result. Treatment options should also be discussed and agreed in advance. Team members attending these meetings should include radiologists, surgeons, pathologists, radiographers, oncologists and nurse counsellors. One member of the team should be nominated as being in charge.
Projecting facilities should be suitable for all those present to see the key imaging and pathological images being presented.

When discussing pre-operative cases it is crucial that the surgeon is made aware of the correct lesion or lesions to be excised and the extent of any disease on imaging. This is especially important if cases have been worked up elsewhere and referred in full surgery.

Similarly in post-operative meetings it is important to correlate the pathology of the excised lesion with the pre-operative findings. If there is sufficient disparity to cause concern a case review may become necessary to ensure that the correct lesion was in fact removed.

4.6 Interval cancers

Definition
Interval cancers are defined as breast cancers arising after a negative screening episode (which may include assessment) and before the next scheduled screening round. It is important not only to register invasive but also in situ (DCIS) interval cancers. Sometimes an interval cancer is not a failure of the screening but a failure of the assessment process. Cancers detected at early recall are not classified as interval cancers, but are screen-detected with a delayed diagnosis (see 4.4.2).

Importance
Interval cancers are inevitable in a screening programme but their number should be kept as low as possible. A high proportion of interval cancers will reduce the effectiveness of screening and the potential mortality reduction will be lowered. The screening process should be optimised and any potential delay in diagnosis must be minimised whether it is due to a failure of the screening process or of assessment. Tracing interval cancers is complex but fundamental to monitor the performance of any screening programme. Mechanisms should be in place to identify all breast cancers arising in the target screened population. Interval cancer monitoring is also important to evaluate the chosen screening interval and radiological performance.

The good practice of performing mammography prior to surgery in all symptomatic cases suspicious for breast cancer will enable more adequate classification of interval cancers as well as demonstrating the extent of malignancy and the presence of contralateral disease.

Reviewing process
Radiologists in each unit must ensure that a suitable mechanism exists for the review and audit of all interval cancers. This review should be an essential part of routine radiological audit, and plays a key role in the continuing medical education of radiologists involved in the programme.

For satisfactory audit purposes a regular review panel should be set up with at least three radiologists so that a consensus on classification can be reached.

Methodology

1. The screening films should first be reviewed without seeing the presentation mammograms taken at the time of diagnosis (blind review). This is in order to make a provisional classification in one of the following categories:

True interval — The screening mammogram is normal, no reason for assessment.

Minimal signs — There is a possible subtle abnormality on the screening film. This would not necessarily be regarded as warranting assessment. A brief description of the lesion and its position should be noted.

False negative — An abnormality is clearly visible and warrants assessment. Description and position should be given.

2. Following provisional classification, the screening mammogram is reviewed again together with the diagnostic mammogram. A new and definitive classification should now be made, which may be different to the provisional classification. For example it may be possible to retrospectively identify minimal signs that were not identified on blind review. It is also important to confirm that minimal signs identified on blind review correlate exactly with the site of interval cancer, otherwise the case, instead of minimal signs, becomes a true interval.

If there is disagreement on classification by the reviewing panel, the opinion of the majority should decide.

If mammography was not performed at the time of the diagnosis it is not possible to classify the interval cancer in a proper way, and the case is categorised as 'unclassifiable'.

In true interval cancers it is important to check the positioning technique and the physico technical quality of the original screening mammogram, in order to identify whether sub-optimal images could have contributed to the cancer not being identified.

Table 3: Classification of interval cancers*

Categories	Subtypes	Screening films	Diagnostic mammogram
True interval		Negative	Positive
Occult		Negative	Negative
Minimal signs		Minimal signs	Minimal signs or positive
False negative	Reading error Technical error	Positive Negative (for technical reasons)	Positive Positive
Unclassifiable		Any	Not available

* Based on the UK Quality Assurance Guidelines for Radiologists, NHSBSP May 1997, page 50.

The group of interval cancers with minimal signs present is very important. It may be possible to split this group into significant and non specific signs. False negative cases should not exceed 20% of the total number of interval cancers. Radiological review of false negatives and minimal signs will directly influence performance and may lead to better screening results. Cancers arising in lapsed attenders are not classified as interval cancers, although it is important to review them. Advanced and node positive screen-detected cancers at subsequent screening should be reviewed in a similar fashion for educational purposes.

The UK NHSBSP Quality Assurance Guidelines for Breast Cancer Screening Radiology (NHSBSP Publication # 59, 2005) proposes a simpler classification of interval cancers, mindful of possible medico-legal consequences of the results of interval cancer review. Following standard review of screening films as outlined above, cases that are classifiable are allocated one of three categories:

1. Normal / benign	Either no abnormality is present on the original screening films, or an abnormality is identified which has benign features.
2. Uncertain	An abnormality is present on the original screening films, either retrospectively or prospectively, which carries radiological features not clearly specific for either a benign or malignant process.
3. Suspicious	The original screening films show an abnormality which in the opinion of the reviewing panel has radiological features suspicious for malignancy.

4.7 Professional requirements

Each screening radiologist should:
- be medically qualified and registered to practise in his/her country
- have had specific training in both diagnostic (symptomatic) mammography and screening mammography
- participate in a continuing medical education programme and in any relevant external quality assessment scheme
- undertake to read a minimum of 5,000 screening cases per year in centralised programmes. This applies to the radiologist carrying out second reading in the non-centralised programmes.

In addition each radiologist should:
- be involved with assessment as well as basic screening
- have access to pathology and surgical follow up data
- attend multidisciplinary review and clinical management meetings
- be involved with symptomatic breast work, ideally having skill in clinical examination of the breast
- be fully experienced in all assessment techniques including the ability to perform ultrasound, FNAC and/or core biopsy

4.8 Screening women at high risk

Women at high risk for developing breast cancer due to hereditary factors such as family history and/or those with genetic factors such as BRCA 1 & 2 gene amplifications can be offered special screening services, following specialist genetic counselling to ascertain the risk level. It must be remembered that the majority (over 90%) of breast cancers arising in a population will not be associated with specific genetic risk factors.

Imaging modalities and screening intervals to be used for these groups have to be selected and planned with a multidisciplinary team. These services should only be offered within special research/study protocols and outside general population screening programs. Nevertheless it is likely to be advantageous to this group of women to be screened by a team which has specific screening expertise.

Women at high risk due to genetic factors belong to the younger age group and often have dense breasts. The sensitivity of both Ultrasound and MRI is not affected in dense breasts but specificity and costs can be a matter of concern. Secondly, access to MRI of the breasts varies considerably in routine Breast Imaging Centres. Therefore screening women at high risk is dependent upon available resources, access to multidisciplinary expertise and adequate planning with research/study protocols for proper monitoring and evaluation. Multiple studies of high risk screening methodology are underway and should clarify the slightly uncertain situation at present.

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5

Multi-disciplinary aspects of quality assurance in the diagnosis of breast disease

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

5.1 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 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). 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. This 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.

5.2 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 these guidelines, a further document on the training of health professionals in breast care has been prepared by EUSOMA and will be 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.

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.

5.3 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 focussed 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 asymmetry 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 patient.

5.4 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.

5.4.1 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. 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.

5.4.1.1 Targets

Analogue targets
High contrast/spatial resolution > 12 lp/mm
Optical density 1.4 – 1.9
Mean glandular dose for standard breast per film <2.5 mGy
Daily processor control maintenance 100%

Digital targets
Contrast – to – noise ratio sufficiently high
Mean glandular dose for standard breast <2.5 mGy
Weekly homogeneity check
Regular monitor check

5.4.2 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.

5.4.3 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 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.

5.4.3.1 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.

5.4.3.2 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 chapters 2 and 3.

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

5.4.4 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.

5.4.5 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 Protocol (chapter 11).

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.
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 2,000 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.

5.5 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 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).

5.5.1 Diagnostic classification

A simple five-point 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.

5.5.2 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%

5.5.3 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%

5.5.4 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 and www.cpo.it/qt

5.5.5 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.

5.5.6 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).

5.6 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 meeting 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.

5.7 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 it's 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.

5.8 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 woman 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. 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.

5.8.1 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 microhistological 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 microcalcification 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.

5.8.2 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 %

5.9 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.

5.9.1 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.

5.10 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) 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.
All pathology laboratories should be accredited according to national standards.

5.11 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.

5.12 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.

5.13 References

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6

Quality assurance guidelines for pathology

6a *Cytological and histological non-operative procedures*

6b *Open biopsy and resection specimens*

Quality assurance guidelines for pathology

6a

Cytological and histological non-operative procedures

Editor
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The previous version of these guidelines are also available in multimedia format as part of the BreakIT project from Giunti Ilabs, Via Ponte Calvi 3/15 1624 Genova Italy.

6a.1 Introduction

Non-operative diagnosis represents the norm in breast screening assessment. Its role in malignancy is to attempt to provide a definitive diagnosis allowing rapid referral for treatment, ideally in one procedure. Definitive non-operative diagnosis of benign conditions is also fundamental, avoiding surgery and allowing return to routine recall.

In this context, needle core biopsy (NCB) by automated biopsy guns and recently by vacuum-assisted systems (VANCB or 'mammotome') are widely accepted tools that have led to the introduction of histology in addition to, or replacement of, traditional fine needle aspiration cytology (FNAC). In all clinical situations, but especially with the impalpable lesions observed in screening pathology, pathologists have to deal with multidisciplinary teams and close communication with the radiologists and the clinicians is essential.

The purpose of these guidelines is to update pathologists on the role and use of minimal invasive diagnostics by FNAC, NCB and VANCB in breast screening assessment. The document and appendices also detail the mechanisms used to assess the quality of non-operative cytological and histological procedures and reporting in breast cancer screening.

6a.2 Use of non-operative diagnostic techniques

All sampling techniques share the same purpose, which is to obtain a representative sample of the targeted mammographic or ultrasound abnormality. This abnormality often represents a lesion, but is sometimes only the expression of a non-pathological tissue distortion of the mammary glandular structure.

All cases should undergo a thorough work up including imaging and clinical examination prior to FNAC or NCB. The imaging characteristics of suspicious lesions are demonstrated using special mammographic views including fine focus magnification views for microcalcification, spot compression views and ultrasound examination. The imaging features of mammographically detected abnormalities are assessed to determine the probability of malignancy. This information together with the result of clinical examination must be considered with the results of FNAC and/or NCB at a multidisciplinary meeting when deciding further management[1].

Cytology and NCB results from non-palpable lesions should not be interpreted in isolation. Inevitably, inadequate and false-negative results are significantly higher for non-palpable lesions. When the imaging findings are considered to be strongly suspicious of malignancy and FNAC or NCB is inadequate, normal or benign then management should be based on the imaging findings. In cases where there is disagreement between modalities with a failure to achieve consensus after multi-disciplinary discussion, the case should be reviewed and a decision made whether to repeat the sampling procedure, to perform VANCB or to refer for open biopsy. If the initial sampling procedure was FNAC then consideration should be given to the use of NCB as the repeat procedure. The non-operative procedures are best carried out by radiologists who are dedicated in breast imaging or in a multidisciplinary team with a specialist radiologist present[1].

The pathologist should receive the radiologic features of the lesion from the operator performing the FNAC/NCB, i.e.: spiculate mass, stellate lesion, well defined mass (solid or complex cyst, microcalcification, architectural distortion, including size, and distribution especially in case of microcalcification. Comparison between the terminology used by radiologists and pathologists is useful to train radiologists and pathologists to share and correlate each other's diagnostic findings (Table 1).

Table 1: Preferred terminology for radiologists, and the main histopathologic differential diagnosis

Spiculate mass	Invasive carcinoma
Stellate lesion	Radial scar, complex sclerosing lesion, invasive carcinoma, usually low/intermediate grade
Well defined mass	Cyst, (fibro)adenoma, hamartoma, phyllodes tumour, invasive carcinoma (high grade), encysted papillary carcinoma, mucinous carcinoma, medullary carcinoma
Microcalcification, coarse branching	Plasma cell mastitis, DCIS high grade
Microcalcification, coarse clustered	Fat necrosis, fibroadenoma, cysts DCIS intermediate/high grade; LCIS (rarely)
Microcalcification, fine clustered	Sclerosing adenosis, cysts, DCIS low/intermediate grade
Architectural distortion	Involution, radial scar, ILC, DCIS (rarely)

Any definitive diagnosis of FNAC/NCB is the result of integrating the data supplied by the pathologist and the radiologist. It includes:

1. The analysis of the pathologist and its diagnostic category, independent of the mammographic/ultrasound image
2. A benign result (C2/B2) should be correlated with the mammographic/ultrasound image and the degree of radiological suspicion, to determine whether the sample is representative to differentiate benign non-representative results from benign representative results
   It should be noted that :
   - the question of whether the sample is representative arises in practice with all cytological or histological benign results
   - a cellular cytological sample does not necessarily mean the sample is adequate
   - comparison of the histological findings with the mammographic/ultrasound image is necessary to judge whether the specimen is representative. Such a comparison requires a close coordination between the radiologist and the pathologist.

Optimal assessment of breast lesions requires dedication and experience. Best results are obtained when only experienced personnel perform FNAC or NCB/VANCB and their performance is audited as a matter of routine.

6a.3 Choice of sampling technique

Significant breast abnormalities should be assessed by NCB or FNAC[2,3]. Current evidence suggests that 14 gauge core biopsy, properly carried out, provides better sensitivity and specificity than FNAC for microcalcification, asymmetry and architectural distortion[4,5].

Core biopsy also facilitates definitive diagnosis of benign lesions. FNAC may be preferred in some centres for sampling mass lesions and obvious carcinoma, but only where a satisfactory standard of excellence has been achieved[6].
Although some screening units provide immediate reporting of FNAC during assessment, this is not essential. Radiologists involved in assessment should ensure that they have the necessary skills to carry out NCB and FNAC under stereotactic and ultrasound control[1]. There should be written local protocols clearly defining the indications for FNAC, NCB and VANCB techniques.

I. Fine needle aspiration cytology (FNAC)

The technical aspects of FNAC sampling are given in Appendix 1.

The accuracy of FNAC depends on three main factors:

- a sample which is adequate and representative of the lesion
- suitable processing and staining without artefacts
- accurate interpretation of the cytological material with a clear report conveyed to the rest of the clinical team

The procedure can fail at any of the stages of preparation (aspiration, spreading and staining) even before diagnostic interpretation. The confidence and experience of the aspirator are vital for obtaining a satisfactory sample. This part of the procedure, like other parts, should not be delegated to the novice.

FNAC is less expensive than NCB and less time consuming. Sampling and processing takes less time, therefore immediate diagnosis is possible. It may also be useful to aspirate clinically or radiologically abnormal axillary nodes as staging of the axilla may be helped by positive cytology obviating the need for a sentinel node procedure[5a,5b]. FNAC does, however, have some weaknesses:

- It may show poor cellularity leading to a 10-15 % inadequate rate[6,7,8,9,10]. Poorly cellular smears are more likely to be obtained from lesions such as sclerosed fibroadenomas, sclerosing adenosis, or invasive lobular carcinoma[11].
- It supplies cells isolated from their environment which does not allow analysis of the tissue architecture. This means that:
  - it requires a highly skilled and well-trained pathologist
  - it is very difficult to distinguish benign proliferating lesions from well differentiated carcinomas[11,12,13,14]
  - it is more difficult to correlate FNAC with the radiological image. An accurate diagnosis of common benign lesions except cysts, intramammary lymph nodes and the most typical fibroadenomas may be difficult leading to uncertainty. This may therefore require histological control by NCB or by surgery if there is doubt after triple assessment[10].

II. Needle core biopsy (NCB)

Needle core biopsies are small volume specimens of tissue, allowing histological analysis. They are obtained using reusable or disposable 'guns' and disposable automatic needles of 18-G to 12-G. The most commonly used is 14-G.

These techniques have been evaluated[15,16] for reliability and limitations depending on the various indications. They are well suited to palpable or non-palpable masses but may be insufficient for microcalcification.

Biopsy is made under local anaesthetic after cutaneous micro-incision; five passes for mass lesions and ten passes for microcalcification gives the highest concordance with open biopsy[16a,17].

- NCB is able to characterize lesions more completely than FNAC and can provide a definitive diagnosis in a higher proportion of cases
- It may differentiate between invasive and in situ carcinoma
- It allows better characterization of lesions associated with microcalcification than FNAC
- It can be used for assessment of important pharmacotherapeutic factors such as steroid receptors and Her2/Neu status

Interpretation of core biopsies requires experience and knowledge of complex breast lesions. Additional immunohistochemical stains may be useful for differential diagnosis. Like FNAC, NCB diagnosis should be part of triple assessment in a multidisciplinary meeting to decide on therapy, as overdiagnosis and underdiagnosis may occur. For example, when stereotactically obtained core biopsies for the diagnosis of microcalcifications contain DCIS, invasive carcinoma is found in up to 20% of cases[18,21].

Published series of image guided breast core biopsies show that high sensitivity and specificity can be obtained using NCB compared to FNAC (see appendix 1). No difference in patient discomfort between FNAC and NCB has been demonstrated.

III. Vacuum-assisted needle core biopsy (VANCB)

For certain types of mammographic abnormality, particularly moderate to low level suspicion microcalcification, a larger volume of tissue is required for accurate diagnosis. This is possible with VANCB. The biopsy probe incorporates a vacuum channel, which applies negative pressure to the biopsy port and thereby sucks the adjacent breast tissue into the port for sampling. The biopsy probe is introduced into the breast and positioned using image guidance. The vacuum is activated and sucks breast tissue into the biopsy port; a rotating cutting cylinder then passes down within the probe and separates the biopsy material from the surrounding tissue. The biopsy specimen is then delivered by withdrawing the cutting cylinder while applying negative pressure and while the main probe remains within the breast. Multiple specimens are obtained by rotating the biopsy probe within the breast so that the biopsy port is applied to different areas of breast tissue.

The potential advantages of this system are the ability to obtain a larger volume of tissue for histological examination and the rapid evacuation of any haematoma which collects at the site of biopsy. This ensures that the specimens obtained are of good quality and are not compromised by the presence of haematoma.

Under local anesthetic, after a cutaneous incision of 5 mm, VANCB allows the radiologist to obtain 5 to 25 8-G or 11-G cores of tissue. These should be X-rayed in cases of micro-calcification. In cases where the whole or a high proportion of the lesion has been removed, a small metal marker should be introduced through the biopsy probe and deployed at the biopsy site.

Consumables are expensive and this technique is often reserved for non-palpable lesions, in particular for microcalcification[19,20] or for the excision of a benign abnormality where the avoidance of an operation is possible. It is usually used under stereotaxis, on digital dedicated tables, but it can also be guided by ultrasound.

Published results on VANCB have demonstrated a lower equivocal sample rate and increased accuracy in the detection of small invasive tumours associated with an area of DCIS[21]. Consideration of the likely underlying histological nature of the lesion from the imaging features should therefore be taken into account when deciding on the sampling method to be used.

6a.4 Indications

A simple imaging classification should be used to indicate the radiologist's degree of suspicion (see chapter on QA in the diagnosis of breast disease) This is useful for multidisciplinary management and audit. The indication and the preferred method for non-operative biopsy is decided according to the degree of suspicion and the nature of the lesion.

R1	Normal/benign
R2	Discrete lesion having a benign appearance
R3	Indeterminate
R4	Suspicious of malignancy
R5	Malignant features

If desired a more complex and numerically precise classification may be used such as the A.C.R.Birads system[21a].

In order to optimize treatment, non-operative histological diagnosis should be the goal replacing open biopsy and frozen section examination[22,23].

6a.5 Complications and changes secondary to FNAC, NCB and VANCB

FNAC, NCB and VANCB are remarkably complication-free, however certain rare problems should be considered such as pain, haematoma, pneumothorax, fainting, removal of lesion by NCB or VANCB, complete infarction of the lesion, reactive stromal changes, and displacement of tumour cells in the biopsy track and by lymphatic drainage. Pathologists are affected by the last four.

I. Removal of lesion by NCB or VANCB

Small lesions, especially very small clusters of microcalcification may, if extensively sampled, be removed completely. In such circumstances, no further residual lesion is found in the excision specimen, despite thorough examination. Careful pathological assessment as advocated in section B with reference to histological evidence of a core biopsy track and discussion at a multidisciplinary meeting to ensure the correct area has been biopsied, should always be performed in these instances. The NCB/VANCB sample can be used to provide prognostic information if no other lesion is found.

II. Displacement of tumour cells

Displacement of tumour cells has become increasingly recognised as a result of NCB[24]. This process has also been described after FNAC[25]. This may cause histopathological diagnostic difficulties in the subsequent excision. Islands of cells are seen outside the main lesion, often within a track with a fibroblastic and histiocytic tissue response indicating the previous sampling site. Displacement is rarely recognised more than a few millimetres from the source of the cells. Recognition of the track makes the correct identification of displacement usually straightforward. Cell groups displaced from 'in situ' papillary lesions or DCIS may mimic invasive carcinoma. The associated signs of trauma from non-operative sampling should be sought. The clinical significance of this phenomenon is not yet clear, however a diagnosis of invasive cancer should be avoided. The observation should be mentioned in the report[24,26,27,28,29]. Lymphatic drainage of epithelial cells displaced by NCB has been observed as emboli in afferent vessels and marginal sinuses of lymph nodes in patients with DCIS or even benign breast lesions[28] but these do not cause a tissue reaction or show evidence of metastatic activity.

III. Complete infarction of the lesion

Complete infarction of a lesion after NCB or FNAC has been reported as a rare occurrence[30] especially in fibroadenoma or encysted lesions such as ductal adenoma and encysted papillary carcinoma. In these cases the needle biopsy should be used for classification of the lesion and further management.

IV. Reactive changes

Both FNAC and NCB may induce a florid (myo)fibroblastic reaction in the needle track which may be a source of misinterpretation (as mesenchymal neoplasia, or metaplastic carcinoma).
Partial infarction and proliferation of spindle cells with squamous metaplasia can be observed after needle biopsy. This may be a source of overdiagnosis.

6a.6 NCB and VANCB reporting guidelines

This section of this document is designed to assist in classification of needle NCB and VANCB samples.

6a.6.1 Specimen information & handling

Proper interpretation of core biopsies requires knowledge of details of both clinical and imaging findings (mammography/US) and this information should be provided on the request form. The completed request form should include clinical details, specifying the imaging findings, the site of biopsies and the number of cores.

The tissue fixation protocol should be based on a standard procedure agreed between the departments involved.

Biopsies performed from microcalcifications should be x-rayed to determine the presence of calcification. A comment regarding the presence of **representative** microcalcification of the mammographic lesion in the sample should be provided along with the specimen x-ray.

Biopsies should be placed in fixative solution immediately and sent promptly to the laboratory.

The specimen x-ray procedure should not interfere with prompt fixation. Before fixation, the specimen should be arranged straight, if multiple in parallel. It is recommended that no more than four NCB specimens should placed into a single cassette.

In cases of mammographic microcalcification, examination of further levels should be performed if calcification is not immediately apparent on histological examination. In problem cases further levels and/or radiography of paraffin blocks may be helpful.

Figure 1a: Specimen NCB/VANCB reporting form

Breast screening NCB/VANCB Form

Surname _____ Forenames _____

Date of Birth _____

Screening No _____ Hospital No _____

Centre _____ Report No _____

Side Right Left Quadrant : _____

Clinical details: _____

_____

_____

Radiological category R1 R2 R3 R4 R5

Radiological Appearance

Spiculate mass Stellate lesion Microcalcification, coarse branching
Well defined mass Architectural distortion fine clustered

Localisation technique Palpation Stereotactic Ultrasound guided

Specimen type NCB VANCB Number of cores _____

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

Histological calcification Absent In benign changes In malignancy In both

Opinion of Pathologist

B1. Uninterpretable/Normal tissue only
B2. Benign
B3. Lesion of uncertain malignant potential
B4. Suspicious of malignancy
B5. Malignant
- a. In situ carcinoma
- b. Invasive carcinoma
- c. Invasive status not assessable
- d. Other malignancy

Pathologist _____ Operator taking biopsy _____

Date _____

Comment _____

_____

_____

_____

Figure 1b: NCB/VANCB reporting form

Optional further information:

Benign lesion

Fibroadenoma	Solitary papilloma	Multiple papilloma
Fibrocystic change	Sclerosing adenosis	Complex sclerosing lesion/radial scar
Periductal mastitis/duct ectasia		Columnar cell change

Other (please specify)_____

Epithelial proliferation

Not present Present without atypia Present with atypia (ductal)

Present with lobular intraepithelial neoplasia

Columnar cell change with atypia

Malignant lesion

In situ carcinoma	Not present	Ductal	Lobular with necrosis
DCIS grade	High	Intermediate	Low Not assessable
Invasive Carcinoma	Not present	Present	
Oestrogen receptor status:	Positive	Negative	_____Quick Score (Allred)
	Not performed		

Comment _____

_____

_____

6a.6.2 Recording basic information

Information on the nature of the mammographic abnormality and clinical characteristics should be provided by the breast screening radiologist requesting the pathology examination.

Centre/Location
Give the name of the assessment centre, clinic, department etc., where the specimen was obtained.

Side
Indicate right or left.
For specimens from both sides use a separate form for each side.

Quadrant
The quadrant of the index lesion can be entered here.

Radiological category
The radiological assessment of the lesion should be entered here.

Radiological appearance
This section of the form is to be filled in by the clinician to indicate the radiological abnormality.
- Spiculate mass
- Stellate lesion
- Well defined mass
- Microcalcification. This should be classified by the requesting radiologist into coarse or fine and branching or clustered
- Architectural distortion

Localisation technique
Please choose one of the following terms:

• Palpation	NCB guided by palpation
• Stereotactic	NCB/VANCB guided by stereotaxis
• Ultrasound guided	CB/VANCB guided by ultrasound.

Number of cores
If known indicate the number of NCB samples taken.
It is recommended that any cores containing calcification are so identified and are sent separately to the pathologist.

Calcification present on specimen X-ray
Indicate whether there is calcification visible on the specimen radiograph if available.

Histological calcification
Indicate whether calcification has been identified in the sample and if present whether it is associated within a benign or malignant lesion.

Pathologist
The name of the pathologist giving the histological opinion. The pathologist should be registered at the screening office.

Operator
Enter the name of the operator performing the biopsy.

Date
Enter the date of reporting the slides.

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

Optional further information
In some cases it may be helpful to record further information. This will be particularly so where

neo-adjuvant or primary chemotherapy is contemplated or for VANCB specimens where the whole lesion may be resected. The fields chosen are the relevant fields from the main histology form (See section B).

6a.6.3 Reporting categories

It is important to remember that histological examination of both NCB and VANCB samples is performed to fulfil the assessment process role by giving a pathology category classification (B1-5) and not designed to give a definitive diagnosis, although this is possible in the majority of cases. Thus whilst most samples can be readily categorised as normal, benign or malignant, it must be recognised that a small proportion (probably less than 10%) of samples cannot. The following reporting guidelines have been devised in recognition of this and should be used for all screen-detected lesions (microcalcification, architectural deformities and mass lesions). It is also important to remember that, although there are five reporting categories similar to those used in fine needle aspiration cytology (FNAC), these are not equivalent.

B1. Normal tissue/uninterpretable

This indicates a core of normal tissue whether or not breast parenchymal structures are present; thus this category is equally appropriate for a core including normal breast ducts and lobules or mature adipose/fibrous tissue only. A B1 report should include a description of the components present and comment should be made regarding the presence of breast epithelial structures.

Cores with B1 diagnoses may contain microcalcification, for example within involutional lobules. It is important in these cases that discussion between pathology and radiology colleagues is undertaken to confirm the appropriateness of the microcalcification in the histological specimen. Small foci of calcification within involuted lobules are common and frequently too small to be visible mammographically, thus a report that merely records the presence of this calcification without additional comment on its nature, size and site may be misleading and lead to false reassurance. Mammograms do not demonstrate microcalcification, either singly or in clusters, less than 100 microns in diameter.

Exceptionally some specimens may be classified as uninterpretable, for example due to excessive crush artefact or composed of blood clot only. Such samples should also be classified as B1 although some experts would prefer these to be classified as B0.

B2. Benign lesion

A core is classified as B2 Benign when it contains a benign abnormality. This category is appropriate for a range of benign lesions including fibroadenomas, fibrocystic changes, sclerosing adenosis and duct ectasia and extends to include other non-parenchymal lesions such as abscesses and fat necrosis.

In some cases it may be difficult to determine whether a specific lesion is present, for example if minor fibrocystic changes are seen. The multi-disciplinary approach is once again vital in these cases to determine whether the histopathological features are in keeping with the radiological and clinical findings. It may be appropriate and prudent to classify the lesion as B1, rather than B2 if only very minor changes are present; such histopathological features would clearly be insufficient to explain a well-defined mass lesion and classification as B2 would be inappropriate.

B3. Lesion of uncertain malignant potential

This category mainly consists of lesions which may provide benign histology on NCB, but either are known to show heterogeneity or to have an increased risk (albeit low) of associated malignancy.

The B3 category has a lower rate of malignancy on further surgical biopsy (25%) when compared with B4 (66%). The majority of B3 lesions require surgical excision, but all these cases should be discussed at a preoperative multidisciplinary meeting.

I. Papillary lesions

Papillary lesions may show intralesional heterogeneity and the limited sampling achieved with NCB may miss areas of in situ cancer. The majority of these lesions should, therefore, also be designated B3 of uncertain malignant potential. On rare occasions when a small lesion has been very widely sampled and submitted for pathological examination, a benign B2 classification may be considered. Conversely, when a sample of a papillary lesion in a NCB shows atypia, for example strongly suspicious of papillary carcinoma in situ, a B4 designation may occasionally be more appropriate.

II. Radial scar/complex sclerosing lesion

Biopsies which show features of a radial scar/complex sclerosing lesion such as areas of hyalinisation, elastosis, or tubular entrapment with epithelial proliferation should be categorised as B3 if they represent the cause of the radiological abnormality[30a.] Actually, these lesions are heterogeneous and a proportion of them are associated with atypia or malignancy (in general LIN or low grade DCIS).

III. Lobular intraepithelial neoplasia (LIN)

A small cell regular epithelial proliferation within moderately distended lobules which is considered by the pathologist to represent lobular intraepithelial neoplasia or LIN (regrouping ALH and LCIS) should be classified as B3: this process does not necessarily have the same management implications as a diagnosis of DCIS but surgical diagnostic excision might be considered. Lobular intraepithelial neoplasia is frequently a co-incidental finding in a core biopsy from a screen-detected lesion however and multidisciplinary discussion is essential as the abnormality identified radiologically may not be represented. Furthermore, it may be that LIN encountered serendipitously in a breast surgical excision does not carry the same risk and prognosis as LIN diagnosed via a targeted NCB/VANCB of a mammographic abnormality[31]. These cases must be managed cautiously.

On occasions it may be impossible to classify a small cell epithelial proliferation in lobules and/or ducts as either lobular neoplasia or low grade DCIS and in these circumstances a numerically higher category (B4 or B5) is prudent and should be considered. In these cases, E-cadherin may help in the differential diagnosis[32]. Pleomorphic LIN may also be classified as B5. There is at present, however, no definite follow-up information on these lesions and management should be discussed in a multidisciplinary forum.

IV. Atypical epithelial proliferation of ductal type

The definition of atypical ductal hyperplasia (ADH) is derived from surgical resection specimens and relies on a combination of histological, morphological and size extent criteria. There is a range of severity from those which are insufficient for a definite diagnosis of DCIS but highly suspicious to those which only show a minor degree of atypia, normally architectural which requires further assessment. In some cases, the appropriate categorisation may be B4 in lesions highly suspicious of DCIS. These proliferations must be clearly separated from usual epithelial hyperplasia (see pitfalls).

A definitive diagnosis of ADH is not possible on NCB. It has been shown that core biopsy samples which include atypical epithelial proliferative foci of ductal type, of insufficient extent for classification as DCIS, on subsequent surgical resection may form part of an established in situ neoplastic lesion with or without associated invasion. This view is based on several studies which describe the subsequent surgical diagnosis in cases described as ADH in NCB. In over 50% of cores surgical excision biopsy has shown either in situ or invasive carcinoma[33]. The limited tissue sampling which can be undertaken by NCB guns (often by stereotactic methods for foci of microcalcification) may thus provide insufficient material for definitive diagnosis of low grade DCIS if only a few involved duct spaces are obtained. In all cases open biopsy is indicated to evaluate the lesion, define its extent, and to exclude invasive growth. It should be clear that ADH cannot be diagnosed on NCB, and that it is incorrect to use the term ADH for cases where core biopsies include atypical intraductal epithelial proliferative foci, or an area of well differentiated DCIS insufficient in extent for classification as DCIS. These should be diagnosed as atypical epithelial proliferation of ductal type.

V. Phyllodes tumour
Fibroepithelial lesions suggesting phyllodes tumour (cellular stroma, stromal overgrowth and possibly some mitotic activity) should also be designated B3. Thus the presence of a cellular stroma within a fibroepithelial lesion should prompt a search for other features that may aid in discrimination from a fibroadenoma. In practice, however, this distinction is often impossible and careful appraisal of the entire clinical picture will usually allow appropriate management to be undertaken. Obviously malignant cases should be classified as B5.

B4. Suspicious of malignancy
Technical problems such as crushed or poorly fixed cores which contain probable carcinoma but cannot provide the definitive diagnosis are best included as B4. Similarly, apparently neoplastic cells contained within blood clot or adherent to the outer aspect of the sample should be classified as B4 suspicious.
A complete single duct space bearing an unequivocal high-grade epithelial proliferative process can be classified as B5 malignant. However care must be taken if one or only part of a duct space is seen containing a highly atypical epithelial process particularly if no necrosis is present; this may be regarded as suspicious rather than definitively malignant. In particular great care should be taken if the epithelial cells show any features of an apocrine phenotype, which may represent an atypical apocrine proliferation rather than DCIS.
The management of cases classified as B4 will usually be either diagnostic excision biopsy of the area or repeat NCB sampling to obtain a definitive diagnosis. **Definitive therapeutic surgery should not be undertaken as a result of a B3 or B4 NCB diagnosis.**

B5. Malignant
This category is appropriate for cases of unequivocal malignancy on NCB. Further categorisation into in situ and invasive malignancy should be undertaken whenever possible. Other forms of malignancy such as malignant lymphoma may also be classified as B5.

I. Lobular intraepithelial neoplasia (see above B3)
Lobular intraepithelial neoplasia is included in the B3 category, as it does not have the same management implications as a diagnosis of DCIS or invasive malignancy. Nevertheless the pleomorphic variant or LIN with comedo-necrosis may be classified as B5.

II. Ductal carcinoma in situ
One of the benefits of NCB is that it can allow distinction between in situ and invasive carcinoma. It should however be borne in mind that, due to sampling error, exclusive presence of DCIS in the core does not exclude the possibility of an invasive focus being present. In approximately 20% of cases sampled by standard methods co-existing invasive carcinoma will be identified in the subsequent surgical excision specimen[21]. The nuclear grade, architecture and the presence of necrosis within the DCIS can be indicated on the NCB report. In particular, the presence of associated calcification should be recorded. Biopsies of skin for Paget's disease may also be recorded as non-operative diagnostic procedures and can be classified accordingly.

III. Invasive carcinoma
An advantage of NCB over FNAC is the ability to diagnose invasion positively. Invasive mammary carcinoma can be unequivocally identified in NCB with a positive predictive value of 98% [34]. As noted above, however, the negative predictive value for invasion is only 80% when only DCIS is identified. Assessment of grade and type of carcinoma may be achieved (although concordance with final grade and type are not absolute and, if performed, should be interpreted with caution)[35,36].

6a.6.4 Problems and pitfalls in diagnosis

Diagnostic pitfalls and problems in diagnosis in NCB include many of the lesions which cause difficulties in FNAC diagnosis (see below). Other lesions, however, may present particular diagnostic problems in core samples.

I. Minor changes
Minor architectural distortions seen mammographically may also result in minimal changes such as a slight increase in stromal fibrosis on biopsy. These should be put in the B1 category with a comment concerning correlation with the mammogram. Asymmetric involution of breast tissue, a common target for biopsy, may lead to such changes.

II. Hamartoma and lipoma
Normal histology may indicate that the lesion has not been sampled. This is, however, not necessarily so. In the case of certain benign lesions such as hamartomas and lipomas apparently normal histological features would be expected on NCB. These should be put in the B1 category with a comment concerning correlation with the mammogram.

III. Pseudoangiomatous stromal hyperplasia (PASH)
PASH consists of anastomosing slit-like pseudovascular spaces, that are either acellular or lined by slender spindle-shaped stromal cells. It may be diffuse and an incidental finding or nodular and indistinguishable from fibroadenoma on imaging.

IV. Usual ductal hyperplasia (UDH)
Usual ductal epithelial hyperplasia (UDH) and other forms of benign hyperplasia such as that of gynaecomastoid type are commonly seen in cores. As with UDH in surgical excision specimens, the lack of uniformity and distribution/streaming of the epithelial cells with bland nuclear features and paucity of mitoses is of assistance in reaching a diagnosis. Usual epithelial hyperplasia of gynaecomastoid type with a micropapillary architecture should not be mistaken for micropapillary DCIS. Immunohistochemical staining with cytokeratin 5/6, may be helpful for the distinction between UDH and DCIS[37]. UDH is a chance finding, and other changes have to be present to explain a radiological abnormality. UDH is not normally associated with microcalcification (but cysts or sclerosing adenosis may be). UDH normally does not form a mass (but may do so when present as part of a complex sclerosing lesion).

V. Epithelial atypia in the terminal duct-lobular unit (TDLU)
Mild atypia of epithelium within lobular units is one of the commonest problems encountered in NCB samples. Care must be taken not to overdiagnose such minimal degrees of atypia, which may represent usual epithelial hyperplasia, apocrine change or reactive changes (for example adjacent to a previous sampling procedure). Such atypia should be classified as B1 (table 4). Conversely more severe degrees of atypia may reflect cancerisation of lobules by high grade DCIS.

VI. Columnar cell changes (CCC) with and without flat epithelial atypia (WHO 2003)
Columnar cell changes of the breast represent a spectrum of lesions, which have in common the presence of columnar epithelial cells lining variably dilated terminal duct lobular units[38,39]. They have been variably recognized as 'atypical cystic lobules', 'columnar cell metaplasia', 'columnar cell hyperplasia', 'columnar alteration with prominent apical snouts and secretions (CAPSS)'. In the 2003 edition of the WHO on the classification of tumours of the breast they are defined as 'flat epithelial lesions'[40]. The interest of these lesions in breast cancer screening pathology is linked to the presence of granular or psammomatous microcalcification within the affected lobules seen on mammography and requiring a core biopsy for histological diagnosis. In fact, a large range of cytological changes, with nuclear enlargement and multilayering, stratification and

tufting of the luminal epithelium, without hyperplasia of the myoepithelium is associated with a basic architectural change of dilated lobules. These parameters have to be considered in order to classify the lesions as 'columnar cell change or hyperplasia without atypia' (B2) (no atypical cells, no cellular tufting), columnar cell change or hyperplasia with atypia (B3) (atypical cells with some cellular tufting and multiple cell layers) and low grade ductal in situ carcinomas (B5) that encompass forms of cribriform to micropapillary in situ (clinging) carcinomas.

VII. Apocrine atypia and apocrine DCIS

Apocrine atypia, particularly in association with a sclerosing lesion such as sclerosing adenosis (called 'apocrine change within sclerosing adenosis') may be especially difficult to identify correctly in non-operative diagnostic samples. In NCB, large nuclei, often with prominent nucleoli may be mistaken for DCIS if pleomorphism is also present. The typical granular eosinophilic cytoplasmic appearance of apocrine cells should be sought. Pure apocrine DCIS is relatively rare; in high grade lesions solid growth in dilated ducts with periductal fibrosis and lymphocytic infiltrate, and features of malignancy such as significant atypia, mitosis, apoptosis, and comedo necrosis are criteria of malignancy[41]. In low grade lesions a complex (cribriform or micropapillary) architecture as well as continuous spread with multiple duct involvement should be sought for confirmatory evidence. Mild or moderate degrees of apocrine proliferation with atypical features in a duct space should be assessed with caution and it may be prudent not to record a definite diagnosis but to classify such a process as B3, of uncertain malignant potential. Conversely intracystic papillary apocrine change should be classified as benign (B2).

VIII. Lactational change

Focal lactational change may be seen in women who are not lactating, or pregnant and may be nulliparous and/or post menopausal. The involved acini are usually lined by plump vacuolated cells with a 'hobnail' architecture but may, less frequently, appear atypical with irregular, large or pyknotic nuclei. The epithelial cells may appear degenerative and rarely the process may be mistaken for cancerisation of lobules by DCIS. The recognition of the vacuolation of the cytoplasm and the typical hobnail architecture will enable the correct diagnosis to be established.

IX. Sclerosing lesions/tubular carcinoma

This is the most common source for overdiagnosis and overtreatment in core biopsies. Both lesions usually present as non-palpable lesions detected as a mammographic stellate mass. There is a risk of over diagnosis of invasive carcinoma when confronted by the centre of a complex sclerosing lesion in a core biopsy, particularly as the normal lobular arrangement may be less apparent than on an excision biopsy specimen. Immunohistochemical staining to demonstrate the presence of an intact myoepithelial cell layer or basement membrane is indicated in cases of doubt.

X. Microglandular adenosis/tubular carcinoma

In microglandular adenosis, the round tubules with open lumina have no myopepithelial cells. The cells have a clear cytoplasm that strongly expresses pS100 and basement membrane is still present[42]. In tubular carcinoma, neither myoepithelial cells nor basement membrane are present.

XI. Stromal proliferations and spindle cell lesions

Stromal proliferations may cause difficulties in diagnosis in NCB samples. Occasionally a second biopsy sample will be taken from a patient containing a fibroblastic proliferation which may represent the target lesion, but which may reflect tissue reaction and repair at the previous biopsy site. If the lesion represents the core site, an associated histiocyte reaction or indeed fat necrosis may be present and haemosiderin can be seen. Sometimes a fibroblastic stroma may be identified in a sample from a patient who has not undergone previous FNAC or NCB and which may represent a spindle cell proliferation such as a fibromatosis or part of a spindle cell tumour

such as a nerve sheath tumour or myofibroblastoma. A stromal proliferation may also be seen in phyllodes tumours and evidence for an epithelial component should be looked for, for example by performing additional levels. Metaplastic carcinomas or rarely primary sarcomas (see rare lesions) may also mimic stromal proliferations. When a definitive histological diagnosis cannot be made the abnormality should be reported as a spindle cell lesion of uncertain histogenesis or nature and classified as B3.

XII. Fibroepithelial tumours

As noted above, phyllodes tumours may rarely be difficult to distinguish from other stromal lesions. More commonly the differential diagnosis lies between a cellular benign fibroadenoma and a phyllodes tumour. Features including stromal atypia, if present, can be useful, but the degree of cellularity of the stroma is the most valuable feature to assess. In rare cases it is not possible to distinguish the two lesions and the sample should be reported as a 'fibroepithelial lesion' and classified as B3, to avoid under diagnosis of a phyllodes tumour. These cases should be discussed at multidisciplinary meetings.

XIII. Radiation induced changes

Radiotherapy changes to the breast may be difficult to differentiate from foci of recurrent or residual carcinoma, both in situ and invasive, or sarcoma. The radiation may induce a degree of epithelial or stromal atypia or stromal changes including vascular changes[43]. Epithelial changes may also follow chemotherapy[44].

XIV. Infiltrating lobular carcinoma

Small foci of invasive lobular carcinoma can be confused with chronic inflammatory cells or reactive stromal cells, and conversely as has been described in lymphocytic lobulitis[45]. The targetoid infiltrative pattern of classical lobular carcinoma may be of assistance but a reactive lymphocytic process can also have a peri-ductal or peri-lobular distribution. Cytokeratin immunohistochemistry, to demonstrate the neoplastic cells is of value in difficult cases but recognition of the abnormal cell proliferation requires vigilance as the features can be subtle.

XV. Mucocoele-like lesions

Mucocoele-like lesions producing extracellular mucin may be associated with ADH, DCIS and even with invasive carcinoma. They are discussed more fully in the FNAC section (see below). Cases uncomplicated by more serious lesions should be classified as B3 on NCB and should be excised.

6a.6.5 Rare lesions

I. Lymphoma

As noted above malignant lymphoma may rarely be identified in core biopsies and should be classified as B5 malignant.

The majority of these lesions are diffuse large B-cell lymphomas which may mimic epithelial malignancy. As in other organs the cells frequently show less cohesion, a higher nuclear to cytoplasmic ratio and do not demonstrate the architectural features of carcinoma. To avoid misclassification as carcinoma, however, the correct diagnosis should be considered and can be supported by immunohistochemistry (CD45, CD20, CD3, CD30 etc.) to demonstrate the appropriate phenotype.

Low-grade lymphomas may be more difficult to distinguish, mimicking a chronic inflammatory process. Infiltration of the lobular epithelium should be sought and the degree of lymphoid infiltrate, if high, should raise the possibility of a neoplastic process. A panel of lymphoid markers will be necessary to demonstrate the immunophenotype of the cells present and to allow the correct diagnosis to be made. These should be classified as B5d.

II. Metastasis to the breast

Metastasis to the breast from malignancies derived elsewhere is well recognised although rarely biopsied. A full clinical history is essential to avoid misdiagnosis of a metastatic adenocarcinoma as a primary breast carcinoma. Lesions which are recognised as metastasising to the breast include lung, especially anaplastic small cell carcinoma, ovarian, renal, prostatic carcinomas, neuroendocrine tumours, and non-epithelial malignancies such as melanoma, myelomas and rhabdomyosarcomas may also be seen. These should be classified as B5d.

A panel of antibodies frequently allows identification of the likely site of a metastatic adenocarcinoma and enables appropriate clinical investigation/management. Breast carcinomas usually express cytokeratin 7 but not cytokeratin 20, epithelial membrane antigen, CEA/NCA, GCDFP-15 and approximately 80% will express oestrogen receptor.

III. Sarcomas

Primary breast sarcomas are rare. They should be classified as B5d and most commonly originate in association with phyllodes tumours but in NCB specimens an epithelial component may not be present. The most common pathways of differentiation in phyllodes tumors are liposarcoma and fibrosarcoma although other differentiation including osteosarcoma, chondrosarcoma and rhabdomyosarcomas can be identified. Angiosarcomas may be a cause of false negative diagnosis as they may be relatively subtle and bland and may be mistaken for radiotherapy changes, particularly when they occur in this situation in the treated breast, or for PASH. Primary leiomyosarcoma (and leiomyoma) may be found in the breast; the latter most commonly seen in a retroareolar site. All these lesions can be difficult to diagnose definitively in core samples. A high index of suspicion and judicious use of immunohistochemistry can facilitate or support a diagnosis but non-diagnostic classification as B3 or B4 is often prudent.

