

Breast Cancer Management Clinical Guidelines



Prepared by the Clinical Guidelines Committee
Royal College of Surgeons in Ireland
November 2000

Mr. T. N. Walsh
Prof. N. O'Higgins



Mr. T. N. Walsh

Senior Lecturer in Surgery
Royal College of Surgeons in Ireland
James Connolly Memorial Hospital, Dublin

Prof. N. O'Higgins

Professor of Surgery, University College Dublin
(St. Vincent's University Hospital)
Member of Council, Royal College of Surgeons in Ireland

Contents

Introduction	2	Management of non-invasive breast cancer	16
Role of Individual Services in a Breast Unit	3	Ductal carcinoma in situ (DCIS)	16
General practitioner	3	Management of DCIS	16
Surgeon	3	Skin-sparing mastectomy	16
Breast-care nurse	3	Factors favouring mastectomy in DCIS	17
Radiologist and radiographer	4	Lobular carcinoma in situ (LCIS)	17
Pathologist	4	Treatment of ductal carcinoma in situ (DCIS) and Paget's Disease	18
Medical oncologist	5	Breast reconstruction	19
Radiation therapist	5	Follow-up of the breast cancer patient	19
Data management	5	Communication with general practitioners	19
Diagnosis of Breast Disease	6	Adjuvant Systemic Therapy in Breast Cancer	20
Mammography	6	Chemotherapy	20
Surveillance of women at special risk for breast cancer	6	Endocrine therapy	20
High risk group	6	Adjuvant therapy in node-negative patients	21
Moderate risk group	7	Adjuvant therapy in node-positive patients	21
Low risk group	7	Radiotherapy	23
Management of a breast lump	7	Management of Recurrent Disease	24
Triple assessment	7	Local recurrence	24
Open surgical biopsy	8	Contralateral primary breast cancer	24
Management of Breast Cancer	9	Locally advanced primary breast cancer	24
Treatment planning	9	Regional recurrence	24
Avoidance of delay in surgical treatment	9	Metastatic breast cancer	25
Decision-making	9	Palliative and terminal care	25
History and physical examination	9	Training and Continuing Education	26
Mammography	11	Surgical training	26
Histology	11	An estimate of the surgical workload in a breast unit	26
Patient preference	11	Standards and audit	26
Pre-operative staging tests	11	References	27
Resection margins	11	Table 1 Survival after BCS	10
Surgery for Primary Operable Breast Cancer	12	Table 2 Recurrence after BCS	10
Surgery of the breast	12	Table 3 Sentinel node data sheet	15
Breast conserving surgery (BCS)	12	Table 4 DCIS and Paget's disease	18
Contraindications to breast conservation	12	Table 5 Risk in node-negative patients	21
Points on surgical technique	12	Table 6 Node-negative patients	22
Risk factors for local recurrence	13	Table 7 Node-positive patients	22
Further surgery following conservative resection	13		
Surgery of the axilla	13		
Evaluation of the sentinel lymph node in breast cancer	14		

Introduction

Guidelines in the management of breast cancer should lead to:

- a uniformly high standard of surgical treatment throughout the country
- reassurance of patients that surgical management is standardised
- standardisation of radiotherapy and chemotherapy
- identification of resources needed to fulfil these guidelines in all hospitals treating breast cancer

In Ireland, most patients with breast cancer present when they are symptomatic. The introduction of screening will increase the number of asymptomatic lesions. The highest quality of care is required to optimise the chances of cure with the least morbidity for all patients. This is best achieved in a multidisciplinary setting with high-quality surgery, medical oncology and radiotherapy together with the support provided by a breast care nursing service.

A team consisting of surgeons, radiologists, pathologists, medical oncologists and nurse specialists, each of whom specialises in breast disease, should manage breast cancer. A Breast Unit should treat a minimum of 100 new primary breast cancer patients annually.

A Breast Unit is defined by the staff, multidisciplinary teams and resources that it applies to the management of breast disease.

Most of the Breast Unit's work is outpatient-based and involves 'reassuring the worried well'. A multidisciplinary approach is more effective if all clinicians follow guidelines. Standards of treatment and outcome of breast cancer vary between and within countries¹. Guidelines can help to reduce these variations and allay public concern.

A breast practice generates a large administrative workload and it is essential that the breast team has adequate clerical support.

Role of Individual Services in a Breast Unit

GENERAL PRACTITIONER

In Ireland, referral to a breast surgeon is usually via a general practitioner (GP). It is essential therefore that the links between GPs and Breast Units be of the best quality to facilitate urgent referral. Breast Units should communicate the diagnosis and proposed treatments to the GP.

Patients who can be managed by the general practitioner include:

- women with minor or moderate degrees of breast pain who do not have a palpable distinct lump.
- women under 50 years of age with multiductal nipple discharge, which is not troublesome or blood-stained.
- asymptomatic women with a negative family history who are at low risk of developing breast cancer.
- young women with tender nodular breasts and older women with symmetrical nodularity who have no focal lesion demonstrable.

When referring patients the term 'urgent' should be used only for patients with symptoms or signs highly suggestive of breast cancer.

'Urgent' referrals include:

- discrete lump in a women over 30 years of age.
- skin ulceration.
- distortion of breast or nipple-areolar complex
- an intradermal nodule
- blood-stained nipple discharge.

This 'urgent' list serves as a guide, and does not imply that all other patients should be considered non-urgent. The decision to refer to the Breast Clinic should be at the discretion of the general practitioner.²

SURGEON

The primary care of breast cancer is the responsibility of the surgeon. In the majority of cases the surgeon establishes the diagnosis and provides the initial treatment. High quality surgery maximises the chance of cure and of local control, reduces morbidity, and provides best pathological information for prognosis and selection of other therapy. The surgeon should remain the primary co-ordinator of care for patients with breast cancer.

It is the duty of the surgeon to discuss the diagnosis and treatment options with the patient and to ensure that the patient has sufficient understanding of the issues to allow her to be an active participant in the decision-making process. The surgeon also has responsibility for co-ordinating the multidisciplinary team. Surgeons with special training and expertise should treat patients with breast cancer because surgical subspecialisation in common cancers improves the standard of care and outcome.³⁻⁶

Follow-up of breast cancer patients involves the surgeon as a member of the multidisciplinary team.

The trained surgeon treating patients with breast disease should demonstrate this interest by participating in audit and by his/her continuing medical education (CME) activity.⁷

BREAST-CARE NURSE

A breast-care nurse should be available for all patients undergoing treatment for breast disease. Breast Units treating 100 breast cancer patients per annum need two breast-care nurses. It is mandatory that these nurses attend the multidisciplinary breast meeting. A suitable room should be available so that consultations can take place in private. The presence of the patient's husband, other relative or friend should be encouraged.

The nurse should see patients on the ward before and after surgery where the patient's concerns and personal problems can be discussed. She should be offered advice on bras, swimwear and choice of permanent prostheses. Temporary prostheses should be fitted by the nurse before discharge and booklets given on treatment, support groups and continuing care.

Following axillary surgery and/or radiotherapy she should advise all patients on arm care. Following surgery for breast cancer, she should observe all patients for signs of anxiety and depression.

The nurse should update herself with knowledge of breast disease. She needs to be involved in the education of nursing staff on breast disease, both in the hospital setting and elsewhere.⁸

RADIOLOGIST AND RADIOGRAPHER

Breast imaging must be performed and reported by radiologists with expertise in breast disease and who reach the appropriate standards. The radiologist is an integral member of the Breast Unit. The surgeon and radiologist must consult regularly about the diagnostic breast clinic.