6a.6.6 Assessment of prognostic information

Grading on NCB can be performed and is reasonably accurate[35,36]. Current evidence suggests that concordance between grade on NCB and that in the definitive excision specimen can be achieved in up to 75% of cases. It should, however, be made clear to the clinicians that the grade may differ (almost invariably by only one level) from that in the subsequent resection specimen. Mitotic count in particular may be lower in the NCB than in the excision specimen, therefore leading to underscore on the core.

Tumours may also often be typed according to the most common categories, such as ductal/NST or classical lobular carcinoma. Invasive carcinoma of special type, however, cannot be accurately predicted although this may be suggested with some degree of accuracy in the NCB report.

6a.6.7 Oestrogen receptor (ER) assessment

ER assessment on core biopsies has been shown to correlate with subsequent surgical excision specimens and also to predict response to hormone therapy[46,47]. As with determination on excision biopsy samples a standard protocol and method of assessment should be used (see section B). Predictive/prognostic factors like ER and HER2 can be performed if patients are candidates for neoadjuvant therapy.

6a.7 FNAC reporting guidelines

The essential role of cytological diagnosis is to distinguish benign from malignant processes. The common general criteria used are illustrated in Table 2. It is important to bear in mind that the morphological and histological patterns seen in both benign and malignant breast disease are quite varied, and this is reflected in the cytological appearances. For this reason, it is useful to have a working understanding of breast histology before approaching breast fine needle aspiration cytology. This knowledge can improve recognition of rare lesions and reduce numbers of false positive and negative diagnoses.

This section of the document is designed to assist classification and reporting of FNAC samples. The

terminology and diagnostic entities referred to are described in more detail in the UK Guidelines[2]. Initially, FNAC was the only method, but now it has been largely replaced by NCB. However, in certain situation and units, FNAC may be useful. Within these guidelines, the cytology chapter is quite large, reflecting the difficulty of the technique rather than its relative importance.

6a.7.1 Using the cytology reporting form

The cytopathology reporting form used may be a separate reporting form (Figure 2) or a form generated specifically by a Breast Screening System with the patient details already filled in by the computer. These both should request essentially the same information although the computer generated form may have spaces for radiographic information such as kV, mAs, side and type of localisation (palpable, ultrasound, stereotactic or other X-ray guided procedure). Information on the nature, size and distribution of the mammographic abnormality and clinical characteristics should be provided by the breast screening radiologist requesting the cytology examination.

Table 2: General diagnostic criteria for the recognition of benign and malignant conditions.

Criterion	Benign	Malignant
Cellularity	Usually poor or moderate	Usually high
Cell to cell cohesion	Good with large defined branching monolayers of cells	Poor with cell separation resulting in dissociated cells with cytoplasm or small clusters of intact cells
Cell arrangement	Usually in flat sheets (monolayers) with even distances between nuclei	Irregular with overlapping nuclei and three-dimensional arrangement
Cell types	Mixtures of epithelial, myo-epithelial and other cells with fragments of stroma	Usually uniform cell population
Bipolar (elliptical) bare nuclei	Present, often in high numbers	Not conspicuous
Background	Generally clean except in inflammatory conditions, or in cystic lesions	Dirty, due to necrotic debris (apoptotic nuclei, calcifications); desmoplasia (magenta stroma with fibroblasts); lymphocytes and macrophages
Nuclear characteristics		
Size (in relation to RBC diameter)	Small	Variable, often large, depending on tumour type
Pleomorphism	Rare	Common
Nuclear membranes (PAP stain)	Smooth	Irregular with indentations
Nucleoli (PAP stain)	Indistinct or small and single	Variable but may be prominent, large and multiple
Chromatin (PAP stain)	Smooth or fine	Clumped and may be irregular
Additional features	Apocrine metaplasia, foamy macrophages	Mucin, intracytoplasmic lumina; psammomatous intraepithelial calcifications

Figure 2: Specimen cytology reporting form

Breast screening Cytopathology

Surname _____ Forenames _____

Date of Birth_____

Screening No _____ Hospital No _____

Centre _____ Report No _____

Side Right Left Quadrant : _____

Clinical details: _____

_____

_____

Radiological category R1 R2 R3 R4 R5

Radiological Appearance

Spiculate mass Stellate lesion Microcalcification, coarse branching
Well defined mass Architectural distortion fine clustered

Localisation technique Palpation Stereotactic Ultrasound guided

Specimen Type

FNA (solid lesion) FNA (cyst) Nipple discharge Nipple or skin scrapings

Opinion of cytologist

C1. Unsatisfactory
C2. Benign
C3. Atypia probably benign
C4. Suspicious of malignancy
C5. Malignant

Cytologist _____ Name of Aspirator_____

Date_____

Comment _____

_____

_____

_____

6a.7.2 Recording basic information

Centre/Location
Give the name of the assessment centre, clinic, department etc., where the specimen was obtained.

Side
Indicate right or left. For specimens from both sides use a separate form for each side.

Quadrant
The quadrant of the index lesion can be entered here.

Clinical Details
A space for recording clinical information e.g. previous carcinoma etc.

Radiological category and appearance
The radiological assessment of the lesion should be entered here.

Specimen Type
Please choose one of the following terms:

• FNA (solid lesion)	Fine needle aspiration of a solid lesion
• FNA (cyst)	Fine needle aspiration of a cyst subjected to cytological examination
• Nipple Discharge	Cytological preparation of a nipple discharge or duct lavage
• Nipple or skin scrapings	Cytological preparation of scrapings from the nipple or skin.

Localisation technique
Please choose one of the following terms:

• Palpation	FNA guided by palpation
• Ultrasound guided	FNA guided by ultrasound
• X-ray guided	FNA guided by X-ray examination (perforated or fenestrated plate)
• Stereotactic	FNA guided by stereotaxis.

Pathologist
The name of the pathologist giving the cytological opinion. The pathologist must be registered at the screening office.

Aspirator
Enter the name of the person performing the fine needle aspiration.

Date
Enter the date of reporting the slides.

Recording the Cytology Opinion
See the section on Reporting Categories below.

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

6a.7.3 Reporting categories

In ideal circumstances one should aim for a definitive diagnosis of malignancy or benignity. The proportion where this is possible will increase with experience of both the pathologist and aspirator. Problems arise where paucity of the sample or interpretation of cell morphology make such a clear distinction impossible.

C1. Unsatisfactory

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

- Hypocellularity
- Error in aspiration, spreading or staining
- Excessive blood.

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

Preparative artefacts include:

- Crush, when too much pressure is used during smearing
- Drying, when the dry smears are allowed to dry too slowly (dry smears should be dried quickly, wafting in the air can speed up drying) or when the wet-fixed smears have been allowed to dry out before fixation
- Thickness of smear, when an overlay of blood, protein rich fluid or cells is obscuring the picture, making assessment impossible.

It is often helpful to make a comment as to the cause of inadequate specimens in the comment box on the form.

A number of methods can be used to spread the specimen by placing a drop of aspirated material from the needle on a glass slide. Many of these are variations on a theme but the essential idea is to get a thin layer of material on the slide to allow rapid drying for air-dried fixation without appreciable squash artefacts due to excess pressure.
All pathologists have received slides from clinicians where the aspirate has been well taken but has been ruined by poor spreading technique. It is sometimes difficult to remedy this but multidisciplinary discussion and making aspirators aware of the problems, especially visually and microscopically often helps to alleviate the problem. Should such problems persist alternative preparative techniques such as cytospin or thin preparations may be considered. The diagnostic criteria remain the same as on traditionally made smears.

C2. Benign

- Indicates an adequate sample showing no evidence of malignancy and, if representative, a negative report.
- The aspirate in this situation is poorly to moderately cellular and tends to consist mainly of regular duct epithelial cells. These are generally arranged as monolayers and the cells have the characteristic benign cytological features. The background is usually composed of dispersed individual and bipolar naked nuclei. Should cystic structures be a component of the aspirated breast, then a mixture of foamy macrophages and apocrine cells may be part of the picture. Fragments of fibrofatty and/or fatty tissue are common findings.
- A positive diagnosis of specific conditions, for example: fibroadenoma, fat necrosis, granulomatous mastitis, breast abscess, lymph node etc., may be suggested if sufficient specific features are present to establish the diagnosis with confidence and may be helpful in multidisciplinary correlation.

C3. Atypia probably benign
The aspirate here can have all the characteristics of a benign aspirate as described in the previous paragraph. There are however, in addition, certain features not commonly seen in benign aspirates[12]. These could be any, or a combination of the following:
1. Nuclear pleomorphism
2. Some loss of cellular cohesiveness
3. Nuclear and cytoplasmic changes resulting from proliferative changes, involutionary changes, pregnancy, or treatment influences (See diagnostic pitfalls)
4. High cellularity may accompany the above features.

C4. Suspicious of malignancy
This category should be used for those aspirates where there are highly atypical features in the smear, such that the pathologist is almost certain that they come from a malignant lesion although a confident diagnosis cannot be made.
This may be for three main reasons:
1. The specimen is scanty, poorly preserved or poorly prepared, but some cells with features of malignancy are present
2. The sample may show some malignant features without overt malignant cells present. The degree of abnormality should be more severe than in the previous (C3) category
3. The sample has an overall benign pattern with large numbers of naked nuclei and/or cohesive sheets of cells, but with occasional cells showing distinct malignant features.

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

C5. Malignant
- Indicates an adequate sample containing cells characteristic of carcinoma, or other malignancy.
- The interpreter should feel at ease in making such a diagnosis. Malignancy should not be diagnosed on the basis of a single criterion. Combination of the features listed in table 3 will be necessary to achieve this diagnosis.

Calcification
It is very useful for the radiologist if the pathologist reports the presence of calcification within specimens taken from stereotactic or perforated plate guided FNAC when the abnormality is one of mammographic microcalcification. If calcification is present in these circumstances the radiologist or multidisciplinary team can be more certain that the lesion has been sampled accurately and that the likelihood of a false negative due to an aspiration miss is lower. Calcification alone does not discriminate between benign and malignant conditions. In cases of calcification in the absence of a mass, NCB is preferable to FNAC.

6a.7.4 Diagnostic pitfalls in interpretation of breast FNAC

1. Potential false positive and suspicious diagnoses

a. Common conditions

I. Fibroadenoma
Smears from fibroadenomas may give very worrisome appearances with marked anisonucleosis and some dissociation. This usually happens in growing lesions as it can be seen in young women and as it may occur in the screened population especially in women with HRT. The clue to the diagnosis is the presence of bare bipolar nuclei in the clean background. Smears containing these in significant numbers should not be diagnosed as malignant unless there are clear features of a benign epithelial lesion (with benign epithelial clumps) and also malignant clumps and dissociated malignant cells recognisable as a distinctly separate cell population. These

smears, where the needle has passed through both a benign and a malignant lesion may be very difficult but the two distinct populations of epithelial cells should aid their recognition. Smears from some malignant tumours contain bare nuclei. These bare nuclei are not bipolar and have obvious malignant features identical to co-existing intact tumour cells. In fibroadenomas two cell types can be recognized in the clusters.

II. Papilloma

Aspiration of papillomas usually produces cellular aspirates with 'staghorn' or 'antler horn' clusters of cells similar on low power appearance to those seen in fibroadenomas although they may appear three-dimensional with well-defined margins. Sometimes connective tissue cores may be seen within these clusters. In some cases magenta (Giemsa) staining basement membrane can be found in columns or spherules (as in collagenous spherulosis). Background features are cyst fluid with macrophages or foam cells, usually in small numbers. Bare bipolar nuclei are seen in papillomas but there are generally not as many as in fibroadenomas. Variation in cell morphology with columnar, cuboidal and flattened epithelial cells with apocrine differentiation is characteristic of papilloma. In contrast to this, FNAC from intracystic papillary carcinoma shows a highly cellular pattern dominated by a single monomorphic columnar or plasmacytoid cell type arranged in overstained well-defined clusters or rows.

III. Apocrine cells

Apocrine cells in smears may appear pleomorphic and may dissociate. Degenerate apocrine cells in cyst fluids may also have a worrisome appearance. Awareness of the cystic nature of the lesion and recognition of the dusty blue cytoplasm, with or without cytoplasmic granules with Giemsa stains or green/pink cytoplasm on Papanicolaou /Haematoxylin & Eosin stains coupled with a prominent central nucleolus is the key to identifying cells as apocrine. Awareness of the marked pleomorphism which may occur in degenerate apocrine cells and careful assessment of the cellularity and chromatin pattern should allow a distinction from the rare apocrine carcinoma. Carcinomas of apocrine cell type occur in the breast but present as a solid mass with all the clinical and radiologic features of malignancy. If one is not dealing with cyst fluid and there is doubt about the nature of apocrine cells it is better to err on the side of caution and give a C3 or C4 report.

IV. Fat necrosis

Fat necrosis is a common occurrence in the breast as result of trauma, noticed or unnoticed. Mammographically fat necrosis may result in variable abnormalities: architectural distortion, a well defined or stellate mass, with or without calcifications which are usually coarsely granular.
FNAC may be overdiagnosed; the smear may be cellular, and overstained clusters of lipophages and histiocytes may resemble atypical epithelial cells.

V. Intra-mammary lymph nodes

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

VI. Radiotherapy changes

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

VII. Smearing and fixation artefacts

Excessive pressure during smear preparation of slides may produce dissociation of cells from benign clumps. The dissociation may cause the cells to resemble dissociated malignant cells.

The clue to this is the finding of nuclear lysis and trails of chromatin due to the over-spreading artefact. Fibroadenomas are the most likely lesions to produce these problems when over-spread.

b. Uncommon lesions

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

II. Granular cell tumour
This can present a worrisome appearance in smears. There is marked dissociation of rather pink cells which, although they have small nuclei generally, may contain occasional larger nuclei giving a pleomorphic appearance. The cells however do not look epithelial and benign epithelial clumps are seen between the dissociated cells of the tumour. The cells have eosinophilic granular cytoplasm on Papanicolaou or Haematoxylin & Eosin staining and a rather mottled pale mauve cytoplasm on Giemsa stains looking rather similar to apocrine cells.

III. Adenomyoepithelial lesions
These difficult and as yet incompletely understood lesions can show malignant cytological features because of dissociation of rather pleomorphic cells which are in fact myoepithelial. However, there is a mixture of different cell types with ductal, apocrine, and squamoid differentiations, and obvious bipolar bare nuclei are present.

IV. Collagenous spherulosis
This lesion produces rounded globules staining a granular purple colour on Giemsa stains with surrounding spindle cells. There is a resemblance to adenoid cystic carcinoma with which the lesion can be confused[48,49]. The globules can also be seen in papilloma and ductal adenoma. Biopsy in these rare conditions is advised.

V. Microglandular adenosis
There is a lack of bare nuclei and the lesion is reported as being a potential problem in the differential diagnosis of tubular carcinoma[42].

VI. Lactational change
Even in the screening age group focal lactational changes can occur. This is uncommon but can produce occasional dissociated cells within an otherwise benign appearing smear. The dissociated cells may possess nucleoli and have larger nuclei than the surrounding benign cells. They do however have a moderate quantity of pale blue cytoplasm on Giemsa staining with lipid droplets in the cytoplasm. Caution in interpreting occasional dissociated cells in an otherwise benign pattern should be exercised even in the screening age range and the question 'could these be lactational/secretory cells' should be specifically asked in these cases. Outside the screening age a history of pregnancy/lactation should always be sought and clinicians should always tell the pathologist of lactation or pregnancy.

VII. Mucocoele-like lesions
Extracellular mucin from non-malignant lesions is a rare event. The mucocoele-like lesion (MLL) as described by Rosen[50] is a well known cause. Extracellular mucin is also occasionally present in association with fibrocystic change, ductal hyperplasia, adenosis, ductal papillomas and fibroadenomas. MLL show scant cellularity with benign cytological features and there are no

specific features apart from extracellular mucin. Cases are often sampled for microcalcification rather than a mass, and when present are indeterminate radiologically. Most invasive mucinous carcinomas have cytological features of malignancy, often with vessels in the mucin which is a very uncommon feature in MLL. It is however documented that MLL may be associated with ADH, DCIS and even invasive mucinous carcinoma[51,52]. This is the rationale behind the recommendation for excisional biopsy, even when the accurate diagnosis has been obtained by NCB[53]. Consequently MLL fall under the category of C3 or C4 and most will require excision.

2. Potential false negative diagnosis

The most common cause of false negative cytological diagnosis is an aspiration miss. There are, however, types of carcinoma[11] which, by their nature, may produce a false negative diagnosis. The most common of these are:

I. Tubular carcinoma/invasive ductal carcinoma grade I[54]

FNAC from low grade invasive carcinomas often have much in common with benign breast epithelial cells, including low to moderate cellularity, cell cohesion, a monomorphic cell type with uniform nuclear size and, often, absence of immediately obvious nuclear abnormalities. Knowledge of the mammographic findings, a lack of bare nuclei, small clusters with microacinar cell arrangement, and irregular nuclear margins with indentations and polygonality are pointers to the diagnosis. Some larger clusters derived from a coincident DCIS component may contain psammomatous calcifications. The background may be red granulated (Giemsa) and contain naked fibroblast nuclei derived from desmoplastic stroma. Often it is not possible to give an unequivocal diagnosis but care should always be taken in interpreting smears from stellate opacities to avoid false negative results from this type of tumour[42,54].

II. Invasive lobular carcinoma[11,55]

Aspirates from this type of carcinoma are often difficult to interpret. The cellularity of these specimens is usually less than that seen in other breast carcinomas. A number of patterns can be observed, ranging in cytological appearance from poorly cellular smears with few benign looking uniform cells to highly cellular smears with cells not dissimilar to those seen in invasive ductal carcinoma. Cell dissociation and signet ring cells with intracytoplasmic lumina (private acini) are indicative of lobular carcinoma, although not specific. Irregularities in the nuclear outline with small protrusions from the nucleus (‘noses’) are also a feature of ILC.

III. Carcinoma with extensive fibro-elastosis

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

3. Recognition of ductal carcinoma in situ (DCIS)

Ductal carcinoma in situ and invasive ductal carcinoma cannot be distinguished accurately by cytology alone and FNAC from DCIS may, therefore, be overdiagnosed. When FNAC is only performed for mass lesions, the risk of overdiagnosis is small, as DCIS rarely presents as a mammographic mass. Some cytologic features may suggest DCIS, and it may be worthwhile to report, as this may be an indication of the presence of an extensive DCIS component. These features vary for different types of DCIS:

- High grade DCIS (comedo type): smears dominated by necrosis with granular calcifications, and with frayed cohesive sheets of large apocrine-like tumor cells with pleomorphic nuclei.
- Low or intermediate grade DCIS (cribriform/micropapillary): cellular smear with cohesive overstained clusters containing psammomatous calcifications; clean background with some macrophages; no or few bipolar naked nuclei.

- Encysted papillary carcinoma: highly cellular smear with overstained well defined clusters, sheets and rows of monomorphic cuboidal or columnar cells; clean background with few macrophages.

Nipple scrapings for Paget's disease should also be recorded as non-operative diagnostic procedures and can be classified accordingly, if diagnostic as C5 or if negative as C2. Uncertain cases should be recorded as C4 and subjected to histological biopsy.

4. Uncommon lesions

I. Silicone, soya oil or paraffin granuloma

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

II. Stromal lesions

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

III. Apocrine carcinoma

This rare type of carcinoma produces cellular smears. Difficulty in interpretation is related to the subtle appearance of the neoplastic apocrine cells and their resemblance to benign apocrine cells with degenerative changes. Clustering of cells and papillary formations are seen in benign as well as malignant lesions and are of little help. The key features of a malignant aspirate are the uniform cell population with nuclear atypia which one should not confuse with degenerative changes. Necrosis is also a helpful feature. Until one is aware of the marked atypical changes associated with apocrine cells in fibrocystic change the diagnosis of apocrine carcinoma should always be approached with caution.

IV. Phyllodes tumours

The benign variants of phyllodes tumour may not be recognised as such on fine needle aspiration and may give a picture similar to fibroadenoma. Clues to the diagnosis include the presence of intact stromal cells, occasionally with nuclear abnormalities and the finding of pieces of cellular mucoid connective tissue in the aspirate. Fibroadenomas can also show both these features however and the recognition of benign phyllodes tumours often depends on clinical and sonographic features.

Occasionally phyllodes tumours can produce a false positive diagnosis of malignancy also.

Malignant phyllodes tumours show a pattern of benign appearing epithelial clumps with spindle cells showing obvious malignant nuclear features.

V. Metastatic tumours[56]

Metastatic tumours in the breast should always be considered in FNAC where a peculiar pattern unusual for breast tumours is seen. Melanoma and oat cell carcinoma are the most common. In melanoma, pigment and large intranuclear cytoplasmic inclusions may be visible. Ovarian metastases are often papillary with psammoma bodies (an uncommon feature of breast tumours), large clear cells full of glycogen may suggest a renal metastasis, squamous carcinoma cells may be from a primary breast lesion but may also be from a metastatic lesion etc. The triple approach may often resolve this problem also.

VI. Lymphoma
The recognition of the lymphoid nature of an apparent primary breast tumour depends on the recognition of the spectrum of lymphoid cell types and the absence of cohesion of cells. Whenever the possibility of lymphoma is considered, haematological assessment and open tissue biopsy is indicated for immunohistologic typing of the lesion.

VII. Malignant stromal tumours
The commonest sarcoma to be aspirated from the breast is angiosarcoma, which is a very uncommon breast tumour without the context of previous radiotherapy.
Whenever the diagnosis of sarcoma in FNAC is considered (usual on the basis of dissociated spindle and/or pleomorphic large cells, and microbiopsies with cells individually surrounded by stroma) there is an indication for histologic classification using immunohistochemistry, to differentiate between metaplastic carcinoma, high grade phyllodes, and sarcoma.

6a.7.5 Prognostic information

Breast FNAC samples are used virtually only for diagnostic purposes. In some centres, however research studies have indicated that additional evaluation is possible on this type of sample[57,58]. Such practice is not, however, recommended as a routine.

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Appendix 1: Quality assurance

A1.1 Definitions

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

Table 1: Definition of QA standards

Absolute sensitivity	The number of carcinomas diagnosed as such (C5 or B5) expressed as a percentage of the total number of carcinomas sampled.
Complete sensitivity	The number of carcinomas that were not definitely negative or inadequate on FNAC or core expressed as a percentage of the total number of carcinomas.
Specificity (full)	The number of correctly identified benign lesions (the number of C2 or B2 results minus the number of false negatives) expressed as a percentage of the total number of benign lesions aspirated.
Positive predictive value of a C5/B5 diagnosis	The number of correctly identified cancers (number of C5 or B5 results minus the number of false positive results) expressed as a percentage of the total number of positive results (C5 or B5).
Positive predictive value of a C4/B4 diagnosis	The number of cancers identified as suspicious (number of C4 or B4 results minus the number of false suspicious results) expressed as a percentage of the total number of suspicious results (C4 or B4).This excludes those not confirmed by histology.
Positive predictive value of a C3/B3 diagnosis	The number of cancers identified as atypical (C3 or B3 results from cancers) expressed as a percentage of the total number of C3 or B3 results.
False negative case	A case which subsequently turns out (over the next 3 years) to be carcinoma having had a negative cytology or core result (This will by necessity include some cases where a different area from the lesion was sampled but who turn up with an interval cancer).
False positive case	A case which was given a C5 or B5 result which turns out at open surgery to have a benign lesion (including atypical hyperplasia).
False negative rate	The number of false negative results expressed as a percentage of the total number of carcinomas sampled.
False positive rate	The number of false positive results expressed as a percentage of the total number of carcinomas sampled.
Inadequate rate	The number of inadequate specimens (C1 or B1) expressed as a percentage of the total number of cases aspirated.

A1.2 How to calculate these figures

The calculation of the figures can be performed for cytology or core biopsy (CQA in the case of cytology, BQA in the case of core). There is also a further calculation which combines the two routines giving the non-operative sensitivity and specificity. This routine takes the worst (highest C or B number) diagnosis of the two techniques where both have been performed on the same patient and calculates the same parameters as the CQA and BQA routines.

Cytology/core biopsy QA standard report

Total cases screened in period _____
Total assessed _____
Total FNA (WBN) performed _____

Test result Subsequent Histology	C5 (B5 for core)	C4 (B4 for core)	C3 (B3 for core)	C2 (B2 for core)	C1 (B1 for core)	Total
Total malignant	**BOX 1**	**BOX 2**	**BOX 3**	**BOX 4**	**BOX 5**	**BOX 6**
Invasive	**BOX 7**	**BOX 8**	**BOX 9**	**BOX 10**	**BOX 11**	**BOX 12**
Non-invasive	**BOX 13**	**BOX 14**	**BOX 15**	**BOX 16**	**BOX 17**	**BOX 18**
Total benign	**BOX 19**	**BOX 20**	**BOX 21**	**BOX 22**	**BOX 23**	**BOX 24**
No histology	**BOX 25**	**BOX 26**	**BOX 27**	**BOX 28**	**BOX 29**	**BOX 30**
Total results	**BOX 31**	**BOX 32**	**BOX 33**	**BOX 34**	**BOX 35**	**BOX 36**

Each box (numbered 1 to 36) of the above table is calculated from the numbers of FNA with a C code (C1,C2 etc) or B code cross-referenced with the worst definitive histology diagnosis. The table and calculations (see below) should be produced for all FNA tests (headed ALL TESTS) and also for all patients (headed ALL PATIENTS) where if two FNA records are present the highest C number is taken. Only final episodes, when all the tests have been completed, should be used.

From the above table is then calculated the sensitivity and specificity in percentages for each of the categories. (**Bold** numbers correspond to BOX NUMBERS in the above table).

Absolute sensitivity (This assumes that all unbiopsied C5 or B5 results are carcinoma and are treated with primary chemotherapy or hormonal therapy.)	$\frac{\mathbf{(1 + 25)}}{\mathbf{6 + 25}}$ x 100
Complete sensitivity	$\frac{\mathbf{1 + 2 + 3 + 25}}{\mathbf{6 + 25}}$ x 100
Specificity (biopsy cases only)	$\frac{\mathbf{22}}{\mathbf{24}}$ x 100
Specificity (full) (This assumes that all cases of atypia (C3 or B3) which are not biopsied are benign.)	$\frac{\mathbf{22 + 28}}{\mathbf{24 + 27 + 28 + 29}}$ x 100

Positive predictive value (C5/B5 diagnosis)	$\frac{31 - 19}{31} \times 100$
Positive predictive value (C4/B4 diagnosis)	$\frac{2}{32 - 26} \times 100$
Postive predictive value (C3/B3 diagnosis)	$\frac{3}{33} \times 100$
Negative predictive value (C2/B2)	$\frac{34 - 4}{34} \times 100$
False negative rate (This EXCLUDES inadequate results)	$\frac{4}{6 + 25} \times 100$
False positive rate	$\frac{19}{6 + 25} \times 100$
Inadequate FNA rate and B1 core biopsy rate	$\frac{35}{36} \times 100$
Inadequate FNA rate and B1 core biopsy rate from cancers	$\frac{5}{6 + 25} \times 100$
Suspicious rate	$\frac{32 + 33}{36} \times 100$
Core biopsy miss rate from cancers	Sum of false negative rate and B1 core biopsy rate from cancers

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

A1.3 Suggested thresholds where therapy is partially based on FNAC/needle core biopsy

A1.3.1 Suggested thresholds for FNA performance

	Minimum	Preferred
Absolute sensitivity (AS)	> 60%	> 70%
Complete sensitivity (CS)	> 80%	> 90%
Specificity (full) (SPEC) (including non-biopsied cases) (as calculated above)	> 55%	> 65%

Positive predictive value (+PV)	> 98%	> 99%
False negative rate (F-)	< 6%	< 4%
False positive rate (F+)	< 1%	< 0.5%
Inadequate rate (INAD)	< 25%	< 15%
Inadequate rate from cancers	< 10%	< 5%
Suspicious rate	< 20%	< 15%

A1.3.2 Suggested thresholds for NCB performance

	Minimum	Preferred
Absolute sensitivity (AS)	> 70%	> 80%
Complete sensitivity (CS)	> 80%	> 90%
Specificity (full) (SPEC) (including non-biopsied cases) (as calculated above)	> 75%	> 85%
Positive predictive value (+PV)	> 99%	> 99.5%
False positive rate (F+)	< 0.5%	< 0.1%
Miss Rate (B1 + B2) from cancer	< 15%	< 10%
Suspicious rate	< 10%	< 5%

These figures will obviously depend on sampling techniques and the experience and care of the aspirator[1] and will vary widely between units.

A1.4 How to interpret the results

The figures are inter-related and strategy to improve one figure will affect others - thus if an attempt is made to reduce the inadequate rate this will often increase the number of suspicious reports, attempts to improve the sensitivity are likely to increase the false positive rate, attempts to improve the specificity will increase the false negative rate and so on. Also attempts to reduce the benign biopsy rate by not biopsying the majority of lesions called benign on cytology will reduce the specificity where this is based on benign histology results rather than on all aspirated cases.

The most common problem encountered in the NHSBSP surveys[3,5] appears to be low sensitivities combined with high false negative rates and high inadequate rates from lesions which subsequently turn out to be cancer. This combination of statistics suggests a problem with the accurate localisation of lesions for aspiration[2]. A significant proportion of these lesions will have been palpable or thought to be palpable as an area of thickening; aspiration of these areas without radiological guidance may have been responsible for some of the problems. It is of interest to note that, in centres where cytology has not been as useful in non-operative diagnosis, there has been a swing towards the use of core biopsy[6] as is commonly reported in publications from the United States[7]. Audit of core biopsy in the breast screening programme, shows similar variability in practice within the NHSBSP[5]. Some units are using both techniques to compliment each other and are achieving higher non-operative diagnosis rates in difficult

cases[8]. This can be especially useful in lobular and tubular carcinomas where cytology is less able to give an unequivocal diagnosis[5,9,10].

In general the cytological performance of pathologists as assessed by the positive predictive values is good although some pathologists are clearly being cautious in diagnosis. This caution can be inferred from the statistics in the units with high positive predictive values for C4 and C3 diagnoses and also in units which have a high suspicious rate. It should be noted that caution by pathologists may be a function of their experience in the technique, previous experience of false positive and false negative results, poorly cellular samples, or local differences in treatment protocols when faced with a C5 diagnosis.

High inadequate rates without a corresponding increase in the inadequate rate from cancers can be seen in occasional units. In these units a high proportion of the women who were recalled for assessment had a needling procedure. This suggests that, in these units, the clinicians were needling lesions with a low predictive value for malignancy in order to reassure either the patient or themselves. This is not necessarily a problem and therefore the crude inadequate rate may not be a good measure of aspiration technique. A better measure appears to be the inadequate rate from lesions which turn out subsequently to be cancer or, for core biopsy, the miss rate (see above).

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Quality assurance guidelines for pathology

6b

Open biopsy and resection specimens

Editor
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The previous version of these guidelines are also available in multimedia format as part of the BreakIT project from Giunti Ilabs, Via Ponte Calvi 3/15 1624 Genova Italy.

6b.1 Introduction

The success of a breast screening programme depends heavily on the quality of the pathological service. Specimens from screened women provide pathologists with particular problems of macroscopic and histological examination; the former principally result from identifying impalpable radiological abnormalities and the latter from classifying complex lesions which are encountered with disproportionate frequency. Accurate pathological diagnoses and the provision of prognostically significant information are important to ensure that patients are managed appropriately and that the programme is properly monitored and evaluated. A standard set of data from each patient, using the same terminology and diagnostic criteria is essential to achieve the latter objective. The opinions expressed represent the consensus view of the E.C. Working Group on Breast Screening Pathology and other pathologists who made written or verbal comments on this document and the United Kingdom document on which it is based. This guidance has been updated since the previous edition of the Guidelines to give clearer and more evidence based help to pathologists. We hope that this new guidance will be at least as useful as the previous version.

6b.2 Macroscopic examination of biopsy and resection specimens

6b.2.1 Introduction

Some general guidelines for specimen handling, both in the operating theatre and in the laboratory can be described. The type of surgical procedure will be influenced by whether a preoperative diagnosis has been achieved and, if so, the nature of the diagnosis whether benign or malignant (in-situ or invasive). If no preoperative diagnosis has been made, the surgical procedure will be in the form of a diagnostic open biopsy. Surgical quality assurance (QA) guidelines indicate that such specimens should be confined to removal of the lesion with a minimal amount of surrounding tissue in order to avoid leaving a cosmetic defect and should generally weigh less than 30 grams; these specimens should therefore be weighed in the pathology laboratory. The lesion may be impalpable and resection may require image-guided localisation using wire, dye or radioisotope. **Frozen section examination is inappropriate for diagnosis of screen-detected lesions.**

If a benign non-operative diagnosis has been made the operation will be undertaken at the patients request for removal. Such resections should be confined to removal of the lesion with a minimal amount of surrounding tissue to avoid leaving a cosmetic defect. In some centres, where available, vacuum-assisted large bore needle resection is being used for resection of benign lesions.

If a malignant diagnosis has been made, the surgical procedure will be influenced by the nature, size and localisation of the lesion, as well as by patient choice. The technique chosen for pathological examination of these specimens requires knowledge of the surgical method used and the anatomical boundaries of the resection. Whichever technique is used, the methodology should enable production of the breast cancer minimum dataset information.

6b.2.2 Surgical handling

It is anticipated that lesions will be resected according to a defined protocol. If the surgical resection differs from the protocol, for example if dissection does not extend to the deep fascia or skin when this is the norm, this should be clearly indicated on the request form.
The surgeon should orientate resection specimens. Each unit should establish a code of orientation using either different lengths of suture or metal staples/clips or ink, which are

anatomically relevant and assist in accurate evaluation of the specimen and the surgical resection lines. The nipple extension/direction of the nipple should be separately marked.
If more than one piece of tissue is removed, it should be made clear how the samples are orientated with respect to each other, in order to simplify assessment of the size of the lesion and the distance to the resection lines.
After surgical excision of the specimen it is appropriate for localisation resections to be X-rayed. In some centres wide local excision specimens are also X-rayed. This allows confirmation of the presence of the abnormality and also its location in the specimen, thus facilitating immediate re-excision if the abnormality is close to a resection line. The X-rays should ideally be reported by the breast radiologist. The specimen X-rays must, however, be available to the pathologist, so that they can be certain of the nature of the lesion i.e. mass, calcification etc. The pathologist can therefore also assess where the lesion is situated in the specimen in order to facilitate histological sampling.
It is to be expected that molecular biologic techniques requiring fresh frozen tumour tissue will be increasingly used for assessment of predictive factors. Therefore the specimen should be sent immediately to the pathology laboratory unfixed. If this is not possible it should be immediately placed in a fixative of a volume at least double the specimen size.

6b.2.3 Laboratory handling

Once received in the laboratory the entire surface of the specimen should be inked so that the lines of excision can be easily determined. This can be performed by blotting the specimen free of blood and moisture, and removal of surface lipid by dipping the specimen in alcohol and drying and then applying an appropriate pigment such as Indian ink, Alcian blue, dyed gelatine or a multiple ink technique. Indian ink can be fixed after painting using 10% acetic acid. The different surfaces can be recognised when different colours are used according to a standard laboratory protocol.
Good fixation is vital to preserve the morphological detail. This is particularly relevant for the diagnosis of intraductal epithelial proliferations and classification and prognostication in malignancy (e.g. histological grade, type and vascular invasion). Specimens must be placed in sufficient neutral buffered formalin (at least twice the volume of the specimen) or other appropriate fixative in an appropriately sized and shaped container either before, or preferably after, receipt by the laboratory.

Where fresh tissue is taken for tissue banking, it should be snap frozen and stored at -70°C, not in contact with air, as a minimum standard.

I. Open biopsy specimens
An open biopsy is performed when a non-operative diagnosis has not been achieved. Many cases are impalpable screen detected lesions, the majority being microcalcification without a mass. These specimens should be handled as wide local excision specimens.

II. Therapeutic wide local excision (surgical part of breast conservative treatment)
Orientation of these specimens is not possible without surgical markers. The surgeon should preferably mark the nipple side and the pectoral side with long and short sutures. The specimen should be weighed and measured. The surgical resection lines should be inked according to laboratory protocol and serial slices made at intervals of 3-5 mm, using one of the methods below. Cooling for 20 minutes at -20°C wrapped in aluminium foil will facilitate the slicing of fresh specimens. When a gross lesion is recognised, tissue may be selected for fresh frozen tissue banking; this should not interfere with histological work-up. Optimal fixation can be achieved by fixing the slices flat between gauze for at least 24 hours.
Cases where block selection is required (i.e. which are not embedded in their entirety) will benefit from specimen slice X-ray examination, particularly those with an impalpable mammographic lesion such as microcalcification. This enables blocks to be taken from the areas corresponding to the mammographic abnormality, as well as any other suspicious areas identified.

The sites of sampling can be marked on the specimen X-ray or the X-ray of specimen slices, by using a white wax (Chinagraph) pencil or other marker.
The sampling technique and the number of blocks taken are clearly dependent on the size of the specimen and the size of the abnormality. If the specimen is small, it is often best to block and examine all of the tissue. Samples approximately 30 mm or less in maximum dimension should be completely sliced, embedded and examined histologically. For larger specimens, sampling should be adequate to determine accurately the size of the lesion. Sampling should include the extremes of the mammographic abnormality and adjacent tissue, in order to avoid underestimation of size. This is particularly important with cases of ductal carcinoma in situ (DCIS) as it is recognised that mammographic size may be an underestimate of true tumour size[1].
A complete cross section of large or ill-defined lesions should be taken in consecutive blocks to allow accurate measurement. Large blocks may be used to embed the entirety of segmental excisions and give valuable information on the extent and distribution of lesions. The blocks taken should be indicated on the report.
If specimens are sent as more than one piece of tissue, it can be impossible to measure the absolute extent of the lesion. In these cases it is appropriate to take a pragmatic approach and to measure the maximum size in each piece of tissue and to add the dimensions to give an estimated total size. If, however, the orientation of the specimens can be determined, the true size can be ascertained more reliably.
It is usual for the surgeon when performing a therapeutic operation to take all the tissue from the subcutaneous to the pectoral fascia. It is essential that the pathologist is informed if this surgical protocol has not been undertaken, as this will affect the optimum specimen handling methodology.
For therapeutic excisions, it is helpful if the surgeon marks the nipple duct excision line; DCIS tracks down towards the nipple and in this plane can be some distance from the obvious area of microcalcification.
The technique for sampling the abnormality will vary somewhat according to the type of sample, specimen size and also pathologist/laboratory preference. A degree of flexibility is needed. Several options are available. Whichever is utilised, as an absolute minimum, the information for the breast cancer minimum dataset, including accurate measurement of size and detailed examination of the margin status and distance to the surgical excision lines must be provided. Three preferred methods for handling these samples are described below.

Method 1. Serial slicing perpendicular to the medial – lateral plane, or nipple-periphery axis
This method is commonly used for examination of non-operatively diagnosed DCIS or microcalcification suspicious for DCIS, as it enables evaluation of the distribution and extent of the lesion towards the nipple (when sliced in the medial-lateral plane), or towards the remaining breast tissue (when sliced in the nipple-periphery axis) and provides a high level of confidence that the lesion has been accurately and adequately sampled and excised.
All specimens benefit from specimen slice X-ray examination, but this may not be absolutely essential for all samples e.g. mass lesions. Where microcalcification is the principle feature by which the lesion was detected, slicing and re-X-raying of the specimen slices is mandatory to enable blocks to be taken most accurately from the areas corresponding to the mammographic abnormality, as well as any other suspicious areas identified. The site of sampling can be marked on the specimen X-ray for radiological-pathological discussion in difficult cases. Slice specimen X-rays may be performed after fixation; care should taken to blot the slices free of moisture to obtain high quality radiographs. It is essential that a laboratory has the facility to perform slice specimen radiography either in the mammography department or using a dedicated X-ray cabinet.
If the excision has been undertaken for calcification or for known DCIS, blocks should be taken to include areas of fibrous breast tissue proximal and distal to the calcification. DCIS, especially the low-grade type, may be much more extensive than the radiologically apparent calcification[1].
In the case of DCIS, blocks of the complete area of microcalcification should be taken to exclude invasive growth and to evaluate the size and distribution of the lesion. This may be best achieved by large block examination.
Altogether blocks should be taken from the main area of calcification but also from proximal (towards the nipple) and distal to the calcification as DCIS extends most frequently in this plane[2].
Measurement can be made in this way from the most distal involved duct across the main area of calcification to the most proximal involved duct (see section on Tumour Size: in situ carcinoma).

Involvement of the surgical resection line is one of the most important risk factors for residual disease in the breast and recurrence. Assessment of resection line involvement and the distance to the resection line should therefore be part of the evaluation of any therapeutic excision specimen. The nearest resection line to the mammographic abnormality must be blocked, as an absolute minimum, in order to facilitate measurement of this distance. Preferably the resection lines should be more widely sampled to allow more accurate assessment of adequacy of excision. The nipple duct resection margin should not be neglected even when the mammographic abnormality is some distance away. The use of different colour inks/markers on an individual section can assist microscopic identification of specific surgical resection lines.

Method 2. Serial slicing perpendicular to the superficial – deep plane
This is a variation of Method 1 and is particularly suitable for smaller specimens or in association with large block techniques. The entire specimen can be examined as a small number of serial large sections.

Method 3. Radial block, with or without shave margin, examination
This method can be used for examination of a specimen containing a palpable or visible macroscopic abnormality. The lesion is sampled as a series of blocks, taken at right angles, as described below.

a. Tumour and surgical resection margin sampling
The specimen is usually incised from the posterior deep fascial plane in a cruciate fashion through the centre of the tumour. This allows the tumour to be sampled as four blocks, which include the anterior/posterior, medial/lateral and superior/inferior dimensions.
It may be possible to take the radial surgical resection line and the lesion in one block from smaller resections. Larger specimens may require tumour and resection margin blocking in 2 (or more) cassettes.
Sections taken for measurement of the distance to resection lines will include a slice through the lesion to the radial edges of the specimen to allow measurement of the distance from the lesion to the resection line.
If the lesion is not centrally placed, one or more additional radial blocks extending to the closest resection line (supero-lateral, supero-medial, infero-medial, infero-lateral) should be taken.

b. Cavity shave/biopsy specimens
The circumferential edge of the sample can be shaved by the pathologist to allow more extensive examination of relevant surgical resection lines. Alternatively the surgeon may provide cavity biopsies.

Surgical bed biopsies or cavity shaves may make the accurate assessment of excision lines impossible and should be discouraged.

This can produce a series of additional shave/cavity blocks: superior shave, supero-lateral shave, lateral shave, infero-lateral shave, inferior shave, infero-medial shave, medial shave and supero-medial shaved edges depending on the size of the specimen. The site of each specimen should be clearly labelled and each specimen examined separately.
It should be noted that shaved edges of the margins of the specimen or examination of 'cavity shaves/bed biopsies' assess adequacy of excision but do not allow measurement of distance between tumour and the surgical resection lines.

c. Re-excision specimens

If the radiological abnormality extends close to a resection margin on the specimen radiograph, the surgeon may undertake an immediate re-excision of that particular margin.

A separate re-excision specimen may therefore be taken (a) at the time of initial surgery, (b) subsequent to the discovery of incomplete excision in a therapeutic excision or (c) following diagnostic localisation biopsy.

The aim is to remove either all of the previous biopsy site, or one or more specific resection margins known (or suspected to be) involved by the disease process. Whenever re-excision has been performed, the surgeon should orientate the re-excision specimen. It is therefore possible to measure the distance of any additional tumour present to the new surgical resection line, or to approximate the distance of the tumour to the new surgical resection line if no tumour is present.

If re-excision specimens have been taken which contain further tumour, it can be extremely difficult to determine the absolute size of lesion. A pragmatic approach is required and the maximum size in each piece of tissue can be measured and added to give an approximate total size of tumour. If, however, the orientation of the specimens can be determined, the size of tumour can be ascertained more reliably. Re-excision specimens at a second operation should be handled as therapeutic excision specimens (see above).

III. Mastectomy specimens

Mastectomy specimens should be orientated by the surgeon, for example by placing a suture in the axillary tail. A diagram indicating the site of the lesion (or lesions) may be helpful.

The specimen should be delivered immediately and fresh to the pathology laboratory, allowing selection of tumour tissue for frozen tissue banking, and immediate incision of the tumour and slicing of the breast to achieve optimal fixation. A method (as discussed above) should be employed to ensure rapid fixation of the tumour and rest of the specimen. Ideally this will be by receipt of the fresh specimen in the pathology laboratory, allowing immediate incision of the tumour and slicing of the breast prior to placing in fixative. If resources do not permit such a procedure, then alternatives must be employed. Mastectomy specimens should not be allowed to fix intact without incision of the tumour. Poor tumour preservation precludes assessment of minimum data set details such as histological grade and vascular invasion and can result in false negative receptor status.

Inking of the resection lines is useful if there are signs of tumour adherence to the fascia, when the mastectomy is performed for extensive DCIS and when mammography mentions an extensive area of microcalcification.

The specimen should be sliced at 0.5-1 cm intervals from the posterior fascial plane perpendicular to the 6-12 o'clock axis. In certain circumstances, such as for correlation with MRI results, slicing in a different plane may be helpful e.g. parallel to the fascial plane.

Grossly recognisable lesions should be reported (size, distribution, and relation to skin and margins). Tumour tissue should be selected for fresh frozen tissue banking without interfering with histopathological work-up.

The slices should be fixed flat optimally between gauze for at least 24 hours in neutral buffered formalin. When the mastectomy is performed for DCIS, or when the mammography mentions extensive microcalcification, X-raying the slices is helpful to pinpoint the lesion, to select areas for blocking, and to define the extent of the lesion and its relation with margins.

A complete cross section through the maximum diameter of any grossly recognisable lesion, including surrounding breast tissue, should be sampled, if necessary in multiple blocks.

Additional sampling of the nipple-areolar complex can be performed to assess the presence of mammary Paget's disease in cases of extensive DCIS, especially when skin sparing surgery has been performed, by a cross section of the nipple perpendicular to the lactiferous ducts, and/or a cross section centrally through the nipple.

Additional sampling of quadrants can be performed if resources permit and can identify occult extensive disease.

6b.3 Guidance for pathological examination of lymph nodes

6b.3.1 Background

Examination of lymph nodes, usually axillary but occasionally internal mammary, should be performed in patients with operable invasive breast carcinoma. The aim is mainly tumour staging, as axillary lymph node involvement is the main prognostic indicator being used to determine the indication for systemic adjuvant therapy. Complete axillary lymph node dissection used to be the preferred method in most countries in Europe, although sampling has been most commonly used in UK. Nowadays sentinel node biopsy is increasingly performed[3] and may replace the other methods in units where it has been validated.

6b.3.2 Lymph node sample specimens

I. Specimen handling
Designated individual lymph node specimens should be identified separately from the breast sample and placed in clearly labelled specimen containers for routine fixation.

II. Tissue blocks
Each lymph node identified should be examined and blocked independently for histological examination.
The methodology used should provide the highest chance of finding metastatic disease by conventional microscopic examination of haematoxylin and eosin (H&E) stained tissue sections.
A representative complete section of any grossly involved lymph node is adequate.
When size permits, lymph nodes should be bisected or serially sliced to obtain slices of 2-3 mm, along the longitudinal axis allowing examination of the largest surface area. This is an effective and simpler alternative to serial sectioning to detect small metastatic deposits in lymph nodes.
All the tissue blocks prepared should be embedded and examined histologically. For larger lymph nodes this may necessitate examination in more than one paraffin block.
Examination of levels is not routinely necessary but may be performed if small groups of worrisome cells are identified, particularly if parenchymal in site.

6b.3.3 Axiliary clearance specimens

I. Specimen handling
Axillary clearance specimens should be placed in clearly labelled containers for routine fixation.

a. Macroscopic examination
Axillary contents received with mastectomy or biopsy specimens should be examined carefully to maximise lymph node yield. This is usually achieved by manual dissection of fixed axillary tissue with careful examination by inspection and palpation. The yield of lymph nodes may be higher in dissection of fresh specimens. The use of clearing agents or Bouin's solution may increase lymph node yield but is time consuming and expensive and is not regarded as essential.
The axillary contents can be divided into 3 levels if the surgeon has marked the specimen appropriately. To facilitate recognition of the apical lymph node the surgeon should mark the apex of the axillary tail of the specimen.
Pathological examination should be performed on all lymph nodes received and the report should state the total number and number containing metastasis.

6b.3.4 Sentinel lymph nodes (SN)

I. Background

The sentinel lymph node procedure is increasingly performed as a staging procedure. Sentinel nodes (SN) are identified either by their colouration (mainly blue in Europe) and/or by their radioactivity, depending on the surgical biopsy method. Several studies have shown that the SN status is a good substitute for nodal status based on complete axillary dissection. Axillary treatment can be withheld from patients with a negative SN. In the case of tumour deposits in SN, the chance of finding more metastases in a subsequent axillary dissection is related to the amount of tumour in the SN.(4) The chance of finding tumour in SNs is related to the proportion of tissue evaluated and the methods that are applied. A balance has to be struck between general applicability and optimal sensitivity.

In accordance with the UICC TNM classification of malignant tumours (5), nodal involvement can be classified as (macro-)metastases (> 2 mm), micrometastases (≤ 2 mm but > 0.2 mm) and isolated tumour cells (ITC)/submicrometastasis (≤ 0.2 mm). The last two terms are used as synonyms, the latter being proposed by the Philadelphia Consensus Meeting (5a) but not a term endorsed by the TNM committee. At the present time, the absolute minimum aim for the histological examination of SNs requires the identification of all macrometastases (an aim that is not currently reached by all laboratories (3). Ideally, micrometastases should be identified, because of their estimated association with further nodal involvement (around 20% in general, and possibly over 30% (6) if the micrometastases are > 1 mm). The demonstration of ITC (submicrometastases) is not an aim of SLN investigations, their identification is a side-effect, but care should be given to their adequate reporting (see later) to avoid classification as a higher stage and subsequent overtreatment.

SN may be supplemented by axillary clearance specimens or lymph node samples, which should be handled according to general guidelines for the histopathological reporting of lymph node specimens.

II. Specimen handling

Designated individual lymph node specimens should be separately identified, and clearly labelled. Specimens should be either sent fresh to the pathology laboratory in the case of intraoperative assessment or fixed in suitable containers. SLNs usually contain ≤ 1% of the total radioactivity, therefore it is generally accepted that they do not represent a special biohazard to the pathology staff.

a. Intraoperative examination

Both frozen sections and imprint cytology have a risk of false negative classification, and false positive results have also been rarely reported. Any of these methods may be suitable for the intraoperative assessment of SNs, but none will adequately identify all metastases in these lymph nodes. Both methods have advantages and disadvantages and, in good hands, both methods have a similar sensitivity and specificity. The choice of the method should be based on institutional resources and preferences. Intraoperative assessment should be restricted to cases where this has an impact on immediate treatment. A learning period is to be expected, and this may justify a preliminary period for the use of intraoperative specimen assessment.

b. Tissue blocks

- Each SN should be blocked independently for histological examination.
- The methodology used should provide the highest chance of finding metastatic disease (macro- and micrometastases) by conventional microscopic examination of HE stained tissue sections.
- A representative complete section of any grossly involved lymph node or intraoperatively positive SN is adequate.
- When size permits, nodes should be bisected or sliced if larger to obtain 2-3 mm slices, across the longitudinal axis.

- All grossly negative SN should be embedded and examined histologically. In larger lymph nodes this may necessitate examination of more than one paraffin block.

c. Sectioning tissue blocks

- At present the absolute minimum requirement in grossly (and/or intraoperatively) negative SNs is that tissue blocks should be sectioned in a way to allow the best identification of metastatic deposits over 2 mm as macrometastatic involvement. In practice this would necessitate step sections through the block with a 1 mm distance between levels.
- Theoretically to identify micrometastatic deposits over 0.2 mm, step sections with a 0.2 mm distance between the levels are necessary. As some tissue loss is expected with sectioning, and when frozen section studies have been performed, it follows that all blocks would need to be sectioned at 150-200 micron intervals through the block[6a].
- More levels, smaller intervals, and use of immunohistochemical staining with keratin antibodies will increase the detection rate of ITC/submicrometastases; this should not be the aim of routine evaluation, but may be part of research or prescribed in trials.
- As an even and complete sampling of the SN tissue blocks leaves no further material for assessment, it is strongly recommended to start with only a few sections keeping in mind that the SNs may be the site of other diseases e.g. lymphoma which may require further investigation.

d. Reporting

Reports should include:

- The total number of sentinel lymph nodes received.
- Any macroscopic involvement if seen.
- The number of lymph nodes involved with metastatic disease.
- The extent of metastatic disease (adherence to the pN categories of the 6th edition of the TNM classification of malignant tumours is recommended)[5]. If several metastatic foci can be detected within one lymph node, the largest should be considered. Alternatively, the size of the largest metastasis, as a more objective feature can be recorded instead of the categories or along with them. When using the TNM categories, the suffix (sn) should be used when nodal status has been determined on the basis of SN biopsy alone.
- If special techniques are used (small distance step sectioning, immunostains, molecular analysis) this should be stated and if nodal involvement is detected only by immunostains or molecular methods, this should also be emphasized in the report. Because the methods may differ from laboratory to laboratory, it is also recommended to include the number of levels assessed and/or their distance from each other.

e. Additional techniques

Additional techniques include further sectioning at multiple levels, use of immunocytochemistry and molecular technology. These tests may all increase the frequency of detection of occult disease (micrometastatic and ITC), therefore they are not mandatory, but may be very useful on some occasions. Their use should be based on local interest and resources.

Specimen European breast pathology data form

Surname _____ Forenames _____ Date of birth _____

Screening no. _____ Hospital no. _____ Health Service Number _____

Pathologist _____ Laboratory _____Date of reporting _____ Report no. _____

Side Right Left

Specimen radiograph seen Yes No

Mammographic abnormality present in specimen Yes No Unsure

Histological calcification Absent In benign changes In malignancy In both

Specimen type Excision biopsy (impalpable lesion) Excision biopsy (palpable lesion)
Therapeutic wide local excision Mastectomy Post treatment excision

Specimen weight _____ g

Axillary Procedure No lymph node procedure Sentinel node biopsy
Axillary node sample Axillary node dissection

Benign lesion present	**Yes**	**No**	**Malignant lesion present**	**Yes**	**No**

Benign lesion
Fibroadenoma Solitary papilloma Multiple papilloma
Sclerosing adenosis Complex sclerosing lesion/radial scar Fibrocystic change
Solitary cyst Periductal mastitis/duct ectasia Columnar cell change
Other (please specify) _____

Epithelial proliferation
Not present Present without atypia
Present with ductal atypia Present with lobular neoplasia
Columnar cell change with atypia

Malignant lesion

In situ carcinoma Not present

Ductal DCIS grade High Intermediate Low Not assessable
Size _____ mm (ductal only)
Lobular with necrosis Paget's disease

Microinvasion Not present Present

Invasive carcinoma Not present

Type No special type (Ductal NST) Pure special type (90% purity specify components below):
Mixed Tumour Type (50-90% special type component, specify component present below):
Other malignant tumour: Specify _____

Specify type component(s) present for pure special type and mixed tumour types:
Tubular Lobular Mucinous Medullary-like with lymphoid stroma Ductal/no special type
Other (please specify) _____

Size Invasive tumour _____ mm (largest dimension of dominant invasive tumour focus)
Whole size of tumour _____ mm (invasive plus surrounding DCIS if DCIS extends >1 mm beyond invasive):

Invasive grade 1 2 3 Not assessable

Tumour extent Localised Multiple invasive foci

Vascular invasion Not seen Present Possible

Axillary nodes present No Yes Total Number _____ Number positive _____
Metastasis (> 2 mm)
Micrometastasis (≤ 2mm - > 0.2 mm)
Isolated tumour cells (≤ 0.2 mm)

Other nodes present No Yes Total Number _____ Number positive _____

Site of other nodes _____

Excision margins (for DCIS or invasive carcinoma)
Not assessable Reaches relevant margin Does not reach relevant margin
Closest relevant margin _____ mm

Oestrogen receptor status Positive Negative _____ Quick Score (Allred) Not performed

Optional additional fields

Progesterone receptor status Positive Negative _____ Quick Score(Allred) Not performed

HER 2 status Positive Negative _____ Score Not performed

Comments/Additional Information

Final Histological Diagnosis	**Normal**	**Benign**	**Malignant**

6b.4 Using the histopathology reporting form

6b.4.1 Introduction

The following section gives guidance on how to use the European Breast Histopathology form and provides definitions of the terms used. The aim is not to replace standard textbooks of breast pathology but to focus on diagnostic criteria for including lesions in the various categories and therefore to help to achieve maximum uniformity of reporting.

The guidance in this section is drawn mainly from texts of breast pathology and the experience gained in External Quality Assurance Schemes in Breast Pathology. It is not necessary to use the form exactly as it appears in this document. It may be found desirable to undertake local modifications, particularly if the form is also to function as the definitive Histopathology report to be entered into the patient's notes and laboratory records. It is, of course, essential to record all the information requested by the form using the same terminology. Evaluation of breast screening programmes depends upon provision of accurate pathology data.

6b.4.2 Recording basic information

Side
Indicate left or right breast. For specimens from both sides, a separate form should be completed for each side.

Pathologist and date
The name of the reporting pathologist and date the specimen was reported should be given here.

Histological calcification
Indicate if calcification observed radiologically was seen on histological sections and, if so, whether it is present in benign or malignant changes, or both.

Specimen radiograph seen
Indicate if a specimen radiograph was present with the specimen or if it was performed within the laboratory.

Mammographic abnormality present in specimen
Are you satisfied that the mammographic abnormality is present in the specimen? This may necessitate consultation with the radiologist responsible for examining the specimen radiograph. It is worth remembering that breast calcification may be due to calcium oxalate salts (Weddelite), which can be detected optimally in histological sections using polarised light.

Specimen type
Choose one of the following terms:

Open surgical biopsy (impalpable lesion)
Select this for a localisation biopsy where the lesion has been localised either by a wire, skin marker or radiotracer for an impalpable lesion.

Open surgical biopsy (palpable lesion)
Select this for a non-guided biopsy/excision including lumpectomy, tylectomy, major duct excision etc.

Therapeutic wide local excision
Includes wedge excisions, segmental excision and quadrantectomy.

Mastectomy

Re-excision (surgical part of breast conserving treatment)
Includes re-excision specimens for clearance of margins.

Specimen weight
Record the weight of all open biopsy and segmental excision specimens. Weight is more reproducible than 3-dimensional measurement to determine volume, even taking into account the different densities of fat and fibrous tissue, which vary in proportion in breast specimens. Specimen weight is also used as the means of determining the likely cosmetic disadvantage to women undergoing a benign biopsy.

Axillary procedure
Choose one of the following terms:
- **No lymph node procedure.**
  Where no axillary procedure was performed
- **Sentinel node biopsy.**
  Where a sentinel node procedure was performed
- **Axillary node sample**
  Where a node sample was performed. Some units refer to this as a level one axillary clearance
- **Axillary node dissection**
  Where an axillary clearance to level 2 or 3 has been performed.

Benign/Malignant Lesion present
Tick the appropriate 'yes' box if any benign or malignant lesion is present and 'no' if none is identified. Both benign and malignant may be ticked as 'yes'.

6b.4.3 Classifying benign lesions

I. Fibroadenoma
A benign lesion composed of connective tissue rarely with other mesenchymal elements and double-layered epithelium exhibiting a pericanalicular and/or intracanalicular growth pattern. Apocrine metaplasia, sclerosing adenosis, blunt duct adenosis, hyperplasia of usual type and other common changes may occur in fibroadenomas but need not be recorded separately unless they amount to atypical hyperplasia or in situ carcinoma. Malignant change occurs rarely in the epithelial component. This is more frequently lobular carcinoma in situ than ductal carcinoma in situ. Fibroadenomas may cause mammographic abnormalities requiring assessment and needle biopsy. They usually present as a well-circumscribed rounded mass. Typical examples are usually not assessed by radiologists in the screening setting but some may be less well-circumscribed on one border leading to uncertainty for the radiologist. Sometimes this is due to individual lobules exhibiting increased stroma producing a fibroadenomatous appearance. These lobules may also be loosely coalescent. These changes are often called fibroadenomatoid hyperplasia or sclerosing lobular hyperplasia but may be recorded as fibroadenoma on the reporting form if they produce a radiologically or macroscopicaly visible or palpable mass. Consequently, fibroadenomas need not be perfectly circumscribed and this may be responsible for uncertainty on the part of the radiologist. Typical differential diagnostic problems for the radiologist include mucinous carcinoma and some well circumscribed grade 3 carcinomas.

Old lesions may show hyalinisation and calcification (or less frequently ossification) of stroma and atrophy of epithelium. These may present as microcalcification, sometimes linear. In this case it may be difficult to exclude DCIS radiologically but more commonly these fibroadenomas will show macrocalcification not requiring assessment.
For the purposes of the screening form, tubular adenomas can be grouped together with fibroadenomas.
Fibroadenomas should be distinguished from **phyllodes tumours.** The high grade or 'malignant' phyllodes tumours are easily identified by their sarcomatous stroma. The low grade variants are more difficult to distinguish but the main feature is the more cellular stroma. In younger women however the stroma in a fibroadenoma may be more cellular. Phyllodes tumours may also exhibit an enhanced intracanalicular growth pattern with club-like projections into cystic spaces and there is often overgrowth of stroma at the expense of the epithelium. Adequate sampling is important as the characteristic stromal features may be seen only in parts of the lesion. Although phyllodes tumours are generally larger than fibroadenomas, size is not an acceptable criterion for diagnosis; fibroadenomas may be very large and phyllodes tumours small. For purposes of convenience, benign and borderline phyllodes tumours should be specified under 'other benign lesions' and malignant phyllodes tumours under 'other malignant tumour' although it is recognised that histological appearance is often not a good predictor of behaviour. The radiological features of benign or borderline phyllodes tumours may not differ significantly from fibroadenomas although ultrasound may show cystic clefts in the lesion. Malignant phyllodes tumours may be more infiltrative and are often more worrying radiologically.

II. Papilloma

A papilloma is defined as a tumour with an arborescent, fibrovascular stroma covered by epithelium generally arranged in an inner myoepithelial and outer epithelial layer. Epithelial hyperplasia without cytological atypia is often present and should not be recorded separately. Atypical hyperplasia is rarely seen and, when present, should be recorded separately under 'Epithelial Proliferation'. Epithelial nuclei are usually vesicular with delicate nuclear membranes and inconspicuous nucleoli. Apocrine metaplasia is frequently observed but should not be recorded separately on the reporting form. Squamous metaplasia is sometimes seen, particularly with infarction. Sclerosis and haemorrhage are not uncommon and, where sclerosis involves the periphery of the lesion, may give rise to epithelial entrapment with the false impression of invasion. The benign cytological features of such areas should enable the correct diagnosis to be made.

The term **'intracystic papilloma'** is sometimes used to describe a papilloma in a widely dilated duct. These tumours should simply be classified as papilloma on the form. For distinction from **encysted papillary carcinoma,** see Table 1.

Papillomas may be **solitary** or **multiple.** The former usually occurs centrally in sub-areolar ducts whereas the latter are more likely to be peripheral and involve terminal duct lobular units. The distinction is important as the multiple form is more frequently associated with atypical hyperplasia and ductal carcinoma **in situ,** the latter usually of low grade type, which should be recorded separately. This malignant change may be focal within the lesion and therefore extensive sampling may be required to detect it. Some sub-areolar papillomas causing nipple discharge may be very small and extensive sampling may be required to detect them. Radiologically papillomas may produce masses or calcification. Multiple papillomas may produce multiple nodular densities, sometimes described as 'papillomatosis'. Sclerosed papillomas may also be difficult as they can be less well circumscribed and may mimic carcinomas.

Lesions termed **ductal adenoma** exhibit a variable appearance, which overlaps with other benign breast lesions. They may resemble papillomas except that they exhibit an adenomatous rather than a papillary growth pattern. These cases should be grouped under papilloma on the form. Indeed, some tumours may exhibit papillary and adenomatous features. Some ductal adenomas may show pronounced central and/or peripheral fibrosis and overlap with complex sclerosing lesions. Radiologically these can be indistinguishable from malignancy forming a mass which is usually poorly circumscribed at one or more margins.

The condition of **adenoma of the nipple** (sub-areolar duct papillomatosis) should not be classified as papilloma on the screening form but specified under 'Benign Lesions, Other'. This should be distinguished from the rare syringomatous adenoma of the nipple composed of ducts and tubules with an apparent infiltrative pattern.

Diffuse microscopic papillary hyperplasia should be recorded under 'Epithelial Proliferation' in the appropriate box depending on whether atypia is present or not.

III. Sclerosing adenosis

Sclerosing adenosis is an organoid lobular enlargement in which increased numbers of acinar structures exhibit elongation and distortion. The normal two-cell lining is retained but there is myoepithelial and stromal hyperplasia. The acinar structures may infiltrate adjacent connective tissue and occasionally nerves and blood vessels. These can lead to an erroneous diagnosis of malignancy. Early lesions of sclerosing adenosis are more cellular and later ones more sclerotic. Calcification may be present.

Sclerosing adenosis may present on mammography as microcalcification but there may be coalescence of adjacent lobules of sclerosing adenosis to form a mass detectable by mammography or macroscopic examination. This has been termed 'nodular sclerosing adenosis' or if poorly circumscribed, may be classified as a complex sclerosing lesion radiologically. It is recommended that sclerosing adenosis is not entered on the screening form if it is a minor change detectable only on histological examination. Although sclerosing adenosis often accompanies fibrocystic change (see below), this is not always the case and the two changes should be recorded separately.

Occasionally apocrine metaplasia is seen in areas of sclerosing adenosis (apocrine adenosis). It can produce a worrying appearance and should not be mistaken for malignancy. This has a low power lobular architecture and there are usually adjacent benign changes with sclerosing adenosis and apocrine metaplasia.

Rarely, the epithelium in sclerosing adenosis may show atypical hyperplasia or in situ carcinoma. In such cases, these changes should be recorded separately on the reporting form.

The differential diagnosis of sclerosing adenosis includes tubular carcinoma, microglandular adenosis and radial scar. In tubular carcinoma, the infiltrating tubules are single layered, with small uniform cells and lack basement membrane, myoepithelium and lobular organoid growth pattern. Ductal carcinoma in situ (DCIS) is a frequent accompaniment. Microglandular adenosis differs from sclerosing adenosis in lacking the lobular organoid growth pattern and being composed of rounded tubules lined by a single layer of cells lacking cytological atypia. The glandular distortion of sclerosing adenosis is lacking. Radial scar is distinguished from sclerosing adenosis by its characteristic floret-type growth pattern with ducto-lobular structures radiating out from a central zone of dense fibro-elastotic tissue. Furthermore, the compression of tubular structures associated with myoepithelial and stromal hyperplasia is lacking. Immunocytochemical studies using antibodies to collagen IV or laminin and muscle specific actin or smooth muscle myosin may be very useful.

IV. Complex sclerosing lesion/radial scar

Under this heading are included sclerosing lesions with a pseudoinfiltrative growth pattern which have been called various names including infiltrating epitheliosis, rosette-like lesions, sclerosing papillary proliferation, complex compound heteromorphic lesions, benign sclerosing ductal proliferation, non-encapsulated sclerosing lesion, indurative mastopathy and proliferation centre of Aschoff.

The radial scar is generally 10 mm or less in diameter and consists of a central fibro-elastic zone from which radiate out tubular structures which may be two-layered or exhibit intra-luminal proliferation. Tubules entrapped within the central zone of fibro-elastosis exhibit a more random, non-organoid arrangement. They are seen radiologically as stellate lesions, classically with a

more lucent centre but may be indistinguishable from tubular and other low grade carcinomas. Lesions greater than 10 mm are generally termed complex sclerosing lesions. They have all the features of radial scars and, in addition to their greater size, exhibit more disturbance of structure, often with nodular masses around the periphery. Changes such as papilloma formation, apocrine metaplasia and sclerosing adenosis may be superimposed on the main lesion. Some complex sclerosing lesions give the impression of being formed by coalescence of several adjacent sclerosing lesions. There is a degree of morphological overlap with some forms of ductal adenoma. These lesions are often thought to be highly suspicious radiologically due to their lack of circumscription and distortion of surrounding tissue.
If the intra-luminal proliferation exhibits atypia or amounts to in situ carcinoma, this should be recorded separately under the appropriate heading on the screening form.

The main differential diagnosis is carcinoma of tubular or low grade 'ductal' type. The major distinguishing features are the presence of myoepithelium and basement membrane around the tubules of the sclerosing lesions. Again immunocytochemical studies for basement membrane proteins and myoepithelial cells are useful. Cytological atypia is also lacking and any intra-tubular proliferation resembles hyperplasia of usual type unless atypical hyperplasia and/or **in situ** carcinoma are superimposed (see above). Tubular carcinomas generally lack the characteristic architecture of sclerosing lesions.

V. Fibrocystic change

This term is used for cases with several to numerous macroscopically visible cysts, the majority of which are usually lined by apocrine epithelium. The term is not intended for use with minimal alterations such as fibrosis, microscopic dilatation of acini or ducts, lobular involution, adenosis and minor degrees of blunt duct adenosis. These changes should be indexed as normal.
Cystic change or apocrine metaplasia occurring within other lesions such as fibroadenoma, papilloma or sclerosing lesions should not be coded here. Apocrine metaplasia occurring in lobules without cystic change may produce a worrisome appearance, occasionally mistaken for carcinoma. This change should be specified as 'apocrine adenosis' under other benign lesions.
Papillary apocrine hyperplasia should be indexed separately under epithelial proliferation with or without atypia, depending on its appearance. Apocrine metaplasia lining cysts is classified into simple, complex (with small papillae) and highly complex (with interconnecting bars and bridges). Apocrine cells often exhibit a degree of pleomorphism greater than is seen in normal breast cells and should be regarded as atypical only when there is a greater than three fold variation in nuclear size. Fibrocystic change is very common and alone rarely produces a radiological abnormality worthy of biopsy but may cause asymmetry or microcalcification classically producing tea-cups on a true lateral projection. Where these are clearly seen radiologically they are not often biopsied and pathologists should be careful not to overlook another cause for the radiological appearance.

VI. Solitary cyst

This term should be used when the abnormality appears to be a solitary cyst. The size is usually greater than 10 mm and the lining attenuated or apocrine in type. The latter may show papillary change, which should be indexed separately under epithelial proliferation of appropriate type. If multiple cysts are present, it is better to use the term 'fibrocystic change' as above. Intra-cystic papillomas and intra-cystic papillary carcinomas should not be entered here but under papilloma or carcinoma.

VII. Periductal mastitis/duct ectasia (plasma cell mastitis)

This process involves larger and intermediate size ducts, generally in a sub-areolar location. The ducts are filled with amorphous, eosinophilic material which may also contain foam cells and calcification which may be linear on mammography. This usually has a characteristic appearance but may occasionally mimic carcinoma in situ. There is often marked periductal chronic inflammation leading to pronounced periductal fibrosis. The inflammatory infiltrate may be granulomatous. The process may ultimately lead to obliteration of ducts leaving dense fibrous masses. Persistence of small tubules of epithelium around the periphery of an obliterated duct

result in a characteristic garland pattern. Duct ectasia is often associated with nipple discharge or retraction.
Cysts are distinguished from duct ectasia by their rounded rather than elongated shape, tendency to cluster, lack of stromal elastin, frequent presence of apocrine metaplasia and less frequent presence of eosinophilic material or foam cells in the lumina.

VIII. Columnar cell change
For a discussion of columnar cell change, see below under epithelial proliferation.

IX. Other (specify)
This category is intended for use with less common conditions which form acceptable entities but cannot be entered into the categories above, e.g. fat necrosis, lipoma, adenoma of nipple, benign and borderline phyllodes tumours and mammary duct fistula (recurring sub-areolar abscess). The index included as appendix 1 should help as a reference for lesions difficult to place in any of the above categories.

6b.4.4 Classifying epithelial proliferation

This section is for recording intra-luminal epithelial proliferation in terminal duct lobular units or inter-lobular ducts.

I. Not present
No epithelial multilayering present (apart from that ascribed to cross-cutting).

II. Present without atypia[7]
This term should be used to describe all cases of intra-luminal proliferation showing no or only mild atypia. The proliferation may vary from mild usual epithelial hyperplasia (up to 4 cell layers thick) to florid hyperplasia. A special form is the gynaecomastoid type of ductal hyperplasia which is usually observed in adenoma of the nipple and also in some fibroadenomas, but which may be found anywhere in the ductal-lobular tree. Immunohistochemically the lesions display the same cytokeratin 5 patchwork pattern as classical usual ductal hyperplasia. The changes may involve terminal duct/lobular units or inter-lobular ducts.
The major features are:
- A mixed cell population comprising epithelial cells and basal cells
- Immunoreactivity for luminal epithelial cytokeratins (CK 8, 18, 19) and basal intermediate epithelial cytokeratins (CK 5, 14) may be helpful in identifying a mixed cell population in usual epithelial hyperplasia. It should be noted however that cells of basal intermediate type are absent in columnar and apocrine proliferations
- Indistinct cell margins leading to a syncytial growth pattern
- Irregular and slit-like peripheral lumina
- Streaming epithelial bridges
- Infrequent mitoses with no abnormal forms.

The distinction from atypical ductal hyperplasia and low grade ductal carcinoma in situ are summarised in Table 6b.1.

Table 6b.1: Comparison of histological features of ductal hyperplasia and DCIS

Histological features	Usual type hyperplasia	Atypical ductal hyperplasia	Low nuclear grade DCIS
Size	Variable size but rarely extensive, unless associated with other benign processes such as papilloma or radial scar	**Usually small (< 2-3 mm)** unless associated with other benign processes such as papilloma or radial scar	Rarely less than 2-3 mm and may be very extensive
Cellular composition	**Mixed. Epithelial cell and spindle-shaped cells* present. Lymphocytes and macrophages may also be present. Myoepithelial hyperplasia may occur around the periphery**	Usually single cell population	**Single cell population.** Spindle-shaped cells not seen. Myoepithelial cells usually in normal location around duct periphery but may be attenuated
Architecture	Variable	Micropapillary, cribriform or solid pattern	**Well-developed micropapillary, cribriform or solid patterns**
Lumina	**Irregular, often ill-defined peripheral slit-like spaces are common and a useful distinguishing feature**	May be distinct, well formed rounded spaces in cribriform type. In less developed forms, bridges and bars. Irregular, ill-defined lumina may also be present	**Well delineated, regular punched out lumina in cribriform type**
Cell Orientation	**Often streaming pattern with long axes of nuclei arranged in parallel to direction of cellular bridges, which often have a 'tapering' appearance**	Cell nuclei may be at right angles to bridges in cribriform type, forming 'rigid' structures	**Micropapillary structures with indiscernible fibro-vascular cores or smooth, well-delineated geometric spaces. Cell bridges 'rigid' in cribriform type with nuclei orientated towards the luminal space**
Nuclear spacing	**Uneven**	Even in the classical type but may be uneven	**Even**
Epithelial/ tumour cell character	Small ovoid but showing variation in shape	Small uniform or medium sized monotonous population present. Some cases may show variation in cell size (CK 5-negative)	**Small uniform monotonous population with cell borders often visible**
Nucleoli	Indistinct	Single small	Single small
Mitoses	Infrequent with no abnormal forms	Infrequent, abnormal forms rare	Infrequent, abnormal forms rare
Necrosis	Rare	Rare	If present, confined to small particulate debris in cribriform and/or luminal spaces

Major diagnostic features shown in bold type.

* These cells are usually called myoepithelial cells but immunohistochemical studies have shown that they have characteristics of basal keratin type epithelial cells.

III. Columnar cell change (with and without atypia)

This includes conditions known as blunt duct adenosis, columnar cell change, columnar cell hyperplasia, unfolded lobule, CAPSS (columnar alteration with prominent apical snouts and secretions), columnar cell atypia[8,9,10]. In the 2003 edition of the WHO on the classification of tumours of the breast they are defined as 'flat epithelial lesions'[10a].

A spectrum of changes ranging from bland columnar cell change to columnar cell hyperplasia with atypia is increasingly recognised, as a result of extensive investigation of radiological calcification.

At present there is no internationally accepted classification or terminology for this range of lesion. In this edition we would endorse the recent overview summary of available data and outline classification proposed by Schnitt[10].

In columnar cell change, lobules are expanded and lined by epithelial cells with a columnar morphology. These may occasionally extend into ducts. A form of the lesion categorised as columnar cell alteration with apical snouts and secretions (CAPSS) in particular is seen as a result of radiologically driven biopsies, as the associated luminal secretions often undergo calcification. Other features may include increased cytoplasm and apical snouts. A single layer of columnar epithelial cells is the norm although minor multilayering and tufting may be present. If greater degrees of multilayering of the epithelial cells are seen the process is classified as columnar cell hyperplasia. This is CK 5-negative in contrast to usual type hyperplasia which has a CK 5-positive patchwork appearance. True micropapillary structures lacking fibrovascular cores and epithelial bridges are not seen in this form. If such architectural atypia, usually in the form of bulbous micropapillary structures, is identified, the lesion is categorised as columnar cell hyperplasia with architectural atypia. This form of atypia is not included in the Page definition of ADH[11].

If superimposed cytological atypia is seen the lesion is classified as columnar cell change with atypia. It is often associated with columnar cell hyperplasia. Less commonly columnar cell change without hyperplasia shows cytological atypia of a degree to cause concern but not amounting to flat in situ carcinoma. The epithelial cells are usually single layered and show mild to moderate degrees of cytonuclear atypia with clumped chromatin or vesicular nuclei or prominent multiple nucleoli.

As the biological significance is unclear, columnar cell change and columnar cell change with hyperplasia should be classified as columnar cell change with or without epithelial proliferation. Neither columnar cell change with atypia or columnar cell change with both hyperplasia and atypia show features which fulfill the criteria for atypical ductal hyperplasia (ADH) (see below) and should be classified as columnar cell change with atypia on the form[8]. However, they may merge or be associated with other epithelial proliferations, including atypical ductal hyperplasia, conventional forms of DCIS (usually of low-grade micropapillary or cribriform type), lobular intraepithelial neoplasia and invasive carcinoma of low-grade tubular or tubulolobular type[9]. The presence of such associations should be recorded as columnar cell change plus the additional lesion.

Proposed categorisation of columnar cell lesions[10]

- Columnar cell change
- Columnar cell hyperplasia
- Columnar cell change with atypia
- Columnar cell hyperplasia with atypia.

It should be noted that the columnar cell epithelial cell proliferation shows homogeneous oestrogen receptor positivity and similarly does not show the heterogeneity of cytokeratin expression of usual epithelial hyperplasia, as described above. These data support the emerging view that the lesions with atypia may be a low-grade form of breast intraepithelial neoplasia.

IV. Present with atypia (ductal)

Atypical Ductal Hyperplasia (as described by Page et al)
Atypical ductal hyperplasia (ADH)[11,12,13] is a rare lesion. In screening it may present as a single cluster of calcification in a non-linear pattern. Its current definition rests on identification of some but not all features of ductal carcinoma in situ[11]. The difficulties are encountered mainly in distinguishing ADH from the low grade variants of DCIS. The diagnosis of ADH is based on both a qualitative and quantitative assessment of the lesion[14].

The *qualitative* assessment is based on cytological features and architectural growth pattern. These include:
- A uniform monomorphic luminal epithelial cell population (CK 8, 18, 19 positive)
- An even cellular distribution
- Secondary lumina some of which are rigid while others are tapering
- Hyperchromatic nuclei
- Cribriform, micropapillary or solid growth pattern.

The *quantitative* assessment is based on assessment of lesion size:
- Areas of ADH are usually small and not exceeding 2-3 mm in size.

Proliferations with high grade cytology (with or without necrosis) qualify as DCIS, regardless of size or quantity of epithelial proliferation.

The diagnosis of ADH is made in those cases in which a diagnosis of DCIS is seriously considered but where the architectural, cytological and quantitative features do not amount to a confident diagnosis of DCIS. If a diagnosis of ADH is contemplated, extensive sampling and/or levels should be undertaken to search for more evidence to establish an unequivocal diagnosis of DCIS.

Table 6b.1 provides details of features to help distinguish ADH from usual type hyperplasia and DCIS.

Useful guides to distinguish ADH from DCIS:
- Restrict diagnosis of ADH to those cases in which DCIS is seriously considered but where the features are not sufficiently developed to make a confident diagnosis.
- DCIS usually extends to involve multiple duct spaces. If a lesion with features of ADH extends widely, the diagnosis of ADH should be questioned.

Proliferations with atypical cytological features, not of Page and Rogers' type are usually of columnar cell type and are dealt with in the columnar cell section (see above). Based on the limited follow-up data, columnar cell change with atypia and columnar cell hyperplasia with atypia in its pure form (see above) should not be classified or treated as DCIS. Columnar cell lesions with the cytological and architectural features of atypical ductal hyperplasia or DCIS should be classified as such.

V. Present with atypia (lobular)

Lobular intraepithelial neoplasia (atypical lobular hyperplasia & lobular carcinoma in situ)
Atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS) do not usually produce a radiological abnormality. They can, very occasionally, form psammomatous calcification but are usually found incidentally during the investigation of another abnormality. ALH and LCIS have traditionally been separated as distinct entities[15, 16, 17]. The difference has been on the basis of cytological and quantitative features relating to the extent of lobular involvement. The justification for separating the entities has been the differing risks of subsequent invasive cancer[17] but molecular analysis suggests that biologically the two appear to be essentially similar. ALH is a neoplastic not a hyperplastic proliferation. In view of the subjective nature of separating ALH from LCIS, the lack of criteria that allows a different management approach and the similar

molecular profiles, some pathologists advocate the use of the term lobular intraepithelial neoplasia (LIN). Very mild forms of ALH can be found in association with fibrocystic change, involution and otherwise normal breast tissue. No attributable risk has been shown for these mild forms and such lesions are often disregarded.

LIN is characterised by proliferation within terminal duct/lobular units of characteristic cells. The defining cell type in LIN is round, cuboidal, or polygonal with clear or light cytoplasm. Nuclei are small, round to oval, cytologically bland, with an occasional small inconspicuous nucleolus. The nucleus may be indented by an intracytoplasmic vacuole containing mucin. The cells have a high nuclear to cytoplasmic ratio. Mitotic figures and hyperchromatism are not often seen. There is an even distribution of cells and cellular monotony is the rule. Cytoplasmic clear vacuoles are often, although not invariably, present, sometimes having a central mucin blob. There is poor cell cohesion and pagetoid spread of cells may be present. This proliferation of neoplastic cells above the basement membrane undermines the normal lining epithelial cells. The distension of lobular units may be variable from mild to gross, resulting in either patent lumina or complete obliteration. Table 6b.2 illustrates the differences between DCIS and LIN.

Table 6b.2 Distinction of low grade ductal carcinoma in situ from lobular intraepithelial neoplasia

Histological features	Low grade DCIS	Lobular intraepithelial neoplasia
Cells	Uniform with small evenly placed nuclei	Small, rounded with granular or hyperchromatic nuclei, inconspicuous nucleoli and high nuclear-cytoplasmic ratio
Intracytoplasmic lumina	Rare	Common
Growth pattern	Very variable e.g. solid, papillary, cribriform	Diffuse monotonous with complete luminal obliteration
Cell cohesion	Usually good with visible cell borders	Usually poor
Degree of distension of involved structures	Moderate to great	Slight to moderate
Pagetoid spread into interlobular ducts	Usually absent	Often present
E-cadherin	Present	Usually absent

NB. All the features of a lesion should be taken into account when making a diagnosis. No criterion is reliable alone.

Variants, particularly the pleomorphic sub-type and LIN with central necrosis, are recognised. In some more extensive lesions distinction between LIN and DCIS may be difficult or impossible. Such cases should be classified as combined DCIS/LIN and accordingly indicated as such on the reporting form. On occasions a regular, evenly-spaced monotonous population is seen within both ducts and lobules; in these circumstances it may also be difficult to classify the lesion as either LIN or DCIS. If only scanty terminal ducts are involved and the proliferation is almost entirely lobular, the lesion is classified as LIN. However, distinguishing DCIS from LIN may be impossible if both an organoid lobular and ductal component is identified. If both ducts and lobules contain epithelial proliferation of this type, categorisation as both LIN and DCIS is recommended to imply the precursor risk of DCIS and the bilateral cancer risk of LIN.

6b.4.5 Classifying malignant non invasive lesions

6b.4.5.1 Ductal carcinoma in situ

Ductal carcinoma in situ (DCIS) is a unicentric[1,18] proliferation of epithelial cells with cytological features of malignancy within parenchymal structures of the breast and is distinguished from invasive carcinoma by the absence of stromal invasion across the basement membrane. Despite the name, most DCIS is generally considered to arise from the terminal duct/lobular units. The main points of distinction from lobular neoplasia are described in Table 6b.2. Features in favour of DCIS are the slightly larger cell size, readily visible cell membranes, cytoplasmic basophilia, and variation in cellular arrangement and size, greater cellular cohesion and lack of intracytoplasmic lumina. The main presenting feature of DCIS on mammography is as microcalcification which may be linear or punctate in clusters but very occasional subtypes may form a mass.

DCIS Classification

a. Grade of DCIS

DCIS varies in cell type, growth pattern and extent of disease and is now considered to represent a group of related in situ neoplastic processes. Classification has historically been according to growth pattern but has been carried out with little enthusiasm due to the perceived lack of reproducibility and lack of clinical relevance. Lesions of high nuclear grade are recognised to be clinically more aggressive. Distinguishing between sub-types of DCIS is also of value for correlating pathological and radiological appearances, improving diagnostic consistency, assessing the likelihood of associated invasion and determining the probability of local recurrence. Various systems have been described, based on combinations of cell morphology, architecture (including polarisation of cells) and the presence of necrosis[19, 20]. Necrosis can be identified by the presence of cell ghosts and is eosinophilic and granular in nature. Karyorrhectic debris is seen. The definition of necrosis does not include single apoptotic individual cells.

A high power lens (40x) should be used to compare size of tumour cell nuclei with normal epithelial nuclear size and red blood cell size[21].

Other features such as mitotic count, presence of prominent nucleoli and polarisation of nuclei may be helpful in assigning grade. In particular a high mitotic count is very rare in DCIS not of high histological grade.

I. High nuclear grade DCIS

Cells have pleomorphic, irregularly spaced, and usually large nuclei exhibiting marked variation in size, irregular nuclear contours, coarse chromatin and prominent nucleoli. Nuclei are typically large and greater than 3 times the size of erythrocytes. Care should be taken with apocrine DCIS where larger nuclei and nucleoli may be present even in low grade lesions. Mitoses are usually frequent and abnormal forms may be seen. If mitoses are prominent there is a high likelihood that a case is of high grade. High grade DCIS may exhibit several growth patterns. It is often solid with comedo type central necrosis, which frequently contains deposits of amorphous calcification. Sometimes a solid proliferation of malignant cells fills the duct without necrosis but this is relatively uncommon and may be confined to nipple/lactiferous ducts in cases presenting with Paget's disease of the nipple. High nuclear grade DCIS may also exhibit micropapillary and cribriform patterns frequently associated with central comedo type necrosis. Unlike low nuclear grade DCIS there is rarely any polarisation of cells covering the micropapillae or lining the intercellular spaces. Radiologically, high nuclear grade DCIS often produces linear branching calcification which is common in this grade but not usually present in other grades or subtypes. High nuclear grade DCIS may also produce clustered calcification, however, and this particular radiological pattern is not discriminatory between grades.

II.Intermediate nuclear grade DCIS
These types cannot be assigned readily to the high or low nuclear grade categories. The nuclei show moderate pleomorphism, less than that seen in the high grade disease, but lack the monotony of the small cell type. The nuclei are typically larger than seen in low grade DCIS and are between two and three times the size of an erythrocyte. The nuclear to cytoplasmic ratio is often high and one or two nucleoli may be identified. The growth pattern may be solid, cribriform or micropapillary and the cells usually exhibit some degree of polarisation covering papillary processes or lining intercellular lumina. Clear cell or apocrine types often fall into this category.

III. Low nuclear grade DCIS
Low grade DCIS is composed of monomorphic evenly spaced cells with rounded, centrally placed nuclei and inconspicuous nucleoli except in apocrine DCIS where lack of pleomorphism is more important. The nuclei are usually, but not invariably, small and typically one to two times the size of an erythrocyte. Mitoses are few and there is rarely individual cell necrosis. These cells are generally arranged in micropapillary and cribriform patterns. Both patterns are frequently present within the same lesion although the cribriform pattern is more common and tends to predominate. There is usually polarisation of cells covering the micropapillae or lining the intercellular lumina. Less frequently low grade DCIS has a solid pattern. Calcification is usually punctate but, apart from linear branching calcification being associated with high-grade lesions, the pattern of calcification is not a good discriminant.

IV. Mixed types of DCIS
A small proportion of cases of DCIS exhibit features of differing nuclear grade. Such variation in cell type is unusual but, if present, the case should be classified by the highest nuclear grade present.

b. Rarer subtypes of DCIS
Other rare, but morphologically distinct, subtypes of DCIS are recognised. There is, however, no firm evidence to support the distinction of special DCIS types from commoner DCIS forms with the exception of encysted papillary carcinoma in situ and apocrine DCIS. The practical problem of inter-observer disagreement in distinction of some special DCIS subtypes, particularly apocrine and micropapillary DCIS, has led to some suggesting a working classification of DCIS with five subtypes: high, intermediate and low grade with in addition apocrine and micropapillary DCIS as separate categories. Simultaneous use of the grading system described above and sub-typing according to architecture is recommended.

I. Apocrine DCIS[22, 23]
The tumour cells show abundant granular cytoplasm, moderate to severe cytological atypia and central necrosis. Apical snouting (cytoplasmic protrusions) are not always seen. The cells may sometimes be highly atypical. In some cases no necrosis may be evident. The diagnosis of apocrine DCIS should be made with caution particularly in the absence of comedo type necrosis when it may be extremely difficult to distinguish atypical apocrine hyperplasia from low grade apocrine DCIS without necrosis. The degree of cytonuclear atypia, the extent of the lesion and altered architectural growth pattern are helpful features used to make this decision. Mitoses are very infrequent or absent in atypical apocrine proliferations. The presence of periductal inflammation and fibrosis may also be helpful and are rarely seen in atypical apocrine hyperplasia or apocrine proliferations other than DCIS. Grading of apocrine DCIS can also be difficult due to the large nuclear size and nucleoli of apocrine cells.
Benign apocrine change is, of course, frequent in breast biopsy material and is recognised to show nuclear atypia, which should not be interpreted as DCIS. Atypical apocrine change in sclerosing adenosis may also mimic apocrine DCIS or even invasive apocrine carcinoma.

II. Encysted (Intracystic) papillary DCIS[24]
This is a rare but distinctive form of DCIS, which is more common in older women. It carries an excellent prognosis if confined within the capsule without surrounding DCIS or foci of invasion.

The presence of associated DCIS in the surrounding tissue is recognised to be of significance regarding local recurrence and should be recorded. Encysted papillary carcinoma in situ is usually circumscribed and accompanied by a hyalinised fibrous wall giving an intracystic (encysted) appearance. Adjacent to the fibrous capsule haemosiderin (or haematoidin) pigment is often seen. Encysted papillary carcinoma has a papillary structure with fibrovascular cores; however these may be absent in at least part of the lesion. The use of immunohistochemistry can be helpful in showing a partial or complete lack of myoepithelial cells lining the papillary structures. Other forms of DCIS, usually of micropapillary or cribriform architecture, may accompany it.

III. Clear cell DCIS
This is an intraductal proliferation of neoplastic cells with optically clear cytoplasm and distinct cell margins forming cribriform and solid structures. Central necrosis may be present. This may be mimicked by poor fixation in other forms of DCIS and care should be taken to achieve optimum fixation of all breast samples, as noted above.

IV. Signet ring DCIS (25)
This is a very rare variant characterised by the proliferation of signet ring cells in solid or papillary growth patterns. The cytoplasm stains positive with diastase-resistant-PAS or alcian blue.

V. Neuroendocrine DCIS
The lesion has an organoid appearance with prominent argyrophilia, resembling a carcinoid tumour. The neoplastic cells may be arranged in a solid pattern or may be papillary, forming tubules, pseudorosettes, palisades or ribbons. Where solid, the proliferation is nearly always punctuated by fine fibrovascular cores. An eosinophilic cytoplasmic granularity or organoid spindle morphology is all supportive of the neuroendocrine phenotype. Because of the lack of microcalcification these tumours tend to present symptomatically, most commonly in elderly patients with blood stained nipple discharge. Immunohistochemical stains for neuroendocrine markers (chromogranin, PGP9.5, synaptophysin) may be helpful in diagnosis of this sub-type of DCIS, which also expresses oestrogen receptor.