Imaging and physics standards are the responsibility of the radiologist(s) on the Breast Unit. Physics services should meet the appropriate guidelines. Each unit should have in place a quality-control programme to monitor and maintain standards.⁹⁻¹³ The radiology service should optimise the quality obtained in their existing equipment including films, screens, cassettes and processors to achieve images of acceptably high quality. Radiological equipment, when due for replacement, should be replaced by equipment which meets internationally accepted standards.

Mammography equipment suitable for magnification and localisation procedures must be available. Ultrasound equipment suitable for breast examination is also essential.

Reports should include details of the site, size, extent and nature of any abnormality, a description of any significant associated features, and an opinion as to the most likely diagnosis. Radiologists should participate in regular audit of individual performance.

Radiologists involved in diagnosis should participate in the imaging of patients following treatment and be familiar with imaging changes. Radiologists should be involved in decisions on the most appropriate imaging investigations.

A standardised proforma for reporting by radiologists should be devised.

Radiographers taking mammograms should hold the appropriate certification of competence. Mammography should be performed only by radiographers with appropriate skills and knowledge. In a centre which has a screening unit the same radiographers should work in the symptomatic Breast Unit.

PATHOLOGIST

The Breast Unit must include pathologist(s) with expertise in breast pathology and cytology. Histopathology laboratories must be accredited. Histopathology departments and surgeons must have access to specimen radiography.

The diagnosis of breast cancer should be made pre-operatively in over 85% of cases. For palpable lesions the surgeon takes the core biopsy specimen while core biopsies of impalpable lesions are carried out by the radiologist under image-guidance by ultrasound or stereotactic methods.

Results of cytology (C) and core biopsy histology (B) specimens are categorised as follows:

C1 or B1 = no diagnosis possible

C2 or B2 = benign

C3 or B3 = atypia, probably benign

C4 or B4 = suspicious for malignancy

C5 or B5 = malignant

Histopathology procedures and reporting should be in accordance with international standards using the TNM system.¹⁴⁻¹⁶ There is a clear need for a defined nationally operated proforma on reporting. Histopathology reports should include information on the following factors:

- the maximum diameter of carcinomas in millimetres (mm)
- the extent of intraductal and invasive disease

- whether the tumour contains an in situ component and if so the size of the invasive component
- the size of the whole tumour
- the distance between the tumour and the surgical excision margins
- tumours identified as multicentric should be so reported
- the histological grade of the cancer
- the presence or absence of lymphovascular invasion
- tumour oestrogen receptor and progesterone receptor status
- the number of axillary lymph nodes examined, their location (Level I, II, and III) and the extent of involvement by metastatic carcinoma.

MEDICAL ONCOLOGIST

Improvements in recurrence-free survival and overall survival for breast cancer patients have been due to the multidisciplinary approach to the problem of breast disease. The development of the speciality of medical oncology has led to significant advances in adjuvant therapies. Such treatments have undoubtedly improved the survival of patients with early breast cancer. The medical oncologist therefore, is an important and intrinsic part of the Breast Unit and should be involved in the multidisciplinary meetings of all patients with breast cancer at a time when treatment is being planned. As primary chemotherapy may become more widely practiced, it is appropriate that the medical oncologist be involved at the early stages of the decision-making process. The input of medical oncology into locally advanced and metastatic breast cancer is also most important and combined clinics with surgeon, medical oncologist and radiotherapist in the follow-up of patients with breast cancer should be routine.

RADIATION THERAPIST

As with the medical oncologist, the radiotherapist should be involved at the early stages of treatment planning for patients with proven carcinoma of the breast. Close consultation between the surgeon and radiotherapist in patients undergoing breast conservation surgery permits the radiotherapist to plan post-operative treatment carefully. The opinion of the radiotherapist is also valuable in post-mastectomy patients where the issue of chest wall irradiation is important. Furthermore, liaison between surgeon and radiotherapist becomes of critical importance in the area of the axilla as radiotherapy to the axilla which has been surgically cleared is inappropriate. New techniques in radiotherapy for breast disease are evolving and the scope and application for radiotherapy is increasing for patients with breast cancer. Therefore, the radiation therapist should be an intrinsic part of the Breast Unit after the primary diagnosis has been made. The radiotherapist will also have a keen interest in follow-up as radiotherapy has an important palliative role to play in both locally advanced and metastatic breast cancer.

DATA MANAGEMENT

The Breast Unit must collect patient data prospectively and requires adequate resources in terms of information technology and data processing. This data must be made available to the National Cancer Registry database for proper epidemiological studies. Breast Units should be audited annually in a similar way to the arrangement for the National Breast Screening Programme, BreastCheck. A National Reference Centre is recommended to co-ordinate annual audit.

Diagnosis of Breast Disease

Diagnosis of breast cancer should be based on triple assessment, where clinical examination is followed by imaging and cytology/pathology as required. The Breast Unit should produce a rapid multidisciplinary assessment for patients with breast disease. For patient convenience diagnostic tests should be arranged to minimise the number of visits.

Patients should receive all the diagnostic tests required at the first visit so that they can be reassured as soon as possible that there is no abnormality or that their lesion is benign. If the lesion is likely to be malignant there is a case to be made for providing time for the patient to adjust to the realisation of the significance of the diagnosis. It is often appropriate to discuss the diagnosis of breast cancer at one visit and the management at a subsequent visit.

Any symptomatic breast referral may be a carcinoma. Patients should be seen soon after referral to identify the problem and to alleviate anxiety. The hospital administration is responsible for providing adequate facilities and personnel to meet these standards.

MAMMOGRAPHY

Decisions as to who should have mammography should be made only by members of the Breast Unit.

Mammography should not be the sole or initial diagnostic test for symptomatic breast disease. A negative mammogram does not exclude cancer. The sensitivity of mammography alone is over 80% but is considerably less in young patients.¹⁷ A mammogram is not required in all women with breast symptoms. Palpable breast cancers may not be visible on a mammogram, particularly in a young woman. Mammography is generally inappropriate under the age of 35 unless there is a specific indication.

Pre-operative mammography is essential for assessment of all patients with operable breast cancer.

There is no evidence that women on hormone replacement therapy (HRT) require more frequent mammograms than received through the National Breast Screening Programme. This also applies to women who are taking HRT under 50 years of age.

Screening is currently advised for women over 50 years of age. Populations of women who are not at high risk of breast cancer do not benefit from routine screening mammography under 50 years of age. The majority of breast cancers are not genetically inherited. The assumption that identification of cancer gene mutations will reduce mortality is unproven. Referral to a Family History Clinic provides an opportunity for proper risk assessment, counselling, and the opportunity to take part in screening or prevention studies and any other research programme.

SURVEILLANCE OF WOMEN AT SPECIAL RISK FOR BREAST CANCER

The following is a management strategy for women with concerns about their family history.

High Risk Group

The high-risk group is defined as:

- breast/ovarian cancer families with 4 or more affected relatives on the same side of the family
- breast cancer families with 3 affected relatives with an age at diagnosis of under 40 years
- breast/ovarian cancer families with 3 affected relatives with breast cancer diagnosed under 60 years
- families with one member with both breast and ovarian cancer.

These patients require consultation with a consultant in human genetics in association with the patient's clinician.