VI. Cystic hypersecretory DCIS (26) and mucocoele-like DCIS
These types of DCIS are variants of micropapillary DCIS. The cells produce mucinous secretions, which distend involved duct spaces giving a cystic appearance. Microcalcifications are often a very prominent feature.

VII. Paget's disease of the nipple
In this condition, there are adenocarcinoma cells within the epidermis of the nipple. Cases where there is direct epidermal invasion by tumour infiltrating the skin are excluded. Paget's disease of the nipple should be reported regardless of whether or not the underlying in situ or invasive carcinoma is identified. The underlying carcinoma should be recorded separately. Her-2 or high molecular weight cytokeratin positivity may be useful in diagnosis.

6b.4.5.2 Lobular carcinoma in situ
See section on lobular neoplasia (LIN) above.

6b.4.6 Microinvasive carcinoma[27,28]

A variety of different diagnostic criteria and definitions have been used for microinvasive carcinoma which has hampered the assessment of its clinicopathological implications. Although it is virtually almost exclusively associated with high nuclear grade/comedo DCIS, it may also be associated with other types of DCIS and with lobular intraepithelial neoplasia. It is related to the

size/extension of associated in situ carcinoma. The current prevailing view is that microinvasive carcinoma appears to have an excellent prognosis with a low risk of associated axillary lymph node metastasis (similar to extensive high nuclear grade DCIS). Reported studies on microinvasive carcinoma have either used variable definitions or none at all preventing reliable analysis and comparison of outcomes and levels of concordance are low in studies of interobserver reproducibility.

I. Definition

A tumour in which the dominant lesion is in situ carcinoma (usually extensive high nuclear grade DCIS, rarely other types of DCIS or lobular intraepithelial neoplasia) but in which there are one or more clearly separate foci of infiltration of non specialized interlobular or interductal fibrous or adipose tissue, none measuring more than 1 mm (about 2 hpf) in maximum diameter[27,28,29]. This definition has been officially reported in the TNM system as pT1mic since 1997 (fifth edition)[30]. It is very restrictive and tumours fulfilling the criteria are consequently rare.

II. Criteria

The tumour focus/foci must invade into nonspecialized interlobular or interductal stroma (extension of the lesion beyond the confines of a ductolobular unit, development of a desmoplastic stroma). The cells deemed to be invasive must be distributed in a fashion (non-organoid pattern) that does not represent tangential sectioning of a duct or a lobular structure with in situ carcinoma. Tangentially sectioned in situ carcinoma foci that simulate microinvasion are distributed in the specialized periductal and intralobular stroma and usually occur as compact groups of tumour cells that have a smooth border surrounded by a circumferential layer of myoepithelial cells and stroma or a thickened basement membrane[29]. At sites of microinvasive foci, tumour cells are distributed singly or as small groups that have irregular shapes reminiscent of conventional invasive carcinoma with no particular orientation[29]. There is complete absence of surrounding basement membrane and myoepithelial cells: immunostains are helpful in demonstrating the presence or absence of basement membrane components (laminin and collagen type IV) or myoepithelial cells (smooth-muscle actin, calponin, smooth-muscle myosin heavy chain). Detecting microinvasion can be difficult when there is marked periductal fibrosis or inflammation because the true boundary of the specialized periductal or lobular stroma is not clear, but immunostaining for cytokeratin may be useful to confirm the presence of separate foci of neoplastic cells embedded in periductal fibrosis or inflammation.

Microinvasive carcinoma can not be reliably excluded unless all tissue is serially sectioned and sequentially submitted. Small excisions (i.e. 3 cm or less in greatest diameter) should be sectioned at 2-3 mm intervals submitting all tissue; cases of extensive in situ carcinoma, especially high nuclear grade/comedo DCIS should be extensively sampled to exclude microinvasion. When there are multiple foci of microinvasive carcinoma only the size of the largest focus is used to classify the microinvasion. Do not use the sum of all individual foci. The presence of multiple foci of microinvasion should however be noted and/or quantified[31] and the size of the whole tumour including the DCIS should be reported. Blocks with microinvasive carcinoma should be cut deeper in order to exclude the possibility of larger invasive foci. Where these are found, the lesion is classified as invasive carcinoma and the maximum diameter measured. A focus of invasive carcinoma 1 mm or less without associated in situ carcinoma is not a 'microinvasive carcinoma' but should be classified as invasive carcinoma and the maximum diameter measured. If there is sufficient doubt about the presence of microinvasion (i.e. in cases with marked fibrosis or inflammation) the case should be classified as in situ carcinoma/microinvasion possible.

In cases with a history of prior needle procedure (FNAC, core biopsy, vacuum assisted core biopsy) diagnosis of microinvasive carcinoma should be made with caution: artefactual disruption of the epithelial-stromal junction of glandular structures involved by in situ carcinoma is not infrequently encountered in a subsequent excisional biopsy. Granulation tissue, old or recent haemorrhage, tissue tears, and a degenerative appearance of the dislodged tumour cells can help distinguish pseudo-invasion from true invasion[32].

6b.4.7 Classifying invasive carcinoma

Typing invasive carcinomas has prognostic value and provides information on pattern of metastatic spread and behaviour. Caution should be exercised in typing carcinomas in poorly fixed specimens or if they have been removed from patients who have been treated by primary chemotherapy or radiotherapy prior to surgery. Typing of breast carcinomas has been shown in EQA schemes to be relatively poorly reproducible and the system has been revised with emphasis on concordance and recognition of pure special types.

I. Pure special type

A classical example, showing the hallmark histological features. You would be confident that other pathologists would recognise this case as a pure special type. **The definitions require 90% purity.** Special type tumours in general have characteristic, usually favourable, clinical prognostic characteristics, as described below.

II. Mixed tumour

This is a relatively common pattern of invasive breast carcinoma. The tumour may be heterogeneous in morphology with some characteristic special type areas **(more than 50% but less than 90%).** For example there may be areas of pure tubular differentiation or one or more characteristics of a special type but lack the full combination of features required for pure special type designation such as a distinctive lobular infiltrative growth pattern with non-lobular cell morphology. This is different from pleomorphic lobular carcinoma and is also different from tumours which include a mixture of specific lobular subtypes. The special type characteristic or area should be identified as an additional feature.

III. No special type

6b.4.7.1 Morphological types of breast cancer

The more common types are described below.

I. 'Ductal' - no specific type (Ductal-NST)

This group contains infiltrating carcinomas which cannot be entered into any other category on the form, or classified as any of the less common variants of infiltrating breast carcinoma. **The tumour shows less than 50% special type characteristics.** Consequently, invasive ductal carcinomas exhibit great variation in appearance and are the most common carcinomas, accounting for up to 75% in published series.

II. Infiltrating lobular carcinoma

Infiltrating lobular carcinoma is composed of small regular cells identical to those seen in situ lobular neoplasia. In its classical form, the cells are dissociated from each other or form single files or targetoid patterns around uninvolved ducts. Several variants have been identified in addition to this classical form but in each case the cell type is the same:

a. The **alveolar** variant exhibits small aggregates of 20 or more cells.
b. The **solid** variant consists of sheets of cells with little stroma.
c. The **tubulo-lobular** type exhibits microtubular formation as part of the classical pattern. Tumours that show mixtures of typical tubular and classical lobular carcinoma should be classified as mixed (see below).
d. The **pleomorphic** variant is uncommon and exhibits the growth pattern of classical lobular carcinoma throughout but the cytological appearances, although retaining lobular characteristics, are more pleomorphic than those seen in classical invasive lobular carcinoma.
e. **Lobular mixed type** lesions consist of mixtures of above sub-types of lobular carcinoma.

At least 90% of the tumour should exhibit one or more of the above patterns to be classified as infiltrating lobular. Lobular carcinomas may be localised or more diffuse. In the latter case they are more difficult to identify on radiography and may be over-represented in studies of interval cancer.

III. Tubular carcinoma

Tubular carcinomas are composed of round, ovoid, or angulated single layered tubules in a cellular fibrous or fibro-elastotic stroma. The neoplastic cells are small, uniform and may show cytoplasmic apical snouting. Nuclei should not show a high degree of atypia. At least 90% of the tumour should exhibit the classical growth pattern to be classified as tubular. However, if the co-existent carcinoma is solely of the invasive cribriform type then the tumour should be typed as tubular if the tubular pattern forms over 50% of the lesion. The characteristic radiological appearance is that of a stellate abnormality which can resemble a radial scar.

IV. Invasive cribriform carcinoma

This tumour is composed of masses of small regular cells as seen in tubular carcinoma. The invasive islands, however, exhibit a cribriform rather than a tubular appearance. Apical snouting is often present. Nuclei should not show a high degree of atypia. More than 90% of the lesion should exhibit a cribriform appearance except in cases where the only co-existent pattern is tubular carcinoma when over 50% must be of a cribriform appearance in order to be classified as of invasive cribriform type. These tumours may produce a well-circumscribed lesion and are not generally stellate as is a tubular carcinoma.

If a diagnosis of invasive cribriform carcinoma is preferred, the 'tubular' box should be ticked and appropriate comment made under 'Comments/Additional Information'.

V. Medullary/atypical medullary carcinoma and medullary-like tumours

Tumours of medullary and atypical medullary types should be recorded as special type on the reporting form and the type component recorded. The three key components of these lesions are syncytial interconnecting masses of grade 3 tumour typically having large vesicular nuclei and prominent nucleoli. The stroma always contains large numbers of lymphoid cells. These features must be present in 90% or more of the tumour. The border of the tumour is predominantly pushing or well-defined. The whole tumour must exhibit these features to be typed as medullary. Surrounding in situ elements are very uncommon. Accordingly they can be difficult on radiology appearing as a well-circumscribed lesion which can be mistaken for a cyst.

The term **atypical medullary carcinoma** has been used for lesions that do not have an entirely well-defined pushing margin or have other features precluding their diagnosis as medullary. This designation does not appear to have any definite prognostic significance and there is doubt as to the value of this category. It may be better to classify these as 'Ductal-NST' and to make a comment about the lymphocytic infiltration and circumscription as below.

An increased frequency of tumours exhibiting some medullary features (high grade, pushing margins, lymphocyte-rich stroma) has been found in patients with inherited BRCA1 gene mutations[33]. The tumours cross the spectrum of pure medullary, atypical medullary and ductal/NST with a lymphocyte rich stroma and have led some to speculate that the current definitions for medullary carcinoma are of limited value. Of all histological tumour types, medullary carcinoma has the worst concordance in EQA schemes. For this reason the Working Group advocates the designation of all these tumours as medullary-like tumours.

VI. Mucinous carcinoma

This type has also been known as mucoid, gelatinous or colloid carcinoma. There are islands of uniform small cells in lakes of extracellular mucin. An in situ component may be present. At least 90% of the tumour must exhibit the mucinous appearance to be so classified. They may also be relatively well circumscribed and resemble fibroadenomas on assessment.

VII. Other primary carcinoma
Other primary breast carcinomas should be entered under this heading and will include variants such as **metaplastic, apocrine, invasive micropapillary, infiltrating papillary etc.**

VIII. Other malignant tumour
Non-epithelial tumours and secondary carcinomas are included in this category. For purposes of convenience, **malignant phyllodes tumours** should be recorded here.

IX. Not assessable
This category should be ticked only if an invasive carcinoma cannot be assigned to any of the previous groups for technical reasons, e.g. the specimen is too small or poorly preserved.

6b.4.8 Recording prognostic data

6b.4.8.1 Tumour size

I. Invasive carcinoma
The maximum dimension of any invasive tumour should be measured in the fresh or fixed state macroscopically. Care should be taken in the case of ovoid tumours that the largest dimension is measured and blocked, bearing in mind that this may not necessarily be the plane of the initial cut into the tumour. If a specimen radiograph is available then the plane of maximum dimension can be better assessed before slicing. It is recognised that for circumscribed tumours, the macroscopic measurement may be very accurate if measured to the nearest millimetre but for diffuse tumours it may be more problematic to define the precise borders of the tumour.

Blocks should also be taken to enable a measurement of the histological size of tumours. Where the maximum macroscopic diameter of a tumour can be blocked directly, it is recommended that a single block across this diameter be taken. Where a tumour is larger than can be assessed in a single block, two or more blocks are recommended from the maximum macroscopic diameter, so that the total tumour size can be estimated by adding the dimensions together or measuring the maximum dimension on the two slides fitted together. Alternatively a large block to encompass the maximum dimension may be taken. If this is the case then at least one other normal sized tumour block should be processed as well, to allow optimal processing and to make receptor studies easier. For diffuse tumours, especially diffuse lobular carcinomas, it may not be possible to macroscopically define the true extent of tumour and in this case, either a large block or consecutive blocks of the whole abnormal area (including adjacent fibrotic tissue) may be necessary.

Occasional cases will have had a diagnostic biopsy before definitive treatment; primary chemotherapy or exceptionally a frozen section may have been performed. Tumour size in these circumstances may be inaccurate but an assessment based on the ultrasound or radiographic size in conjunction with the histology may be necessary. There may also be a problem where multiple core biopsies have completely or partially removed a small tumour. (See also the needle core histology form in section A.) In these situations an estimate of the original tumour size should be given. This may need discussion with the radiologist and correlation with ultrasound, mammographic, or other radiological features. An estimate of the tumour size should be ascertained and a comment made in the comments/additional information box.

Tumour size should be measured in millimetres and the invasive tumour size entered in the field ‘MAXIMUM DIMENSION (invasive component)……’ on the reporting form. Satellite lesions should not be included in the measurement of the maximum invasive tumour dimension, nor should foci of vascular or lymphatic invasion. (Fig 1). On occasions it may be difficult to be certain whether foci of invasive carcinoma close to each other within a section represent a main mass in continuity or one a satellite focus from the other. Features that may be of assistance include the presence of normal breast parenchymal structures between the two deposits and the distance between the foci. It is impossible to strictly define a distance between the foci that can

be used to decide whether one is a satellite deposit from another; if however the foci are 5 mm or more apart the chances of the deposits representing one tumour appearing as separate foci due to plane of slicing are low. A pragmatic approach must be taken however to measurement of invasive tumour size and common sense applied when a definitive size measurement cannot be given. In addition comparison with ultrasound or magnetic resonance imaging size may be helpful. If these are not available, mammographic size can be utilised, although less accurate. Finally (and least accurately) clinical size can be compared.

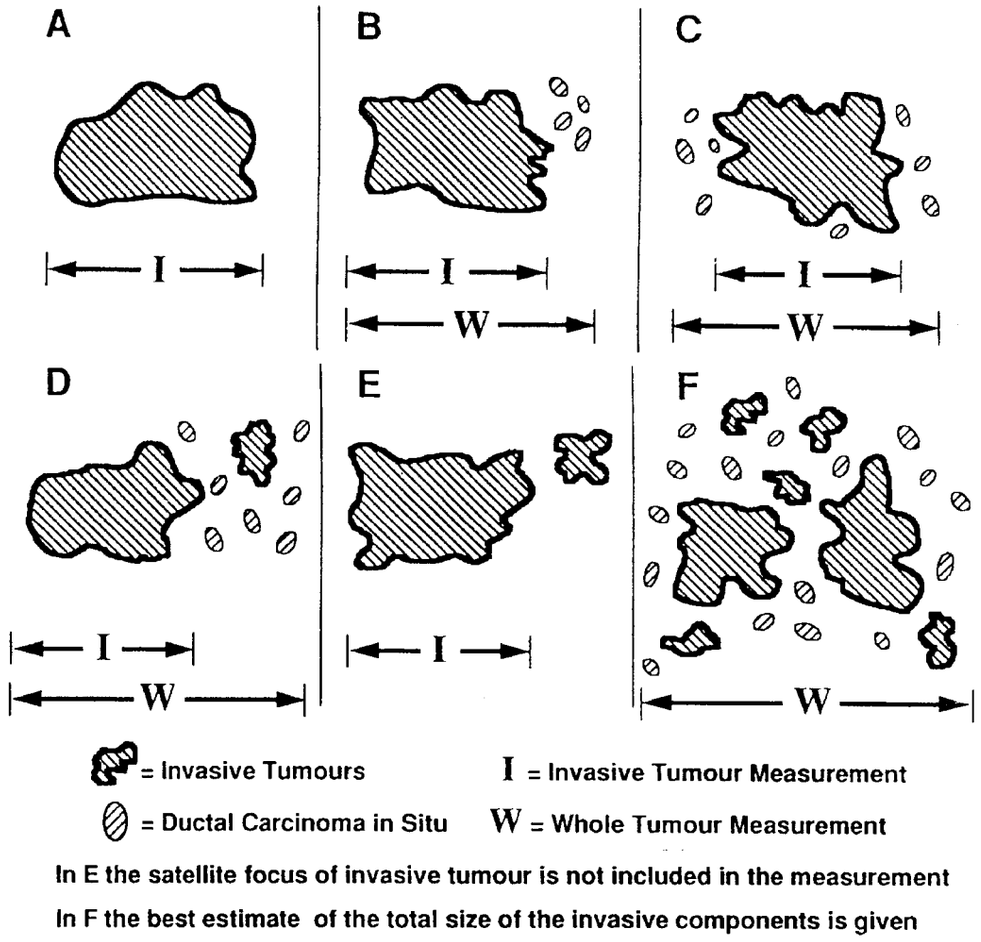

Figure 1

Where there is a discrepancy between the macroscopic size and the microscopic size then the latter should be recorded provided it is certain that the true plane of maximum dimension has been included in the slide or slides. For example an ovoid tumour 11 x 8 x 8 mm may be underestimated histologically as 8 mm if the plane of block selection is through the centre and not in the plane of the long axis.

Measurement of histological size from the tissue sections can be made using the Vernier stage micrometer. The slide should be placed at an angle on the microscope stage so that the largest dimension is determined. Other methods include inking the edges of the tumour on the slide with marker pen and then measuring the distance between the points with a ruler or using a magnifying device with a graticule applied directly over the histological slide.

II. In situ carcinoma

Lobular intraepithelial neoplasia is generally multifocal and measurement of the extent of this disease is unreliable, unnecessary and unhelpful. **Only DCIS should be measured.** Undoubtedly, however, the measurement of DCIS in two-dimensional slides is at best an underestimate of the total size of the in situ change. The tree-like branching structure of normal breast ducts means that ductal carcinoma in situ generally very rarely forms a rounded mass and ramifies within the affected duct system. Of especial note is the extension of the in situ tumour into the major duct running towards the nipple[2].

Large blocks can help to delineate in situ disease. The two dimensional nature of slides may not give the true extent of disease and block taking and measurement should be correlated with the specimen radiograph. Where the size measured is less than the size on the radiograph then further blocks should be taken to identify the limit of the calcification seen on radiography.

The measurement of the size of ductal carcinoma in situ should be recorded on the reporting form in the field under non-invasive tumour 'SIZE (ductal only) .....', **not** in the whole tumour size field under invasive carcinoma.

III. Invasive carcinoma with surrounding in situ carcinoma

There is no internationally recognised definition of extensive in situ carcinoma but it has been reported that, on excision of an invasive carcinoma with a small margin of normal tissue, surrounding extensive in situ carcinoma is associated with increased risk of local recurrence. Where more extensive excision is performed, however, the significance of this factor is markedly reduced. This problem relates to adequate excision of tumour with associated in situ component and is considered to be the same problem as evaluating complete excision of pure DCIS.

The invasive tumour should be measured, as above, but the assessment of the whole tumour size including in situ carcinoma presents the same problems as in the previous section (see figure 1). The measurement of DCIS associated with invasive carcinoma should be recorded in the whole tumour size field on the reporting form, including tumours which are predominantly composed of DCIS but have multiple foci of invasion. Measurement of the invasive component in this latter case can be problematic, as in Figure 1 case F where the best estimate of the invasive tumour burden should be given in the 'size of invasive tumour field'. It is recommended that pathologists take blocks from macroscopically normal tissue between an excised tumour and the excision lines in all three planes of section. Slice specimen radiography may help in this assessment.

If a tumour is insufficiently delineated to be measured accurately, a comment should be made in the Comments/Additional information field on the reporting form.

6b.4.8.2 Disease extent

The fields for disease extent on the form have been a source of confusion in the past due to debates about the definition of multicentric or multifocal. The fields are hence now given as **localised or multiple invasive foci.** The field is present to record the presence or absence of multiple foci of invasive tumour within the specimen, clearly separate from each other and not connected by associated DCIS.

It is not intended that a tumour with multiple areas of invasion from a continuous area of DCIS be classified as multiple.

It should be noted that DCIS is a unifocal disease although it may be widespread[1,18].

The designation of multiple foci should be reserved for multiple **separate** areas of invasive tumour, such as occurs with lobular carcinoma or tumours with extensive vascular invasion where there are multiple areas of invasive tumour due to extravasation of tumour cells from lymphatics and establishment of separate satellite invasive tumour foci. As noted above (in tumour size section) it can be difficult, if not impossible, on rare occasions to determine whether two

adjacent foci represent satellite foci or one lesion mimicking this process due to plane of sectioning. A pragmatic approach is required; the presence of intervening normal tissue and increasing distance between foci are features that indicate that these are more likely to be multiple foci than a localised process.

Multiple synchronous primary tumours of different types should be categorised as multiple. It is recognised that this may be difficult to assess.

6b.4.8.3 Histological grade

Histological grading provides powerful prognostic information[34,35]. It requires some commitment and strict adherence to the accepted protocol. The method is that described originally by Elston and Ellis[34]. The method involves the assessment of three components of tumour morphology: tubule/acinar/glandular formation, nuclear atypia/pleomorphism and frequency of mitoses. Each is scored from 1 to 3. Adding the scores gives the overall histological grade, as shown below.

Some degree of variation in appearance from one part of a tumour to another undoubtedly occurs; this is particularly true of tumours of mixed type[34]. Assessment of tubular differentiation is made on the overall appearances of the tumour and so account is taken of any variation. Nuclear appearances are evaluated at the periphery and/or least differentiated area of the tumour to obviate differences between the growing edge and the less active centre.

Do not expect equal numbers of cancers to fall in each grade category. Published ratios for grades 1, 2 and 3 are approximately 2:3:5 in symptomatic breast cancer[34], so about half of all symptomatic cancers are grade 3. If audit of grade distribution shows substantially fewer grade 3 cases, or a majority of grade 2 cases, grading protocols should be carefully reviewed. Screen detected cancer series are likely to include a smaller proportion of high grade cases. In the case of multiple tumours, the worst tumour grade should apply.

I. Tubule/acinar formation

All parts of the tumour are scanned and the proportion occupied by tumour islands showing clear acinar or gland formation or defined tubular structures with a central luminal space is assessed semi-quantitatively. This assessment is generally carried out during the initial low power scan of the tumour sections.

Score

1. > 75% of tumour forming tubular structures
2. 10-75% of tumour
3. < 10% of tumour

In the assessment of tubule formation, only structures in which there are clearly defined central lumens, surrounded by polarised tumour cells, should be counted. A tumour in which 75% or more of its area is composed of such structures would score 1 point for tubule formation.

II. Nuclear atypia/pleomorphism

Individual pathologists differ markedly in their approach to nuclear grading, and breast specialists appear to allocate higher grades than non-specialists[36]. Few cancers possess the very bland nuclei warranting an atypia/pleomorphism score 1, and obvious atypia/pleomorphism should attract a score of 3. The minimum proportion of tumour nuclei which should show marked nuclear atypia/pleomorphism before a score of 3 is allocated has not been defined but the finding of an occasional enlarged or bizarre nucleus should not be used to give a score of 3 rather than 2. Pleomorphism should be assessed with the x40 objective.

Score

1. Nuclei small with little increase in size in comparison with normal breast epithelial cells, regular outlines, uniform nuclear chromatin, little variation in size.
2. Cells larger than normal with open vesicular nuclei, visible nucleoli and moderate variability in both size and shape.
3. Vesicular nuclei, often with prominent nucleoli, exhibiting marked variation in size and shape, occasionally with very large and bizarre forms.

III. Mitoses

Accurate mitosis counting requires high quality fixation, obtained when fresh specimens are sectioned promptly as well as tumour blocks of optimal thickness (3-4 mm) fixed immediately in neutral buffered formalin. This can be achieved without compromising evaluation of resection margins.

Mitosis score depends on the number of mitoses per 10 high power fields. The size of high power fields is very variable, so it is necessary to standardise the mitotic count using the table below. Measure the field diameter of the microscope using a stage graticule or Vernier scale, and read the scoring categories from the corresponding line of the table or graph. Field diameter is a function of objective and eyepiece, so if **either** of these is changed, this exercise **must** be repeated.

A minimum of 10 fields with the x40 objective should be counted at the periphery of the tumour, where it has been demonstrated that proliferative activity is greatest[37]. If there is variation in the number of mitoses in different areas of the tumour the least differentiated area (i.e. with the highest mitotic count) should be assessed. If the mitotic frequency score falls very close to a score cut point then one or more further groups of 10 high power fields should be assessed to establish the correct (highest) score. It is recommended that identification of the most mitotically active or least differentiated part of the tumour forms part of the low magnification preliminary assessment of the histological section. This area should be used for mitotic count scoring. If there is no evidence of heterogeneity, then mitotic scoring should be carried out at a part of the tumour periphery chosen at random. Fields chosen for scoring are selected during a random meander along the peripheral margin of the selected tumour area. Only fields with a representative tumour burden should be used. The low power scan of the tumour can be used to provide an assessment of the typical tumour to stromal ratio. Only definite mitotic figures (in any phase of the growth cycle) should be counted. Hyperchromatic nuclei and/or apoptotic nuclei should not be scored. Poor quality fixation can result in underscoring of mitotic frequency and optimal fixation is essential.

	Number of mitoses corresponding to		
Field diameter in mm	**Score 1**	**Score 2**	**Score 3**
0.40	up to 4	5 to 8	9 or more
0.41	up to 4	5 to 9	10 or more
0.42	up to 4	5 to 9	10 or more
0.43	up to 4	5 to 10	11 or more
0.44	up to 5	6 to 10	11 or more
0.45	up to 5	6 to 11	12 or more
0.46	up to 5	6 to 11	12 or more
0.47	up to 5	6 to 12	13 or more
0.48	up to 6	7 to 12	13 or more

0.49	up to 6	7 to 13	14 or more
0.50	up to 6	7 to 13	14 or more
0.51	up to 6	7 to 14	15 or more
0.52	up to 7	8 to 14	15 or more
0.53	up to 7	8 to 15	16 or more
0.54	up to 7	8 to 16	17 or more
0.55	up to 8	9 to 16	17 or more
0.56	up to 8	9 to 17	18 or more
0.57	up to 8	9 to 17	18 or more
0.58	up to 9	10 to 18	19 or more
0.59	up to 9	10 to 19	20 or more
0.60	up to 9	10 to 19	20 or more
0.61	up to 9	10 to 20	21 or more
0.62	up to 10	11 to 21	22 or more
0.63	up to 10	11 to 21	22 or more
0.64	up to 11	12 to 22	23 or more
0.65	up to 11	12 to 23	24 or more
0.66	up to 11	12 to 24	25 or more
0.67	up to 12	13 to 25	26 or more
0.68	up to 12	13 to 25	26 or more
0.69	up to 12	13 to 26	27 or more
0.70	up to 13	14 to 27	28 or more

Overall Grade

The use of terms such as well differentiated or poorly differentiated in the absence of a numerical grade is inappropriate. The scores for tubule formation, nuclear pleomorphism and mitoses are then added together and assigned to grades, as below:

Grade 1 = scores of 3 - 5
Grade 2 = scores of 6 or 7
Grade 3 = scores of 8 or 9

It is recommended that grading is not restricted to invasive carcinoma of ductal-NST but is undertaken on all histological sub-types. There are two major reasons for this recommendation:

1. There are occasionally problems in deciding whether to classify a tumour as NST or some other sub-type.

2. There may be significant variation in prognosis within certain sub-types, e.g. lobular carcinoma and grading provides additional information (38).

'Not assessable' should be ticked if for any reason the grade cannot be determined, e.g. specimen poorly preserved or too small.

Grading systems other than that described above should not be used.

For audit and other purposes, it may be appropriate to record individual components of grade, including actual mitosis count and field size, which may have added prognostic significance within grade categories[39].

6b.4.8.4 Lymph node stage

All lymph nodes must be examined histologically, as noted above in the macroscopic examination section. Please record data from axillary nodes separate from nodes from other sites.
Record as positive only lymph nodes that contain micrometastases or larger (see below). If only isolated tumour cells are identified, they can be mentioned under additional comments, and should be recorded in the appropriate pN0 category. If no lymph nodes are sent for histopathological assessment, the number of all nodes received should be 0. Any non-axillary lymph nodes (including intramammary nodes), whether removed by sentinel node biopsy or any other means should be included under **other nodes**. The removal of non-axillary sentinel nodes can be mentioned under additional comments. Extracapsular involvement can also be recorded under additional comments.

Histological reports should include:

- The total number of lymph nodes identified.
- The number of lymph nodes involved with metastatic disease.
- Specific axillary levels and nodes, i.e. the apical node, may have been identified by the surgeon and can be recorded independently, but they should also be included in the total lymph node figures.
- The presence of extracapsular spread can be noted under 'Comments/additional information' but is considered to be of limited clinical value.

Whilst it is recognised that the evidence base for the stratification of lymph node stage is limited, adoption of the approach outlined below and described in the new TNM staging system is encouraged as it offers a pragmatic solution to the issues of classification of small metastatic deposits. It is felt appropriate for Europe to adopt an international consensus classification system to support evidence accrual based on common definitions. The system outlined below is adapted from the TNM classification of malignant tumours[5,31].

6b.4.8.5 Reporting and definitions of micrometastatic disease and isolated tumour cells[40]

I. Micrometastasis

The current pTNM definition is recommended: Micrometastasis is defined as one or more deposits of metastatic carcinoma within the lymph node more than 0.2 mm in size but none of which are larger than 2 mm in greatest dimension.

II. Isolated tumour cells (ITC)

Either single tumour cells or small clusters of tumour cells none of which is > 0.2 mm. ITC are typically located in the sinuses or the capsular lymphatics, and often identified with immunostains (or molecular methods), but sometimes verified by HE stains. Typically, ITC do not show malignant activity (proliferation or stromal reaction) or penetration of the vascular or lymphatic sinus wall. For staging and treatment purposes, these are *not considered metastases;* pN0. The pTNM classification distinguishes between pN0(i+), where nodal involvement of the isolated tumour cells category is present and pN0(i-), where the presence of isolated tumour

cells has been looked for by special/additional morphological (microscopic) methods, but no such involvement was found.

III. Submicrometastasis
This is synonymous with the 'isolated tumour cells' category and is not defined in the TNM publications[41].

Some members of the group advocate including the method of nodal assessment in the pathology report.

6b.4.8.6 Vascular invasion

The presence of vascular invasion is generally considered to be an adverse feature providing independent prognostic information about both local recurrence and survival[42,43]. It is therefore important to record whether or not it is present. Because it is difficult to distinguish between lymphatic and venous channels, findings should be categorized as 'vascular spaces', rather than specific channels.

One of the major problems in trying to determine whether tumour cells are in a vessel or not is shrinkage artefact, so care should be taken, wherever possible, in ensuring that there is optimal tissue fixation and processing. A clear rim of endothelium should be present before considering that a vascular space has been identified. The **presence** of unequivocal tumour in vascular spaces should be recorded; if there is doubt but is considered very likely it should be recorded as **possible** and if not present it is categorised as **not seen.** Perineural invasion should not be recorded as vascular invasion.

There are various features that may be helpful in trying to identify vascular invasion and to recognise whether tumour cells are in definite vascular spaces. These are:
- Groups of tumour cells in spaces around the main tumour mass; make sure any spaces are lined by endothelial cells and are not fat spaces.
- The presence of adjacent vascular channels that may be of varying sizes.
- The presence within the space of erythrocytes and/or thrombus.
- Shrinkage artefact results in nests of cells having the shape of the space in which they lie; endothelial cells will not be seen. Shrinkage artefact in DCIS may leave the myoepithelial layer attached to the basement membrane and this may simulate an endothelial lining.

The best method for assessing vascular invasion is the use of good quality, optimally fixed and processed haematoxylin and eosin stained sections. Immunostaining for endothelial markers does not generally contribute further but could be considered for difficult, critical cases.

6b.4.8.7 Excision margins

Assessment of adequacy of excision requires close correlation between the surgical excision procedure and pathological examination[44]. In particular it is essential that the pathologist is made aware of the depth of tissue excised and whether the surgeon has excised all the tissue from the subcutaneous to the pectoral fascia.

I. Invasive carcinoma
The excision margins of a well-circumscribed invasive carcinoma without a significant in situ component are usually relatively simple to assess. The distance from the tumour to the nearest radial resection line (medial, lateral, superior or inferior) and to the deep and superficial resection lines (if surgically relevant, as described above in *surgical handling – principle*s) should both be measured macroscopically. If the surgeon has orientated the specimen with clips or sutures then the resection margin assessed should be related to these. To some extent this depends on local issues, especially where the surgeon has not excised the complete depth of breast tissue from subcutaneous to pectoral fascia. In this case the superficial and deep resection margins may become more important and should in this instance be adequately assessed.

The relevant resection lines should be painted with ink and blocks taken so that the macroscopic measurement can be confirmed microscopically. The distance from the nearest radial resection line (unless the deep resection line is involved) should be given in the distance field on the form.

The most problematic areas of resection margin assessment are related either to diffuse tumours that are not easily visible macroscopically or to DCIS, whether alone or associated with invasive carcinoma. In the former situation it may not be easy to define the nearest resection margin and a number of blocks from the nearest area of firm fatty or fibrous tissue to this resection edge may need to be taken. Some units employ shaved resection margins or large blocks in this instance and these can be very helpful, although with the former it may not be possible to give an exact distance from the resection line.

II. DCIS and invasive carcinoma with an extensive In situ component

In the case of DCIS or invasive tumours with an extensive in situ component, it is not possible to accurately assess the distance of the in situ lesion from the nearest surgical resection line by the common method of a single block taken from the tumour to the nearest resection line such as is used for circumscribed invasive tumours. This is because of the ramifying nature of the duct system within the breast, which may contain in situ disease. This can therefore potentially extend to any resection edge of the specimen, even at some distance from the main area of calcification or invasive tumour. There are a number of methods of assessing this problem.

Undoubtedly large blocks are the best for measurement of the distance of the nearest focus of in situ carcinoma from the surgical excision line. However, they can only assess these margins two dimensionally and there is a possibility of unrecognised in situ tumour extending to the resection edge outside the plane of the large block. The previous edition of these guidelines recommended that 'pathologists take blocks from macroscopically normal tissue between an excised tumour and the margin in all three planes of section to allow comment on the extent of DCIS and its relationship to the margin' in cases of extensive in situ carcinoma. Similarly for pure DCIS, the previous guidelines stated that 'the distance from the nearest excision margin should be recorded if the lesion is sufficiently delineated. If not make a comment under 'Comments/ Additional information'. The presence of non-neoplastic breast parenchyma between the DCIS and the surgical resection line is usually associated with adequate excision.'

It now appears from the UK DCIS Trial and other studies of recurrent/residual disease post-conservation therapy that such simple rules may not be sufficient to ensure complete excision. Some units now take blocks of the major area of calcification, blocks from this area to the nearest inked resection line and then take shaved surgical margin specimens with particular reference to the nipple duct margin. It is helpful if the surgeon marks this margin especially in cases of DCIS as, although it may be some distance from the main area of calcification, it is sometimes the only margin to be involved. The specimen radiograph may also be a helpful adjunct in assessing surgical clearance although it should be borne in mind that in situ disease may be more extensive than the calcification seen mammographically, particularly for low grade disease.

6b.4.9 Steroid receptors

6b.4.9.1 Recommendations for steroid receptor testing

(Adapted from working protocol see Appendix 2)

The steroid receptor (oestrogen and progesterone receptor) status of a breast cancer is used to determine whether or not a patient will benefit from anti oestrogen treatment[45], either as adjuvant therapy or for metastatic disease. Previously, assays depended on the homogenisation of fresh tumour tissue followed by ligand or antibody binding. Immunohistochemistry is now the method of choice for assessing steroid receptor status[46]. It has the advantage that it can be used for both core biopsies and therapeutic excisions, and is widely applicable. However, any laboratory undertaking immunohistochemistry must ensure that results are highly reproducible, and can be assessed semi-quantitatively. These guidelines have been formulated to give advice.

6b.4.9.2 Principles

I. Fixation

Poor fixation will affect results, particularly for oestrogen receptor. To obtain optimum fixation it is preferable for specimens to be received as soon as possible after surgery and sliced to allow rapid and even penetration of the fixative. This should be either formal-saline or neutral buffered formalin. The rapid fixation achieved with core biopsies is a benefit.

II. Methods

1. Antigen retrieval in 0.01M citrate buffer pH 6.0 is required. The duration of antigen retrieval is critical; too short a heating time can be a major cause of poor and variable results[47].
2. Well-characterised antibodies against oestrogen receptor and progesterone receptor that have been validated against other methodologies for detecting steroid receptors e.g. ligand binding assays, should be used.
3. A sensitive detection method should be employed.
4. If changes are made to either the duration of antigen retrieval or the detection system, as new reagents become available, it is important that all antibody titres are optimised to ensure clear nuclear staining with no cytoplasmic or background reactivity.
5. The optimum method for core biopsies and resection specimens may differ and this should be taken into account when organising samples for staining.
6. Nuclear counterstaining should not obscure weak positive staining.

III. Controls

These are particularly important and must be used for each staining run. A composite block containing receptor rich, receptor poor and negative tissues should be used. Tissues to be tested should have normal breast tissue present wherever possible as well as cancer; this acts as a good internal positive control and is particularly important if fixation is sub-optimal. Negative controls should always be included. If there are any problems with the standard control or the staining of internal normal tissue, staining should be repeated. The type and grade of the carcinoma should also be taken into account since better differentiated cases are highly unlikely to be negative.

IV. Scoring

There are several different scoring systems[46,48] in place. Only nuclear staining is considered and all of the invasive component should be assessed. In order to ensure uniformity between different laboratories we recommend that the **quick (Allred) score** is used. This is based on assessment of the proportion and the average intensity of staining. For example a heterogenous tumour having 30% weak positive cells, 30% moderately staining cells and 30% strong staining cells would have an average intensity of moderate (score 2).

Score for proportion	**Score for intensity**
0 = no staining	0 = no staining
1 = < 1% nuclei staining	1 = weak staining
2 = 1-10% nuclei staining	2 = moderate staining
3 = 11-33% nuclei staining	3 = strong staining
4 = 34-66% nuclei staining	
5 = 67-100% nuclei staining	

The scores are summated to give a maximum of 8.

There are several reasons for evaluating the extent of reactivity of a carcinoma:

1. Much of the data relate to treatment of metastatic disease where it has been shown that the higher the level of receptor, the greater the chance of response to endocrine therapy.
2. Patients whose carcinomas have no evidence of staining have essentially no chance of responding to endocrine treatment.

3. Determination of progesterone receptor as well as oestrogen receptor can be of value e.g. for patients whose tumour has low oestrogen receptor, high progesterone receptor endocrine treatment is worthwhile.
4. Patients whose breast cancers have very low levels of staining (2 in quick score) benefit from adjuvant endocrine treatment[46]. This emphasises the need to have sensitive, reproducible techniques that can detect these very low levels.

Because most information comes from response in metastatic disease it is difficult to define cut-off points that are applicable to the adjuvant setting but this data will become available.

6b.4.9.3 Ductal carcinoma in situ

Trials are being introduced to determine the value of endocrine therapy in ductal carcinoma in situ and a requirement for entry will be knowledge of the oestrogen receptor status. Currently there is no scoring system as for invasive disease but a cut-off point of > 10% cells staining has been used for defining positive in the NSABP B24 trial. Until further evidence becomes available this should be used.

Adequate quality assurance in oestrogen and progesterone receptor testing is essential and participation in a standardised EQA scheme for technical aspects is mandatory to ensure accurate receptor estimation[49].

The fields for oestrogen receptor on the form should be filled in as positive or negative and a score given as above.

Optional additional fields on the form include progesterone receptor scored as for oestrogen receptor above and Her-2 if performed (see Appendix 3).

6b.4.10 Comments/additional information

Any relevant information should be entered here as free text. Please also state if any further special investigations have been undertaken such as other receptor assessment, oncogene analysis etc.

6b.4.11 Histological diagnosis

If normal, tick the box and do not complete the remainder of the form. ‘Normal’ includes minimal alterations such as fibrosis and microscopic dilatation of acini or ducts, lobular involution and enlargement and blunt duct adenosis.

If malignant and benign changes are found, tick only the ‘malignant’ box. Tick the ‘benign’ box when the breast is neither normal nor exhibits malignancy.

6b.5 Quality assurance

It is vital that laboratories are enrolled in relevant quality assurance schemes both for laboratory techniques (standard and special techniques e.g. immunohistochemistry) and diagnostic accuracy.
In countries where screening is established then external quality assurance for laboratories involved in screening should be included as part of the screening process.