Moderate Risk Group

The moderate risk group includes women with:

- one first-degree relative with breast cancer diagnosed under the age of 40 years
- two first-or second-degree relatives with breast cancer diagnosed under the age of 60 years, or ovarian cancer at any age
- three first-or second-degree relatives with breast or ovarian cancer diagnosed at any age
- a first-degree relative with bilateral cancer under the age of 60 years
- a first-degree male relative with breast cancer at any age.

The relative risk for breast cancer in these women is at least 3 times that of the general population.

A possible age-dependent screening protocol for high-risk and moderate-risk groups might be:

- Over age 50 Mammography every 18 months
- Age 35-49 Annual mammography (consider screening from 5 years prior to age at diagnosis in relative if this is age under 39 years).
- Below age 35 No mammography.

Low-Risk Group

The strategy for these women should be to discuss the difference between familial and non-familial cancer and to explain that that individual's risk is not significantly elevated. They should be informed that the risk of non-familial breast cancer remains and be encouraged to participate in the breast screening at an appropriate age. The advice offered to women should be the same, whether in primary care or in the Breast Unit.

MANAGEMENT OF A PATIENT WITH A BREAST LUMP

Patients should be encouraged to bring somebody with them when the results are being discussed. Breaking bad news should be done in a professional way by the surgeon with a breast-care nurse in attendance. The consultation should be conducted

in a sensitive fashion and should not be rushed. It should take place in an appropriate environment with adequate privacy.

The follow-up arrangements should be clear to patient, doctor and breast-care nurse. The patient must have a contact telephone number for the breast-care nurse.

Triple Assessment

Assessment of a patient with a breast lump requires a careful history and clinical examination by the surgeon.¹⁸ Further assessment of a discrete breast lump is based on Triple Assessment.

If a discrete lump is found fine needle aspiration is performed.¹⁹ If the aspirate contains fluid which is not blood stained and the lump disappears, the fluid need not be sent for cytology and no further action is needed other than an imaging procedure. If the aspirate is blood-stained or the mass remains the aspirate should be sent for cytology.

If the breast lump is solid, fine needle aspiration cytology (FNAC) provides useful information. The results of FNAC are variable and are operator - and pathologist - dependent. FNAC is valuable in that patients with clinically benign and cytologically benign lesions may be reassured. Where the diagnosis is positive on cytology confirmatory tests can be performed.

FNAC cannot distinguish between invasive and in-situ carcinoma. Core biopsy provides tissue for histological examination and therefore allows definition of whether a tumour is invasive or non-invasive, provided a representative sample of tissue has been taken. Core biopsy sensitivity varies between 67% and 95%.²⁰⁻²¹ Advantages of core biopsy over FNAC are that tissue can be processed as ordinary histology and oestrogen receptor status determined. The use of automated core biopsy devices increases sensitivity of core needle biopsy.

Open surgical biopsy can be performed if core biopsy is negative or inappropriate. However, over 90% of patients should be diagnosed without open biopsy. The diagnosis of breast cancer should be established before definitive treatment is undertaken.

A mammogram should be performed in women over 35 years of age or if the mass is clinically malignant.²² Mammography should be performed before FNAC if the mass is suspected to be malignant as haematoma can interfere with interpretation. Mammography in this setting assesses the risk of malignancy and screens both breasts for non-palpable lesions that may affect the surgery performed. Mammography has a false negative rate of up to 20% in palpable breast cancer.

Open Surgical Biopsy

In the small number of cases in which open surgical biopsy is needed for diagnosis (e.g. needle localisation for calcification) the surgeon or pathologist should weigh the specimens. Biopsies for diagnosis of impalpable lesions that prove to be benign should weigh less than 15 grams in 90% of cases.

Some breast operations are suitable for day-case surgery but this is not always so. There must be recognition of the emotional needs and general health of the woman. The decision as to whether day case surgery is appropriate should be made on an individual basis by the surgeon and not dictated by a general management policy by hospital administration.

Management of Breast Cancer

TREATMENT PLANNING

Treatment of the primary tumour must follow written protocols agreed by the Breast Unit.²³ Following diagnosis, women must be given adequate time, information and support in order to make a fully informed decisions about treatment. This must include discussion of treatment options with the surgeon with the breast-care nurse in attendance.

The treatment options offered and the decisions agreed with the patient must be recorded. In the event of a patient refusing the treatment options recommended this should also be recorded. There must be close communication between the surgeon, the medical oncologist and the radiotherapist to plan primary treatment and facilitate adjuvant therapy.

A care plan must be drawn up and recorded for each woman. This must take account of predictive factors of local or regional recurrence and of survival, of social circumstances and patient preferences. Planning should also allow discussion of reconstructive surgery options.

Consultants within the Breast Unit (surgery, radiology, pathology, medical oncology, and radiotherapy) must have contractual time for attendance at the multidisciplinary meeting. Breast surgery trainees, and breast-care nurses must attend multidisciplinary meeting.

All patients should receive advice on reconstructive breast surgery where appropriate. There should be adequate facilities for outpatients, inpatients, day patients and theatre sessions.

AVOIDANCE OF DELAY IN SURGICAL TREATMENT

When a decision has been reached on surgery, patients should be offered a date for operation. Diagnostic or therapeutic surgery is associated with a great deal of patient anxiety. Such surgery should therefore be classified as 'urgent'.

The date offered for surgery should be within 2 – 3 weeks of the diagnosis to minimise patient anxiety.²⁴ There is no evidence, however, that a delay of 4 weeks has any effect on survival. Management must make resources available to achieve these targets.

DECISION-MAKING

Evidence is available at 18 years follow-up on six prospective trials comparing mastectomy and axillary clearance with breast conservation and axillary clearance.²⁵⁻³¹ Whole breast irradiation with doses of 45 to 50Gy were used in all these trials. (Tables 1 and 2). None of the trials demonstrated significant differences in overall or disease-free survival with either treatment. In only one trial²⁹ was a significantly higher risk of local recurrence identified in the breast conservation group. In this study, however, only gross tumour removal was required for entry to the trial.

Local recurrence after breast conservation may be the result of inappropriate patient selection, inadequate surgery or inadequate radiation therapy. The incidence of local recurrence in the treated breast varies between 3 and 19%. Most of these recurrences can be treated by mastectomy and survival after such an event is approximately 75% at 5 years. The incidence of chest wall recurrence after primary mastectomy ranges between 4 and 14%.

The critical elements in selection of patients for breast conservation are:

- history and physical examination
- mammography
- histology
- assessment of the patient's needs and expectations

History and Physical Examination

A young age is not a contraindication to breast conservation. In elderly women, the physiological rather than the chronological age and the presence or absence of co-morbidity should be the determining factors. A family history of breast cancer, including the age at diagnosis and whether the family member had bilateral breast cancer are relevant. A family history of ovarian, endometrial or other tumours is also taken into account.

On physical examination, the tumour size and location are important as is the size of the breast. A 3 cm tumour in the periphery of a large breast may be suitable for breast conservation while a similar lesion in a small breast may make a satisfactory result from breast conservation less likely, both in

Table 1

Comparison of Survival after Breast Conserving Surgery and Radiotherapy with Mastectomy – Prospective Randomized Trials							
Trial	Endpoint (years)	Overall Survival (%)			Disease Free Survival (%)		
		CS & R	(P Value)	Mastectomy	CS & R	(P Value)	Mastectomy
National Cancer Institute, Milan ²⁶	18	65%	(NS)	65%	N/A		N/A
Institut Gustave-Roussy ²⁷	15	73%	(.19)	65%	N/A		N/A
NSABP B-06 ²⁸	12	63%	(.12)	59%	50%	(.21)	49%
National Cancer Institute, U.S.A. ²⁹	10	77%	(.89)	75%	72%	(.93)	69%
EORTC ³⁰	8	54%	(NS)	61%	N/A		N/A
Danish Breast Cancer Group ³¹	6	79%	(NS)	82%	70%	(NS)	66%

CS & R = conservative therapy and radiation; EORTC = European Organization for Research and Treatment of Cancer; N/A = data not available; NS = not significant; NSABP = National Surgical Adjuvant Breast and Bowel Project

Winchester, Cox²⁵

Table 2

Comparison of Local Recurrence after Breast Conserving Surgery and Radiation with Mastectomy – Prospective Randomized Trials				
Trial	Endpoint	Local Recurrence (%)		
		CS & R	(P Value)	Mastectomy
National Cancer Institute, Milan ²⁶	Cumulative incidence at 18 years	7%	(NS)	4%
Institut Gustave-Roussy ²⁷	Cumulative incidence at 15 years	9%	(NS)	14%
NSABP B-06 ²⁸	Cumulative incidence at 8 years	10%	(NS)	8%
National Cancer Institute, USA ²⁹	Crude incidence, median follow-up 10.1 years	19%	(.01)	6%
EORTC ³⁰	Crude incidence at 14 years	17%	(NS)	4%
Danish Breast Cancer Group ³¹	Crude incidence, median follow-up 3.3 years	3%	(NS)	4%

CS & R = conservative therapy and radiation; EORTC = European Organization for Research and Treatment of Cancer; N/A = data not available; NS = not significant; NSABP = National Surgical Adjuvant Breast and Bowel Project

Winchester, Cox²⁵

terms or histological clearance and acceptable cosmesis. Patients with multiple primary breast tumours are unlikely to be suitable for breast conservation. If there is evidence of locally advanced breast cancer, such as skin ulceration, the presence of satellite nodules, inflammatory carcinoma, fixed axillary lymph nodes or lymphoedema, the patient should be considered for primary systemic therapy. It should be noted that skin tethering or retraction of the nipple or of breast parenchyma are not signs of locally advanced breast cancer and are not contraindications to breast conservation.

Mammography

Mammography is a requirement for patients with breast cancer and is a prerequisite in determining suitability for breast conservation. It defines the extent of the disease and whether the tumour is unicentric or multicentric. It also indicates the presence and extent of microcalcification and allows evaluation of the opposite breast.

Histology

The histological features indicating an increased risk of local recurrence after breast conservation are listed under 'Risk Factors for Local Recurrence' and are taken into account when planning primary surgery.

Patient Preference

The surgeon should discuss with the patient, in the presence of the breast-care nurse, the benefits and risks of breast conservation compared with those of mastectomy. Issues of survival, local recurrence, psychological adjustment, cosmetic outcome, functional capacity and sexuality should be taken into account.

PRE-OPERATIVE STAGING TESTS

All patients should have a chest x-ray and liver function tests. Bone scanning and liver ultrasound may be done on a selective basis.^{32,33} There is good evidence that a peri-operative search for occult metastases (e.g. bone scan, liver ultrasound) does not yield useful information in a woman with operable primary breast cancer. These investigations should be carried out only if the patient is symptomatic or for the investigation of symptoms in the follow-up clinic or as part of a clinical trial. The goals of breast cancer surgery are cure of cancer, local disease control with the provision of accurate pathological staging and a satisfactory cosmetic result. This should occur where there is infrastructure to ensure physical and psychological rehabilitation.

Resection margins

All tumours should be removed with an adequate surgical margin. If resection margins are not clear further surgery should be recommended. An adequate margin may be defined as that which results in a local recurrence of less than 5% at 5 years, in the conserved breast. Clear margins of 1 cm should be the aim but this is not always possible, particularly for tumours situated close to the pectoralis major muscle. To minimise the number of therapeutic operations in women undergoing conservation surgery the number of operations should be recorded.

To ensure that all necessary data are obtained histological node status should have been obtained in patients with invasive breast cancer. Formal axillary dissection should be performed. The morbidity of the procedure can be minimised with meticulous surgery, physiotherapy and by avoiding irradiation to the surgically cleared axilla.

Appropriate treatment should be given to patients with ductal carcinoma in situ (DCIS) in the absence of invasive breast cancer. A local excision is not appropriate for extensive or multifocal DCIS. Patients with previously diagnosed DCIS should not undergo an axillary clearance.

Surgery for Primary Operable Breast Cancer

SURGERY OF THE BREAST

Breast Conserving Surgery (BCS)

All patients should be considered, but not all patients are suitable, for BCS. Conservation of the breast without compromising the goals of breast cancer surgery is the preferred option. Appropriate conservative surgery to the breast followed by radiotherapy gives similar survival to more radical surgery.

Breast conserving surgery (followed by radiation therapy to the conserved breast) is the treatment of choice for unifocal invasive breast cancer provided that the disease can be excised with histologically clear margins of at least 5mm around the tumour.^{34,35} The use of metallic clips to the tumour bed facilitates subsequent radiotherapy. The tumour bed can be seen on x-ray films taken during simulation so that a radiation boost can be given to this area if indicated. Rigorous histopathological assessment of the margins of the excised specimen is required. The excised specimen should be orientated for the pathologist. This can be done conveniently by the use of sutures according to the locally agreed protocol. The specimen should be inked by the pathologist. Oestrogen and progesterone receptor status can be measured by ELISA at designated centres. Receptor status can also be estimated by immunohistochemistry on fixed sections.

Some patients who have undergone conservative resection for invasive breast cancer require further excision or completion mastectomy once the full histological report is available as the risk of local recurrence within the breast is unacceptably high if the resection margins are involved by tumour. Studies have found variation in the rates of breast conservation treatments in the United Kingdom. Not all patients are suitable for breast conservation surgery. Mastectomy is indicated in situations where the disease is multifocal or in situations where radiotherapy is contra-indicated. The possibility of breast reconstruction should be offered to all patients undergoing mastectomy.

Contraindications to Breast Conservation

Indications for total mastectomy are:

- multifocal disease
- two or more primary tumours in separate quadrants of the breast
- anticipated poor cosmetic result
- breast cancer occurring in the 1st and 2nd trimester of pregnancy
- inability to obtain histologically clear margins
- patient preference and
- contraindications to radiotherapy.

Patients undergoing mastectomy or/and certain patient after BCS should be considered for breast reconstruction.

Relative contraindications to breast conservation include collagen vascular disease as such patients tolerate radiotherapy poorly. Tumour size *per se* is not a contraindication to breast conservation although adequate resection of a large tumour in a small breast might result in unacceptable cosmetic deformity.

Points on Surgical Technique

There are several technical considerations which the surgeon should take into account to minimise risks of local recurrence and to maximise the cosmetic result.

- curvilinear incision (radial for large mass in lower quadrants)
- incision directly over the lesion
- separate incision for the axillary surgery
- at least 1cm gross margin (margins must be histologically clear)
- pectoralis fascia removed in deep lesions
- metallic clips (titanium) to the tumour bed
- no drain or deep sutures to the breast are recommended but drainage of the axilla is advised.
- subcuticular suture

Risk Factors for Local Recurrence

Risk factors for local recurrence, following BCS include:

- positive surgical margins for tumour
- tumour near the margin
- radiotherapy not given
- extensive DCIS or extensive intraduct component (EIC) associated with an invasive cancer
- extensive lymph node involvement (more than 4 nodes)
- young age
- multiple tumours
- high grade tumours
- lymphovascular invasion
- tumour necrosis.