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Appendix 2

Index for screening office pathology system

Term	Place to classify on form
A	
Abscess	Other benign pathology (specify)
Adenocarcinoma (no specific type)	Invasive ductal NST
Adenoid cystic carcinoma	Other primary carcinoma (specify)
Adenoma, apocrine	Other benign pathology (specify)
Adenoma intraduct	Enter as papilloma
Adenoma of nipple	Other benign pathology (specify)
Adenoma, pleomorphic	Other benign pathology (specify)
Adenoma, tubular	Fibroadenoma
Adenomyoepithelioma	Other primary carcinoma (specify), or Other benign pathology (specify)
Adenosis, NOS	Histology normal
Adenosis, apocrine	Other benign pathology (specify)
Adenosis, apocrine with atypia	Other benign pathology (specify) Epithelial proliferation-atypia (ductal)
Adenosis, blunt duct	Histology normal
Adenosis, microglandular	Other benign pathology (specify)
Adenosis, sclerosing with atypia	Sclerosing adenosis Epithelial proliferation atypia ductal or lobular
Adnexal tumours	Other benign pathology (specify)
Alveolar variant of lobular carcinoma	Invasive lobular
Aneurysm	Other benign pathology (specify)
Angiosarcoma	Other malignant tumour (specify)
Apocrine adenoma	Other benign pathology (specify)
Apocrine adenosis	Other benign pathology (specify)
Apocrine carcinoma (in situ)	Non-invasive malignant, ductal (specify type)
Apocrine carcinoma (invasive)	Other primary carcinoma (if pure) or ductal NST
Apocrine metaplasia	Fibrocystic change
Multilayered/papillary	Epithelial proliferation present
Argyrophil carcinoma	Other primary carcinoma (specify)
Arteritis	Other benign pathology (specify)
Atypical blunt duct adenosis	Columnar cell change Epithelial proliferation-atypia (ductal)
Atypical ductal hyperplasia	Epithelial proliferation-atypia (ductal)
Atypical epitheliosis (ductal)	Epithelial proliferation-atypia (ductal)
Atypical lobular hyperplasia	Epithelial proliferation-atypia (lobular)
B	
B-cell lymphoma	Other malignant tumour (specify)
Benign phyllodes tumour	Other benign pathology (specify)
Blunt duct adenosis	Histology normal
Blunt duct adenosis (atypical)	Columnar cell change Epithelial proliferation-atypia (ductal)
Breast abscess	Other benign pathology (specify)
C	
Calcification (benign)	Calcification present, benign
Calcification (malignant)	Calcification present, malignant
Carcinoma, apocrine (in situ)	Non-invasive malignant, ductal (specify type)
Carcinoma, apocrine (invasive)	Other primary carcinoma (if pure) or ductal NST
Carcinoma, clear cell	Other primary carcinoma (specify)

Carcinoma, colloid	Invasive mucinous carcinoma
Carcinoma, comedo-in situ	Non-invasive malignant, ductal (specify type)
Carcinoma, cribriform (in situ)	Non-invasive malignant, ductal (specify type)
Carcinoma, cribriform (invasive)	Invasive tubular or cribriform
Carcinoma, ductal in situ	Non-invasive malignant, ductal (specify subtype)
Carcinoma, lobular in situ	Non-invasive malignant, lobular
Carcinoma, lobular (invasive)	Invasive lobular
Carcinoma, lobular variant	Invasive lobular
Carcinoma, medullary	Invasive medullary
Carcinoma, metastatic	Other malignant tumour (specify)
Carcinoma, mixed	Other primary carcinoma (specify types)
Carcinoma, mucinous	Invasive mucinous carcinoma
Carcinoma, papillary	Other primary carcinoma (specify)
Carcinoma, signet ring	Other primary carcinoma (specify)
Carcinoma, spindle cell	Other primary carcinoma (specify)
Carcinoma, squamous	Other primary carcinoma (specify)
Carcinosarcoma	Other primary carcinoma (specify)
Cellular fibroadenoma	Fibroadenoma
Clear cell carcinoma	Other primary carcinoma (specify)
Clear cell hidradenoma	Other benign pathology (specify)
Clear cell metaplasia	Other benign pathology (specify)
Collagenous spherulosis	Other benign pathology (specify)
Columnar cell change	Columnar cell change
Columnar cell change with atypia	Columnar cell change Epithelial proliferation-atypia (ductal)
Columnar cell hyperplasia	Columnar cell change Epithelial proliferation present without atypia
Columnar cell hyperplasia with atypia	Columnar cell change Epithelial proliferation-atypia (ductal)
Comedocarcinoma	Non-invasive malignant, ductal
Comedocarcinoma invasive	Invasive ductal NST
Complex sclerosing lesion	Complex sclerosing lesion/radial scar
Cribriform carcinoma (in situ)	Non-invasive malignant, ductal (specify type)
Cribriform carcinoma (invasive)	Invasive tubular or cribriform
Cyclical menstrual changes	Histology normal
Cyst, epidermoid	Other benign pathology (specify)
Cyst, single	Solitary cyst
Cyst, multiple	Fibrocystic change
Cystic disease	Enter components
Cystic mastopathia	Enter components
Cystic hypersecretory hyperplasia	Other benign pathology (specify)
Cystic hypersecretory carcinoma	Non-invasive malignant, ductal

D

Ductal carcinoma in situ	Non-invasive malignant, ductal
Ductal carcinoma invasive	Invasive ductal NST
Ductal hyperplasia (regular)	Epithelial proliferation present without atypia
Ductal hyperplasia (atypical)	Epithelial proliferation, atypical (ductal)
Duct ectasia	Periductal mastitis/duct ectasia
Duct papilloma	Papilloma, single
Dysplasia, mammary	Enter components

E

Eccrine tumours	Other benign pathology (specify)
Epidermoid cyst	Other benign pathology (specify)
Epitheliosis (regular)	Epithelial proliferation present without atypia

Epitheliosis (atypical)	Epithelial proliferation, atypical (ductal)
Epitheliosis (infiltrating)	Complex sclerosing lesion/radial scar

F

Fat necrosis	Other benign pathology (specify)
Fibroadenoma	Fibroadenoma
Fibroadenoma, giant	Fibroadenoma
Fibroadenoma, juvenile	Fibroadenoma
Fibrocystic disease	Enter components
Fibromatosis	Other benign pathology (specify)
Fistula, mammillary	Other benign pathology (specify)
Focal lactational change	Histology normal
Foreign body reaction	Other benign pathology (specify)

G

Galactocoele	Other benign pathology (specify)
Giant fibroadenoma	Fibroadenoma
Glycogen-rich carcinoma	Other primary carcinoma (specify)
Grading of carcinomas	See Text
Granulomatous mastitis	Other benign pathology (specify)

H

Haematoma	Other benign pathology (specify)
Haemangioma	Other benign pathology (specify)
Hamartoma	Other benign pathology (specify)
Hyaline epithelial inclusions	Other benign pathology (specify)
Hyperplasia, ductal (regular)	Epithelial proliferation present without atypia
Hyperplasia, ductal (atypical)	Epithelial proliferation-atypia (ductal)
Hyperplasia, lobular (= adenosis)	Histology normal
Hyperplasia, lobular (atypical)	Epithelial proliferation-atypia (lobular)

I

Infarct	Other benign pathology (specify)
'Inflammatory carcinoma'	Specify by type (usually ductal NST)
Invasive carcinoma	Specify by type
Invasive comedocarcinoma	Invasive ductal NST
Invasive cribriform carcinoma	Invasive tubular or cribriform
Involution	Histology normal

J

Juvenile fibroadenoma	Fibroadenoma
Juvenile papillomatosis	Other benign pathology (specify)

L

Lactation	Histology normal
Lactational change, focal	Histology normal
Lipoma	Other benign pathology (specify)
Lipid-rich carcinoma	Other primary carcinoma (specify)
Lobular carcinoma in situ	Non-invasive malignant, lobular
Lobular carcinoma invasive	Invasive lobular
Lobular hyperplasia (= adenosis)	Histology normal
Lobular hyperplasia (atypical)	Epithelial proliferation-atypia (lobular)
Lymphoma	Other malignant tumour (specify)

M

Malignant phyllodes tumour	Other malignant tumour (specify)
Mammary duct ectasia	Periductal mastitis/duct ectasia
Mammillary fistula	Other benign pathology (specify)
Mastitis, acute	Other benign pathology (specify)
Mastitis, granulomatous	Other benign pathology (specify)
Mastitis, plasma cell	Periductal mastitis/duct ectasia
Mastopathia, cystic	Enter components
Medullary carcinoma	Invasive medullary
Menopausal changes	Histology normal
Metaplasia, apocrine (single layer)	Fibrocystic change
Metaplasia, apocrine Multilayered/papillary	Fibrocystic change Epithelial proliferation present
Metaplasia, clear cell	Other benign pathology (specify)
Metaplasia, mucoid	Other benign pathology (specify)
Metaplasia, squamous	Other benign pathology (specify)
Metastatic lesion	Other malignant tumour (specify)
Microcysts	Histology normal
Microglandular adenosis	Other benign pathology (specify)
Microinvasive carcinoma	Code by in situ component and specify microinvasion present
Micropapillary change	Epithelial proliferation present
Mixed carcinoma	Other primary carcinoma (specify types)
Mondor's disease	Other benign pathology (specify)
Mucinous carcinoma	Invasive mucinous carcinoma
Mucoele-like lesion	Other benign pathology (specify)
Mucoid metaplasia	Other benign pathology (specify)
Multiple papilloma syndrome	Papilloma, multiple
Multiple papilloma syndrome with atypia	Papilloma, multiple Epithelial proliferation-atypia (ductal)
Myoepithelial hyperplasia	Other benign pathology (specify)

N

Necrosis, fat	Other benign pathology (specify)
Nipple adenoma	Other benign pathology (specify)
Nipple - Paget's disease	Non-invasive malignant Paget's disease
Normal breast	Histology normal

P

Paget's disease of nipple	Non-invasive malignant, Paget's disease
Panniculitis	Other benign pathology (specify)
Papillary carcinoma (in situ)	Non-invasive malignant, ductal (specify type)
Papillary carcinoma (invasive)	Other primary carcinoma (specify)
Papilloma, duct	Papilloma
Papillomatosis	Epithelial proliferation (with or without atypia)
Papillomatosis, juvenile	Other benign pathology (specify)
Papillomatosis, sclerosing	Other benign pathology (specify)
Phyllodes tumour (low grade)	Other benign pathology (specify)
Phyllodes tumour (high grade)	Other malignant tumour (specify)
Pregnancy changes	Histology normal

R

Radial scar	Complex sclerosing lesion/radial scar
Regular hyperplasia	Epithelial proliferation present without atypia

S	
Sarcoidosis	Other benign pathology (specify)
Sarcoma	Other malignant tumour (specify)
Sclerosing adenosis	Sclerosing adenosis
Sclerosing adenosis with atypia	Sclerosing adenosis Epithelial proliferation-atypia
Sclerosing subareolar proliferation	Specify under other benign pathology as adenoma of nipple
Squamous carcinoma	Invasive malignant, other (specify)
Squamous metaplasia	Other benign pathology (specify)
Spindle cell carcinoma	Invasive malignant, other (specify)
Scar, radial	Complex sclerosing lesion/radial scar
T	
Trauma	Other benign pathology (specify)
Tuberculosis	Other benign pathology (specify)
Tubular adenoma	Fibrodenoma
Tubular carcinoma	Invasive malignant, tubular or cribriform
W	
Wegener's granulomatosis	Other benign pathology (specify)

Appendix 3

Immunohistochemical detection of steroid receptors in breast cancer

A Working Protocol Produced By The Uk Receptor Group, Uk Neqas, The Scottish Breast Cancer Pathology Group And The Receptor And Biomarker Study Group Of The EORTC

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Appendix 4

Recommendations for HER2 testing

A4.1 Introduction

The humanised anti-HER-2/neu (also known as c-erbB-2, further denoted HER2) monoclonal antibody trastuzumab (Herceptin)[1], has recently been endorsed for the treatment of metastatic disease[2, 3] Establishing tumour HER2 status is a prerequisite for the use of trastuzumab[1, 2, 4]. These guidelines, based on the updated UK guidelines[5] and on a review of National Testing Guidelines[6], have been formulated to give advice on methodology and quality assurance for local testing to ensure that HER2 testing results are accurate and reliable, regardless of the test that is used.

A4.2 General principles

A4.2.1 Suitable samples

Formalin fixed paraffin embedded tumour tissue samples are appropriate for assay [7,8,9,10,11,12]. Ideally buffered formalin should be used for fixation, use of Bouin's fixative will preclude testing by fluorescence in situ based methods. Other methods of tissue fixation can also adversely affect antigen reactivity.

A4.2.2 Caseload

Laboratories providing a testing service should be carrying out a minimum of 250 assays per year for immunohistochemical detection of HER2. There is evidence of higher consistency of assay quality when tests are performed by high volume reference laboratories[13, 14]. This target level has also been set to ensure continuing expertise of assay providers.

Centres with low numbers of cases < 250 p.a. requiring IHC assay should consider using a reference laboratory service.

Similar principles apply to FISH testing and it is recommended that laboratories testing < 100 cases per year consider referral of their workload to a reference laboratory. A smaller caseload has been set for FISH assay as it is generally accepted to be a more discriminant test at the positive negative-borderline, has greater ease of methodological standardisation and less observer variation.

A4.2.3 Appropriate laboratory assay methods

Immunohistochemistry (IHC) and fluorescent in situ hybridisation (FISH) [8, 9, 10, 11, 12, 15, 16] are the techniques recommended for determining HER2 status. Currently, other available HER2 testing techniques (CISH, polymerase chain reaction, enzyme-linked immunosorbent assay, Southern blotting) should be used for research only.

For both immunohistochemical and FISH based HER2 testing, comprehensive standardisation of methodology, including monitoring of scoring procedures and the inclusion of validated controls are mandatory. In the UK, participation and satisfactory performance in the current NEQAS scheme for IHC and the forthcoming NEQAS scheme for HER2 FISH is a requirement. These schemes are open to laboratories across Europe and participation in a recognised EQA scheme is advised. Although published data support the use of FISH for the selection of patients most likely to respond to trastuzumab, many protocols allow treatment of patients with tumours strongly staining by IHC. Worldwide there remains an ongoing debate as to whether laboratories should switch to the use of FISH for all specimens, removing the need for a second tier of testing to identify HER2 positive cases, or whether laboratories should adopt a two tier testing. Current results from reference centres suggest that there is a very high level of correlation between IHC and FISH assay results in the 0/1+ and 3+ IHC categories, negating the need for dual IHC and FISH based assay in the majority of cases[17], however other published studies show higher rates of discordance. Caution may be needed before extrapolating the experience of reference centres

to laboratories with lower case loads.
It is logical, in the light of published data, to use FISH as a secondary test in the equivocal (2+) IHC category to clarify the HER2 status of these cases, however, once trastuzumab is licensed for both FISH and IHC positive cases it is possible that any advantage of the current two tier testing system will be scrutinised. In this case, as at present in other countries, some laboratories will choose to use FISH as a front line diagnostic test without the use of IHC. It is also expected that emerging data on accuracy of prediction of response to HER2 targeted therapies will influence the choice of testing method.
In summary, the current recommendations are for a two tier testing strategy, but this does not preclude laboratories from using primary FISH testing.

A4.2.4 Controls

The inclusion of controls and their detailed scrutiny are essential to ensure test accuracy. A recommended positive control or controls producing results close to important decision making points and a negative control are recommended.

Cell line preparations containing multiple samples of known HER2 status characterised by FISH and IHC are useful as controls[18]. Where possible tissue based controls, preferably from breast cancers, should also be used in all assay runs.

Excessive antigen retrieval can be monitored by an evaluation of normal breast epithelial cells as an internal control. Should membrane reactivity be identified in the normal cell population, excessive antigen retrieval may have occurred and re-testing of the entire run should be considered.

A4.2.5 Evaluation

For assessment of both IHC and FISH preparations, training and experience in interpretation of histological characteristics of breast tissue is essential. Recognition of different histological tumour types is required. In particular HER2 status should only be determined on the invasive portion of the tumour and IHC positivity or FISH amplification should not be reported as a positive result in isolation. Image analysis systems are currently under investigation and may provide alternatives to manual scoring for both IHC and FISH in the future. At present insufficient evidence is available to recommend their routine use in the diagnostic setting.

A4.2.5.1 Immunohistochemistry

For all IHC tests, antigen retrieval processes are critical, must be standardised and follow strict protocols. The antibody used and its titre should be predefined. Standardisation can be achieved using commercial assay systems such as the Herceptest (DakoCytomation). For in-house assays no single antibody has been consistently demonstrated to be superior in terms of specificity and sensitivity. At present, antibody clones CB11 (Novocastra, Newcastle upon Tyne, UK), TAB 250 (Zymed, San Francisco, California, USA) and polyclonal anti-sera A0485 (DakoCytomation, Ely, Cambridgeshire, UK) are the most widely used for all assay methods. Test conditions (temperature, exposure time, etc) should be standardised[19].

I. Validation Of Standardised Assay Method

Test conditions should be optimised so that distinct moderate or strong membrane staining identifies FISH positive samples. This can be achieved by:

1. Dual IHC and FISH assay of a contemporary series of breast carcinomas. (Minimum 100 cases). Use of tumour tissue array blocks for this purpose may reduce costs. FISH assay can be confined to those cases demonstrating membrane reactivity (1, 2 or 3+).
2. The use of tumour tissue array blocks for validation may reduce costs. It may be possible to obtain such sections, which have already been scored for IHC and FISH, from a research laboratory or reference source.

Laboratories not wishing to standardise in-house methodology should consider using a commercial kit assay system such as the Herceptest (DakoCytomation).

II. Scoring IHC

Only membrane staining of the invasive tumour should be considered when scoring IHC tests. If a commercial kit assay system is used, it is recommended that laboratories adhere strictly to the kit assay protocol and scoring methodology. Local modifications of techniques can lead to false positive and negative assay results. The scoring method recommended is a semi-quantitative system based on the intensity of reaction product and percentage of membrane positive cells, giving a score range of 0-3+. Samples scoring 3+ are regarded as unequivocally positive and 0/1+ as negative. Borderline 2+ results require confirmation using another analysis system, ideally FISH.

Non commercial kit assay methods can be scored on a similar basis or by modification to a 3 tier system of positive, borderline and negative. Until better evidence on scoring methodology emerges, the cut off points for such simplified assay scoring systems should be based on the existing HercepTest kit method with a positive score being based on 3+ score, borderline 2+ score and negative 1+ or 0 score.

Inter-observer variation in the assessment of staining can lead to misclassification of HER2 status[20]. Each individual assessor should standardise scoring against known positive, negative and borderline cases. It is also preferable to assess comparability of scoring with a colleague on a regular basis.

III. Quality assurance

All clinical laboratories utilising assays for HER2 as predictive or prognostic tests must participate in an appropriate external quality assurance (EQA) programme.

A4.2.5.2 Fluorescence in situ hybridisation (FISH)

FISH testing for HER2 should meet the following criteria:

1. Comprehensive standardisation of methodology.
2. Validated controls. The inclusion of a chromosome 17 control to allow for correction of the HER2 signal number for chromosome 17 aneusomy (seen in over 50% of cases) is considered beneficial by many laboratories and is recommended.
3. Validated scoring procedures.

I. General principles

There is no evidence that storage of blocks leads to deterioration of signal. It is recommended that storage of cut sections from controls or samples for over 6 to 12 months should be avoided.

It is advisable to locate areas of invasive tumour using a serial section stained with haematoxylin and eosin (H&E) and to use this to locate tumour areas to be scored after testing. Care should be taken to avoid areas of ductal carcinoma in situ, which can show amplification even when adjacent invasive tumour cells are negative. With experience such features can be identified under fluorescence microscopy, however the use of serial H&E sections is essential should there be any uncertainty in this area.

Tissue digestion should be standardised to maintain nuclear morphology and should follow strict protocols[21]. Some laboratories find it helpful to evaluate nuclear structure before hybridisation and adjust digestion, where appropriate, to preserve nuclear integrity. This may be particularly valuable with difficult sections, cytology samples, bone biopsies etc. Evaluation of sections before hybridisation can also improve efficiency and is recommended. Hybridisation and washing steps should be standardised. Guidance can be provided by reference laboratories. Use of automated tissue processors and standardised commercial tissue digestion kits can improve consistency and should be considered.

It is recommended that commercially available probes are used. For systems using in-house nick-translated probes, attention should be given to batch variability of nick translation enzymes, etc.

Laboratories not wishing to use in-house methods should consider using a commercial system such as PathVysion (Abbott Vysis). Other commercial systems currently available, are not yet widely validated or lack the chromosome 17 control discussed above.

II. Scoring FISH

HER2 FISH testing results are conventionally expressed as the ratio of HER2 signal to chromosome 17 signal. Tumours showing a ratio of > 2 should be considered positive. Cut off values for HER2 gene amplification when chromosome 17 probes are not used have not been established.

The number of chromosome 17 and HER2 signals is scored for between 20-60 cells, where possible using at least three distinct tumour fields, and the mean HER2 to chromosome 17 copy ratio is calculated. In most cases where either clear amplification is observed or the ratio is below 1.5 scoring of 20 cells is sufficient. In cases where either tumour heterogeneity is seen (1-2% of cases) or the ratio is close to 2.0 (between 1.5-2.3) more cells should be scored (up to 60). Samples with > 2.0 copies of HER2 for each chromosome 17 are considered to be amplified. Published data suggests that inter-observer variation is significantly lower for FISH than for IHC. However, especially when developing a new service, care needs to be taken. The recommendation is that laboratories should perform validation studies by dual observer scoring when training new staff until inter-observer variation for normal specimens and those with low level amplification is routinely below 15%. Continued monitoring of scoring offers advantages in quality control and training but is not a requirement. Variation increases with highly amplified samples, and is not critical where the ratio exceeds 4.

III. Quality assurance

To ensure adequate quality assurance, laboratories wishing to set up independent FISH testing are recommended to join an EQA scheme.

A good current review of the Her-2 literature can be found on http://www.mcponline.org[22].

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Appendix 5

Definitions of the pTNM categories

pTx Primary tumour cannot be assessed
pT0 No evidence of primary tumour
pTis Carcinoma in situ
- **pTis(DCIS)** ductal carcinoma in situ
- **pTis(LCIS)** lobular carcinoma in situ
- **pTis(Paget)** Paget's disease of the nipple with no tumour (Note: if there is an associated tumour, the disease is classified on the basis of the size of that tumour)

pT1 Tumour 2 cm or less in greatest dimension
- **pT1mic** Microinvasion 0.1 cm or less in greatest dimension
- **pT1a** (If associated with in situ carcinoma, more than 0.1 cm) but not more than 0.5 cm in greatest dimension
- **pT1b** More than 0.5 cm but not more than 1 cm in greatest dimension
- **pT1c** More than 1 cm but not more than 2 cm in greatest dimension

pT2 More than 2 cm but not more than 5 cm in greatest dimension
pT3 Tumour more than 5 cm in greatest dimension
pT4 Tumour of any size with direct extension to chest wall or skin only as described in pT4a to pT4d
- **pT4a** Extension to chest wall
- **pT4b** Oedema (including peau d'orange), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
- **pT4c** Both pT4a and pT4b
- **pT4d** Inflammatory carcinoma

pNx Regional lymph nodes cannot be assessed (not removed for study or previously removed)
pN0 No regional lymph node metastasis
pN1mi Micrometastasis (larger than 0.2 mm, but none larger than 2 mm in greatest dimension)
pN1 Metastasis in 1-3 ipsilateral axillary lymph node(s), and/or in ipsilateral internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent (i.e. not detected by clinical examination or imaging studies excluding lymphoscintigraphy)
- **pN1a** Metastasis in 1-3 axillary lymph node(s), including at least one larger than 2 mm in greatest dimension
- **pN1b** Internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent
- **pN1c** Metastasis in 1-3 axillary lymph nodes and internal mammary lymph nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent

pN2 Metastasis in 4-9 ipsilateral axillary lymph nodes, or in clinically apparent ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis
- **pN2a** Metastasis in 4-9 axillary lymph nodes, or including at least one that is larger than 2 mm
- **pN2b** Metastasis in clinically apparent internal mammary lymph node(s) in the absence of axillary lymph node metastasis

pN3 Metastasis in 10 or more ipsilateral axillary lymph nodes; or in ipsilateral infraclavicular lymph nodes; or in clinically apparent ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes; or in more than 3 axillary lymph nodes with clinically negative, microscopic metastasis in internal mammary lymph nodes; or in ipsilateral supraclavicular lymph nodes
- **pN3a** Metastasis in 10 or more axillary lymph nodes (at least one larger than 2 mm) or metastasis in infraclavicular lymph nodes
- **pN3b** Metastasis in clinically apparent internal mammary lymph node(s) in the presence of positive axillary lymph node(s); or metastasis in more than 3 axillary lymph nodes and in internal mammary lymph

nodes with microscopic metastasis detected by sentinel lymph node dissection but not clinically apparent

pN3c Metastasis in supraclavicular lymph node(s)

Mx Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis

The pN categories of the TNM classification and advice on how to use them

Number of metastatic axillary lymph nodes	Metastases in internal mammary (parasternal) lymph nodes	Others[1]	pN categories, subgroups[2]
		Lymph nodes are not assessable (eg. previous removal, lack of removal)	pNx
		Lymph node(s) containing isolated tumour cells (ITC) only	pN0(i+)[3]
		0.2 mm < metastasis ≤ 2 mm	pN1mi[4]
0	None (unknown)	No regional lymph node metastasis	pN0
	Microscopically detected[5]		pN1b[6]
	Clinically evident[7]		pN2b
1-3	None (unknown)		pN1a[4]
	Microscopically detected[5]		pN1c
	Clinically evident[7]		pN3b
4-9	None (unknown)		pN2a
	Microscopically detected[5]		pN3b
	Clinically evident[7]		pN3b
≥10	None (unknown)		pN3a
	Microscopically detected[5]		pN3b
	Clinically evident[7]		pN3b
		Infraclavicular lymph node metastasis	pN3a
		Supraclavicular lymph node metastasis	pN3c[8]

The table has been prepared on the basis of the TNM classification of malignant tumours 6th edition.

1. Factors defining pN categories others than those reported under the statuses of axillary and parasternal lymph nodes in the first two columns.
2. The use of subgroups makes the classification of tumours more precise.
3. The pN0(i+) category was variously defined, but now there is consensus that its meaning is 'No regional lymph node metastasis histologically, **positive morphological findings** for ITC', therefore microscopically identified ITC are given a category pN0(i+) independently of their detection by e.g. serial sectioning and HE staining or immunohistochemistry. The subcategory pN0(i-) denotes negative findings after special morphological investigation (e.g. step sectioning or immunohistochemistry) for ITC. pN0(mol+) has also been defined: this relates to the positivity of molecular markers (e.g. RT-PCR or flow cytometry) of regional nodal involvement by ITC, but negative morphological findings. pN0(mol-) in this setting defines those node negative cases that have no metastasis histologically and are negative for ITC with non-morphological methods.
4. Micrometastasis was defined as pN1a in the 5th edition of the TNM classification, and this has a different meaning in the 6th edition. Whenever any of the metastases is greater than this, the largest metastasis should be used to classify the tumour.
5. Clinically not evident, e.g. identified via sentinel lymph node biopsy or internal mammary sampling.
6. In the 5th edition of the TNM classification pN1b referred to macrometastases (metastases >2 mm).
7. Detected by physical examination, imaging (excluding lymphoscintigraphy) or macroscopic pathologic examination.
8. In the previous edition supraclavicular lymph node metastasis was classified M1.

If only sentinel lymph node biopsy was used for staging, the (sn) symbol is to be put after the pN category; the use of (sn) is inappropriate if axillary clearance was also performed.

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7

Quality assurance guidelines for surgery

7a *European guidelines for quality assurance in the surgical management of mammographically detected lesions*

7b *Quality control in the locoregional treatment of breast cancer*

The third edition of these Guidelines were screening orientated and describe the relevant surgical aspects of dealing with screen detected lesions. This chapter has now been updated. The fourth edition is designed to cover aspects of breast care and diagnosis, as well as screening. Accordingly we have supplemented this chapter with the addition of the previously published EUSOMA document on quality control in the locoregional treatment of breast cancer.

7a

Quality assurance guidelines for surgery

European guidelines for quality assurance in the surgical management of mammographically detected lesions

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Preface

European Guidelines developed for mammography screening have contributed to the general discussion on quality assurance and on the important tasks of the health professionals dealing with breast cancer screening. The cooperation of each medical discipline is of utmost importance in order to achieve optimal results and eventually a mortality reduction. These guidelines are based on the British NHS quality assurance guidelines for surgeons in breast cancer screening. They are based on several meetings held during 1997 under the auspices and with the support of the Europe Against Cancer Program of the European Commission and with the support and participation of representatives of the European Society of Surgical Oncology and the national surgical oncology groups in Europe. In June 2003, the European parliament decided in an official political decision and call to the member states, to support this strategy. To create, by 2008, the conditions required for a 25% reduction in the breast cancer mortality rate in the EU and, at the same time, for a reduction to 5% in the disparity in the survival rates between the Member States. This can currently be as high as 16%.

7a.1 Introduction

Mortality reduction for breast cancer is the ultimate endpoint of any screening programme. To meet this endpoint, it is essential that all elements of the screening service achieve and maintain high levels of quality if it is to be of significant benefit to women. The screening process can only be successful if followed by timely and appropriate management by surgeons.

These guidelines for surgeons are set out to identify quality objectives and targets, to suggest a framework for surgical quality assurance and to put forward ways in which the quality of performance of each surgical unit can be measured.
Some of the general quality assurance objectives and standards lie outside the influence of the surgeon alone, but the surgeon is a member of the multidisciplinary breast screening team responsible for achieving these objectives. The quality assurance standards achieved should be monitored by the responsible surgeon and one surgeon should be responsible for quality assurance audit in his/her centre.

These guidelines should be periodically reviewed. The service should be consultant based. Assessment clinics and specialist operations e.g. marker-guided biopsy, should not be delegated to unsupervised trainees.

The surgeon must have sufficient identified operating times for cases arising from the screening programme. This time depends on the population covered but should be at least one operating list per week for a screening population of 41,000 (based on the average size of a screening unit as recommended in the UK original guidelines). The surgeon should have access to cytology/histopathology services, which conform to established quality assurance guidelines.

7a.2 General performance of a breast screening unit

The surgeon is a member of a multidisciplinary team. He/she expects the availability and close communication with professionals with specialist knowledge in imaging techniques, plastic and reconstructive surgery, pathology, radiotherapy, medical oncology, specialist nursing, psychological guidance and counseling - all conforming to established quality assurance guidelines. Conversely, the patients and the other members of the team expect specialist knowledge in the surgical management of screen-detected lesions from the surgeon. Regular multidisciplinary review meetings involving surgeons, radiologists, medical oncologists and pathologists are essential for audit and represent a fundamental part of quality assurance guidelines for all disciplines involved in the screening process.
Breast Units should be able to report on long-term outcome measures in treating women with breast cancer. These measures include information on local and regional recurrence, long-term morbidity following the primary treatment, metastatic disease and death. In June 2003, the European parliament decided in an official political decision and call to the member states, to support the need for multidisciplinary breast centres throughout the EU. In Member States, where such breast centres already exist, studies have shown, that women have better chances of being cured.

The interval from the screening mammogram to assessment should be minimised, so that 90% of patients attend an assessment centre within one week of the decision that further investigation is necessary, and within three weeks of attendance for the screening mammogram.

The number of small (less than 15 mm in diameter) invasive cancers should be at a minimum of 50% of invasive cancers detected at screening.

The surgeon should be fully involved in the assessment of screen-detected cancers and he/she should always see the patient before accepting her for surgery. No more than one week should elapse between the first recall appointment and an appointment for surgical assessment.

7a.3 Surgical diagnosis

The majority (more than 70%) of both palpable and impalpable cancers should receive a pre-operative diagnosis by fine needle cytology or core needle histology. Core needle histology can provide more detailed information as to whether the lesion is benign or malignant, its tumour invasiveness and grade in addition to other biological features, such as receptor status.

Unnecessary surgical excision should be minimised. For open surgical biopsies the ratio of benign to malignant should not exceed 0.5 to 1.

The operative identification (i.e. successful removal) of lesions producing mammographic abnormalities should be successful in more than 95% of impalpable lesions at the first localisation biopsy operation. In 90% of cases with clear malignant diagnosis, the definitive surgical treatment should be performed in one operation.
The standard approach to tumour localisation has been hook wire. An ultrasound- or mammographic-guided hook wire is inserted in the breast and placed by the radiologist within 1 cm from the lesion, in at least 90% of cases. Other techniques of localisation are possible, such as a) ROLL (Radioguided Occult Lesion Localisation) which includes the use of 99m Tc-labelled colloid particles of human serum albumin injected in the center of the suspicious lesion and detected intraoperatively using a gamma detecting probe, b) the use of charcoal suspension injected under stereotactic or ultrasound examination and, c) insertion of stainless steel marker at the time of the core biopsy, using an ultrasound device for identification intraoperatively.
Surgeons are encouraged to familiarize themselves with the use of ultrasound for the intraoperative localization of suspicious lesions.
The surgeon should remove the radiological lesion with a certain additional amount of grossly free margin. The correct identification and removal of the radiological lesion must be confirmed by the presence of the lesion on specimen radiography, which is mandatory in cases of microcalcifications. This procedure should be carried out by the staff of the radiological department, so that the radiologist can determine whether the relevant lesion has been excised. There will be a few occasions when the mammographic abnormality cannot be identified in the specimen. This may result from the excision of a lesion producing only change in the clinical mammogram or from unsuccessful surgical localisation. Detailed pathological examination, including radiology of the sliced specimen, should still be undertaken and the findings communicated to the surgeon. Clinical mammography must subsequently be repeated to determine if the lesion is still present in the breast following multidisciplinary review.
Frozen sectioning is generally inappropriate in the assessment of clinically impalpable lesions. Rarely, however, it may be justified to enable a firm diagnosis of invasive carcinoma to be made in order to allow definitive surgery to be carried out in one operation. **Three essential criteria, however, must be fulfilled:**

1. The mammographic abnormality must be clearly and unequivocally identified on macroscopic examination.
2. It must be large enough (generally at least 10 mm) to allow an adequate proportion of the lesion to be fixed and processed without prior freezing.
3. It must have proved impossible to make a definitive diagnosis pre-operatively.

The surgeon should be discouraged from cutting the specimen open after removal before sending it to the pathologist. The specimen should be marked according to local protocols. The pathologist should perform the definitive written diagnosis and description in 90% of cases in the time of one working week. The interval from the surgeon's decision to operate for diagnostic purposes and the first offered admission date should be minimised. Waiting time for operation should not exceed two weeks in 90% of patients in order to reduce patient anxiety.

To minimise the adverse cosmetic effects of operative biopsies carried out for diagnostic (not therapeutic) purposes placement and length of the incision should be considered. Ninety percent of those biopsies that prove benign should weigh less than 30 grams fresh or fixed weight. It is recommended that the surgeon ensure that the weight is recorded.

7a.4 Management

The surgical treatment of screen-detected cancers should follow the same guidelines for treating symptomatic breast cancer that is total removal of the malignant lesion with clear margins. For patients with a pre-operative diagnosis, the surgeon should endeavour to obtain a clear margin and to obtain a rim of uninvolved breast tissue around the primary lesion. The minimal distance from the primary lesion to the margins should be clearly documented by the pathologist. Standard descriptions by the pathologist should be tumor size, grading, typing, resection margins, biological characterisation, the sentinel lymphnode(s) and/or the histological evaluation of all nodes with the number of positive nodes numerically compared to the examined nodes.

All surgeons involved in the treatment of screen-detected cancers must be aware that different treatment options are available for each woman, so that overtreatment or undertreatment is avoided. Breast conserving surgery is the treatment of choice for the majority of small sized screen-detected cancers, and should be provided in 70-80% over all cases.

Every woman should receive information on treatment options (breast conserving surgery versus total mastectomy). The patient, where appropriate, should be offered a choice of treatment, including immediate or delayed breast reconstruction. She may also be offered allocation of treatment within a clinical trial. A specialist breast care nurse should be present when the diagnosis of cancer is given.

The surgeon should ensure completeness of excision. Specimens must be orientated by the surgeon. Intra-operative assessment of margins may be improved by the use of two-plane specimen radiography in order to facilitate re-excision of margins which are too close to the tumour in one operation.

The surgeon should aim at minimising the number of operations carried out for therapeutic purposes in patients with proven pre-operative or intra-operative diagnosis of cancer (in situ to invasive). Thus repeat operations needed after incomplete excision should be reduced to a minimum and should not exceed 10%.

Sentinel node technology has transformed the management of the axilla in patients with mammographically-detected breast cancer. Identification, removal and analysis of the sentinel node or nodes has significantly reduced the need for complete axillary dissection in patients whose sentinel node is uninvolved by metastatic breast cancer. The sentinel node can be identified by injection of blue dye, by the injection of radio-isotope or by using both methods. The combination of blue dye and isotope increases the accuracy of sentinel node detection, but the major success of each technique depends upon the experience of the surgeon. When the histological diagnosis confirms the presence of axillary node metastasis, axillary dissection is generally recommended. Evolving techniques of increasing sophistication for detecting the presence of isolated tumour cells in axillary lymph nodes remain under evaluation. In particular, uncertainty exists about the management of patients whose sentinel node is demonstrated to be clear on routine histology but proven to be affected by tumour cells when examined by immunohistochemistry. As the accuracy in identifying the sentinel node improves with practice and training, all surgeons undertaking this procedure should receive specific training and each surgeon should have the accuracy of his or her sentinel node experience validated.

When breast conserving surgery is selected, radiation therapy to the conserved breast is indicated for most invasive tumours. Systemic treatment should be considered for all patients tailored according to individual prognostic factors.

Local excision is not considered appropriate for extensive, multicentric DCIS lesions which cannot be excised with clear margins and cosmetically acceptable results. Axillary dissection is contraindicated. In cases of high-grade or extensive DCIS where there is concern about the possibility of microinvasion, evaluation of the axilla by sentinel node biopsy is being utilised increasingly and is under active evaluation.

Following breast conservation surgery for DCIS, radiotherapy to the conserved breast is recommended.

After diagnosis of lobular carcinoma in situ (LCIS) in a surgical excision, the need for careful surveillance rather than further surgical intervention is recommended.

The interval from a surgical decision to operate for therapeutic purposes (i.e. where there is a pre-operative definitive diagnosis of cancer) and the first offered admission date should be minimised so that 90% of patients should be offered surgical treatment within three weeks of informing the patients who need surgical management.

7a.5 Follow up

Adequate follow up of screen-detected cancers must be ensured, so that all women diagnosed with cancer and appropriately treated should be examined at least at annual intervals. The surgeon, as an active member of the screening unit, should be involved in the follow up process. Each screening centre must nominate a surgeon responsible for recording of the audit procedures for breast cancer screening, treatment and outcome, to generate reports on these issues and to report annually on results. The surgeon must be given clerical help as the collection of this data is mandatory. Mammography of the treated and/or contralateral breast to a radiological standard equivalent to that performed within the screening programme should be included.

Extensive laboratory investigation, including multiple tumour markers, is not necessary for asymptomatic patients.

Follow up should be audited according to an agreed standard.

7a.6 Training

The management of cases coming to surgery from the screening programme should be carried out only by surgeons who have acquired the necessary specialist knowledge. All surgeons treating patients with breast cancer should have developed a special expertise and have undergone specific formal training in a multidisciplinary program, which should include courses in communication and counselling. No surgeon should undertake ultrasound of the breast without appropriate training.

7a.7 Bibliography

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7b

Quality assurance guidelines for surgery

Quality control in the locoregional treatment of breast cancer

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7b.1 Introduction

This document provides guidelines for the control of the quality of locoregional treatment of invasive breast cancer.
This document does not provide specific treatment guidelines, but tries to set out the objectives which locoregional treatment in breast cancer should meet, and to determine the outcome measures to these objectives. This document is partly based on the guidelines for symptomatic breast disease of the British Association of Sugical Oncology (BASO) Breast Group[1], the European Society of Surgical Oncology (ESSO) principles and guidelines for surgeons in the management of symptomatic breast cancer[2], the European guidelines for quality assurance in the surgical management of mammographically-detected lesions[3]. As the measurement of outcome is an essential part of the quality control process, prospective registration of all relevant clinical, treatment-related and follow-up data on patients is mandatory[4]. The input criteria are mentioned in the text as operational procedures. Next, this document describes the most relevant outcome measures related to the quality of the locoregional treatment.
It should be stated here that breast cancer should be diagnosed and treated in a comprehensive environment as described in the EUSOMA document 'The requirements of a specialist breast unit'[5].

7b.2 Diagnosis of the primary lesion

Statement: The surgeon should aim to treat invasive breast cancer either:

1. If the triple diagnosis (including fine needle aspiration (FNA) result C-5) is concordant with invasive breast cancer, or
2. A core-biopsy shows invasive breast cancer, or
3. An in- or excisional biopsy shows invasive breast cancer (note: this procedure is not recommended as an initial step in the diagnosis of breast cancer).

The diagnostic work-up of patients with breast abnormalities should be performed as described in the EUSOMA document 'Diagnosis of breast cancer'[6].
For locoregional treatment, the following diagnostic steps should be taken in every patient suspected to have invasive breast cancer. The diagnosis is based on the triple assessment:

- Physical examination (by a surgeon)
- Bilateral mammography in two projections
- Ultrasound for symptomatic lesions and for clinical occult mammographically-detected densities
- FNA cytology/core biopsy (depending on the expertise and availability)

Results of diagnostic tests must have been discussed in the multidisciplinary team[6, 7]. After diagnosis of breast cancer, patients must have had a full explanation of the treatment options. In general, the surgeon can be considered as the coordinator of the patient with breast cancer during her diagnostic process, treatment and follow-up.

Outcome measure:	In over 95% of the patients with palpable breast cancer triple assessment is performed.
Outcome measure:	More than 90% of patients subsequently proven to have breast cancer should have a pre-operative FNA or core biopsy at the diagnosis of cancer.
Outcome measure:	More than 70% of patients subsequently proven to have clinically occult breast cancer should have had a pre-operative FNA/core biopsy that is diagnostic for cancer.

7b.3 Diagnosis of distant disease

No evidence exists that any subset of tests is sufficiently accurate to exclude distant disease in primary operable breast cancer[8]. Therefore any tests will be performed on indication of symptoms and extent of local disease.
For patients with tumours suitable for primary surgery, with no clinical evidence of dissemination, a preoperative screening test should be chest X-ray, full blood count and liver function tests. For patients with clinically involved axillary nodes or being considered for neo-adjuvant therapy by the size and extent of the primary tumour, further screening tests should be arranged. These include liver imaging (computed tomography (CT)-scan or ultra sound) and skeletal survey (bone scan); tumour markers are optional.

7b.4 Surgery of the breast

Statement: Surgery for breast cancer must be carried out or directly supervised by a fully trained surgeon, specialised in breast surgery[1, 2, 7, 9].

The aim of surgery in invasive breast cancer is to achieve tumour-free margins with the least possible mutilation, in accordance with the needs of the well informed patient. To reach this goal, the surgeons must be seen after an optimal pre-operative imaging process, depending on the clinical problem.
The results of imaging should be available in the operating theatre. The surgeon must have seen the patient before any surgery and have been completely informed about the clinical situation of the patient.
Patients where breast conserving therapy (BCT) seems feasible, must have been informed about the options: BCT, mastectomy and/or immediate reconstruction.
In cases of clinically-occult lesions or doubts of the location of the tumour, pre-operative localisation guided by ultrasound or stereotactic mammography equipment is mandatory.
The pre-operative histological or cytological diagnosis of malignant lesions improve the quality and completeness of therapeutical excisional biopsies (lumpectomies)[6, 9]. Bracketing wires facilitate the completeness of excison of microcalcifications. Local excision in BCT aims at tumour-free margins and – as good as possible – cosmetic outcome. Consequently, the size of the lesion, i.e. the size of the excision, is limited and related to the size of the breast. No upper size limit for BCT for invasive cancer can be given.
The surgeon should aim to perform wide local excision in one complete specimen and mark the specimen for the pathologist. Margin assessment is preferably performed in one complete specimen. Margin assessment by so-called touch prep-imprint-cytology or random shave biopsies from the cavity might be helpful, but has not proven to be superior over a complete careful assessment of the wide local excision specimen.
Incisions are placed to ensure best possible cosmetic result and the possibility of mastectomy should be taken into account. Closure of breast tissue, use of drains and closure of skin depends on local anatomy, width of excision and location of the tumour in the breast. Every measure should be taken to achieve the best possible cosmetic result[10].

Outcome measure:	Every patient with an invasive cancer considered to be suitable for breast conservation must have had information about the possibility of BCT.
Outcome measure:	Over 90% of women having conservation surgery should have 3 or less therapeutic operations.

7b.5 Breast conserving treatment

BCT is a combination of a surgical excison aiming at microscopically-free margins and of radiotherapy of the breast. It generally applies to small (arbitrarily up to 4 cm) unifocal invasive breast cancer. The aims are:

1. To achieve local control
2. To preserve breast cosmesis

The requirements for breast surgery are described in the previous paragraph. In breast conservation, the surgeon aims at 1 cm free margins.
Requirements for breast radiotherapy are:

- High energy photons
- Simulation and treatment planning
- Use of appropriate beam modifiers to achieve homogeneity of dose distribution: dose should not exceed 110% and should not be under 95% of the prescribed dose
- Avoidance of heart, lung and contralateral breast irradiation
- Interval between surgery and initiation of radiotherapy should preferably not exceed 8 weeks

Indications for BCT should take into account the risk factors for local recurrence and the determinants for cosmetic outcome[11, 12].
The aim for BCT is to keep the breast relapse rate of invasive cancer less then 1 - 2% per annum follow-up (< 15% at 10 years)[13, 14]. If known risk factors indicate a higher risk for breast relapse (young age, incompletely excised infiltrating or in situ cancer, impossibility to deliver an adequate dose of radiation therapy), either a re-excision (when cosmetically feasible) or mastectomy has to be considered[15].

Outcome measure:	The breast relapse rate for invasive cancer after BCT should not exceed 15% at 10 years.
Outcome measure:	Excellent or good cosmetic result from a patient's point of view should be at least 80% at 3 years.

Recommendation: As radiation therapy substantially improves breast tumour control (by a factor of 2 - 3), every patient (> 95%) with invasive cancer who have had breast conservation surgery must have had a consultation with a radiation oncologist to ensure sufficient information has been given on how to achieve the best tumour control with the least morbidity.

7b.6 Mastectomy

A mastectomy is the en bloc removal of the complete breast parenchyma including parts of overlaying skin with the nipple areola complex.
Criteria for mastectomy are:

1. Patients who are not eligible for BCT
2. Patient's preference

The aim of mastectomy is to achieve tumour-free margins.
Mastectomy remains a reasonable option to achieve local control in invasive breast cancer. The patient should be informed about this option, including the possibility of immediate breast reconstruction. Breast reconstruction can be offered, but may not delay or hamper locoregional treatment. In extensive disease (either clinically or after histological work-up of the excisional specimen) mastectomy may not result in sufficient local control. Factors associated with a high risk for local recurrence after mastectomy are:

1. Invasive tumour > 5 cm (measured by pathologist)
2. Vascular invasion
3. Skin or muscle involvement
4. Involved or close (< 1 mm) surgical margins
5. Extensive nodal involvement (≥ 4 positive nodes)

In the presence of these risk factors, adjuvant chest wall radiation treatment must be discussed with the patient[16, 17].

Outcome measure: The chest wall relapse rate after mastectomy for invasive breast cancer should be less than 10% after 10 years.

Recommendation: In the presence of high risk factors for local relapse after mastectomy, more than 90% of the patients should have had a consultation with a radiation oncologist to inform them about the possibility of adjuvant radiation therapy of the chest wall and regional lymph node area.

Recommendation: Patients with primary operable breast cancer for whom mastectomy is advised or preferred by the patient should have been informed by the surgeon or plastic reconstructive surgeon about the possibilities of breast reconstruction.

7b.7 Preoperative chemotherapy (for tumours too large for breast conserving treatment)

A number of studies have shown that different regimens of preoperative chemotherapy lead to a remission of primary invasive breast cancer in over 80% of the patients, with a pathological complete remission varying from 7 to 15%[18, 19]. A number of trials show different rates (30 - 85%) of patients who could be treated with BCT for cancers initially considered too large for conservation treatment[20, 21]. To date, after a limited follow-up, these trials showed equal survival rates in patients who had preoperative chemotherapy compared with postoperative chemotherapy[18, 19, 20, 21]. In some studies, however, local failure rates are unacceptably high, so that the same surgical conditions apply for patients who are eligible for BCT without chemotherapy[21].

There is no role for preoperative chemotherapy in patients with invasive breast cancer who are already candidates for BCT. If tumours are too large for BCT, a core needle biopsy with histologically-confirmed invasive breast cancer is mandatory. Dispersed microcalcifications and multi-focal diseases appear contra-indications for preoperative chemotherapy[22]. Since at this moment neither the optimal combination nor duration of chemotherapy have been clearly evaluated, preoperative chemotherapy to downstage the tumour in order to facilitate BCT should be applied with caution. In those patients in whom this treatment is considered, the patient should be informed only after histological confirmation of the diagnosis of breast cancer and optimal imaging by mammography at least. After completing chemotherapy, a second mammogram prior to the surgical treatment should be performed to evaluate the feasibility of BCT. After every course of chemotherapy, local tumour progression should be excluded by clinical examination[18, 19].

Outcome measure: Breast conservation therapy after preoperative chemotherapy for histologically-confirmed invasive breast cancer (more than 50% reduction) in tumours considered too large for BCT should result in a breast relapse rate of less than 15% after 10 years.

7b.8 Locally advanced breast cancer (LABC)

Definition:

- Tumour > 5 cm (stage III) measured clinically, by ultrasound or mammography
- Proven skin involvement
- Chest wall muscle or chest wall skeletal involvement
- Fixed axillary lymph nodes
- Clinical signs of a mastitis carcinomatosa
- Tumour-positive apical (infraclavicular) node

There is sufficient evidence that combined modality treatment is superior to ensure lasting locoregional control in locally advanced breast cancer. The influence on overall survival is uncertain[23, 24].
The timing of each of the components of the multimodality treatment remains to be established. The advantage of upfront chemotherapy, in general accepted as the first step in LABC, is that the primary cancer functions as its own chemotherapy sensitivity test. For instance, in the situation of progressive disease after two courses of chemotherapy, one can decide to stop the applied chemotherapy. On the other hand, it has been convincingly shown that a partial or complete remission after upfront chemotherapy is an important favourable prognostic factor for local control and survival[24]. Overall, in the majority (> 80%) of patients, a remission of tumour volume after upfront chemotherapy can be observed. Radiotherapy to the breast, chest wall and regional lymph nodes is an integral part of the treatment of LABC.
If, and to what extent, surgery should be applied is uncertain. For macroscopic invasive cancer, radiotherapy alone will provide a lasting local control in approximately 60 - 70% of the patients[25]. The situation of clinically-overt remaining invasive cancer, tumour reduction (debulking) by surgery will improve local control. In general, if upfront chemotherapy for LABC results in a partial remission, surgery (BCT, mastectomy or more extensive procedures depending on the extend of the remaining disease) is indicated to ensure a better local control in combination with adjuvant radiotherapy. However, the same holds true if upfront chemotherapy does not have any effect.
Adjuvant hormonal treatment should always be considered in patients with oestrogen receptor (ER)- and/or progesterone receptor (PgR)-positive tumors[26]. Tamoxifen is an equivalent to chemotherapy in elderly patients with receptor-sensitive tumours.