Further Surgery following Conservative Resection

Some patients, having undergone conservative resection, may require further excision or completion mastectomy when the full histological report is available. It should be explained to the patient in advance that the risk of local recurrence is unacceptably high if resection margins are involved

The risk of local recurrence after breast conserving surgery, if radiotherapy is not given, is up to 43% at 9 years compared with 12% if radiotherapy is used. Patients having BCS should therefore have radiotherapy to the residual breast.

SURGERY OF THE AXILLA

The aims of axillary surgery are:

- to accurately stage the disease
- to provide prognostic information
- to provide a rational basis for subsequent systemic therapy
- to prevent axillary recurrence
- to increase the likelihood of cure.

Clinical examination of the axilla is inaccurate with false positive and false negative rates of 30% so axillary surgery is needed to stage the disease. The chances of axillary involvement is high even when the primary tumour is small. The number of nodes involved is also important.

Formal axillary clearance involves removal of Levels I, II, and III nodes. The number of nodes involved is important in estimation of prognosis and hence in the selection of adjuvant therapy.³⁶⁻⁴⁴ Lymph node sampling frequently does not provide sufficient number of nodes for accurate staging as no nodes may be retrieved. Sampling missed nodal metastases in 14% of patients in one study. The technique of axillary lymph node sampling is, therefore, poorly defined and provides an uncertain yield of nodes.

Level I removal of axillary contents from the lateral border of latissimus dorsi to the lateral border of pectoralis minor up to the axillary vein; this usually involves complete dissection of the axillary vein on its anterior and inferior surfaces for a distance of 6 to 8cms.

Level I-II Level I and, in addition, removal of the contents posterior to pectoralis minor.

Level I-III Level I-II and contents medial to the medial border of pectoralis minor up to the subclavius muscle (Halsted's ligament)

- If Level I nodes are involved the chances of Level II-III being involved is 41%.
- Level I clearance will miss the 3% of cases that have skip lesions - involvement of Level II and III with negative Level I.
- If a Level I-II clearance is performed only 0.5% of skip metastases to Level III would be missed

- Level I-III provides the best staging information. Although Level I-II will also provide accurate information, 22% of patients with positive Level I-II nodes will have positive nodes at Level III. The average number of lymph nodes in a complete axillary dissection is around 25.
- With a full Level I-III clearance the incidence of local axillary recurrence is 1%. This contrasts with a relapse rate of 8% with radiotherapy alone and 21% with an expectant policy.

The thoraco-dorsal nerve and vessels and the long thoracic nerve are isolated and protected throughout their extent in the axilla and the intercosto-brachial nerve is protected if this is feasible, unless it is surrounded by tumour. Formal axillary dissection (Levels I, II and III) provides the most accurate staging information on the axilla. A relationship exists between the size of the tumour and the likelihood of the axillary lymph nodes being affected. If a tumour is more than 5cms in diameter, more than 60% of patients have involved axillary lymph nodes whereas when the tumour is less than 0.5cms only 3% of the nodes are affected.

Disadvantages of formal axillary clearance are seroma formation, arm swelling and shoulder stiffness. Significant arm swelling after axillary clearance or radiotherapy occurs in 2% of cases. This increases to at least 30% if axillary radiotherapy is added to surgical clearance. Axillary irradiation should, therefore, generally be avoided after axillary clearance.

Evaluation of the Sentinel Lymph Node in Breast Cancer

Patient with uninvolved axillary lymph nodes do not benefit from axillary dissection and identification of such patients before the lymph nodes are completely excised, would obviously be desirable. Evaluation of the first lymph node that drains the tumour area (sentinel node) is under investigation in an attempt to avoid extensive surgery on a "negative" axilla. Sentinel lymph node mapping may identify patients most likely to benefit from axillary dissection and avoid the need for axillary clearance by identifying node-negative patients. The ideal technique, the extent of the histopathological examination and the training required for accurate and reproducible results have yet to be determined. For this reason the sentinel node method remains investigational and should be carried out only in the context of a promising method under evaluation.

A multicentre trial has demonstrated marked variations among surgeons in the performance of sentinel lymph node dissection.⁴⁵ The adverse oncological consequences of this surgical procedure being poorly performed are serious. The results of individual surgeons should be audited before the sentinel node assessment becomes the only axillary intervention. Because the procedure, whether done by blue dye, by radio-isotope or by both, remains under evaluation, it should be performed only in the context of a subsequent verifiable axillary clearance on each individual patient and the information required for such an evaluation is demonstrated in Table 3. Most studies indicate that the combination of blue dye and radio-isotope provides the most accurate means available at present.

Table 3

SENTINEL NODE DATA SHEET

Side:	1. Right	2. Left	3. Bilateral		
Palpable mass:	0. No	1. Yes			
Diagnosis:	1. FNA	2. Core	3. Surgical Biopsy		
Location:	1. UOQ	2. LOQ	3. UIQ	4. LIQ	5. Central
Clinical size:	_____				
Pathological size:	_____				
Date of procedure:	/ /				
Surgeon:	_____				
Number of nodes seen (approx)	_____				
Counts: Background	_____				
Injection site	_____				

	Nodes Level I	Nodes Level II	Nodes Level III
Location (level) of node			
Blue dye 0. No 1. Yes			
Counts over skin			
Counts in situ			
Counts ex vivo			
Bed count post excision			

OPERATION: 1. Breast Conservation 2. Mastectomy

Number of sentinel nodes excised:	_____			
Number of sentinel nodes positive:	_____			
Number of axillary nodes excised:	_____			
Number of axillary nodes positive:	_____			
Total number of nodes excised:	_____			
Total number of nodes positive:	_____			
	1. Dye only	2. Isotope only	3. Dye + Isotope	4. Failure

Comments about procedure:

MANAGEMENT OF NON-INVASIVE BREAST CANCER

Non-invasive breast cancer includes ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS).

Ductal carcinoma in situ (DCIS)

DCIS can present clinically by the presence of a lump, Paget's disease of the nipple or a bloody nipple discharge. DCIS may be detected clinically or by screening mammography. With the widespread use of mammography DCIS accounts for up to 30% of breast cancers. DCIS is a spectrum of histological subtypes of diseases of different biological behaviours; comedo, cribriform, micropapillary and solid.⁴⁶⁻⁴⁸

Pathological reports should include the histological sub-type, its extent and margin involvement. Attempts have been made to classify DCIS according to prognosis. The comedo-type has the greatest potential for recurrence after local treatment.⁴⁹

When excision alone was compared with excision and radiotherapy for DCIS there was a significant reduction in the local recurrence rates at 5 years in irradiated patients.⁵¹

The National Surgical Adjuvant Breast and Bowel Project (NSABP B-17) was a prospective randomised trial comprising excision alone with excision and radiotherapy in the treatment of ductal carcinoma in situ (DCIS). The first report in 1993 indicated a significant reduction in the 5-year rates of local recurrence in the irradiation group of patients from 10.4% to 7.5% for non-invasive recurrences and from 10.5% to 2.9% for invasive recurrences. The European Organisation for Research and Treatment of Cancer (EORTC) has recently published the results of a trial confirming that radiation decreases rates of local recurrence in DCIS patients treated with breast conservation.⁵⁰ The reduction in invasive recurrence, noted in NSABP B-17, was not confirmed in the EORTC study and neither trial provided a subset analysis giving comparative rates of local recurrence for various subgroups of DCIS. Of concern is the observation in the EORTC study of an increased rate of contralateral breast cancer in the irradiated

group. At present, the evidence is that radiotherapy to the breast in DCIS patients following breast conservation is beneficial, reducing local recurrence rates but it is not yet known which subgroups benefit.

Management of DCIS

- DCIS less than 0.5cm Segmental mastectomy
- DCIS 0.5-1.9cm Segmental mastectomy + radiotherapy
- DCIS more than 2.0cm Total mastectomy

Thirty percent of patients with DCIS treated by biopsy alone develop invasive breast cancer within 10 years.

Total mastectomy had in the past been the standard treatment for DCIS with a local recurrence of 0.75% and an overall cancer-related mortality of 1.7%. Wide excision plus radiotherapy gives a recurrence rate at 5 years of 10% versus 21% if radiotherapy not given.⁵⁰

Skin-sparing Mastectomy

Wide excision alone is indicated for a small focus of mammography-detected non-comedo DCIS. When BCS is performed the margins must be histologically free as for invasive breast cancer. BCS mandates frequent follow up as 50% of the recurrences will be invasive breast cancer. The 7-year disease free survival after excision and radiotherapy was 84% compared to 98% for mastectomy.

Skin-sparing mastectomy involves a procedure whereby the breast tissue is excised whilst preserving the overlying skin. This procedure combines the possibility of removing all the underlying breast tissue and affords the opportunity of placing an implant under the skin to preserve the breast contour. In some circumstances this procedure may be carried out with preservation of the nipple-areolar complex but care must be taken to ensure that resection margins are clear of DCIS.

Factors Favouring Mastectomy in DCIS include:

- the presence of comedo necrosis
- extensive disease on mammography
- clinically palpable lump greater than 2cm
- bloody nipple discharge
- Paget's disease
- involved margins after resection
- biological data indicating poorer prognosis e.g. high nuclear grade, high proliferation index, negative oestrogen receptor status
- diffuse pattern of growth.

Axillary surgery is unnecessary in patients with DCIS as the risk of nodal involvement is 2%.⁵² Low Level I axillary clearance is indicated for extensive disease or microinvasion. The place of tamoxifen in the management of DCIS remains to be established. An algorithm for the management of DCIS and Paget's disease is presented in Table 4.

Lobular Carcinoma in situ (LCIS)

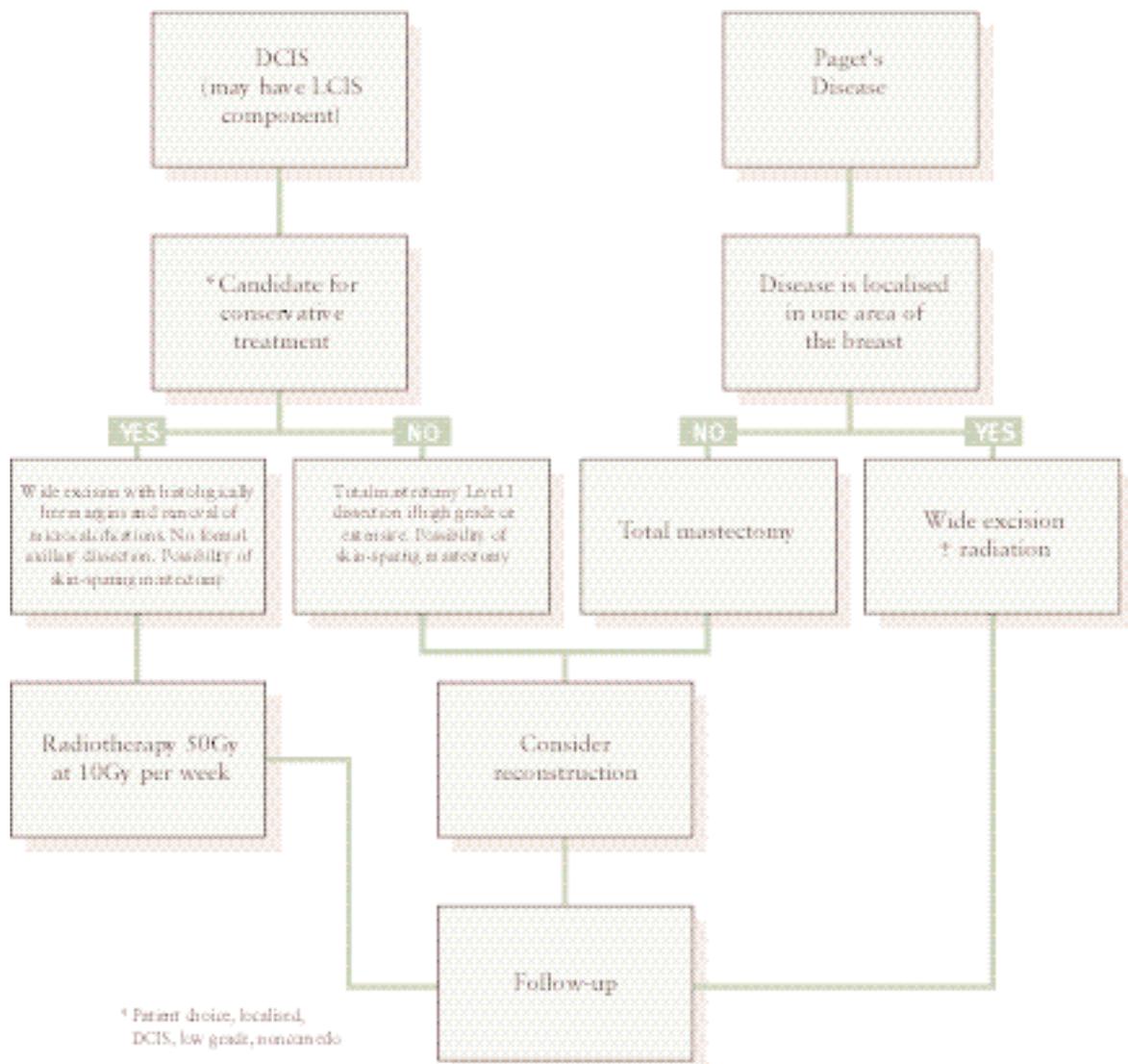
LCIS is an incidental finding in pre-menopausal women. It has no clinical, mammographic or gross pathological features. LCIS does not require treatment. Its significance is that it is a "marker" of increased risk for the development of breast cancer.

The risk of breast cancer, equal for both breasts, is 1% per annum for 15-20 years.⁵³ This represents a 12-fold risk over the general population. Close surveillance with clinical examination and annual mammography is indicated. In spite of this there is a 7% breast cancer mortality rate in patients followed up for LCIS.

Table 4

TREATMENT OF DUCTAL CARCINOMA IN SITU (DCIS) AND PAGET'S DISEASE

Eligibility into approved clinical trials should be considered. If not appropriate for a trial, the following schema can be recommended.



BREAST RECONSTRUCTION

Breast reconstruction should be considered for all patients who have undergone mastectomy. Consideration of this procedure may take place before or after mastectomy depending on the circumstances. Evidence is accumulating that the long-term results of immediate breast reconstruction are no worse than in delayed reconstruction. Reconstruction takes the form of synthetic implants, myocutaneous flaps or frequently a combination of both.