Outcome measure: Over 80% of the patients with a locally advanced breast cancer should have had combined modality treatment including upfront chemotherapy, cytoreductive surgery for clinically overt disease and radiation therapy.

7b.9 Lymphatic dissemination

Invasive cancer may lead to lymphatic dissemination. The most important primary tumour factors related to the risk of lymphatic dissemination are:

- Size of the tumour
- Grade
- Vascular invasion

Patients with micro-invasive (< 2 mm) or tubular cancer up to 10 mm have a very low probability of lymph node metastasis. For these patients the search for lymph node metastasis or elective treatment of lymph nodes can be omitted[27, 28, 29].
The presence of lymph node metastasis is the most important prognostic factor for survival; the more involved the lymph nodes, the worse the prognosis[30]. Treatment of lymph node metastasis will result in a better lasting regional control of the disease[31]. Whether early treatment for clinically-occult lymph node metastasis has an impact on overall survival is not proven.

Indirect evidence strongly suggests a small, but significant, positive effect on survival[32-34].
In conclusion, the knowledge of lymph node dissemination will result in treatment adjustment to improve the outcome of the patient.

Measures to diagnose lymphatic dissemination are:
1. FNA cytology of clinically-overt enlarged regional lymph nodes
2. Ultrasound-directed FNA cytology of suspicious lymph nodes
3. Non-selective lymph node sampling
4. Axillary lymph node dissection (ALND), level I - II
5. Full axillary lymph node dissection, level I - II - III
6. Lymphatic mapping by the sentinel node (SN) procedure

Every method has its own accuracy depending on experience, the a priori chance of lymph node involvement, the applied techniques. ALND (at least level I - II) resulting in the examination of at least 10 lymph nodes by the pathologists, has proven to give an excellent prognostic information on nodal status and axillary tumour control at the expense of certain morbidity, which is particularly a price to pay for node-negative patients[35]. If ALND is used as a staging procedure, it is recommended to perform a complete axillary clearance which results in sufficient axillary tumour control in the majority of node-positive patients[33, 34]. Non-selective lymph node sampling may result in a sampling error, but has proven to provide sufficient prognostic information with less morbidity[36].
Maturing data from many prospective studies indicate that lymphatic mapping by the sentinel node technique may be an equal staging procedure compared with ALND[37, 38]. However, the sentinel node technique is laborious, demands expertise and a careful mapping of the sentinel nodes with tracers (lymphoscintigraphy, intraoperative use of the probe and dye). However, anyone involved in this new technique should be subject to a certain learning phase, including a training course and the verification of the procedure by an ALND in at least 25 and preferably 50 patients[39].
Once lymphatic dissemination to the axilla is established, it is generally accepted that treatment of the axilla is indicated[31-34]. In clinically-overt disease, complete ALND (on indication followed by radiotherapy) provide the best axillary tumour control. If lymph node metastasis are found in the ALND specimen, in general the axilla is sufficiently treated except in extensive dissemination: arbitrarily more than four positive lymph nodes, a positive apical node, extra nodal growth are indications for adjuvant radiotherapy[32]. In these situations, the option of regional radiotherapy should be discussed with the patient. If, after non-selective lymph nodal sampling or after the sentinel node procedure, lymph node metastasis are found, there is a substantial risk that there are more tumour-positive nodes left behind in the axilla (after sentinel node procedures varying from 10 to 50%). These findings justify elective treatment of the axilla. The options for treatment of the axilla after lymph node sampling or sentinel node procedure are either complete ALND or radiation therapy of the axilla. What treatment leads to the best regional control with the least toxicity and long term morbidity remains to be established[34, 40].
The elective treatment of internal mammary chain (IMC) nodes is heavily debated[41]. If lymphatic mapping locates sentinel nodes at the internal mammary chain, these nodes can be removed if they appear. If tumour-positive, the internal mammary chain area can be irradiated. When lymphoscintigraphy does not show drainage to the internal mammary chain, it is uncertain whether this implicates that there is a low risk of tumour dissemination to this region. The role of IMC node biopsy is currently under investigation.
The value of elective irradiation of the internal mammary chain nodes is currently investigated in a large European Organization for Research and Treatment of Cancer (EORTC) trial in patients with a positive axilla or medial located tumours.

Outcome measure: For patients with invasive breast cancer of less than 2 mm or tubular cancer of less than 10 mm do not need lymphatic mapping or elective treatment of axillary lymph nodes.

Outcome measure: For patients with an invasive cancer, information on the nodal status should have been obtained (lymph node sampling > 4 nodes, ALND more than 10 nodes, sentinel node procedure).

Outcome measure: More than 90% of the patients with invasive cancer and proven lymph node metastasis should have had axillary treatment (ALND, radiotherapy to the axilla or combined in extensive nodal involvement).

7b.10 Ductal carcinoma in situ

Ductal carcinoma in situ (DCIS) is defined as a malignant transformation of the ductal lining cells within an intact basal membrane. DCIS is more frequently diagnosed following the increased breast screening. Nowadays, over 15% of the screen-detected malignancies are DCIS[42]. DCIS may appear in different histological variants with specific cyto-nuclear, architectural and molecular-pathological features[43]. As invasive cancer, poorly differentiated DCIS is related to a more aggressive behaviour, particularly with respect to an invasive recurrence and consequent metastatic disease.
The aim of surgical treatment of DCIS is to achieve tumour-free margins[44, 45]. To reach this goal, all requirements related to the treatment of invasive cancer are applicable to DCIS[42]:

- Optimal imaging (including magnification views in cases of microcalcifications)
- Presurgery diagnosis of microcalcifications or density by histological core (stereotactic or ultrasound-guided) biopsies
- Discussion of the patient in the multidisciplinary team
- Specimen radiography after diagnostic and/or therapeutic excisional surgery
- Guide-wire localisation preceding any surgery of a clinically-occult lesion
- The surgical resection should aim to result in at least 1-cm tumour-free margin.
- Marking of the specimen after excision to guide the pathologist
- Diagnostic work-up by the pathologist according to established guidelines

DCIS should be excised completely. If margins are involved a re-excision (guided by post-operative mammography and if necessary again a guide-wire localisation) should be attempted. When a re-excision will result in poor cosmesis, a mastectomy (with or without reconstruction) should be considered and offered. If on basis of mammographical findings, the DCIS is considered to be too large for breast conservation (usually exceeding a 3 cm area of microcalcifications) immediate mastectomy with or without reconstruction should be discussed. In 'true' DCIS, treatment of the axilla is not recommended[42].
Radiotherapy reduces breast relapse rates by 40% after a complete excision of DCIS, irrespective the histological features of the DCIS[46, 47]. Therefore, the possibility of radiotherapy should always be discussed with the patient who desires to conserve her breast after complete excision of DCIS. There are instances where the risk of invasive local relapse, which may lead to dissemination, is extremely low[44]:

- Small (< 2 cm) foci of DCIS
- Low grade of DCIS
- Histologically-confirmed wide margins more than 10 mm.

In these situations, the adjuvant value of radiotherapy is very limited.
After BCT for DCIS, patients should be followed carefully with at least annual mammography. It should be kept in mind that DCIS is a potentially curable disease (by mastectomy). Therefore, BCT should carry a very limited risk for the development of invasive cancer.

Recommendation: After complete excision of DCIS, adjuvant radiotherapy of the breast should be discussed with the patient.

Outcome measure: The breast relapse rate (invasive cancer) after BCT for DCIS should be less than 10% at 10 years.

Outcome measure: The chest wall relapse rate after mastectomy for DCIS should be less than 5% at 10 years.

7b.11 Follow-up

Follow-up after treatment for breast cancer is mandatory for the following reasons[48]:

- For the measurement of outcome, at least annually, indefinitely
- For the measurement of recurrences
- For screening for second primaries:
  - Annual mammography is advised
  - For screening for distant disease
  - Asymptomatic detection of distant disease does not lead to a prolonged survival
  - Other diagnostic means should be applied in cases of symptoms

7b.12 Participants

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8

Data collection and monitoring in breast cancer screening and care

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8.1 Background and aims

Professional organisations and health administrators increasingly recognise the need for audit of quality assurance in health care. According to the consensus statement on breast cancer formulated within the 1st Joint Breast Cancer Conference in Florence[1], 'quality assurance programmes should become mandatory for breast cancer services to qualify for funding from healthcare providers'. The Brussels statement at the 2nd Joint Breast Cancer Conference suggests that all breast units develop quality assurance programmes entering their data onto a common European database[2].

The mammography screening movement in Europe has been in the front line in introducing quality assurance and monitoring in all stages of breast cancer management and care: screening, but also diagnosis and treatment[3,4]. The Surgical Guidelines that precede this section make clear that the collection of data for auditing surgical treatment is mandatory for screening programmes and that a nominated surgeon should be given adequate resources and made responsible for the audit procedures. The same should be true for the other specialists involved and audit should be a responsibility of the multidisciplinary Breast Unit as a whole[5] and the basis for self-assessment and participation in voluntary accreditation/certification programmes.

The aim of this section is to suggest how recommendations included in this 4th Edition of the European Guidelines for Breast Cancer Screening and Diagnosis can be monitored in practice to facilitate their implementation and to allow the best possible outcomes.

8.2 Definitions

The evaluation of quality in health care can be defined as 'measuring to what extent health services increase the probability of favourable outcomes for the individuals and the population and are conform to up-to-date scientific and professional knowledge'[6]. Monitoring can be designed to measure outcomes (such as mortality, recurrences, quality of life …), which at times might prove to be impractical or untimely, or to use indirect measures (indicators) of structure or process of care. According to Avedis Donabedian[7], a pioneer in the conceptualisation and measure of health care quality, structure includes the characteristics of health workers and of the physical, technical, organisational resources they use, while process concerns all events deriving from the interaction between patients and providers.

A quality assurance programme, to be effective, should conform to criteria of validity (are indicators employed accurately measured and relevant to the pertinent health care objectives and is bias minimised?), precision (is random error minimised?) and, last but not least, feasibility. Validity requires that indicators are derived from up-to-date and evidence based guidelines, or that they refer to aspects of health care on which there is clear consensus by professional and the public (say waiting times or cosmetic outcomes). The need to include measures that are based on consensus statements or expert opinion arises from the fact that many relevant aspects of the quality of care have not been evaluated in trials[8]. The employment of universally recognised classification and coding also improves validity and helps in reducing bias in time and area comparisons. Furthermore, accuracy of measurement is improved by employing, when possible, multiple sources and by careful data verification. To maximise precision events should be frequent enough to allow stable estimates and provide sufficient statistical power. Feasibility requires the avoidance of duplication of effort as much as possible, by including quality assurance in routine reporting from health care or screening, and, even more importantly, the consensus and motivation of professionals involved. The latter is more likely to be achieved if professionals in the different disciplines are involved in the setting up of the monitoring system, if this is kept reasonably simple and if they are regularly and timely informed of results that apply to their work.

Other desirable characteristics of measures of the quality of care are the following [6,9]:

- Process of care pictured by the indicator should be potentially modifiable and it should exist a potential area for improvement
- Reproducibility should have been demonstrated
- The way the indicator is calculated and reported (eligible case, numerator, denominator, the management of missing values, targets) should be clearly specified
- Potential confounders should be measured
- Monitoring costs should be acceptable
- Results should be accessible to patients and advocacy organisations

8.3 Data reporting and audit systems

This edition of the European Guidelines defines a number of performance and early impact parameters that each programme should monitor, with suggested targets. These parameters concern the entire range of activities related to breast cancer detection and care, ranging from screening to assessment, diagnosis and treatment. They are listed in relevant chapters and in the executive summary.

In order to facilitate implementation of the recommendations into practice and to standardise monitoring, the European Guidelines also offer some useful tools. In the first place data collection forms for grouped data are shown in the Epidemiology chapter. These have been developed within an EBCN multi-centre project[10] and revised according to the current Guidelines.

Standard data reporting forms should be used in every-day practice for individual patients, including essential items and their appropriate coding, relating to assessment, cyto-histo-pathological diagnosis and treatment (see relevant chapters).

Finally, European Guidelines offer the option to use computerised audit systems capable of calculating the great majority of recommended quality indicators. In fact, within projects sponsored by the 'Europe Against Cancer' programme of the European Commission, EBCN acquired experience in collecting individual data on screening, diagnosis and treatment for breast cancer and produced computerised audit systems on breast cancer screening and management. These systems, described in the following paragraphs, are named QT and SEED. They are public domain and can also be used as a model for adapting accordingly local documentation systems.

Case notes are often incomplete and procedures, or results, can be reported in different ways. Implementing more uniform and consistent item coding is one of the major advantages that an audit system can bring about. Of course, the audit systems should use certified clinical and pathological reporting forms such as those suggested by professional and scientific groups and keep them updated. This is the case for the systems proposed by these Guidelines. Recording of clinically relevant data and the adoption of up-to-date classifications and reporting would benefit the quality of care as well as facilitate its measurement.

Another advantage of audit systems is that precisely defined outcome measures, such as those recommended by these Guidelines, may involve complicated calculations which are unlikely to be consistently performed by the user. Standard reports that can be easily produced directly in the screening programme evaluation Unit or at the multidisciplinary Breast Unit are therefore in order. User-driven analyses on recorded data must also be allowed in order to select subsets of cases, check results of standard reports and understand the reasons for inconsistencies or failure. Often, automated clinical information systems swallow data more easily than they let it out. Such systems are useless for quality assurance, for which feed back is essential. QT and SEED have been developed in a multidisciplinary setting keeping in mind both the soundness of screening and clinical information included and the ease of data analysis.

Quality objectives, recorded items and clinical classifications, once defined, need to be periodically updated. The audit systems must be linked to professional and scientific organisations capable of certifying and confirming its appropriateness while knowledge accumulates, or to suggest modifications. The same organisations could promote reviews and data comparison. Experience in data collection following the publication of the Third Edition of the European Guidelines has been valuable for editing this edition and for updating audit systems.

Another requirement of an audit system is being easy-to-use. Clinical databases, at least at specialised Breast Units, should preferably be employed in everyday practice rather than for retrospective data collection. For this reason they should be accessible in a network to the different specialties involved in breast cancer care, and should be capable to be locally adapted in order not to duplicate, as far as possible, data recording made for routine or administrative reasons.

8.3.1 The European Screening Evaluation Database (SEED)

This prototype web database and audit system (www.cpo.it/seed) based on individual records is capable of calculating, at a local or regional level, a number of process and early impact indicators of breast cancer screening, such as those recommended by the European Guidelines, and of producing reports and statistics relevant to the running of a screening programme. It can also support multi-centre projects aimed at comparing on a common individual data set performance parameters of screening programmes in Europe. SEED is produced with Oracle© technology and is fed by data transfer files. It can be accessed securely by internet with the required standards for sensitive information. Patient data are anonymous and each centre can access uniquely its own data.

Breast cancer screening programmes use a great variety of software for issuing invitations and recording results. The idea behind SEED is to provide the screening community with a standard European evaluation system, no matter the information system is locally used for running the programme.

The algorithms used to calculate the indicators are documented at the web address specified above. This also allows a user to test the system on simulation data from approximately 100,000 screening episodes from two screening programmes linked to a regional organisation. A minimum data set containing items required to calculate these parameters has been defined. This is also described in the SEED website together with transfer files requirements. The database includes all relevant stratification variables (calendar time, age, screening units, etc.) and is structured in such a way to incorporate the appropriate screening organisation scales (invitation round, first and subsequent tests, screening and assessment, routine recalls and intermediate mammography, etc.). The database has a record for each woman and each screening episode.

SEED, being capable of calculating European screening performance parameters and including a database containing the required items should contribute to the standardisation of screening evaluation in Europe both by facilitating joint data collection and multi-centre comparisons and by helping individual programmes to evaluate their own performance in a standard way.

The sections of the database related to diagnosis, treatment and follow up largely overlap with QT (see next paragraph) so that the two systems may be easily inter-connected and have been designed to work in a modular fashion. SEED can also calculate some quality indicators of cancer diagnosis and treatment.

8.3.2 Audit system on Quality of breast cancer diagnosis and Treatment (QT)

The report of the European Society of Mastology (EUSOMA) on 'Breast Units: future standards and minimum requirements'[5], states that performance figures on precisely defined quality objectives and outcome measures must be produced by Breast Units yearly.

At the same workshop the QT Audit System has been endorsed as the EUSOMA database as it was deemed capable of assisting Breast Units in this activity. QT is a Microsoft Access© individual records database produced with funding by the 'Europe Against Cancer' Programme of the European Commission, which can be freely downloaded from www.cpo.it/qt or the EUSOMA website (www.eusoma.org). It is available in five languages (English, French, German, Italian, Spanish; a Hungarian version is in preparation) and has users in several European countries. A web version, which would not require the use of Microsoft Access©, is under construction. Useful features of QT are that it is being kept updated with guidelines and the availability within the same package of data entry and data analysis facilities, ranging from free analysis with use of the main statistical procedures to the production of several standard reports. QT allows recording of data on all women recalled for assessment in a screening programme (or assessed for clinical suspicion). Data items included in QT are numerous, serving different needs by clinicians which are related not only to monitoring but also to patient care. However, the minimum data set necessary to calculate European indicators is much more limited and is clearly identifiable by the user. QT includes a section with screening history to allow its use for screening evaluation purposes, allowing to classify population breast cancer cases as Never Invited, Never Attenders, Screen Detected, Interval (see Epidemiology Chapter). In addition to the monitoring of process indicators, the system allows data recording and analysis on long term follow up for recurrences and survival.

QT has been designed for and is being used by clinical Breast Units for monitoring diagnosis and treatment of breast lesions in symptomatic as well as asymptomatic women. The same database is used by screening programmes for collecting information and calculating quality indicators on the management of screen detected cases. Furthermore, it can assist Cancer Registries for high resolution population studies. The use in different settings in Europe of a common database on breast cancer, reflecting agreed guidelines and benchmarks, can contribute to achieving a greater collaboration and understanding between these different areas of medicine and a better evaluation of the impact of screening and the quality of care.

The system is easy-to-use and, at least in specialised Breast Units, it should preferably be employed in everyday practice rather than for retrospective data collection. For this reason it should be made accessible in a network to the different specialties involved in breast cancer care. Furthermore, wherever possible, it should be connected with the local hospital information systems.

8.4 The quality cycle

Running a monitoring system for quality of screening and care requires resources, particularly data managers with some clinical expertise, and an appropriate organisation for collecting data and making the best use of them. An individual, be it a physician, a breast nurse or a data manager should be made responsible for co-ordinating data collection and reporting at the screening programme evaluation Unit as well as at each Breast Unit collaborating with the programme (see Chapter on requirements of Breast Units). For auditing to produce change, feed back and careful analysis of emerging problems is necessary, and the best setting for these activities is multidisciplinary meetings. Although many of the indicators relate to individual skill or knowledge of recommendations, most involve the team as well. Discussion of data analysis reports during multidisciplinary meetings often prompts improvement of quality of data itself, such as reduction of missing values and accurate item definition, classification and coding.

Voluntary certification of Units conducting specialised work in the field of breast cancer treatment is desirable, in the form required by regional, national or European authorities or professional organisations. By using a quality assurance programme monitoring well-defined targets, Breast Units in Europe have the opportunity to demonstrate their excellence. The potential benefits of audit are unlikely to be accomplished unless clinicians take responsibility for it and value it as an opportunity for permanent education and improvement.

The feed back process is likely to be easier in a centralised screening programme with nominated clinical staff. However, whatever the organisation of the screening programme, efforts should be made to perform audit and to do this in connection with all clinicians involved and with epidemiologists engaged in population cancer registration. Quality improvement and experience gained during audit are likely to promote update and corrections in guidelines and in the monitoring system itself, through closing the quality circle.

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9

The requirements of a specialist Breast Unit

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9.1 Introduction

In October 1998 in Florence the First European Breast Cancer Conference took place, jointly organised by the European Organization for the Research and Treatment of Cancer Breast Cancer Cooperative Group (EORTC-BCCG), the European Society of Mastology (EUSOMA) and Europa Donna. Delegates agreed a consensus on research, genetic predisposition, psycho-social status, treatment and notably quality of care. 'The Florence Statement'[1] demanding that all women have access to multidisciplinary breast clinics based on populations of around 250,000; also it called for mandatory quality assurance programmes for breast services.
With the intention of assuring a high quality specialist service Europe-wide, a working party was established to consider what should comprise a specialist service. These resulted in the publication of The 'Requirements of a Specialist Breast Unit', which represents the opinion of the European Society of Mastology (EUSOMA) and EORTC on the standards required for forming high quality Breast Units across Europe[2].

These Guidelines have been generally well received and have been influential in the introduction of the multidisciplinary working in several countries. 'The Brussels Statement'[3], following EBCC2 drew attention to these guidelines and demanded that processes of accreditation of breast units be implemented. The importance of the establishment of multidisciplinary breast units was again stressed in 'The Hamburg Statement'[4], which followed EBCC4. Attention was drawn to the approval given to this in the European Parliament (OJ C 68 E (18.03.2004), p.611).

9.2 Objectives

- To make available for all women in Europe a high quality specialist Breast Service.
- To define the standards for such a service.
- To recommend that a means of accreditation and audit of Breast Units be established in order that units providing this service should be recognisable to patients, practitioners and health authorities as being of high quality.

9.3 Background

In the UK the recommendations of the report 'A Policy Framework for Commissioning Cancer Services'[5] were that specialist breast units be established, staffed by clinicians and other professionals specialising in single 'anatomical areas', such as in the breast.
A number of reports from groups concerned in the management of breast disease were published, by the British Breast Group[6]; by the Breast Specialty Group of the British Association of Surgical Oncology (BASO)[7,8] and by the UK NHS Executive[9]. The European Society of Surgical Oncology (ESSO) has published similar guidelines[10] to those of BASO and European Guidelines for Quality Assurance in Mammographic Screening have been published[11]. All these reports recommend that breast disease be cared for by specialists in breast disease working as teams in Breast Units.

Across Europe an increasing number of well organised multidisciplinary Breast Units have been established but overall the quality of each service is variable. It is the hope of those working in the field that the recommendations in this report will become mandatory thus building a breast cancer service of the highest quality throughout Europe.

In order that this may be assured it is necessary that standards are set which any hospital wishing to form a recognised Breast Unit must meet.

Further EUSOMA working parties have made recommendations to establish quality standards in the separate aspects of breast cancer care and have published Guidelines on diagnosis, local treatment of the primary tumour, management of risk and reconstruction, endocrine therapy and radiotherapy[12, 13, 14, 15, 16].

9.4 General recommendations

Definitions

- Unit: Essentially a group of specialists in breast cancer and need not necessarily be a geographically single entity, although the separate buildings must be within reasonable proximity, sufficient to allow multidisciplinary working
- Clinic: used to mean a session, usually around 3 hours at which a number of patients are seen for clinical examination and investigations
- Specialists: completed training and certified in own discipline (e.g.) Surgery, Radiology etc and for Core Team members, spending half their working time (clinics, operating, pathology or imaging reading, multidisciplinary meetings, inpatient care etc in breast cancer
- Radiologist: a specialist in imaging for diagnosis
- Radiographer: a technician, taking the mammograms and responsible for mammographic quality
- Radiation Oncologist: specialist in radiotherapy only
- Medical Oncologist: specialist in medical oncology
- Breast Care Nurse: qualified nurse, trained to give psychological support to breast cancer patients (especially at the time diagnosis is given) and to act in follow up as link between patient and breast Team
- Psychiatrist: medically qualified specialist in pharmacological treatment of patients with psychiatric and psychological problems
- Psychologist: not usually medically qualified and therefore unable to prescribe pharmacological therapies
- Surgeon: gynaecological surgeons specialising in breast cancer are included in this term

9.4.1 Recognition of a Breast Unit must be based on mandatory requirements.

9.4.2 A European process of voluntary accreditation of Breast Units, based on the fulfilment of mandatory requirements should be established. To give uniformity a standard database should be made available.

9.4.3 Units must record the basic data on diagnosis, pathology, primary treatment and clinical outcomes. The data must be available for audit and the Unit team should hold regular audit meetings inspecting separate topics and designing and amending protocols and QA systems. These meetings must be minuted.
Performance and audit figures must be produced yearly and set alongside defined quality objectives and outcome measures, such as those laid down in the EUSOMA Guidelines on the various aspects of care[12, 13, 14, 15, 16] or in other suitable guidelines.

9.4.4 The Unit must have written protocols for diagnosis and for the management of cancer at all stages (primary and advanced cancer). All protocols must be agreed upon by the core team members.
New protocols and protocol amendments should be discussed by the core team at the audit meetings (see 9.4.3).

9.4.5 Breast Units will most often be established in large or medium sized hospitals; they should generally cover one-quarter to one-third of a million total population. Some highly specialised units will be larger.

9.4.6 Population Breast Screening programmes should be based within or be closely associated with a recognised Breast Unit and not work as a separate service. The radiologists, surgeons and pathologists working in the screening programme must be core members of the associated Breast Unit.

9.4.7 There has to be a minimum size for a Breast Unit from the point of view of numbers of specialist staff required, arrangement of frequent clinics, provision of equipment and cost-effectiveness. If two hospitals are close together it is more practical for only one of them to establish a functional breast unit serving both hospitals, i.e., the breast team works at both centres.

9.4.8 A Breast Unit should hold outreach clinics for symptomatic referred women, screening assessment and follow-up, in the smaller hospitals in the neighbourhood if these are at a distance from the Breast Unit. In areas with low population density, out-reach arrangements are preferable to the establishment of small Breast Units without the clinical volume to allow expertise. In that circumstance outreach clinics may be only held as infrequently as once per month; such scheduling may prolong waiting times for appointments but clinical evaluation by an expert team is considered preferable to maintaining short waiting times.

9.4.9 Breast Units must provide care of breast disease at all its stages - from screening through to the care of advanced disease. Occasionally the patient may need to be sent to an associated large oncology centre for radiotherapy but the patient must essentially be managed and followed-up at her Breast Unit.

9.4.10 Breast Units should manage their own budget, covering all the work of the unit.

9.5 Mandatory requirements

9.5.1 Critical mass

A Unit must be of sufficient size to have more than 150, newly diagnosed cases of primary breast cancer (at all ages and stages) coming under its care each year.
Note: these are newly diagnosed breast cancers. They may have been diagnosed elsewhere but if they have received any prior treatment and have been transferred, for example, to receive radiotherapy, they should not be counted.

All primary treatment must be carried out under the direction of the Unit (operation must be in the unit, adjuvant therapies must be directed by the unit but may have been received in other settings e.g. RT and chemotherapy). Follow up should be under the control of the Unit.

The reason for recommending a minimum number is to ensure a caseload sufficient to maintain expertise for each team member and to ensure cost-effective working of the Breast Unit: the establishment of a clinic staffed by experts is expensive and must have a high through-put of patients.

A number of Units will be recognised as teaching centres, nationally or internationally. They may be recognised for teaching overall breast cancer management or special aspects (e.g.) screening, reconstruction, pathology.

9.5.2 Core team

Each member of the core team must have special training in breast cancer; for standards see Chapter 10.

Each member of the breast unit core team must undertake continuing professional education on a regular basis. Breast Unit budgets must include provision for this.

9.5.2.1 The Breast Unit must have an identified Clinical Director of Breast Services.

9.5.2.2 Breast Surgeons (including Gynaecologists performing breast surgery)

Two or more nominated surgeons specially trained in breast disease, each of whom must personally carry out the primary surgery on at least 50 newly diagnosed cancers per annum and must attend at least one diagnostic clinic per week.

For an average sized unit the surgeons will need at least eight identified ca. 4 hr sessions per week in Breast Disease. These sessions will allow for operating time, participation in diagnostic clinics, a follow-up clinic and, where appropriate, screening assessment clinics. A session must be allowed for attendance at a weekly team case management and audit meeting.

A Unit team must provide breast surgical reconstruction when required for those patients not suitable for breast conserving therapy and be able to apply special techniques for patients with extensive local disease. The breast surgeons in the team should be able to undertake basic reconstruction or recontouring and there should be a standard arrangement or joint reconstruction clinic with one or two nominated Plastic Surgeons (non-core team member) who take a special interest in breast reconstructive and recontouring techniques.

9.5.2.3 Breast Radiologists

There must be at least two nominated radiologists, fully trained and with continuing experience in all aspects of breast disease and associated imaging, tissue sampling and localisation procedures under image control. Ideally any radiologist investigating breast patients should participate in the screening programme in countries in which this is established and must participate in a national or regional QA scheme.

They must fulfil the volume requirements as laid down for breast assessment in Chapter 5 and the previously published document 'Quality Assurance in the Diagnosis of Breast Disease'[12], reading a minimum of 1000 mammograms per year (5000 for those participating in a screening programme).

They must attend multidisciplinary meetings for case management and audit purposes. They must be present in diagnostic assessment clinics with the surgeon. Each radiologist must attend at least one diagnostic clinic per week for symptomatic patients or screening assessment.

9.5.2.4 Breast Pathologists

A lead pathologist plus usually not more than one other nominated pathologist, specialising in Breast Disease, will be responsible for all breast pathology and cytology. Pathologists carrying out these roles must have contractual sessions to attend team case management and audit meetings. They must be familiar with national and/or European performance quality standards and guidelines. They must take part in available European, National and Regional quality assurance schemes.

9.5.2.5 Breast Oncologists

(a) A nominated radiation oncologist must arrange the appropriate delivery of radiotherapy[16]. He/she must hold advanced disease clinics with other members of the breast team at the Breast Unit and must take part in the case management and audit meetings of the Unit.

(b) In some countries, Clinical Oncologists carry out both radiation therapy and prescribe the chemotherapy. In centres in which a Medical Oncologist gives the chemotherapy he/she should be a member of the core team and take a full part in case management and audit meetings.

9.5.2.6 Breast Diagnostic Radiographers (Technicians)

Radiographers with the necessary expertise and training in mammography are essential members of the team. They must fulfil the training and working practice recommendations as laid down in Chapters 3, 5, and 10. They must be responsible for

taking the mammograms, which must not be performed by radiographic or non-radiographic personnel without the above training.

9.5.2.7 Data Managers

There must be a system covering audit. A data manager must enter data on diagnosis, treatment, pathology and clinical outcomes contemporaneously.

9.5.2.8 Patient Support staff

Regular support (advice, counselling, psychological help) is given by Breast Care Nurses in some countries and psychologically professionally trained persons with expertise in Breast Cancer in others. These persons must be members of the core team. They must be available to counsel and offer practical advice and emotional support to newly diagnosed patients at the time the diagnosis is given, so as to further explain treatment plans. They should also be available on demand from patients in the Primary Breast Cancer Follow up clinic and in the Advanced Breast Clinic. Particularly they must be present to support women when the diagnosis is given that the disease has become advanced.

At least two Breast Care Nurses are needed per breast unit.

9.6 Equipment

9.6.1 The unit must be in possession of all necessary imaging equipment for complete and adequate breast diagnosis.

9.6.2 The minimum equipment in a department giving radiotherapy must be two megavoltage units, a brachytherapy unit, a simulator and a computerised planning system. The department must have a radiotherapeutic quality control programme for breast cases.

9.7 Facilities/Services

Clinics (see definition in Section 9.4). Consultations for Breast patients should be held separately, i.e., not as part of general surgery.

9.7.1 New patient clinics

At least one clinic per week for newly referred symptomatic women must be held. A Unit diagnosing 150 new cancers per year must expect over 1500 new referrals of symptomatic women (= approximately 30 per week).

Suggested outcome measures for the waiting times are given in Chapter 5. A suggested good practice is that all newly referred women with breast symptoms should be offered an appointment within 10 working days of receipt of the referral.

Clinics to which patients are referred or self-referred must be staffed by a surgeon, a radiologist and radiographers from the breast care team. Multidisciplinary working must allow all standard investigations for triple assessment (clinical examination and all appropriate imaging and tissue diagnostic procedures) to be completed at one visit. Where possible the finding of no abnormality or a confirmed diagnosis of a benign lesion should be communicated to the patient at that visit.

9.7.2 Communication of the Diagnosis and Treatment Plan

It may not be possible (now that core biopsy is most often used) or may not be considered appropriate by the unit to give the diagnosis of cancer at the initial visit. Women found to have breast cancer should receive that diagnosis within 5 working days. The diagnosis should be

ideally communicated personally by the surgeon: if it is communicated by the radiologist, then the surgeon (±) the oncologist must personally advice the patient on treatment. It is recommended that a breast care nurse (or) psychologically trained person (see 9.5.2.8) be present to discuss fully with the patient the options for treatment and to give emotional support. If a patient has clear advanced breast cancer it may be more appropriate that an oncologist rather than a surgeon gives the diagnosis if the patient's treatment does not involve surgery.
A suitable room with sufficient privacy must be available. In units in which preoperative irradiation or primary medical therapies are used, cases which might be suitable for these should be seen jointly by a surgeon and radiation or medical oncologist before treatment commences.
A diagnosis should not be given to a patient by letter or on the telephone, unless at the specific request of the patient given adequate and full informed choice.

9.7.3 Multidisciplinary Case Management Meetings (MDM's)

All members of the core team must attend the Multidisciplinary Meeting (MDM), which must be held at least weekly.

The following should be discussed:
- cases in which the diagnosis is as yet uncertain e.g., following core biopsy
- cases in whom the diagnosis of cancer is confirmed and who may be considered for primary medical therapy
- all cases following surgery on receipt of the histopathology for discussion of further care and
- cases in follow-up who recently have undergone diagnostic investigations for possible symptoms of recurrent or advanced disease

It is possibly more convenient to have two MDM's per week:
- one for cases in diagnosis attended by surgeons, radiologists and pathologists and
- one for post-operative consideration of prognosis and adjuvant therapies and for cases investigated for disease recurrence (oncologists, surgeons, radiologists and pathologists)

9.7.4 Physiotherapy

Physiotherapy must be available for the post-operative recovery period to ensure good shoulder mobility, etc.

9.7.5 Adjuvant Therapies

- The multidisciplinary team (MDT) must decide on the appropriate adjuvant therapies in light of the pathology of the surgical specimen.
- Radiotherapy may be delivered within the same hospital or patients may have to travel to a Radiotherapy Unit in another Hospital (at which the core team radiation oncologist must be able to supervise their treatment).
- The administration of cytotoxic therapy as adjuvant therapy or for advanced disease must be by an accredited oncologist (member of the core team) with proper facilities. Cytotoxic therapies may be given in another hospital but the decisions regarding their application must be made by the MDT of the Unit.

9.7.6 Advanced and Recurrent Breast Cancer

- There must be one Advanced Breast Cancer Clinic at least every 2 weeks at the Breast Unit, separate from the general oncology clinics (although sometimes combined with gynaecological oncology) and attended by the Clinical Oncologist ± Medical Oncologist (see 9.5.2.5 b). The surgeon must be available if required for consultation and must be in full attendance if the breast surgeons supervise the endocrine therapies. Patients with distant metastases locally

advanced primary breast cancer and local or regional recurrence, must be managed in this clinic according to protocols agreed by the multidisciplinary team.
- Patients who have received radiotherapy or chemotherapy at another Cancer Centre should normally be referred back to the Breast Team at their Breast Unit for further follow-up and decision making in the Advanced Breast Cancer Clinic.
- A palliative care/pain control service must be easily accessible.

9.7.7 Follow-up of primary breast cancer

- All patients with primary breast cancer must be followed-up in a Clinic directly supervised by one of the surgeons. Any necessary imaging or other investigations should be carried out at the same visit.
- Although the patient may have to visit a separate Hospital to receive radiotherapy or specialised chemotherapy, the decisions on the case management and the subsequent follow-up should be by the team members of her Breast Unit. The skills of the diagnostic breast team are then available for the detection and investigation of a possible recurrence.

9.7.8 Benign disease

The Breast Unit must also advise and where necessary treat women with benign disease (e.g.) cysts, fibroadenoma, mastalgia, inflammatory conditions, mammillary fistula and phyllodes tumour.

9.7.9 Family History/genetics

Advice is best given in a multidisciplinary clinic, the specialists involved are a clinical geneticist and from the team a breast surgeon with reconstructive skills, radiologist and psychiatrist or clinical psychologist. Gene probing must be available when required and ideally a molecular geneticist should be accessible for consultation by the specialists in the clinic.

9.7.10 Reconstruction

(See 9.8.2 below)

9.7.11 Breast Screening

Ideally breast screening centres should be a part of Breast Units and the same radiologists should be members of the Unit team and work in screen detection and the diagnosis of symptomatic disease. Assessment centres should be placed in Breast Units.

9.7.12 Patient Information

Women must be offered clear written and oral information regarding their diagnosis and/or treatment options. The Breast Unit should also provide written information concerning local out patient support groups and advocacy organisations and should also respect the patients rights as outlined in the Breast Cancer Resolution of the European Parliament (OJ C 68 E (18.03.2004), p.611). Patients should be provided with a list of their rights as outlined in the breast cancer resolution

9.8 Associated Services and non-core personnel

These are services for which it cannot be expected that staff will spend the majority of their time on breast disease.

9.8.1 Extra Psychological Support

If the patient is experiencing psychological morbidity that cannot be dealt with effectively by members (usually breast care nurse or psycho-oncologist) of the Unit team, she should be referred to a psychiatrist with whom there are particular arrangements to see breast patients for the Breast Unit (non-core team member).

9.8.2 Plastic Surgeon

The Breast Unit should make arrangement with one or two nominated plastic surgeons with a special interest in breast reconstructive and recontouring techniques.

9.8.3 Geneticists

Women seeking advice with regard to risk, e.g., family history, must be able to receive advice from the Breast team, which must include a clinical geneticist with a specialist interest in breast cancer (see 9.7.9).

9.8.4 Palliative Care

A specialist palliative care service must be available for the referral of patients with advanced breast cancer. A close working relationship must be established between members of the Breast Unit (especially the breast care nurse) and the palliative care service to ensure that breakdowns in continuity of care do not occur and also with the local network for home assistance.

9.8.5 Prosthesis

There must be provision for a Prosthesis fitting service within the unit.

9.8.6 Physiotherapy and Lymphoedema

An identified Physiotherapist or a Breast Care Nurse for the treatment of lymphoedema and late sequeale.

9.9 Research

Research is one of the essential parts of training of specialists. As part of Audit Units must record numbers of patients entered into clinical trials and details of all other research.
Units should be encouraged to provide research opportunities and this must be taken into account when assessing units for their suitability for accepting trainees.

9.10 Teaching

The Unit must provide teaching, whether simply for junior staff or for students or on a national or international basis. Some units may particularly concentrate on certain areas (e.g.) Reconstruction, Screening, Pathology, etc.

9.11 Additional points

The implementation of the suggested structure of Breast Units requires a reorganisation of time in each discipline, so that as a consultant spends more time in breast disease, his or her colleagues no longer treat breast cancer and specialise in other areas. Rationalisation of work patterns, in this way would provide sufficient staff for the Breast Units. Such a move would coincide with changes that are already occurring within all disciplines, for example, from General Surgery the emergence of specialist surgeons for urology, microinvasive techniques, vascular surgery, upper GI, hepatic and colon.

All work must be carried out or directly supervised by specialists specifically trained in breast disease. A service provided by a trained specialist is more efficient and more cost effective – diagnostic decisions are made earlier whereas junior staff are more likely to call a patient back several times unnecessarily and to carry out unnecessary investigations; operating by consultants gives better results for technical reasons; the interpretation of imaging techniques and the reading of histology is much more likely to produce definitive opinions if carried out by experts.

We estimate that for a 10 million total population base 30-40 Breast Units are required for the ideal service and that reorganisation in this way will provide considerable financial savings. This could easily be achieved and should be attractive to many countries.

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10

Guidelines for training

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10.1 Introduction

The success of a screening programme is largely dependent on the availability of specially trained staff committed to implementation, provision and evaluation of a high quality, efficient service.

Multidisciplinary communication should be maintained between the members of the team as follows:

- Epidemiologist
- Physicist
- Breast Radiographer
- Breast Radiologist
- Breast Pathologist
- Breast Surgeon
- Breast Care Nurse
- Medical Oncologist/Radiotherapist

All staff involved in a programme must have knowledge of the basic principles of breast cancer screening. In order to achieve this they could preferably attend a course of instruction at an approved training centre prior to the commencement of the programme. The need of training differs between different disciplines and is most important for those involved in the links related to screening in the chain of breast cancer diagnosis and care. E.g., surgery, radiology, pathology, and postoperative treatment is not performed differently depending on whether a cancer is screen detected or clinically detected. High quality screening performance is based on a multidisciplinary approach, therefore both unidisciplinary and multidisciplinary training packages should be offered. Updating of knowledge within the framework of Continuing Medical Education should be encouraged.
Participation in training courses should be carefully documented and a certificate of attendance should be issued based on level of skills and performance check.
Specific training requirements in terms of quality and volumes should determine eligibility for any certification process, which must be applied only to centres with sufficiently skilled personnel. The EUREF and EUSOMA organisations can be contacted for advice on sources of training and coordination (www.EUREF.org).

10.2 General requirements

- There is general agreement at present based on research evidence that **multidisciplinary services** provide better patient care. Effective communication between the various professionals of a Breast Care Team is essential. Therefore, training courses should also focus on the good interprofessional communication. Joint courses given for the multidisciplinary team may facilitate this goal.

- **Continuing education,** including refresher courses at various intervals are essential to gain information on new developments and to improve the quality of the diagnostic and therapeutic process. It is important to keep records of training activities as they are useful indicators of the quality of a given centre. They will be part of a certification review process.

- All medical staff involved in a screening programme should acquire a basic knowledge of the **epidemiological aspects and the philosophy** of such a programme.

  Relevant topics are:
  - Breast cancer epidemiology (incidence, prognosis, mortality)
  - Introduction to screening philosophy (concept of secondary prevention)
  - Breast cancer screening terminology (sensitivity, specificity, predictive value, etc.)

- Evaluation of screening effectiveness (performance parameters, detection rate, recall rate, tumour stage distribution, mortality reduction)
- Current screening practices (centralised and decentralised programmes, population based programmes, methods of invitation, response rate)

10.3 Epidemiologist

A breast cancer screening programme is, of necessity, a multidisciplinary undertaking. Many disciplines will contribute to monitoring and evaluating the programme. It is essential therefore that directly from the start of the programme, a designated individual with relevant epidemiological knowledge, is given the task of overlooking the data generation process which should be designed to facilitate evaluation. Assessing the programme's impact on breast cancer mortality is only possible if adequate provision has been made in the planning process for the complete and accurate recording of the data required. The 'Epidemiological guidelines for quality assurance in breast cancer screening' (chapter 1) and the Executive Summary give more detailed guidance for this effort.

Basic training:
The person overseeing data generation and evaluation should have attended a basic training course in clinical epidemiology.

Training for epidemiologists prior to their involvement in a breast cancer screening programme should give specific emphasis to:
- Breast cancer epidemiology: incidence, prevalence, mortality, trends
- Screening philosophy: preclinical lesions, lead time
- Breast cancer screening terminology: sensitivity, specificity, predictive value, etc.
- Breast cancer screening programme: sources of bias, current screening practices
- Ethical and confidentiality issues
- Setting up a mammography screening programme: identification and invitation of target population, call-recall system, follow up system
- Strategies for data collection and management: use of appropriate databases, individual files, computerised archives, linkage to appropriate registries, classification of screening outcomes, quality control procedures in data collection
- Statistical analysis and interpretation of results: performance indicators for process evaluation, predictors of screening impact, assessing screening impact and effectiveness, basic cost-effectiveness calculations, sources of bias, outcomes, adherence to the programme, side-effects of screening
- Presentation of data and report writing

The training programme should preferably be organised as secondments for a period of at least one week to one or two established screening centres running population-based screening programmes. In addition, international courses on relevant aspects of the work involved should be attended if appropriate.

10.4 Physicist

Involvement of a qualified physicist is required within any breast cancer screening programme. Each physicist should have a degree in physics (or physics engineering, biomedical engineering or technical physics) and have undergone further postgraduate training, or may comply with the EFOMP (European Federation of Organisations for Medical Physics) training recommendations.

- The physicist should be able to set up and maintain a quality assurance system.
- The physicist should be able to advise on the purchase and use of mammography equipment

in general, and must be able to communicate the current standards of practice in a concise way to radiologists, radiographers and manufacturers alike. He or she must have a broad knowledge of imaging techniques in general but be an expert in imaging techniques of breast tissue.
- The physicist must be able to build up and maintain a network of professionals in order to keep these skills in touch with the current technology. In some of the tasks (e.g. solving conflicting interests) management skills are necessary. With an eye on the (near) future it is also necessary to be a skilled computer user for e.g. digital mammography, building databases and developing specific local software.

Ongoing education and training is indispensable for achieving professional standards. As a guide, the physicist should spend about 5% of working time on these aspects.

The theoretical and practical training in the physics of breast screening should cover at least the following topics:
- Organisation of a quality assurance programme
- Physics of medical imaging in mammography (both film-screen and digital)
- Principles of film processing (including film artefacts and their causes)
- Principles of basic image processing techniques in digital mammography
- Principles of image presentation techniques in digital mammography
- Basics of DICOM applicable for mammography
- Quality assurance measurements on mammography X-ray sets, stereotactic accessories, specimen cabinets (including image quality and radiation dose measurements)
- Radiation risks associated with mammography (screening)
- Quality assurance testing of processors, films and screens (including sensitometric techniques)
- Quality assurance measurements on workstations and printers

Specific training in the physics of mammography in both theoretical and practical matters at an established institute or training centre is obligatory.

Trainees should attend about 20 hours of formal lectures or equivalent theoretical training, supplemented by 20 hours of personal study about the topics of the formal lectures and at least 4 weeks of practical training. We recommend that physicists should visit at least two different appropriate training centres.

In order to maintain skill levels it is desirable that each physicist has a fairly substantial involvement in breast imaging systems. If for practical reasons some physicists look after relatively small numbers of systems e.g. 1 or 2, then additional steps must be taken to coordinate and compare their work with other more experienced physicists.

10.5 Breast Radiographer

Radiographers have a key role in obtaining and maintaining recognised targets for the success of a mammography screening programme.

Diagnostic accuracy is highly dependent on correct breast positioning. This is a specialised task requiring a good knowledge of the standard and additional views, a high level of skills, and above all good communication with the woman undergoing the mammographic examination.

Specialist Breast Diagnostic Radiographers should be expected to update their knowledge and develop their skills in line with continuing professional development. They should be responsible for regular audit and should review their own performance against international standards and objectives.

Training in the various aspects of their work is mandatory.
Outlines of the radiographic quality objectives are summarised in chapter 3. In order to achieve these objectives, all radiographers participating in a breast screening programme are expected to undergo a programme of training which should consist of two parts: academic & clinical.

The academic component should include:
- The normal breast, anatomy and physiology
- Radiology and pathology of benign and malignant lesions
- Basic physical principles of medical imaging in film-screen and digital mammography (including image quality, radiation protection and quality assurance)
- Basic principles of image processing and presentation (including quality assurance of image presentation)
- The management of breast cancer
- Organisation of a breast screening programme
- Epidemiological aspects
- Communication and social skills
- Patient confidentiality and data protection

The course may include lectures, tutorials, demonstrations and reading.

The clinical component should include:
- Standard and additional views e.g. magnification, coned views and specimen radiography
- Daily and weekly technical quality control procedures
- The assessment of the quality of the images from the positioning as well as the technical point of view
- Relevant administrative procedures
- Additional imaging techniques e.g. ultrasound and MRI
- Localisation and biopsy techniques for impalpable lesions

Candidates for accreditation as specialist breast radiographers must have undergone at least 40 hours of documented training specific to the radiographic aspects of mammography and regularly participate in External Quality Assessment schemes as well as radiographic update courses.
During training, the trainee should perform at least 75 mammograms and, if required for assessment of a possible abnormality in the breast, further mammographic projections under supervision of a recognised training radiographer. Depending on the experience and existing skills of the radiographer, the training will last 2-6 weeks.

At least 150 mammograms (including additional views) must be completed after the training before a certificate can be applied for.

The mammographic examinations should be adequate for radiological interpretation in >97% of cases.

10.6 Breast Radiologist

The radiologist is responsible for high image quality and for ensuring that all the physico-technical and professional quality control processes have been satisfactorily carried out.

Radiologists responsible for the radiological aspects of breast screening must have undergone formal training and have experience in mammography and in the radiological assessment of women with screen-detected abnormalities.

For this reason, we have recommended the following. The radiologist must also be conversant with the important aspects of processing techniques and exposure which play a vital role in final image quality in analogue setting. The basic inter-relationship of kV, film-screen type, contrast, resolution, processing time and temperature must be understood, likewise the importance of

sufficiently high optical density for the detection of small invasive cancers. Adequate compression and lack of motion artefact are also important diagnostically. Film artefacts such as scratches and skin folds indicate sub-optimal technique, but may not be sufficient to interfere with diagnosis. Further details of these issues may be found in the physico-technical chapter.

Training programmes should include at least the following subjects:

- Basic physical principles of medical imaging in film-screen and digital mammography (including image quality, radiation protection and quality assurance)
- Basic principles of image processing and presentation (including quality assurance of image presentation on digital workstations)
- Radiographic positioning, standard views, additional views, magnification, coned views and specimen radiography
- Radiology of the normal breast and variants of normal
- The radiology and pathology of benign lesions, especially those which simulate malignancy
- The radiology and pathology of malignant breast disease
- The differential diagnosis of mass lesions, microcalcifications, parenchymal distortion and asymmetrical density
- The importance of radiologic-pathologic correlation in cases where there is an extensive intraductal disease component, and the implications for management and treatment
- The use and place of ultrasound in the diagnosis and management of breast lesions
- Localisation and biopsy techniques for impalpable lesions, fine needle aspiration cytology, and needle core biopsy
- Involvement in the daily reading of screening and clinical mammograms
- Self-assessment procedures, review of interval cancers,
- The epidemiological aspects of breast screening
- Participation in multidisciplinary pre-operative and postoperative meetings
- Additional imaging techniques including MRI
- Current issues of breast diagnosis and treatment

In contrast with the highly academic courses that currently dominate the post-graduate teaching of radiology the training programme should preferably have a tutorial structure and a multidisciplinary approach with direct interaction between the participants and the experts.

It is the experience of most of the recognised training centres that even a long clinical experience in radiological breast diagnosis will not substitute for a comprehensive training in screening mammography.

Before undertaking screen film reading or screening assessment radiologists should be seconded to a screening and assessment centre. This should be an approved training centre with a throughput of at least 10,000 screens per year, for a period of time which, depending on experience and aptitude, could vary from some days to some weeks.

10.7 Breast Pathologist

The quality of the pathology service is crucial in order to provide the definitive diagnosis of a mammographically detected lesion and to give information on its prognostic and predictive significance. In addition, the pathology data, e.g. tumour size, grade and axillary node status, are essential indicators of screening performance. Each screening programme should have access to high quality pathology services provided by pathologists with special expertise in breast pathology. Pathologists involved in a screening programme should have undergone specialist training for at least one to two weeks in an approved training centre.

Such a training programme should include both theoretical and practical sections on the following subjects:

- Optimal handling of biopsy specimens, the use of specimen radiography and the extent of sampling of the specimen for histological examination

- The classification of malignant invasive and non-invasive lesions
- Recording prognostic data: tumour size, malignancy grade, axillary node status and assessment of relevant immuno-histochemical tests e.g. hormone receptor- and HER2-status, including FISH-test
- radiologic-pathologic correlation of benign and malignant lesions: mass lesions, microcalcifications, parenchymal distortions and asymmetrical densities
- The importance of radiologic-pathologic correlation in cases where there is an extensive intraductal disease component, and the implications for management and treatment
- Common pitfalls in histological diagnosis, e.g. atypical ductal hyperplasia vs. ductal carcinoma in situ, florid adenosis vs. tubular carcinoma, 'microinvasion', benign vs. malignant papillary lesions
- The interpretation of fine needle aspiration cytology and needle core biopsy samples, and the associated pitfalls in diagnosis
- The pathologist's role in the sentinel-node biopsy technique
- The assessment of margins and consequences for treatment modalities
- Participation in multidisciplinary pre-operative and postoperative meetings
- Principles of imaging of breast lesions
- Principles of breast cancer treatment; surgery, radiotherapy and medical treatment
- Hereditary breast cancer and genetic counseling
- The epidemiological aspects of breast screening

10.8 Breast Surgeon

The management of patients referred to surgery from the screening programme should be carried out only by surgeons/gynaecologists/plastic surgeons who have undergone specific training and have acquired the necessary specialist knowledge to be entitled as specialist Breast Surgeon. Attendance at an approved training course is mandatory since data show that sub-specialization guarantees a better quality of treatment in terms of loco-regional control, cosmetic results and survival.

The EUSOMA guidelines on **'Training of Specialized Health Professionals dealing with Breast Cancer'** (in press) provide a detailed list of training requirements including entry requirements, theoretical and practical training requirements and outcome measures of training for Breast Surgeons.

The list below contains the most essential topics of the theoretical training courses:

- Breast imaging: mammography, ultrasound, MRI, localization techniques
- Radiologic-pathologic correlation of benign and malignant lesions
- The classification and management of invasive and in situ breast cancer
- The classification and management of benign breast disease
- The management of screen-detected breast disease
- Breast reconstruction
- Radiotherapy relating to breast cancer
- The use of chemotherapy and hormonal therapy for breast cancer in the pre-operative and adjuvant setting
- Psychological evaluation, communication and counseling
- Hereditary breast cancer and genetic counseling
- Epidemiology and principles of screening for breast cancer
- Multidisciplinary pre- and post-surgical case management meetings
- Principles and practice of audit procedures
- Clinical trials and statistics

Following the theoretical and practical training, the candidate should have sufficient knowledge, expertise and skill to enable independent practice within the setting of a multidisciplinary team.

10.9 Breast Care Nurse

The role of the Breast Care Nurse (BCN) has become increasingly recognised within the multidisciplinary breast care team. In a rather short time the BCN has turned out to be an indispensable position in a high quality breast care team.

The BCN is a prototype of the clinical nurse specialist whose role can be summarized in:
- Providing information
- Monitoring physical and psychological progress
- Providing emotional support and counseling
- Giving practical advice at all points in the disease process about all aspects of diagnosis, management and impact of breast cancer

Adoption of extended skills into specialist nursing roles has validated the position of BCN as a full partner in the multidisciplinary team.

The EUSOMA guidelines on **'Training of Specialized Health Professionals dealing with Breast Cancer'** (in press) provide a detailed list of training requirements including entry requirements, theoretical and practical training requirements and outcome measures of training for Breast Care Nurses.

Some essential topics of the theoretical and practical training include:

General knowledge on the nature of breast disease:
- Epidemiology and risk factors
- Benign breast disease
- Malignant breast disease, classification and staging
- Breast screening and early detection
- Diagnosis including clinical examination and imaging techniques
- Breast cancer genetics

Treatment approaches, implications and impact:
- Surgery
- Radiotherapy
- Chemotherapy and endocrine therapy

The experience of breast cancer:
Reactions to diagnosis, treatment options, recovery and rehabilitation, follow-up and survival, altered body image and sexuality, premature menopause, treatment induced fertility issues, lymphoedema, prosthesis, etc.

Additional topics:
Shared decision making, informed consent, audit and performance standards.

10.10 Medical Oncologist/Radiotherapist

In some countries, Clinical Oncologists carry out both radiation therapy and prescribe the chemotherapy. In centres in which a Medical Oncologist gives the chemotherapy he/she should be a member of the core team and take a full part in case management and audit meetings.
The management of screen detected breast cancer patients referred to oncological treatment should be carried out by Oncologists/Radiotherapists who have undergone specific training and have acquired the necessary specialist knowledge in the field of screening. Preferably, training courses could be organized at a regional level where oncologists/radiotherapists share knowledge in breast cancer screening with other members of the core team.

The list below contains the most essential topics of the theoretical training courses:

- Breast imaging: mammography, ultrasound, MRI, localization techniques
- Radiologic-pathologic correlation of benign and malignant lesions
- The classification and management of invasive and in situ breast cancer
- The classification and management of benign breast disease
- The management of screen-detected breast disease
- Breast reconstruction
- Radiotherapy relating to breast cancer
- The use of chemotherapy and hormonal therapy for breast cancer in the pre-operative and adjuvant setting
- Psychological evaluation, communication and counseling
- Hereditary breast cancer and genetic counseling
- Epidemiology and principles of screening for breast cancer
- Multidisciplinary pre- and post-surgical case management meetings
- Principles and practice of audit procedures
- Clinical trials and statistics

Following the theoretical and practical training, the candidate should have sufficient knowledge, expertise and skill to enable independent practice within the setting of a multidisciplinary team.

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11

Certification protocol for breast screening and breast diagnostic services

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This is a revised version of the original EUREF certification protocol - working document, published as Annex IV in the third edition of the European Guidelines for quality assurance in mammography screening (2001).

11.1 Executive Summary

Mammography (x-ray examination of the breast) is a widely used imaging procedure - undergone by at least 10 million women per year in the European Member States. The main benefits are those of early detection of breast cancer, reduction in mortality from breast cancer by mammography screening and reassurance of normality, The potential harm in terms of the creation of unnecessary anxiety and morbidity, untoward economic costs and the use of ionising radiation should not be underestimated.

Use of sub-optimal equipment by insufficiently trained and skilled professional staff will negate the major benefits of screening and result in poorly effective and cost ineffective mammography services. We believe that positive steps are necessary to abolish such practice and that it is important to help consumers, health care professionals, government authorities and other interested parties to identify high quality mammography services.

We have therefore developed a European programme for:

Voluntary certification of high quality
diagnostic breast imaging and breast screening services

This certification allows tangible and demonstrable recognition of adherence to a recognised quality system and will take into account the special requirements of both breast diagnostic and screening services. It has been developed for the European Commission by EUREF in co-operation with the European Network of Breast Screening programmes, competent departments of the European Commission, European agencies and other interested national authorities in Member States.

Methodology and criteria are described for four chosen certification categories, two for the provision of **diagnostic breast imaging services** and two for the provision of **breast screening programmes.** These categories range from the ability to produce an adequate quality mammogram up to a centre performing population screening to European Reference Centre level.

In addition to these four certification categories an Advisory Visit and a Pre-certification Visit will be offered to screening programmes on request.

11.2 Introduction

Europe currently leads the world in implementation of organised population based breast cancer screening programmes using mammography of demonstrable high quality. Considerable progress has been made with effective population based screening in several Member States. The experience gained in these activities has demonstrated the complex technical, organisational and professional aspects of maintaining an appropriate balance between the beneficial and potentially harmful effects of mammography. This need for a high quality service in mammography and breast screening has become increasingly recognised over recent years. Attention to technical detail has been scientifically demonstrated to increase cancer detection rates and in particular to increase detection of small invasive cancers[1], a major pre-requisite for maximising mortality reduction from breast cancer screening by mammography.

Training and adherence to audit have played a significant part in such advances. One of the lessons learnt is that effective mammography screening cannot be established in the framework of opportunistic screening within a symptomatic mammography service. It is essential to have in place high quality diagnostic mammography imaging services, which may or may not participate within a fully organised quality assured breast screening process. Benefits and advances gained by quality assured screening programmes working to recognised high standards should be introduced into programmes that are less experienced and also into the realms of diagnostic mammography.

In 1988 the European Commission funded the Europe Against Cancer Programme and initiated a Pilot Project Network in the Member States. This would examine and develop the methodologies of breast cancer screening in different health care environments, share knowledge, experience and provide reliable information for political decision making in each Member State as to the future of any national breast screening programmes. After the first few years, the pilot projects matured into a more quality based network for breast cancer screening, with funding only provided for quality improvement initiatives. EUREF - The European Network of Reference Centres for Breast Cancer Screening - was set up in order to facilitate and co-ordinate training in these screening centres. It would provide epidemiological and physico-technical support and ultimately have the aim of bringing each of the network members to Reference Centre status within its own country. The breast screening network has received funding from The Europe Against Cancer programme and up until now the provision of such funding for quality assurance measures, the co-ordinating of training and the site visits performed by consultants to the programme have been the major means by which a quality service has been documented and recognised. EUREF has now further refined its role towards certification and is redefined as the European Reference Organisation for Quality Assured Breast Screening and Diagnostic Services, while the Network continued its activities, with a number of highly successful projects, as the European Breast Cancer Network (EBCN).

We regard it as crucial that adherence to a quality system receives tangible and demonstrable recognition by way of certification. Certification of health care services is an endeavour receiving increasing attention from government agencies, professional bodies and health care purchasers and providers in Europe. There is an increasing awareness of the benefits of this process in improving the outcome and the cost effectiveness of health care services through successful implementation of quality assurance systems. The inference from certification is two fold. Firstly that a certain level of performance has been achieved, secondly that a certificate may be withdrawn if standards are not maintained. In order to ensure that previous standards have not deteriorated, it is suggested that recertification must be obtained every five years.

Certification in this instance may be defined as the granting of documentation in the form of a certificate to signify that set standards as laid out in the European Guidelines have been achieved. The certificate will be time limited and will state that a recognised international visiting team of professionals, of an approved standard, has visited the unit/organisation concerned and has found it to have achieved satisfactory standards to the level of certification granted in accordance with the protocol.

In this manner, commitment to quality assurance activities will be increased throughout Europe, including the new Member States, and this will bring benefit from an extensive team of associated experts to those European areas not currently experienced in high quality mammography.

Some workers believe that the way forward in this matter is to undergo the process of obtaining the ISO 9000 Standard. Experience in the UK Breast Screening Programme has shown that this methodology is not optimal for the purpose required in breast cancer screening. The voluntary accreditation system for mammography in the United States organised initially by The American College of Radiology demonstrated most effectively how such a system rapidly takes hold and may become mandatory in the short to medium term. Ultimately, 'purchasing power' from general practitioners, women's groups or health insurance agencies is likely to be of great significance. Certification can act in support of this.

All requests for certification will be of a voluntary nature until such time in the future that the European Commission or other authorities consider this to be mandatory. These certification activities should not be detrimental to any worthwhile local quality initiatives taking place in units or programmes, and as far as possible should eventually become integrated with, and work alongside initiatives being taken at national level by recognized authorities in each Member State.

11.3 Breast screening versus diagnostic breast imaging activity

It is important to distinguish clearly between the differing requirements for a breast diagnostic service and a breast screening programme. It is important to avoid confusion between the wider organisational and epidemiological support that will be necessary for a screening programme and to some extent the differing facilities that may be required between both services.

To this end we have separated the certification categories between breast screening and breast diagnostic activity. We intend to further clarify this issue by issuing certificates, which will be marked as Diagnostic Breast Imaging or Breast Screening. The issuing of a Diagnostic Breast Imaging Certificate will therefore make no judgement or reference to the ability to perform screening, likewise the possession of a Diagnostic Breast Imaging Certificate in no way implies that this unit is suitable to perform screening activities. Breast Screening Certificates will only be available to organised population based screening programmes, not to individual 'screening' units outside a screening programme.

11.4 Certification categories and visits

Four certification categories and two specialised visits are described:

1. Diagnostic Breast Imaging Unit

2. Diagnostic Breast Assessment Unit

3. Loco-regional Breast Screening Programme

4. European Reference Centre for Breast Screening

5. Advisory Visit (A) & Pre-certification Visit (B)

Different categories and visits of certification should be acknowledged from the ability to produce an adequate quality mammogram in an individual Diagnostic Breast Imaging Unit, up to a facility that is capable of acting as a European Reference Centre for population based breast screening activities. Reference will be made to whether the programme is working in a centralised or decentralised setting.

Also in a decentralised setting all participating offices (Diagnostic Breast Imaging Units and Diagnostic Breast Assessment Units) will be required to form part of the centralized physico-technical and professional quality control requirements as described, and comply with all relevant criteria. The mammographic image quality will be assured, as will the experience of the second radiologist performing centralised double reading. Volume requirements as stated in the following sections are regarded as the absolute minimum required to allow the production of adequate diagnostic quality images. Greater numbers may not guarantee higher quality, but are much 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. 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.

11.4.1 Category 1. Certification protocol of a diagnostic breast imaging unit

This level reflects the ability of any office or clinic to provide mammographic and sonographic image quality of satisfactory physico-technical and professional standards according to published criteria in the European Guidelines[2]. The visiting team must be satisfied that the performance levels of equipment, radiographic staff, radiological staff and physics support services as laid out in the European Guidelines have been achieved, and that adequate and regular Quality Control procedures will be followed. The following basic criteria will be required from a Diagnostic Breast Imaging Unit:

A) General
- Perform at least 1,000 mammograms per year.
- Keep a record of mammogram results and monitor numbers of women referred for further assessment and for assessment outcomes.

B) Physico-technical
- Have dedicated equipment specifically designed for application in diagnostic mammography e.g. mammography system with magnification ability and dedicated processing, and be able to provide adequate viewing conditions for mammograms.
- Have dedicated ultrasound system.
- Comply with the physico-technical protocol in the European Guidelines.

C) Radiographers
- The radiographers, technologists or other members of staff performing the mammographic examination must have had at least 40 hours of documented training specific to the radiographic aspects of mammography and regularly participate in External Quality Assessment Schemes and radiographic update courses. These persons must be able to perform good quality mammograms. There should be a nominated lead in the radiographic aspects of quality control.

D) Radiologists
- 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.

11.4.2 Category 2. Certification protocol of a diagnostic breast assessment unit

In addition to the standards achieved by the Diagnostic Breast Imaging Unit, a centralized 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 following basic criteria will be required from a Diagnostic Breast Assessment Unit:

A) General
- Perform at least 2,000 mammograms a year.
- 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 (including stereotactic) or sonographic guidance.
- Monitor data and feedback of results.
- Keep a formal record of mammogram results, assessment processes and outcomes.

B) Physico-technical
- Have dedicated equipment specifically designed for application in diagnostic mammography e.g. mammography system with magnification ability and dedicated processing, and be able to provide adequate viewing conditions for mammograms.
- Have dedicated ultrasound and stereotactic system and needle biopsy device for preoperative tissue diagnosis.
- Comply with the physico-technical protocol in the European Guidelines.

C) Radiographers
- The radiographers, technologists or other members 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 and radiographic update courses. These persons must be able to perform good quality mammograms. There should be a nominated lead in the radiographic aspects of quality control.

D) Radiologists
- Employ a trained radiologist, i.e. a person who has had at least 60 hours of training specific to mammography and who in volume reads at least 1,000 mammograms per year.

E) Pathology support
- Have organised and specialist cyto / histopathological support services.

F) Multidisciplinary activities.
- Participate in multidisciplinary communication and review meetings with others responsible for diagnostic and treatment services.

11.4.3 Category 3. Certification protocol of a loco-regional breast screening programme

In addition to the physico-technical and professional standards required for high quality breast imaging, it will be necessary to demonstrate a significant level of organizational success with regard to population based mammographic screening, and in addition to meet recognised performance standards and targets widely regarded as essential for successful screening.

Certification of a loco-regional screening programme requires that all diagnostic breast imaging units and diagnostic breast assessment units operating within the screening programme meet the required standards.

The following basic criteria will be required from a Loco-regional Breast Screening Programme:

A) General
- Perform at least 5,000 examinations a year
- Serve an area and age defined target population of at least 20,000 eligible women.
- Have undergone at least two full screening rounds.
- Ensure that there is a nominated Programme Director with overall responsibility for the programme, having the authority to suspend unsatisfactory smaller units in a decentralised system, where repeated attempts at image quality improvement have failed.

B) Invitation scheme
- Operate a successful personalised invitation system and/or a promotional campaign as well as an organised system for re-inviting all previously screened women.

C) Physico-technical quality control
- Have a centralised physico-technical quality control service.
- Comply with all physico-technical criteria set out in the European Guidelines and ensure that adequate technical and professional quality assurance procedures are carried out in all units participating in the programme.
- Have adequate and satisfactory equipment in all units dedicated to the use of mammography, and dedicated processing with all necessary facilities for full and complete assessment of women with screen detected abnormalities.
- Have adequate viewing conditions including the use of roller viewers for multiple screen film reading by more than one reader if necessary in the most effective manner.

D) Radiographers
- The radiographers, technologists or other members 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 and radiographic update courses. These persons must be able to perform high quality mammograms. There should be a nominated lead in the radiographic aspects of quality control.

E) Radiologists
- Employ trained radiologists, i.e. a person who has had at least 60 hours of training specific to mammography.
- Have centralised reading or, in a case of a decentralised programme, centralised double reading by one or more fully trained and experienced radiologists each reading at least 5,000 mammograms per year.
- Ensure that in a decentralised programme with multiple smaller screening offices participating, the central and experienced double reading radiologist judges the mammograms from both the diagnostic and an image quality point of view. This radiologist must take full responsibility for the image quality of the mammograms reported and ensure that where necessary images are repeated until they be of satisfactory standard.
- Observe all radiographic image quality criteria.

F) Referral, assessment and feedback
- Keep a formal record of referrals, mammogram results, assessment processes and outcomes.
- Have an approved protocol for referral of women with screen detected abnormalities within a decentralised screening programme to centres with adequate and full assessment facilities.
- Process feedback of data and results to the professional staff involved in the programme.

G) Pathology support
- Have organised and specialist cyto / histopathological support services.

H) Multidisciplinary activities
- Participate in multidisciplinary communication and review meetings with others responsible for diagnostic and treatment services.

I) Identification and peer review of interval cancers and screen-detected cases
- Have a mechanism for identification and peer review of interval cancers and screen-detected cases. Interval cancer review will also form part of the certification visit.

J) Epidemiology support
- Ensure satisfactory epidemiological support particularly with regard to the organisational, implementation and evaluation aspects as described in the European Guidelines - Quality Assurance in the Epidemiology of Breast Cancer Screening[2].
- Collect and monitor data according to the European Guidelines.
- Evaluate and report on the performance of the screening programme annually.

11.4.4 Category 4. Certification protocol of a European reference centre for breast screening

In this context European refers to the performance of a centre according to the best European standards as opposed to its geographical connotations. In addition to the requirements listed and the fulfilment of all published targets and conditions at organisational, professional and physico-technical levels, the Centre must be considered capable of providing consultation services and training both internally and externally. It will be expected to function on a more global level of furthering the processes of mammographic quality improvement regionally and nationally, both justifying and promoting the values of population screening by mammography for breast cancer.

Certification of a European Reference Centre for Breast Screening requires that all diagnostic breast imaging units and diagnostic breast assessment units operating within the screening programme meet the required standards.

As certification becomes more widely used, it is anticipated that 'franchised' certification activities will be placed in the hands of a limited number of highly regarded and recognised centres. Only programmes that have achieved category 4 certification will be considered as suitable candidates for this extension of certification within their own Member States. The granting of category 4 certification however does not place any obligation in this regard either on the part of the programme concerned or the certifying organisation.

The following basic criteria will be required from a European Reference Centre for Breast Screening:

A) General
- Perform at least 10,000 mammograms a year.
- Serve an area and age defined target population of at least 20,000 eligible women.
- Have undergone at least two full screening rounds.
- Ensure that there is a nominated Programme Director with overall responsibility for the programme, having the authority to suspend unsatisfactory smaller units in a decentralised system, where repeated attempts at image quality improvement have failed.

B) Invitation scheme
- Operate a successful personalised invitation system and/or a promotional campaign as well as an organised system for re-inviting all previously screened women.

C) Physico-technical quality control

- Have a centralised physico-technical quality control service.
- Comply with all physico-technical criteria set out in the European Guidelines and ensure that adequate technical and professional quality assurance procedures are carried out in all units participating in the programme.
- Have adequate and satisfactory equipment in all units dedicated to the use of mammography, and dedicated processing with all necessary facilities for full and complete assessment of women with screen detected abnormalities.
- Have adequate viewing conditions including the use of roller viewers for multiple screen film reading by more than one reader if necessary in the most effective manner.

D) Radiographers

- The radiographers, technologists or other members 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 and radiographic update courses. These persons must be able to perform high quality mammograms. There should be a nominated lead in the radiographic aspects of quality control.

E) Radiologists

- Employ trained radiologists, i.e. a person who has had at least 60 hours of training specific to mammography.
- Have centralised reading or, in a case of a decentralised programme, centralised double reading by one or more fully trained and experienced radiologists each reading at least 5,000 mammograms per year.
- Ensure that in a decentralised programme with multiple smaller screening offices participating, the central and experienced double reading radiologist judges the mammograms from both the diagnostic and an image quality point of view. This radiologist must take full responsibility for the image quality of the mammograms reported and ensure that where necessary images are repeated until they be of satisfactory standard.
- Observe all radiographic image quality criteria.

F) Referral, assessment and feedback

- Keep a formal record of referrals, mammogram results, assessment processes and outcomes.
- Have an approved protocol for referral of women with screen detected abnormalities within a decentralised screening programme to centres with adequate and full assessment facilities.
- Process feedback of data and results to the professional staff involved in the programme.

G) Pathology support

- Have organised and specialist cyto / histopathological support services.

H) Multidisciplinary activities

- Participate in multidisciplinary communication and review meetings with others responsible for diagnostic and treatment services.

I) Identification and peer review of interval cancers and screen-detected cases

- Have a mechanism for identification and peer review of interval cancers and screen-detected cases. Interval cancer review will also form part of the certification visit.

J) Training

Provide training by means of

- Teaching files including interval cancers and recalled cases.

- Training programmes with performance evaluation for radiologists and radiographers
- Training programmes for multidisciplinary diagnostic and treatment teams.

K) Epidemiology support
- Ensure satisfactory epidemiological support particularly with regard to the organisational, implementation and evaluation aspects.
- Collect and monitor data according to the European Guidelines.
- Evaluate and report on the performance of the screening programme annually.

11.4.5 Category 5. Specialised visits

• Certification protocol of an Advisory Visit (A) & • Pre-certification Visit (B)

This type of visits will be offered to screening programmes on request in addition to the four certification categories.

(A) The **Advisory Visit** may take place around the commencement or during the first year of a screening programme. The aim of such a visit is to assess whether the design of the programme is in line with the recommendations of the European Guidelines. The visiting team will in addition highlight any possible shortcomings of the programme and offer appropriate advice and support to overcome these.

(B) The **Pre-certification Visit** may take place during the second screening round and before applying for a full certification of the screening programme. The aim of this visit is to ensure a successful certification. The visiting team will highlight the remaining possible shortcomings that could hamper a successful certification and offer appropriate advice and support to overcome these.

Support means here that for those specific subjects in which the European targets were not met 'coaching' can be provided by specialized experts.
This can be requested both after the advisory and the pre-certification visits.

The protocols of the above visits are based on the category 3 and 4 certification protocols with the exception that no review of interval cancers will be carried out on site.

11.4.6 Sources and criteria

The major source for physico-technical and professional standards is the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis[2]. Reference has been given to the American Mammography Quality Standards Act and in particular the Small Entity Compliance Guide - An Overview of the Final regulations Implementing the Mammography Quality Standards Act of 1992[3]. Reference is also made, and should be made by any office or programme wishing certification, to Council Directive 97/43/EURATOM[4], referring to the radiation protection of the exposure of individuals as part of health screening programmes.

11.4.7 Methodology

All requests for certification should be made to the Professional Co-ordinator by filing an application form. This form will include preliminary questions, and the applicant should demonstrate that checklist criteria have been achieved. Each request will then be considered and on the basis of this checklist, the decision whether or not the site in question can be deemed viable for certification will be taken. In this case a site visit will be scheduled and a suitable international expert team allocated. A protocol will be sent to the local unit laying out the time schedules involved and describing precisely the actions to be followed, the criteria which

need to be achieved, and the documents and results that should be available for the visiting team to review. All visits will include a review of films, technical and patient facilities.

The visiting team for the Diagnostic Breast Imaging Unit will consist of a radiologist and a radiographer, for the Diagnostic Breast Assessment Unit a physicist and a pathologist in addition. The visiting teams for the Loco-regional Breast Screening Programme and European Reference Centre for Breast Screening will include the above nominated members with the addition of an epidemiologist. For certain certification visits also a specialist breast surgeon will be invited to the visiting team. The membership will be stated prior to the visit and will be drawn from a pool of acknowledged international experts from recognised European centres. The team leader may, or may not, be one of the professional representatives participating in the visit.

The certification visit will take place at the offices of the unit or organisation requesting certification and it is expected that the relevant senior professionals involved in that programme will also be present. Following the visit and while still on site, the visiting team will have an informal feedback session with each other. Provisional and brief comments on initial impressions will then be passed on confidentially by the leader of the team to the Senior Executive present at the local unit. Although the prime purpose of the visit will be to assess the suitability for certification, the visiting team will still make constructive suggestions as to any local improvements which could be made to further best practice.

The full written report in draft will be sent to the nominated representative of the local unit within six weeks of the date of the visit. A formal reply must be made by the local unit within a further four weeks responding to issues of accuracy or interpretation. Following receipt of this response. A final report will be issued within three weeks and will state whether certification has been granted or withheld. There will be a mechanism for the right of appeal in cases of dispute.

When all procedures have been satisfactorily completed, full DIAGNOSTIC BREAST IMAGING or BREAST SCREENING Certification will be issued. This signed certificate will state quite clearly the name of the unit or organisation concerned and the category of certification granted. Such a certificate may be displayed by the units or programmes concerned, and the relevant logo utilised on notepaper, reports etc as appropriate.

11.4.8 Frequency of certification

Re-certification should take place every five years with at least one data update in between full visits, so that the co-ordinating office may ensure that technical and professional standards are being adhered to.

11.5 References

1. Young KC, Wallis MG, Ramsdale ML. 1994
   Mammographic film density and detection of small breast cancers. – Clinical Radiology 49, 461 - 465

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3. Small Entity Compliance Guide - An Overview of the Final Regulations Implementing the Mammography Quality Standards Act of 1992.
   Report to Mammography Facilities and the Public. United States Department of Health and Human Services. October 1997.

4. Health Protection of Individuals Against the Dangers of Ionising Radiation. Council Directive 97/43/EURATOM. European Commission. June 1997.

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Guidance on breast screening communication

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Introduction

Screening is a medical investigation differing from other health care activities in that it is usually addressed to a healthy and asymptomatic population. Compared to general medical practice, where patients apply to the physician for a specific complaint, in the screening scenario people are invited by a population-organised programme to undergo a preventative test in order to detect diseases before symptoms occur and receive more effective and less invasive treatment.
It is therefore imperative to ensure that those invited to take part in screening programmes are given adequate information about screening. Furthermore, this information must be communicated in an appropriate and unbiased manner to enable women to make an informed choice about attending screening. In order for this to happen, screening operators have to understand the complexity of appropriate communication with women invited to attend screening, and develop new and innovative approaches of communicating information to these women. To this end, ten European countries and Europa Donna have been involved in projects concerning communication, within the framework of the European Breast Cancer Network (EBCN). This chapter represents the outcome of this collaboration.

The objective of this chapter is to give an insight into the issues relating to communicating information about screening and provide those involved in screening with some pragmatic suggestions on how to plan and develop written screening information tools.

FIRST PART

12.1 Communicating information to enable decision-making

While the term 'information' means the mere transfer of data, communication is a more complex process. Communication implies that the person who receives the information can understand and make use of it. Communicating about health does not just include transmitting information. In order to communicate effectively and appropriately about health, it is important to interpret the social and cultural factors that influence individuals' needs and behaviours. In addition, health communication has become more complex due to the exponential growth of scientific knowledge. This can generate confusion and lead to difficulties in the process of decision-making[1].
It has been suggested that providing information to individuals with the purpose of helping them make choices and decisions requires new ways of interacting and communicating[2]. Questions such as: What background information must individuals receive? How deeply should health professionals probe for understanding? What constitutes irrelevant information that only tends to confuse? What words and explanations facilitate comprehension? need to be answered. Health professionals have not been in the habit of asking such questions[2].

Health professionals must provide individuals with such information that will allow them to 'knowledgeably' decide whether or not to undergo an intervention, taking into consideration available alternatives, potential risks and foreseeable outcomes[3 4]. However, in the screening context the issue of communication becomes more complex because here it is the health professional (generally both administrative staff and medical personnel) who approaches an apparently healthy individual to undergo a test. Women invited to attend breast screening are not ill, and only few of them will develop breast cancer during the course of their lives. It is therefore vital that these women know the pros and cons of breast screening to help them make an informed decision about whether or not to attend screening[5,6,7,8,9]. When a woman chooses to attend screening mammography, she voluntarily agrees to do so. However, this does not imply that she has knowledge and understanding of what is proposed.

The following factors have to be taken into account when developing communication strategies for those invited for mammography.

12.1.1 Ethical principles

Any framework developed to communicate health information needs to be underpinned by the following ethical principles[10]:
1. Autonomy: the obligation to respect the decision making capacities of autonomous persons. It emphasises that patients should normally be in a position to choose whether to accept an intervention or not as part of their general right to determine their own lives.
2. Non maleficence: the obligation to avoid causing harm intentionally or directly (the principle is not necessarily violated if a proper balance of benefits exists; that is, if the harm is not directly intended, but is an unfortunate side effect of attempts to improve a person's health).
3. Beneficence: the obligation to provide benefits balancing them against risks.
4. Justice: obligation of fairness in the distribution of benefits and risks.

These four principles provide a useful framework for health professionals (including those offering screening) to use when developing appropriate ways of communicating with client groups.

12.1.2 Population heterogeneity and informed choice

There is a growing concern that individuals invited for screening are often told about the positive aspects of screening, ignoring any negative aspects in order to increase the attendance rate and

ensure the effectiveness of the screening programme[6,11,12]. Women cannot be expected to make an informed choice about participation in a screening programme unless they are given sufficient and adequate information. This information should be honest, adequate, evidence based, accessible, unbiased, respectful, and tailored to individual needs[4,8,13-15]. Otherwise, problems could emerge. For example, misconceptions about cancer and the screening process may lead to high anxiety levels[16].

In the screening context there does not exist a monolithic 'public', but a diversity of 'publics' with specific characteristics to consider. Thus while breast cancer screening is a population programme, the issues that health professionals offering population screening have to face are individuals with specific needs and different values and beliefs. In addition, contextual, cultural or personality factors may directly influence the way an individual processes health information and impact on the motivations to attend screening. Educational status can also have an impact on how the presented information is understood[17-19].

12.1.3 The role of the media

An important factor that must be noted by health professionals is the influence of the mass media on individuals' perception and understanding of health issues. Research has shown that the media plays an important role in influencing opinion in the use of medical interventions such as breast screening[20]. Generally, the media has favoured the optimistic message of the 'mythical' view that, medicine in general and screening in particular can cure all diseases. The information disseminated by the media has often underlined only benefits of medical services, glossing over uncertainties, adverse events and side effects and ignoring legitimate scientific controversies[21,22,23,24]. With respect to screening programmes the message from the media appears to be that screening is 100% accurate and therefore any false positives or negatives must be due to errors on the part of those providing the screening. This has lead to the perception that all cancers arising after a normal screening examination must have been 'missed' and that delays in diagnosis have prognostic significance[25]. This misunderstanding of the effectiveness of screening has resulted in high expectations on the part of the public and anger and resentment (often resulting in litigation) when this is not the case[25].

It is therefore vital that health professionals are aware of the role of the media in providing information and subsequently influencing individuals' decisions. It is important that health service providers work closely with the media and provide them with current, accurate and comprehensive information proactively and regularly. Such information disseminated by the media may engender informed debate that empowers the public rather than give rise to false expectations that cannot be realistically met by the services.

12.2 Problems related to effective communication in screening

Problems related to effective communication can be associated both with providers and consumers[17,18,26] and include the following:

12.2.1 Access to the information about breast screening

Appropriate information in suitable formats should be available and accessible to all women who would benefit from breast screening. It is important that women are informed about where they can get information about breast screening, what kind of information is available and in what format (written materials, web-site, information phone lines etc.). Accessibility also includes the provision of such information to disadvantaged groups (i.e. disabled, ethnic groups).

12.2.2 Lack of clarity of health professionals involved in the screening programme

Women obtain breast cancer information from a variety of sources, among which health professionals are one of the most obvious.
The health professionals that play a central role in the provision of information include staff working in primary care and in the breast screening units. It is important that these people acquire comprehensive knowledge needed to inform women about the pros and cons of screening. This is not always the case. Biomedical ethics is rarely covered in the curriculum of health operators. Risk communication, i.e. communication of benefits, the potential harm from medical interventions, and the subtleties of what genuine informed consent involve are seldom covered in medical and health education programmes. In addition, not all health professionals understand and accurately interpret epidemiological data (e.g. relative or absolute risk reduction)[27].

12.2.3 Communication skills of primary care and health professionals

In most EU countries, the specific role of General Practitioners (GPs) or Gynaecologists in providing information about breast screening is well-documented[28]. In particular, the personal and continuing relationship of GPs with their patients puts them in a privileged position for providing relevant and specific information to these women. This can contribute to reducing anxiety and fear about the test. GPs are also usually trusted by their patients and overall, their involvement in the decision making process is accepted by women. Research indicates that their involvement is an important factor associated with mammography use[29,30].
If GPs' involvement in communicating information about breast cancer screening is important, it follows that they need to be well informed about the various issues and processes. Educating, training and motivating GPs to play an appropriate role in enabling and empowering women to make informed decisions about participation in breast screening is an important part of the proper running of a screening programme.
The way in which information is presented is as important as the information itself. Accuracy of information depends not only on its content but also on the communication skills of the health professionals involved in providing it. Health professionals need to be sensitive to the educational, linguistic and religious differences among women and recognise the potential impact of race, ethnicity, class and culture on the decision whether or not to participate in screening. They should use jargon-free language and avoid incomprehensible mathematical or statistical concepts expressing risk[31] as this makes it very difficult for lay people to understand what is being communicated. To overcome these problems, it is essential that health professionals are given appropriate training in communication skills.

12.2.4 Consumers' health literacy skills

On the part of the consumers, low health literacy skills can represent a major obstacle in understanding information. Individuals vary in their ability to read, understand and use information. Poverty, ethnicity and age are also considered predictors of limited literacy[19].
Providers of screening programmes have to frequently face multicultural and multi-linguistic populations with all the related communication problems. To tackle these problems does not entail just translating the information materials, but also gaining an understanding of ethno-cultural values, beliefs, health practices and communication styles of these varied groups and identification of their specific information needs[32].

In addition to the above barriers identified by research the following factors can also have an impact on providing appropriate and relevant information to women invited for mammography screening.

12.2.5 The communication paradox

As noted above, screening is offered on a population basis, and information pertains to the population level. This diversity between personal and population information needs can lead to the conundrum of the communication paradox. For example, information sent to the population should include lifetime risk of getting breast cancer, but it cannot include the individual's risk (as this would have to take into account individual characteristics, i.e. family history, age at menarche and other possible risk factors). It may therefore be necessary to 'customise' or 'tailor' information to fit individual needs. Evidence shows that such tailored messages are likely to increase the effectiveness of the information[33,34]. However, problems can arise with using 'customised information' as it is not an inexpensive option and it is not feasible to provide tailored information to cater for the individual needs of 'large' groups of several thousand women, such as those enrolled in population programmes. Pragmatically, what may be possible is to 'customise' information for sub-groups e.g. ethnic minorities and different age groups, or people recalled for further tests to address their specific and different needs.

However, it should also be borne in mind that tailored messages are not always effective for all groups. As research suggests, tailored messages are 'far superior to non-tailored messages for some people, only slightly better for others, and, for some, no different or less effective than non tailored messages'[35].

12.2.6 Developing client-centred information

The starting point for good quality information to enable decision-making is to provide information about the issues of importance to those who are receiving it. Some phases of the screening process, especially the invitation phase, do not usually permit one-to-one communication between health professional and the individual, and consist of one-way transmission of information from the health professional that is often developed without any input from the client group, or evaluated to determine its appropriateness to the needs of this group. An important aspect of decision-making is that individuals have access to relevant and appropriate information, relevant not just from the health professional's point of view but also from the individual's point of view. It is therefore vital to ascertain the views of those invited for screening on what information they need to make an informed choice in order to make the communication process more effective and appropriate.

SECOND PART

As underlined in the first part of this chapter, women cannot make informed decisions unless they are provided with sufficient and appropriate information about breast cancer and screening. The information women are given should be underpinned by available evidence and presented in an appropriate form.

12.3 Improving the quality of breast screening communications

Several tools have been used to convey information to individuals about screening interventions (videos, leaflets, audio cassettes, touch screens, etc.). A systematic review looking at informed use or non-use of screening concluded 'there is currently limited evidence available about the most effective ways of presenting information about the risks and benefits of screening'[36]. The following questions should be asked when developing a communication tool and information packages for breast cancer screening[3] (table 1):

- Which is the most accessible media format?
- Can it be shared with family and friends?
- How easy would it be to update?
- What about the costs of updating, reproduction and distribution?
- Would it be appropriate and acceptable to the intended audience?

Table 1 - Attributes of a good communication tool

1. Easy to understand
2. Accessible and comprehensive
3. User-friendly
4. Easy and cost-effective to update, reproduce and distribute

Information provided to women invited to attend breast cancer screening should be accessible, relevant, comprehensible, comprehensive, including benefits as well as risks and disadvantages, and tailored to meet needs of special groups. In addition information provided should be phase specific and multilevel to take into account the needs of women recalled and those who may need additional information on specific areas (table 2).

Accessible

Information should be accessible to all women who would benefit from breast screening. It is important that a woman who needs information about breast screening should be able to find and access it easily.

Relevant

Screening information should be relevant to the women for whom it is intended. It should be 'women centred' and meet women's needs. In the past, screening professionals tended to assume that they knew best what information women needed and wanted. Unfortunately, the majority of the materials they developed failed to address issues that women thought important[37]. It is vital to gain an insight into women's understanding of the information about breast screening and involve women in developing information materials. However, this is rarely done and screening providers need to find out what information women need and want, and involve them in the development of appropriate and timely information materials.

Comprehensible
Information should be clear, avoiding jargon and technical language. Guidelines have been produced to enable the production of good written material[38]. They include the following:
- Women's interest should be paramount
- Use concepts the women will understand
- Avoid unnecessary words
- Be personal
- Use short sentences and short words
- Follow rules of grammar and syntax

Comprehensive
Information should be comprehensive and messages should not be biased to encourage participation. It is imperative that the information is well balanced, i.e. it should include information on risks, false positives, false negatives, and uncertainties. Communications should also contain information about the benefits and the quality of the breast cancer screening programme. It may be appropriate to add information about process indicators like participation rate, waiting times, recall rate and the proportion of breast cancers detected by mammography, to help women understand the screening programme and to verify its results.

Tailored
Information should be tailored as far as is possible and adapted to suit the specific needs of different groups and different situations. This will ensure that the information has more personal relevance and contains less redundant information. While it is difficult to provide individually tailored information for population programmes, it should be possible to provide particular sub-groups with relevant information tailored to their specific needs at a given stage of the screening process.

Phase-specific information
Women will need different levels of information at the different phases of screening. Research has shown that the high level of anxiety experienced by women recalled for further assessment[39] can be diminished initially by informing about the possibility of recall in the first invitation letter and then by giving further relevant information at the time of assessment[40].

It would be appropriate to provide women with different types of information according to the different screening phases (i.e. first invitation, recall, etc.). For example, women recalled for further assessment might need information on what these procedures consist of and on the resulting outcomes. At this stage it would be appropriate to provide women with additional and more detailed information using different formats. It is important that during this phase women have the opportunity to meet health professionals such as a breast care nurse or radiologist, and be able to discuss various options and outcomes with professionals in a supportive environment.

Multi-level information
Basic information can be considered as the information handed out to all women (generally at the time of the first invitation). It must be complete, honest and comprehensive and conform to the guidance on readability and clarity, such as avoiding too much information, badly presented and using jargon that may lead to confusion. Information given should be appropriate and brief, preferably in a question and answer format. However this may limit the amount of information delivered and women in the same screening phase may require different degrees of information i.e. from a basic level of information to more detailed information on specific areas. It is therefore important that women requiring additional and in-depth information should be able to access it. Basic information provided to all women should also indicate where more detailed information may be obtained (i.e. phone-line, screening operators, GPs, web-site, etc.). It is important that screening programmes provide this supplemental information, using different communication instruments for this purpose.

Table 2 summarises the characteristics that information provided to women invited to attend breast cancer screening should include.

Table 2 – Characteristics that information provided to women invited to attend breast cancer screening should include

Accessible:	Women should be able to find information easily.
Relevant:	Information should be 'women centred' and include information that women want to know.
Comprehensible:	Information should be clear, avoiding jargon and technical language.
Comprehensive:	Information should cover both the positive and negative aspects of screening.
Tailored:	Information should be customised to suit the specific needs of different groups and different situations.
Phase specific:	Women should be provided with appropriate information according to the different screening phases (i.e. first invitation, recall, etc.)
Multi-level:	The range of information provided should meet the needs of different users from basic information to more detailed information on specific aspects of screening.