FOLLOW-UP OF THE BREAST CANCER PATIENT

Patients should be supported by a specialist breast care nurse who is a member of the Breast Unit and who should have links with the ward nurses to assist in continuity of care. Following surgery, the fitting and supply of breast prostheses should be explained to patients.

Patients should be informed about the range of services available and provided with literature including details of follow-up treatment and information about local support groups. Support groups should preferably work with patients under the direction of the breast-care nurse. Clinical follow-up involving the surgeon should take place at regular intervals and annual mammography is recommended.

On outpatient visits women may receive results and further treatment may be discussed. A telephone contact number to discuss treatment and answer questions is important. Women with benign conditions need similar opportunities.

Following diagnosis of cancer the patient must be given adequate time, information and support in order to make a fully informed decision about their treatment. This should include discussion with the surgeon, in liaison with a breast-care nurse, of appropriate treatment options. It is often preferable to have this discussion at a separate interview in an appropriately calm setting.

COMMUNICATION WITH GENERAL PRACTITIONERS

The Breast Unit should ensure that GPs receive communications that gives them a clear understanding of the diagnosis, care plan and toxicity profile of any proposed systemic treatment. Such communications must follow the first post-operative review and any subsequent change of treatment.

Clinical trialists must ensure that GPs are fully briefed about any trial that the patient is entering and any potential side-effects which may ensue.

Adjuvant Systemic Therapy in Breast Cancer

Radiotherapy and chemotherapy should be directed by radiation oncologists and medical oncologists who specialise in breast cancer. They should be active members of the Breast Unit.

Treatment should be provided at the Breast Unit whenever practicable. Standard chemotherapy may be carried out at the Breast Unit or at another centre but arrangements must comply with the requirements for the safe handling of cytotoxic drugs and has trained supervision.

Radiotherapy has to be provided at a Radiotherapy Centre but the patient should be cared for at the centre by the radiotherapist attached to her own Breast Unit.

Many issues in adjuvant therapies remain unresolved and await the outcome of carefully designed and rigorously conducted clinical trials. As large numbers of patients are needed for these studies, multicentre collaboration is needed. Surgeons, radiotherapists and medical oncologists are encouraged to seek recruitment of their patients in ethically approved international clinical trials in Europe and the United States in addition to inter-hospital studies within Ireland. A surgeon should be involved as a principal investigator in all trials involving surgery, either as part of diagnostic or therapeutic intervention.

CHEMOTHERAPY

Most patients with breast cancer will require some form of adjuvant therapy. This will depend on tumour pathological characteristics, lymph node involvement, oestrogen receptor status and age of the patient.⁵⁴⁻⁵⁶

The role of chemotherapy is best defined in a multidisciplinary conference when all of the pathology information is available. In cases in which adjuvant chemotherapy is required, the time interval between the decision to give chemotherapy and the start of treatment should not exceed three weeks. These target times include any waiting time for ward or hostel accommodation. Local protocols may vary.

Delivery of cytotoxic chemotherapy should be carried out under the supervision of a medical oncologist who is a member of the Breast Unit and is treating the majority of patients from that unit. There should be adequate pharmacy support. There must also be adequate facilities for the management of complications that may arise.

ENDOCRINE THERAPY

The benefits achievable by endocrine manipulation in ER-positive breast cancer may exceed gains from cytotoxic therapy for both early and advanced disease.

The Early Breast Cancer Trialists Collaborative Groups overview demonstrated that ovarian ablation significantly improved the long term survival for women under 50 years of age. The overview indicated that further trials of the addition of chemotherapy to ovarian ablation were needed. Issues arise about the safety of inducing menopause in young women, particularly in relation to concerns about delayed side-effects such as skeletal and cardiovascular disease. In patients with advanced breast cancer similar disease-free survival and overall survival was noted for those treated by oophorectomy as with the GnRH analogue, goserelin. The value of GnRH analogues in the adjuvant setting is under investigation in clinical trials.

Tamoxifen remains an important agent as adjuvant treatment for patients whose tumours express steroid hormone receptor. While initial trials indicate that the protective effect of tamoxifen against relapse lasted for 2 years, more recent studies indicate that its value extends for at least 5 years. The evidence for tamoxifen efficiency for longer than 5 years remains inconclusive and is currently under study.

The use of selective oestrogen-receptor modifier (SERM) drugs and selective aromatase inhibitors are being used increasingly both in the adjuvant setting and for locally advanced or metastatic breast cancer. Their precise role in clinical practice remains to be established after evaluation in clinical trials.

ADJUVANT THERAPY IN NODE-NEGATIVE PATIENTS

The following guidelines, supplied by the International Consensus Panel⁵⁴ are based on clinical trials which indicate that adjuvant systemic therapy can reduce the risk of relapse and increase length of survival. They should not be taken as definitive requirements to be applied to all patients since individual circumstances vary.

The Consensus Panel divided node-negative patients into minimal/low risk, intermediate risk and high risk as shown below (Table 5).

For node-negative patients considered at high risk of recurrence the choice of treatment follows similar guidelines to that for node-positive disease, after which the prognosis is similar (Table 6).

For high-risk patients with negative hormone receptors, chemotherapy alone is considered to be appropriate.^{55,56} The addition of tamoxifen to chemotherapy is suitable for tumours which express oestrogen or progesterone receptors. Combining chemotherapy with tamoxifen in ER or PgR-positive tumours is more effective than endocrine therapy alone, irrespective of menopausal status. The use of anthracyclines for these patients probably results in a small but statistically significant improvement over the oral cyclophosphamide (Days 1 and 14), intravenous methotrexate and 5-fluorouracil (day 1 and 8) regimen.

For patients at minimal or low risk, account should be taken of the low relapse rate within 10 years without adjuvant treatment and the potential reduction of contralateral breast cancer by the use

of tamoxifen. In premenopausal women classified as having an intermediate risk, the value of endocrine therapy other than tamoxifen remains investigational considering the long-term side-effects of these treatments. This includes ovarian ablation either by oophorectomy or by gonadotropin-releasing hormone (GnRH) analogue.

ADJUVANT THERAPY IN NODE-POSITIVE PATIENTS

For oestrogen-receptor (ER) or progesterone-receptor (PgR) positive patients with positive nodes, chemotherapy in the form of cyclophosphamide, methotrexate, fluorouracil (CMF) or anthracycline-based chemotherapy in addition to tamoxifen has been demonstrated to be better than tamoxifen alone in terms of prolonging disease-free survival (Table 7). Tamoxifen alone in postmenopausal women may be justified when other factors, such as age, co-morbidity, risk of recurrence and patient preference are taken into account. Anthracycline-based regimens indicate a small but significant advantage over CMF treatments. The use of taxanes, dose intensification and more novel combinations of chemotherapeutic agents are under evaluation.

The International Consensus Panel⁵⁴ agreed that patients with less than 10% chance of relapse within 10 years should not be candidates for routine adjuvant systemic therapy. The most relevant factors involved in estimating the risk of relapse are the presence and number of axillary lymph nodes involved and the size of the tumour.