12.4 Recommendations on the contents of written information (invitation letter/leaflet)

The invitation letter is usually the first communication tool directly sent to women, to invite them to participate in the screening programme. It usually includes logistic/organisational information relating to the screening appointment.
As the first contact with women, the invitation letter must be written in a simple, clear and readable style and include information about the purpose of breast screening. It is recommended that all relevant additional information is provided in a leaflet or other communication instruments included with the letter. The letter should refer to the leaflet and encourage women to read it[16].
Table 3 lists the topics that should be covered in the invitation letter.

Table 3 - Contents of the invitation letter
Invitation letters should include information on:

1.	The purpose of screening - Who the test is for (target population - age group)
2.	The test – what type of test mammography is
3.	The screening interval
4.	If the test is free or not
5.	The appointment - how to make it, how to change it

6.	When and how to get the results (mentioning approximate waiting times)
7.	Mention the possibility of being recalled for further tests
8.	Other logistical information: e.g. to bring previous mammograms, clothes to wear
9.	Where women can get further information (e.g. information services, telephone hotlines, patient groups and web-sites)
10.	Data protection/confidentiality.

Invitation letters and leaflets are usually designed to complement each other and information contained in the former can be reiterated in the latter. The leaflet included with the invitation letter usually provides descriptive information about the screening programme, the test and its effects. It often reinforces information already mentioned in the invitation letter and adds extra information that may be useful to women.
The benefits and disadvantages should be explained in the leaflet. The leaflet should be well written and visually acceptable to the audience. It is therefore important that different formats and structures are tested with the target population.
Table 4 lists the information that should be included in the leaflet.

Table 4 - Contents of the invitation leaflet
The invitation leaflet should include information about:

1.	Who the test is for
2.	The test – nature, purpose, validity
3.	The process of the test - who performs the test, how long does it take, what does it involve?
4.	The screening interval
5.	What does early detection mean?
6.	Benefits and disadvantages of breast cancer screening (including information on side effects i.e. pain, discomfort and radiation risk)
7.	How to obtain the result and how to interpret it (negative, positive, uncertainties)
8.	Further assessments - explaining the possibility of further tests (why and what?) and the possibility of false positive results and uncertainties
9.	Quality controls of the screening procedure
10.	Where women can get further information (e.g. information services, telephone hotlines, patient groups and web-sites)
11.	Date and sources of information provided

It is essential that written information is guided by good communication principles because the way information is presented plays an important role in determining comprehension and acceptance. Some recommendations on text and language style, wording, and formatting are listed in table 5. They should be carefully considered by the screening staff to make the communication more effective and easily understandable to women.

Table 5 - Stylistic advice

Language:

- clear (about the topic: clarify points with examples)
- honest, respectful, polite
- simple everyday language (no technical terms, jargon, abbreviations and acronyms)
- informal (use of pronouns like 'we' and 'you' to personalise the text)
- impartial
- not top-down (no prescriptive style or paternalistic tone)
- written in the active voice

Text style and wording:

- credible, reliable (indicating the source of information)
- up to date
- friendly and sympathetic
- contemporary
- positively framed (e.g. 9 out of 10 recalled women are found to be normal rather than 1 out of 10 recalled women will have cancer)
- positive tone (alarming statements should be avoided)

Text format:

- preferably plain layout
- short sentences and brief paragraphs
- use of diagrams and pictures
- use of titles and subtitles (to distinguish different areas)
- bold or capital letters (to underline important points)
- larger print (essential for older target populations)
- use of white spaces (to facilitate the reading)
- preferably question/answer and paragraphs formats
- appropriate colours (as some colours are difficult for colour blind people to read)
- logo

12.5 Other issues to consider when developing communication strategies for breast screening

12.5.1 Relationship between information provision and participation in breast cancer screening

It has been argued that the provision of explicit information on the limitations of screening could result in:

- decreased participation and reduction in population benefits
- possible inequity, as those most likely to be deterred may be the most socially disadvantaged
- increased costs as more staff time is required to explain screening and its consequences
- reduced cost-effectiveness if participation falls so low that the service becomes unviable[6]

There have been many debates in past years, about the desirability of attaining high rates of participation in screening 'per se', without allowing participants to make an informed decision about whether or not to be screened. As a result, tensions still exist between promoting informed decision making, where the individual may decide not to undergo screening, and strategies promoting participation as an effective form of health-care[8,14,36,41].

The concept of recognising the active and responsible role of women and their participation in screening programmes, based on informed choice, has been proposed as a replacement of the idea of compliance[42].

The question as to how many people would refuse screening if the limitations were included in the information can be considered an empirical one, as very little work has been carried out in this area[43,44]. Research is needed to assess the impact of the 'information factor' on participation.

12.5.2 The role of advocacy groups

The function of advocacy groups in breast screening is increasingly essential[45]. In the recent years they have empowered women to evolve from the position of passive participants into influential partners[46]. The role of women's advocacy groups (such as Europa Donna which is an active member of the EBCN communication group) in the breast screening context can be varied. Their role includes emphasising the need for appropriate screening and early detection, ensuring that women fully understand any proposed treatment option and providing high quality supportive care during and after treatment. Other aims of these associations are to advocate appropriate training for health professionals, to promote the advancement of breast cancer research and to promote the dissemination and exchange of factual, up to date information on breast cancer[47].

12.5.3 The Internet

The advent of the Internet has added a new dimension in the dissemination of information. While research indicates that presently a small minority of younger and more educated women use the Internet to access information on breast screening, it will be useful in the future to explore the use of this growing and increasingly accessible technology as a source of information[48].

12.5.4 Communication quality indicators

The development of indicators to evaluate the quality of the information provided to women in each programme needs to be an important aspect of the communication strategy in the future. Several technical indicators already exist to evaluate the performance of the screening procedure and the programme's activities. These have been incorporated into the quality assurance process of many ongoing breast screening programmes and are constantly reviewed and revised in the light of recent experience and research. In addition, minimum quality standards are recommended to evaluate programmes. However, no quality indicators are available to evaluate the standard of communication in breast screening. It is crucial that such standards are developed to assess the relevance and appropriateness of the information provided. In addition indicators should be developed to assess how information about breast screening is communicated to the women invited for screening and to the women in the different phases of screening. Among the potential communication quality indicators, some are more easily quantifiable than others, which are more conceptual.
Table 6 outlines some potential quality indicators and evaluation parameters that could be refined and implemented to ensure good quality screening communication.

Table 6. Potential communication quality indicators (in parentheses examples of possible evaluation parameters)

• The availability of a telephone information service for women invited for screening (YES/NO; number of calls received per 1000 invited women)
• The availability of different formats from which women can get information about the screening programme (YES/NO; types of formats)
• Written information material which was tested on the target population for their acceptability and readability (YES/NO; evaluation outcomes)
• Information materials available for different ethnic groups or special needs groups (e.g. visually impaired) (YES/NO; proportion of specific communication materials for ethnic and/or

disadvantaged minority groups compared to those present in the population)

- The involvement of non-medical organisations (churches, markets, etc.) in the dissemination of information (YES/NO)
- The implementation of counselling protocols (YES/NO; proportion of counselling sessions per 1000 invited women)
- The availability of face-to-face communication for women on request (YES/NO)
- The organisation of courses on communication for screening providers (front office staff, radiologists, radiographers etc.) (YES/NO; number of courses/year; proportion of participants who took up the training compared to those who were eligible)
- Women's involvement in developing and assessing the information material (YES/NO)
- The administration of satisfaction questionnaires to the target population (YES/NO; evaluation outcomes)
- The availability of a web site (YES/NO; updating level, number of contacts)

12.6 Developing a communication strategy for breast cancer screening – a summary

A communication strategy for breast cancer screening must be underpinned by robust ethical principles and ensure that the information developed is evidence-based, 'women centred' and delivered effectively.
Breast screening providers should therefore consider the following key points when planning and developing communication strategies for breast screening:

- Take into account the principles of bioethics (autonomy, non maleficence, beneficence, justice)
- Have conclusive evidence that screening procedures meet the appropriate criteria and can be of potential benefit to individuals
- Provide individuals with information that will allow them to make an informed choice
- Acquire the comprehensive knowledge needed to inform people about the pros and cons of screening
- Be sensitive to educational, linguistic, cultural and religious differences among individuals and tailor information to suit personal needs
- Explore women's information needs and involve them in developing information materials
- Take into account the needs of disadvantaged groups (disabled, ethnic minority groups, visually impaired, etc.)
- Give appropriate information in suitable formats available and accessible to the target population
- Test the different information aids on a sample of the target population to evaluate their effectiveness
- Evaluate women's satisfaction with the screening service (i.e. by surveys or questionnaires)
- Develop standards to evaluate the quality of the provided information
- Give women opportunities to discuss the mammography outcomes and other options with screening professionals in a supportive environment
- Avoid situations where economic or political incentives could affect the messages
- Involve GPs in breast cancer screening programmes as women usually know them and tend to have a good relationship with them
- Collaborate with advocacy groups
- Collaborate with the media to ensure the dissemination of accurate information on breast cancer screening
- Exploit new communication tools (Internet, videos, touch screen computers)
- Reserve funds and personnel dedicated to communication
- Receive adequate and on-going training in communication skills

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Annex I

Council Recommendation of 2 December 2003 on cancer screening

(2003/878/EC)

The Council of the European Union,

- Having regard to the Treaty establishing the European Community, and in particular Article 152(4), second subparagraph, thereof,

- Having regard to the proposal from the Commission,

- Having regard to the opinion of the European Parliament,

Whereas:

1) Article 152 of the Treaty provides that Community action is to complement national policies and be directed towards improving public health, preventing human illness and diseases, and obviating sources of danger to human health. Such action shall cover the fight against the major health scourges, by promoting research into their causes, their transmission and their prevention, as well as health information and education. Community action in the field of public health shall fully respect the responsibilities of the Member States for the organisation and delivery of health services and medical care.

2) Further development of cancer screening programmes should be implemented in accordance with national law and national and regional responsibilities for the organization and delivery of health services and medical care.

3) Cancer is a major disease and cause of death throughout Europe, including the future Member States. An estimated number of 1 580 096 new cancer cases, excluding non-melanoma skin cancer, occurred in the European Union in 1998. Of these, 1,4% were cervical cancers, 13% breast cancers, 14% colorectal cancers and 9% prostate cancers. Cervical and breast cancer constituted 3% and 29%, respectively, of new cancers in women. Prostate cancer constituted 17% of new cancers in men.

4) Principles for screening as a tool for the prevention of chronic non-communicable diseases were published by the World Health Organisation in 1968 and by the Council of Europe in 1994. These two documents form, together with the current best practice in each of the cancer screening fields, the basis for the present recommendations.

5) Additionally, these recommendations are based on the 'Recommendations on cancer screening' of the Advisory Committee on Cancer Prevention together with the experience gathered under the different actions sustained under the Europe against Cancer programme where European collaboration has helped, for example, high quality cancer screening programmes to provide efficient European guidelines of best practice and to protect the population from poor quality screening.

6) Important factors which have to be assessed before a population-wide implementation is decided upon include, inter alia, the frequency and interval of the application of the screening test as well as other national or regional epidemiological specificities.

7) Screening allows detection of cancers at an early stage of invasiveness or possibly even before they become invasive. Some lesions can then be treated more effectively and the patients can expect to be cured. The main indicator for the effectiveness of screening is a decrease in disease-specific mortality. As in the case of cervical cancer, cancer precursors are detected, a reduction in cervical cancer incidence can be considered a very helpful indicator.

8) Evidence exists concerning the efficacy of screening for breast cancer and colorectal cancer, derived from randomized trials, and for cervical cancer, derived from observational studies.

9) Screening is, however, the testing for diseases of people for which no symptoms have been detected. In addition to its beneficial effect on the disease-specific mortality, screening can also have negative side effects for the screened population. Healthcare providers should be

aware of all the potential benefits and risks of screening for a given cancer site before embarking on new population- based cancer screening programmes. Furthermore, for the informed public of today, these benefits and risks need to be presented in a way that allows individual citizens to decide on participation in the screening programmes for themselves.

10) Ethical, legal, social, medical, organisational and economic aspects have to be considered before decisions can be made on the implementation of cancer screening programmes

11) Due account should be taken of specific needs of persons who may be at higher cancer risk for particular reasons (e.g. biological, genetic, lifestyle and environmental, including occupational).

12) The public health benefits and cost efficiency of a screening programme are achieved if the programme is implemented systematically, covering the whole target population and following best-practice guidelines.

13) The cost-effectiveness of cancer screening depends on several factors such as epidemiology, and healthcare organisation and delivery.

14) Systematic implementation requires an organisation with a call/recall system and with quality assurance at all levels, and an effective and appropriate diagnostic, treatment and after-care service following evidence-based guidelines.

15) Centralised data systems, including a list of all categories of persons to be targeted by the screening programme and data on all screening tests, assessment and final diagnoses, are needed to run organised screening programmes.

16) All procedures for collecting, storing, transmitting and analysing data in the medical registers involved must be in full compliance with the level of protection referred to in Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data[1], as well as in full compliance with the relevant provisions of Member States on the management and processing of health data in accordance with Article 8 of the Directive.

17) Quality screening includes analysis of the process and outcome of the screening and rapid reporting of these results to the population and screening providers.

18) This analysis is facilitated if the screening database can be linked to cancer registries and mortality databases.

19) Adequate training of personnel is a prerequisite for high quality screening.

20) Specific performance indicators have been established for cancer screening tests. These should be monitored regularly.

21) Adequate human and financial resources should be available in order to assure the appropriate organisation and quality control in all the Member States.

22) Action should be taken to ensure equal access to screening taking due account of the possible need to target particular socioeconomic groups.

23) It is an ethical, legal and social prerequisite that cancer screening should only be offered to fully informed people with no symptoms if the screening is proved to decrease disease-specific mortality, if the benefits and risks are well known, and if the cost-effectiveness of the screening is acceptable.

[1] OJ L 281, 23.11.1995, p. 31.

24) The screening methods which presently meet these strict prerequisites are listed in the Annex.

25) No screening test other than those listed in the Annex is scientifically justified to be offered to people with no symptoms in an organised population-based programme before it has been shown in randomised controlled trials to decrease disease-specific mortality in particular.

26) The screening tests listed in the Annex can only be offered on a population basis in organised screening programmes with quality assurance at all levels, if good information about benefits and risks, adequate resources for screening, follow-up with complementary diagnostic procedures and, if necessary, treatment of those with a positive screening test are available.

27) The introduction of the recommended screening tests in the Annex, which have demonstrated their efficacy, should be seriously considered, the decision being based on available professional expertise and priority-setting for healthcare resources in each Member State.

28) Once there is evidence that a new screening test is effective, evaluation of modified tests may be possible using other epidemiologically validated surrogate endpoints if the predictive value of these endpoints is established.

29) Screening methodologies are subject to ongoing development. The application of recommended screening methodologies should therefore be accompanied by simultaneous assessments of the quality, applicability and costeffectiveness of new methods if available epidemiological data justify this. In fact, the ongoing work may lead to new methods, which could ultimately replace or complement the tests listed in the Annex or be applicable to other types of cancer,

Hereby recommends that member states:

1. Implementation of cancer screening programmes

a) offer evidence-based cancer screening through a systematic population-based approach with quality assurance at all appropriate levels. The tests which should be considered in this context are listed in the Annex;

b) implement screening programmes in accordance with European guidelines on best practice where they exist and facilitate the further development of best practice for high quality cancer screening programmes on a national and, where appropriate, regional level;

c) ensure that the people participating in a screening programme are fully informed about the benefits and risks;

d) ensure that adequate complementary diagnostic procedures, treatment, psychological support and after-care following evidence-based guidelines of those with a positive screening test are provided for;

e) make available human and financial resources in order to assure appropriate organisation and quality control;

f) assess and take decisions on the implementation of a cancer screening programme nationally or regionally depending on the disease burden and the healthcare resources available, the side effects and cost effects of cancer screening, and experience from scientific trials and pilot projects;

g) set up a systematic call/recall system and quality assurance at all appropriate levels, together with an effective and appropriate diagnostic and treatment and after-care service following evidence-based guidelines;

h) ensure that due regard is paid to data protection legislation, particularly as it applies to personal health data, prior to implementing cancer screening programmes.

2. Registration and management of screening data

a) make available centralised data systems needed to run organised screening programmes;

b) ensure by appropriate means that all persons targeted by the screening programme are invited, by means of a call/recall system, to take part in the programme;

c) collect, manage and evaluate data on all screening tests, assessment and final diagnoses;

d) collect, manage and evaluate the data in full accordance with relevant legislation on personal data protection.

3. Monitoring

a) regularly monitor the process and outcome of organized screening and report these results quickly to the public and the personnel providing the screening;

b) adhere to the standards defined by the European Network of Cancer Registries in establishing and maintaining the screening databases in full accordance with relevant legislation on personal data protection;

c) monitor the screening programmes at adequate intervals.

4. Training

adequately train personnel at all levels to ensure that they are able to deliver high quality screening.

5. Compliance

a) seek a high level of compliance, based on fully informed consent, when organised screening is offered;

b) take action to ensure equal access to screening taking due account of the possible need to target particular socioeconomic groups.

6. Introduction of novel screening tests taking into account international research results

a) implement new cancer screening tests in routine healthcare only after they have been evaluated in randomized controlled trials;

b) run trials, in addition to those on screening-specific parameters and mortality, on subsequent treatment procedures, clinical outcome, side effects, morbidity and quality of life;

c) assess level of evidence concerning effects of new methods by pooling of trial results from representative settings;

d) consider the introduction into routine healthcare of potentially promising new screening tests, which are currently being evaluated in randomised controlled trials, once the evidence is conclusive and other relevant aspects, such as cost-effectiveness in the different healthcare systems, have been taken into account;

e) consider the introduction into routine healthcare of potentially promising new modifications of established screening tests, once the effectiveness of the modification has been successfully evaluated, possibly using other epidemiologically validated surrogate endpoints.

7. Implementation report and follow-up

report to the Commission on the implementation of this Recommendation within three years of its adoption and subsequently at the request of the Commission with a view to contributing to the follow-up of this Recommendation at Community level.

Hereby invites the commission:

1. To report on the implementation of cancer screening programmes, on the basis of the information provided by Member States, not later than the end of the fourth year after the date of adoption of this Recommendation, to consider the extent to which the proposed measures are working effectively, and to consider the need for further action.

2. To encourage cooperation between Member States in research and exchange of best practices as regards cancer screening with a view to developing and evaluating new screening methods or improving existing ones.

3. To support European research on cancer screening including the development of new guidelines and the updating of existing guidelines for cancer screening.

Done at Brussels, 2 December 2003.

For the Council
The President
R. MARONI

Annex
Screening tests which fulfil the requirements of the recommendation*:

- pap smear screening for cervical cancer precursors starting not before the age of 20 and not later than the age of 30;

- mammography screening for breast cancer in women aged 50 to 69 in accordance with European guidelines on quality assurance in mammography;

- faecal occult blood screening for colorectal cancer in men and women aged 50 to 74.

* The indicated age ranges are to be understood as maximum ranges; subject to national epidemiological evidence and prioritisation, smaller age ranges may be appropriate.

Annex II

European Parliament resolution on breast cancer in the European Union

(2002/2279(INI))

The European Parliament,

- having regard to Article 152 of the EC Treaty as amended by the Treaty of Nice,
- having regard to Article 35 of the Charter of Fundamental Rights of the European Union[1],
- having regard to its resolution of 9 March 1999 on the report from the Commission to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions on the state of women's health in the European Community[2],
- having regard to its resolution of 13 February 2003 on the Commission communication on Community and national measures in relation to breast implants[3],
- having regard to its resolution of 4 October 2001 on the patenting of BRCA1 and BRCA2 breast cancer genes[4],
- having regard to its resolution of 15 January 2003 on the Commission communication to the Council, the European Parliament, the Economic and Social Committee and the Committee of the Regions on the future of health care and care for the elderly: guaranteeing accessibility, quality and financial viability[5],
- having regard to Decision No 646/96/EC of the European Parliament and of the Council of 29 March 1996 adopting an action plan to combat cancer within the framework for action in the field of public health (1996 to 2000)[6], which was extended by Decision No 521/2001/EC of the European Parliament and of the Council[7],
- having regard to Decision No 1786/2002/EC of the European Parliament and of the Council of 23 September 2002 adopting a programme of Community action in the field of public health (2003-2008)[8],
- having regard to Decision No 1513/2002/EC of the European Parliament and of the Council of 27 June 2002, concerning the sixth framework programme of the European Community for research, technological development and demonstration activities, contributing to the creation of the European Research Area and to innovation (2002-2006)[9],
- having regard to Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001, on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use[10],
- having regard to Charter Against Cancer, adopted on 4 February 2000 at the first World Summit Against Cancer, which was held in Paris,
- having regard to the 'European Guidelines for Quality Assurance in Mammography Screening'[11],

[1] OJ C 364, 18.12.2000, p.1.
[2] OJ C 175, 21.6.1999, p. 68.
[3] P5_TA(2003)0063.
[4] OJ C 87 E, 11.4.2002, p. 265.
[5] P5_TA(2003)0015.
[6] OJ L 95, 16.4.1996, p. 9.
[7] OJ L 79, 17.03.2001, p. 1.
[8] OJ L 271, 9.10.2002, p. 1.
[9] OJ L 232, 29.8.2002, p. 1.
[10] OJ L 121, 1.5.2001, p. 34.
[11] In 2001, the Commission published the third edition of this European Breast Cancer Network publication.

- having regard to the recommendations of the European Society of Mastology (EUSOMA) set out in 'The requirements of a specialist breast unit'[12],

- having regard to the 'Recommendations on cancer screening in the European Union' of the Advisory Committee on Cancer Prevention[13],

- having regard to Rule 163 of its Rules of Procedure,

- having regard to the report of the Committee on Women's Rights and Equal Opportunities (A5-0159/2003).

A. whereas Article 152 of the EC Treaty provides that a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities and that Community action, which shall complement national policies, shall be directed towards preventing major health scourges, such as cancer, by promoting research into their causes and their prevention, as well as health information and education,

B. whereas, in 2000, the World Health Organisation (WHO) reported more than 216 000 newly diagnosed cases of breast cancer and 79 000 deaths from breast cancer in women, whereas breast cancer is the most frequent cancer affecting women, with one woman in nine suffering from the disease, and whereas breast cancer is the most frequent cause of death in women between the ages of 35 and 55 in the European Union,

C. whereas the Charter of Fundamental Rights of the European Union recognises that everyone has the right of access to preventive health care and the right to benefit from medical treatment,

D. whereas every woman, irrespective of place of residence, social status, occupation and education, should have access to high-quality screening for treatment and aftercare in the event of cancer, but whereas huge disparities exist in the quality of breast cancer services and, hence, in the chances of survival of women in the various Member States, the regions and even between individual hospitals in a given city,

E. whereas the 1999 Eurocare Study demonstrated that in the various Member States, there were unacceptable disparities by up to 16% in the survival rates of breast cancer patients which were attributed to, inter alia, disparities in access to screening, diagnosis and treatment1,

F. whereas research has not yet developed effective measures for the prevention of breast cancer or for curing the disease irrespective of the diagnosis stage, and whereas up to 90% of breast cancer patients may be cured if diagnosed and correctly treated at an early stage,

G. whereas the Community programme entitled 'Europe Against Cancer' has given a significant boost to the fight against breast cancer, with the 'European Guidelines for Quality Assurance in Mammography Screening', which were originally drawn up in 1992, setting a good example for quality standards and best practice in European health policy,

H. whereas, according to the WHO, high-quality mammography screening, i.e. regular invitations to women to undergo free, voluntary mammographies and follow-up diagnoses as part of an organised population-based regional or national programme, can reduce breast-cancer mortality in women aged between 50 and 69 by up to 35% and whereas, according to scientific studies, breast-cancer mortality in women aged between 40 and 49 can also be reduced by up to 20%,

I. whereas women with breast implants must be offered ultrasound screening, since they are more difficult to screen,

[12] Published in the European Journal of Cancer 36 (2000) 2288-2293.
[13] Published in the European Journal of Cancer, 36 (2000) 1473-1478.

J. whereas breast self-examination is a valuable tool for increasing women's self-awareness of health, although it may never constitute an alternative to early diagnosis based on screening, and whereas the WHO has also concluded that there is still insufficient evidence that clinical breast examination or self-examination reduces mortality from breast cancer,

K. whereas a clinical examination of the breast constitutes an important tool for the early detection of carcinomas in the interval between two screenings and in the case of women who, because of their age, are not entitled to take part in organised screening programmes,

L. whereas early detection, diagnosis, treatment and aftercare of breast cancer should be performed only by an multidisciplinary team of fully trained physicians, since that may significantly increase the survival rates of the women involved,

M. whereas high-quality breast cancer services may lead to savings for health care systems in the medium and long term, with unnecessary examinations and treatment being avoided and mammary cancer detected at an earlier stage and, therefore, requiring less expensive operations and aftercare,

N. whereas the highest possible quality of life must be achieved for patients, since the treatment of breast cancer involves substantial physical and psychological burdens,

O. whereas breast cancer patients should be adequately informed by the attending physician of their diagnosis and treatment and should be involved in decisions about therapy options, while also being made aware of any possible side-effects,

P. whereas not all Member States have yet adopted a specific regulation on patients' rights, and thus the relevant rights are currently far from transparent for patients,

1. Calls on the Member States and on the Commission to make the fight against breast cancer a health policy priority and to develop and implement effective strategies for improved preventive health care: screening, diagnosis, treatment and aftercare in order to achieve the highest quality breast-cancer treatment throughout Europe;

2. Calls on the Member States to set themselves the target of creating, by 2008, the conditions required for a 25% reduction in the average breast-cancer mortality rate in the EU and of reducing to 5% the disparity between the Member States in the five-year survival rate;

3. Is dismayed to note that, to date, only eight of the 15 Member States have taken measures based on the 'European Guidelines for Quality Assurance in Mammography Screening' to introduce nation-wide screening programmes; calls, therefore, on the Member States to offer, at the earliest possible opportunity, mammographies at two-year intervals to all women between the ages of 50 and at least 69, with the following quality criteria being observed in a population-based programme where voluntary participation in the programme achieves a participation rate of over 70%:

   - screening shall take place in dedicated and certified units, or in fixed or mobile units under the authority of such centres, with the assessment of cases with suspicious results also being carried out by a multidisciplinary team in dedicated units,

   - each mammogram shall be read independently and double-blind by two radiologists, each of whom reads the screening mammograms of a minimum of 5 000 women per year,

   - the image quality and radiation dose of the screening equipment shall be monitored regularly; the development process should also be checked,

   - physicians and paramedical staff shall regularly attend further training courses;

4. Calls for the presence in screening programmes of equipment for ultrasound screening for women with breast implants which inhibit the penetration of x-rays;

5. Calls for all women suffering from breast cancer to be entitled to be treated by an multidisciplinary team and calls on the Member States, therefore, to establish a network of certified multidisciplinary breast centres which cover the entire population and fulfil the following criteria:

   - each breast centre shall perform a minimum of 150 primary breast cancer operations per year,

   - each breast centre shall operate under the direction of a highly qualified physician who specialises in breast disease, while the multidisciplinary team shall consist of physicians experienced in and performing only breast surgery, together with radiologists, oncologists, pathologists, nurses and radiographers who also specialize in breast disease, as well as a data manager,

   - multidisciplinary pre-operative and post-operative case conferences shall be held at least once a week,

   - the quality of the results shall be guaranteed by means of clinical research,

   - physicians and paramedical staff shall regularly attend further training courses,

   - physicians and paramedical staff shall be required to pass a test at regular Intervals to demonstrate that they have sufficient up-to-date knowledge and skills,

   - follow-up and aftercare examinations shall be carried out in close cooperation with the relevant multidisciplinary breast centre,

   - patients shall receive onco-psychological counselling, psychotherapeutic support and physiotherapy services, as well as social services;

6. Welcomes the allocation of EUR 400 million for cancer research in the sixth framework programme of research and calls on the Commission and the Member States to:

   a) ensure more effective coordination between national and European research,

   b) ensure that evidence-based medicine also constitutes the basis for breast cancer treatment in Europe,

   c) incorporate the positive findings of fundamental research into treatment as soon as possible and further strengthen clinical research, in particular the clinical trials coordinated by the European Organisation for Research and Treatment of Cancer (EORTC) and conducted in cancer centres and clinics across the European Union,

   d) provide more funding than previously allocated for breast cancer research, in order to:
      – step up the search for the causes of the disease and for forms of therapy,
      – improve prediction of the effect of treatment and certainty of outcomes,
      – further investigate the relationship between breast cancer and potential risk factors such as tobacco, diet, hormones and life-style (body weight, physical activity),
      – increase research into in-patient and out-patient treatment protocols, with a view to reducing the unnecessary burden on patients of clinical and medical treatment services,
      – develop a method for the standardised risk assessment of women potentially in danger of developing a hereditary breast disease;

7. Calls on the Member States, within the limits of their powers and responsibilities, to:

   a) comply with the WHO recommendation and, with the involvement of all the major actors concerned, draw up national action plans against cancer,

   b) develop and continuously update further evidence-based guidelines on breast-cancer screening, diagnosis, treatment and aftercare, establish a national breast-cancer coordination office and ensure the implementation of the guidelines by means of a transparent auditing process,

   c) protect the psychological well-being and physical integrity of women by ensuring that:

      – every woman is informed of the results of a clinical examination and of a screening examination within five working days and that no woman who has been diagnosed as suffering from breast cancer need wait more than four weeks before treatment begins,

      – in order to reduce the number of breast amputations, breast-conserving surgery is available to every woman in every instance where it is medically justified and that, wherever possible, breast reconstruction operations are performed using the patient's own tissue and within the shortest possible time,

      – every woman receives a reliable pre-operation diagnosis (in particular through minimal invasive biopsy),

      – women who have received breast implants are issued with a patient's pass which includes an indication of the specific features and requisite postoperative aftercare measures,

   d) ensure that the cost of any supplementary aids, such as wigs and bra prostheses and lymphatic drains in follow-up care, is reimbursed,

   e) expand medical specialisation schemes leading to qualifications, for example, as breast surgeon, breast cancer nurse or onco-psychologist which have already proved their worth in some Member States, by setting up appropriate training and further training facilities,

   f) set up establishments for the medical and psychological counselling of women with a presumed risk of hereditary breast cancer and offer an intensified screening programme for women whose test results are positive,

   g) adopt a specific regulation on individual patients' rights, giving patients the following rights:

      – the right to appropriate and qualified medical care provided by qualified medical staff in suitably equipped and organised practices and hospitals,

      – the right to easily understandable, expert and appropriate information and advice from the physician, before, during and after treatment,

      – the right to self-determination based on full information,

      – the right to treatment records and to inspection thereof,

      – the right to confidentiality and data protection,

      – the right to lodge a complaint,

      – the right to a second medical opinion in the case of cancer,

h) involve patients' organisations in health-policy decisions more heavily than in the past and support their activities in an appropriate manner,

i) improve data compilation and, at the earliest possible opportunity, set up national cancer registers which meet the standards set by the European Network of Cancer Registries, so that the EU may finally have available informative and comparable European data about the development of cancer and breast cancer;

8. Calls on the Commission to:

a) promote in an appropriate manner, in future as well, the innovative projects such as the European Breast Cancer Network, the European Network of Cancer Registries and the European Prospective Investigation into Cancer and Nutrition (EPIC) network, set up on the basis of the earlier Europe Against Cancer programme which formed part of the programme of Community action in the field of public health (2003-2008),

b) combine the current activities of the Directorates-General for Health, Research andthe Information Society and create a common EU website on cancer on which individual citizens and lay persons, as well as medical experts and research workers, may find information about cancer variously compiled by European and national research workers, medical societies and patients' organisations, etc., written in easily comprehensible terms and in various languages,

c) come forward at short notice with a proposal for a Council recommendation on cancer screening based on the 'Recommendations on cancer screening in the European Union' of the Advisory Committee on Cancer Prevention, which emphasises an organised and consistent approach to cancer screening (breast cancer, cervical cancer, colorectal cancer and prostate cancer); considers that a Europe-wide coordinated approach is essential in order to prevent inefficient, low-quality and opportunistic screening; the European Parliament undertakes to participate in this process;

9. Emphasises the importance of clinical studies for medical progress; welcomes the adoption of the aforementioned Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use; believes that the requirements of research bodies should be taken into account when the relevant implementing provisions are being drafted, that the objective of the harmonisation of the legal and regulatory arrangements for clinical research will not be attained and that the current obstacles to clinical studies involving several Member States will not be eliminated;

10. Calls on the Member States with Objective 1 regions to allocate more Structural Fund resources to financing investment in the healthcare system in view of the significant regional disparities in access to early detection, diagnosis and treatment of breast cancer;

11. Reiterates its concern at the possible consequences of the granting by the European Patent Office of patents on BRC AC 1 and BRC A2 ('breast cancer') genes; calls on the EPO to reconsider the patenting of these genes and calls on the Council, the Commission and the Member States to ensure that the human genetic code is freely available for research throughout the world and that medical applications of certain human genes are not impeded by monopolies based on patents;

12. Calls on the Commission to organise a conference, jointly with the Italian Presidency in late 2003, when the final projects come to an end, in order to draw up a final summary of the successes and failures of the 'Europe Against Cancer' programme, partly with a view to the new action programme in the field of public health (2003-2008);

13. Is concerned at the comparatively poor survival rates for women suffering from breast cancer in the accession countries; calls on the accession countries to step up their efforts

to fight breast cancer and calls on the Commission to arrange a structured exchange of experience with the future Member States;

14. Calls on the Commission, jointly with the Member States, to draw up, in time for the spring 2006 summit, a report on the measures taken by the Member States and, in the light of the progress achieved, to take a decision on further steps to be taken in the fight against breast cancer;

15. Instructs its President to forward this resolution to the Council, the Commission and the parliaments of the Member States.

Annex III

Council of Europe | Committee of Ministers

Recommendation No. R (94) 11

Of the Committee of ministers to member states on screening as a tool of preventive medicine

(Adopted by the Committee of Ministers on 10 October 1994 at the 518th meeting of the Ministers' Deputies)

The Committee of Ministers,

Considering that the aim of the Council of Europe is to achieve a greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common action in the public health field;

Noting that chronic diseases are the major causes of death and a high social and economic burden in developed countries;

Considering that screening for the early detection of some of these diseases could, in principle, provide a method for their control;

Considering that, as yet, there is no absolute proof of the value of screening and early treatment in most diseases;

Considering that few, if any, diseases can at the present time be regarded as fulfilling all the desirable criteria for screening, and that the recommended evaluative procedures are not often carried out in full;

Recognising that the implementation of widespread screening programmes raises major ethical, legal, social, medical, organisational and economic problems which require initial and ongoing evaluation;

Taking into account the provisions of the Europe an Convention on Human Rights and of the European Social Charter;

Bearing in mind the Convention for the protection of individuals with regard to automatic processing of personal data of 28 January 1981, as well as the provisions of Recommendation No. R (81) 1 on regulations for automated medical banks and Recommendation No. R (83) 10 on the protection of personal data used for purposes of scientific research and statistics;

Recommends to governments of member states that they take account in their national health planning regulations and legislation of the conclusions and recommendations set out in the appendix to this recommendation.

Appendix to Recommendation No. R (94) 11

1. Introduction

1.1 For the purposes of this recommendation, screening means applying a test to a defined group of persons in order to identify an early stage, a preliminary stage, a risk factor or a combination of risk factors of a disease. In any case it is a question of detecting phenomena, which can be identified prior to the outbreak of the disease.

1.2 The object of screening as a service is to identify a certain disease or risk factor for a disease before the affected person spontaneously seeks treatment, in order to cure the disease or prevent or delay its progression or onset by (early) intervention.

1.3 The value of existing forms of screening for infectious diseases is fully acknowledged but these established methods are not considered in detail in this recommendation. Emphasis is made on screening for chronic degenerative non-communicable disorders.

1.4 Screening is only one method of controlling disease. It should be viewed in the whole context of reducing the burden of ill health to the individual and the community by, for example, socio-economic, environmental measures, health education and improvement of existing health care and disease prevention systems.

1.5 Environmental factors are recognised as important contributors to disease, but inherited factors may also play an important role. With the advent of new genetic knowledge, an increasing number of genetic diseases and genetic risk factors for disease will be identified and offer the possibility for new screening procedures. As the procedures for genetic screening are not fully established nor fully evaluated, they have not been included in this recommendation.

1.6 The present position is that the implementation of screening in European countries is fragmentary, with few national screening programmes for the total population but many screening schemes restricted to population groups.

1.7 Because there are differences in health needs and health services, as well as in ethical values and in legal norms and rules between countries, the decision to implement a particular screening programme should be taken in cooperation with the medical profession by each country. Nevertheless there are common general principles and problems which are equally relevant to all systems.

1.8 Screening is a tool which is potentially capable of improving the health of the population but it also has adverse effects. Constant care should be taken to ensure that in any screening programme the advantages prevail over the disadvantages.

1.9 The general benefits of screening are often described. It is, however, also important to be aware of the adverse effects which can be:
- stigmatisation and/or discrimination of (non) participants;
- social pressure to participate in the screening and undergo the intended treatment/intervention;
- psychological distress where there is no cure for the disease or where the treatment and/or intervention is morally unacceptable to the individual concerned;
- exposure to physical and psychological risks with limited health gains;
- creation of expectations which probably cannot be fulfilled;
- individuals who are positively screened might experience difficulties such as access to insurance, employment, etc.;
- severe side effects of invasive clinical diagnosis of false positives;
- delay in diagnosing false negatives;
- unfavourable cost-benefit relationship of a screening programme.

1.10 The various problems which are encountered in the introduction and provision of screening interrelated. Nevertheless, a distinction may be made between those concerned with:
i. ethical and legal issues;
ii. selection of diseases (medically) suitable for screening;
iii. economic aspects and evaluation of screening;
iv. quality assurance;
v. organisation of a screening programme;
vi. scientific research.

2. Ethical and legal values

2.1 Effectiveness is a necessary prerequisite for the screening to be ethical. It should none the less be kept in mind that screening can be effective and still unethical.

2.2 Advantages and disadvantages of screening for the target population and the individual must be well balanced, taking into account social and economic costs, equity as well as individual rights and freedoms.

2.3 Failure to make known information on the positive and negative aspects of the screening is unethical and infringes the autonomy of the individual.

2.4 The decision to participate in a screening programme should be taken freely. The diagnoses and treatments which may follow the screening should also require a free and separate consent. No pressure should be used to lead somebody to undergo any of these procedures.

2.5 The right to privacy requires that the results of the tests as a general rule are not communicated to those who do not wish to be informed, are collected, stored, and handled confidentially, and adequately protected. It is preferable not to screen individuals who do not wish to be informed of the results of the screening.

2.6 Neonatal screening can only be justified if the intervention is of direct health benefit to the child. Otherwise screening should be postponed until the child can decide for itself.

2.7 No personal data derived from the screening should be communicated to third parties unless the data subject has given consent to it or in accordance with national law.

2.8 When a screening programme is provided as a service and conducted also for research purposes, the decision to make available personal medical data stemming from the screening programme for research purposes should be taken freely, without undue pressure.

The decision not to take part in the research should not in any way prevent the individual from participating in the screening programme.

3. Criteria for selecting diseases suitable for screening

3.1 The disease should be an obvious burden for the individual and/or the community in terms of death, suffering, economic or social costs.

3.2 The natural course of the disease should be well-known and the disease should go through an initial latent stage or be determined by risk factors, which can be detected by appropriate tests. An appropriate test is highly sensitive and specific for the disease as well as being acceptable to the person screened.

3.3 Adequate treatment or other intervention possibilities are indispensable. Adequacy is determined both by proven medical effect and ethical and legal acceptability.

3.4 Screening followed by diagnosis and intervention in an early stage of the disease should provide a better prognosis than intervention after spontaneously sought treatment.

4. Economic aspects

4.1 The increasing financial burden of health care makes it necessary to assess the economic aspects of screening. However these aspects should not be the overriding consideration. In all screening programmes human consideration regarding the value and quality of life, life expectancy as well as respect for individual rights are of prime importance.

4.2 Economic assessments are necessary to enable rational decisions to be made on the priority to be given to alternative ways of using health resources.

4.3 Measurement of the economic aspects of screening is not fully mastered. Early detection and treatment may be less expensive than late treatment. However, available studies relate only to present screening costs and further work is necessary to determine possible cost control in the long term.

4.4 Non systematic screening or spontaneous screening results in high marginal costs. Only systematic screening is able to provide means for controlling cost. Therefore, constant care should be taken to ensure that in any screening programme the allocated resources are used in an optimal way.

5. Quality assurance

5.1 Screening should aim at the highest possible standards of quality from the medical and organisational point of view.

5.2 Because of the expectations that screening creates as well as its adverse effects, screening should meet the highest quality assurance standards in all its aspects.

5.3 An assessment of the scientific evidence of the effectiveness of screening in the control of a disease should be made by experimental studies before introducing a screening programme as a service. The practical arrangements for a mass screening, which are directly linked to the health structures and systems, should obtain the same effectiveness as that obtained in the randomised trial.

5.4 Having implemented a screening programme, it should be subjected to continuous independent evaluation. Evaluation will facilitate adaptation of the programme, correction of deficiencies noted and verification of achievement of objectives. The adverse effects of the screening programme should not be ignored in the evaluation which should be carried out by independent public health experts.

5.5 If quality assurance standards are not met in the long term it should be possible for the screening programme to be corrected, and, if this is not possible, stopped.

5.6 The programme must evaluate participation, and the percentage of people screened in the target population, the technical quality of testing and the quality of diagnosis and treatment provided as a follow-up for persons with a positive test result.
Severe side effects of false positives should be revealed and evaluated.

5.7 There is a need for more teaching of medical students in epidemiology and its application to measuring the effects of screening. Similarly post-graduate education in this field is also needed to enable practising doctors to understand the principles and evaluation of screening.

5.8 Provision of screening programmes requires that training in techniques and interpretation of screening tests is included in undergraduate and post-graduate medical teaching programmes.

5.9 A screening programme requires resources in both staff and technical facilities for carrying out the screening tests. In many instances tests can be performed by non medical staff. Provision should be made for initial and further training of the medical and technical staff who will be involved in performing the screening tests and interpreting their results. Technical methods, including automated techniques, are useful in screening for some diseases. Quality of screening methods should be monitored.

6. Organisation

6.1 The organising body of a screening programme should be held responsible throughout the programme. The organisation of a screening programme should comply with what is described in national guidelines and protocols.

6.2 Within the organisational framework the target population should be defined (by age or otherwise) as well as the frequency of screening tests and the general and specific objectives and quality assurance guidelines.

6.3 It must be stressed that screening cannot succeed without co-operation between preventive and curative systems. Organisation must be tailored to the structures of the health system. If appropriate structures in the curative health care system are lacking, screening should not be implemented until they are developed (pilot programmes, for example). There are various degrees to which screening services may be integrated with curative services or develop as a separate speciality. The advantages and disadvantages of these should be assessed separately in different health care systems.

6.4 Provisions should be made for the financing of the programme, the cost of organising and evaluating the structure, the cost of testing, the cost of quality assessment and monitoring, and the cost of the follow-up care of those people who screen positively.

6.5 Process and outcome indicators should be constantly evaluated.

6.6 Systematic collection of data is required in screening programmes to serve the needs of the individual and of the health service. To that end, data should be collected on the target population, on persons screened (with dates and the results of the test carried out), and on the results of eventual diagnostic examinations. Access to a morbidity register considerably facilitates evaluation.

6.7 Adequate protection of all data collected by means of a screening programme should be guaranteed.

6.8 Participation of the public in screening programmes is determined by personal factors (for example attitudes, motivation and anxiety) and by situational factors (waiting time and efficient organisation, for example). These can be influenced for instance by health education and by good organisation of the screening procedure.

6.9 In order to ensure optimal participation by the target population, the best possible information should be widely provided and awareness-raising and education programmes should be organised for both the target population and the health professionals.

6.10 Invitations should be accompanied by written information on the purposes and effectiveness of the programme, on the test, on potential advantages and disadvantages, on the voluntary nature of participation and on how data will be protected. An address should be provided for those who require further information.

6.11 Participants should be informed on how, when and where their test results will be available or will be communicated to them.

6.12 The positive results found at screening should always be confirmed by subsequent diagnostic tests before commencing a treatment/intervention, unless the screening test is a diagnostic test. It is absolutely essential that adequate diagnostic facilities are available to confirm or reject the screening finding as soon as possible. Similarly, treatment facilities must be available and easily accessible to the confirmed cases. The work load placed on the health services by screening can be very large, especially since most screening programmes also lead to incidental pathological findings unrelated to the disease at which the programme is aimed.

6.13 Combining screening for several diseases into a multiple screening procedure may seem to be convenient to the individual and economic to the programme, but such a 'package deal' may negatively influence the extent to which most of the criteria for screening including age limit and frequency would be met.

7. Research

7.1 Research into new, more effective, screening tests must be encouraged and the long-term effects of the various methods of treatment and provision for positive subjects studied. Research must be further developed to answer the numerous social, ethical, legal, medical, organisational and economic questions as well as psychological problems raised by screening, on which evidence is incomplete.

7.2 Quality assurance concerning research programmes should be conducted into the effectiveness of the various screening tests, the practical arrangements for screening, the measures to increase participation, the means of improving test efficiency, follow-up to and provisions for those screened positive, an assessment process and all the economic aspects.

7.3 Information gathered during screening should be available for the purpose of scientific research, for the improvement of health services, and for the benefit of future screening, taking into account full respect of autonomy and confidentiality and the protection of personal privacy.

8. General remarks

8.1 It is particularly important that political decision-makers and target groups should be kept informed of the current state of knowledge about the value of screening for particular diseases. Improved communication should be encouraged.

8.2 Governments should promote the research and evaluation necessary for assessing the value of both new and existing programmes. This form of research necessarily means large-scale research which, in some instances, may be designed as international collaborative studies. Scientific evaluation is the only way in which the positive and negative effects of screening can be assessed in order that a rational decision can be taken on whether a screening programme should be implemented and what resources should be allocated.

Quality assurance (as defined by World Health Organization):
'All those planned and systematic actions necessary to provide adequate confidence that a structure, system or component will perform satisfactorily in service (ISO 6215 1980). Satisfactory performance in service implies the optimum quality of the entire diagnostic process i.e., the consistent production of adequate diagnostic information with minimum exposure of both patients and personnel.'

Quality control (as defined by World Health Organization):
'The set of operations (programming, co-ordinating, carrying out) intended to maintain or to improve [...] (ISO 35341977). As applied to a diagnostic procedure, it covers monitoring, evaluation and maintenance at optimum levels of all characteristics of performance that can be defined, measured, and controlled.'