Table 5

Risk in node-negative patients			
FACTORS	MINIMAL/LOW (has all listed factors)	INTERMEDIATE	HIGH (has at least one listed factor)
Tumour Size	≤1cm	1-2cm	> 2cm
Oestrogen and/or progesterone receptor status	Positive	Positive	Negative
Grade	Grade 1 (uncertain relevance for tumours < 1cm)	Grade 1-2	Grade 2-3
Age (years)	≥35		< 35

Table 6

Node-Negative Patients			
Patient Group	Minimal/Low Risk	Intermediate Risk	High Risk
Premenopausal ER or PgR positive	NONE OR TAMOXIFEN	TAMOXIFEN± CHEMOTHERAPY▲ Ovarian ablation◆ GnRH analogue◆	CHEMOTHERAPY+ TAMOXIFEN▲ Ovarian ablation◆ GnRH analogue◆
Premenopausal ER and PgR negative	not applicable●	not applicable●	CHEMOTHERAPY■
Postmenopausal ER or PgR positive	NONE OR TAMOXIFEN	TAMOXIFEN± CHEMOTHERAPY▲	TAMOXIFEN CHEMOTHERAPY▲
Postmenopausal ER or PgR negative	not applicable●	not applicable●	CHEMOTHERAPY■
Elderly	NONE OR TAMOXIFEN	TAMOXIFEN± Chemotherapy	TAMOXIFEN (If no ER or PgR expression: CHEMOTHERAPY)
<p>WORDS IN CAPITAL LETTERS Based directly on randomised controlled trials or internationally accepted for routine use</p> <p>GnRH Gonadotropin releasing hormone</p> <p>◆ Still under evaluation</p> <p>■ The addition of Tamoxifen following chemotherapy might be considered for ER and PgR (-) patients who have minimal traces of ER or PgR</p> <p>▲ The addition of chemotherapy is considered an acceptable option based on evidence from clinical trials, considerations based on low relative risk of relapse are toxicity, socio-economic implications and patient preference might justify use of Tamoxifen alone</p> <p>● 'Not applicable' because these patients are, by definition, at high risk</p>			

Goldhirsch, Glick, Gelber, Senn⁵⁴

Table 7

Node-Positive Patients	
Patient Group	
Premenopausal ER or PgR positive	CHEMOTHERAPY + TAMOXIFEN OVARIAN ABLATION (or GnRH analogue ± Tamoxifen)◆ Chemotherapy ± ovarian ablation or (GnRH analogue) ± Tamoxifen◆
Premenopausal ER and PgR negative	CHEMOTHERAPY▲
Postmenopausal ER or PgR positive	TAMOXIFEN / CHEMOTHERAPY■
Postmenopausal ER or PgR negative	CHEMOTHERAPY▲
Elderly	TAMOXIFEN (If no ER or PgR expression: CHEMOTHERAPY)
<p>WORDS IN CAPITAL LETTERS Based directly on randomised controlled trials or internationally accepted for routine use</p> <p>GnRH Gonadotropin releasing hormone</p> <p>◆ Therapies under evaluation in clinical trials</p> <p>■ The addition of chemotherapy is considered to be an acceptable option based on evidence from clinical trials. Considerations about the low relative risk of relapse, age, toxicity, socio-economic implications and patient preference might justify use of Tamoxifen alone.</p> <p>▲ The addition of Tamoxifen following chemotherapy might be considered for patients whose tumours are classified as ER and PgR negative but which exhibit minimal or trace levels of either ER or PgR.</p>	

Goldhirsch, Glick, Gelber, Senn⁵⁴

For node-negative patients, differential prognosis can be defined and therefore selection of adjuvant therapy should be considered, according to:

- tumour size
- histological and nuclear grade
- steroid hormone receptor status
- lymphovascular invasion
- age

New developments may alter the estimation of risk and require validation before they are accepted for routine practice outside of clinical trials. Surgery of the axilla might change if sentinel node biopsy and evaluation replaces formal axillary clearance in 'sentinel node-negative' patients.

Furthermore the use of primary, or pre-operative, systemic therapy will influence the prognostic information available and assessment on the pathological features will depend on analysis of the limited material obtained from a core biopsy.

Finally, although steroid hormonal receptor status is a most important feature, methodology used to assess receptors varies and correlating responsiveness with immunohistochemical cut-off parameters is still under evaluation.

RADIOTHERAPY

In the case of patients with early breast cancer treated by wide local excision and post-operative radiotherapy, the time interval between the two should not exceed 4 weeks. The precise time should be determined by clinical assessment and should take into account any time needed for wound healing.

Patients should be seen at a combined clinic by the surgeon and medical oncologist. Where chemotherapy and radiotherapy are both required phasing of treatments is decided for clinical reasons and the planned interval should be strictly adhered to.

The radiation oncologist who is a member of the Breast Unit should see the majority of breast-cancer patients from that Unit and should direct radiotherapy techniques. Therapeutic radiographers should be appropriately trained, and staffing should be as recommended by appropriate authorities. Patients should be reviewed by the medical oncologist regularly throughout their radiation therapy.

Post-operative breast irradiation after breast conservation is routinely given as it reduces the risk of in-breast recurrence and probably reduces the disease specific mortality. Previous radiotherapy to the breast, collagen vascular disease and pregnancy are contraindications.

Chemotherapy and radiotherapy are usually given in sequence rather than concurrently as increased toxicity is seen with concurrent regimens especially when anthracyclines are used. Radiotherapy to the chest wall after mastectomy should be considered in patients who have a higher risk of local chest wall recurrence. These include patients in which the described tumour was at or within 3 mms of the pectoral fascia or those who have heavy axillary nodal disease (more than 4 nodes positive).

Management of Recurrent Disease

Although early diagnosis and new modality treatments have improved prognosis, many will have some form of recurrence and metastases and die of the disease. Prognostic scores should be defined at the time of treatment. More than two-thirds of all recurrences occur within the first 5 years after treatment, the incidence of events decreasing exponentially with time

LOCAL RECURRENCE

Local recurrence after breast conservation is defined as further breast cancer within the skin or parenchyma of the treated breast (whether considered a recurrence or a new primary tumour).

All breast cancer patients should be followed up by the Breast Unit as recurrence is sometimes difficult to recognise. Recurrence in the conserved breast or in the mastectomy flaps may pose diagnostic difficulties. Distant recurrence may also present clinical dilemmas (for example, hypercalcaemia, endobronchial disease, lymphangitis of the lung or bone pain). These are most likely to be recognised and appropriately treated by a breast cancer specialist.

The GP will see on average only one new patient with metastatic breast cancer every 3-4 years. The GP should refer suspected recurrence back to the Breast Unit so there must be a clear line of contact for the GP to the Breast Unit.

The surgeon is responsible for patient follow-up in a breast clinic with the co-operation of other members of the breast team. They must work to standards that are the same as for the diagnosis of primary breast cancer. It is inappropriate for patients treated by conservation surgery and radiotherapy to be followed solely by the medical oncologist, who should have combined responsibility with the surgeon and radiotherapist for patients who have received radiotherapy and/or chemotherapy

Regular clinical follow-up is routine in most centres. The purpose of follow-up is to provide psychological support (especially in the first year) and to detect loco-regional recurrence or distant metastases. The ideal frequency for mammographic follow-up is unclear and current practice is variable. At present annual mammography is recommended. Patients' follow-up after treatment for breast cancer is part of the management and facilities must be available.

The incidence of local recurrence in mastectomy flaps is influenced by the extent of the operation and by the use of radiotherapy. Local recurrence presenting as a single lesion within the flap may be treated by simple excision. More extensive recurrence such as dermal lymphatic invasion reflects more aggressive disease and should be managed by a multidisciplinary approach from the surgeon, medical oncologist and radiation oncologist.

The breast surgeon should be able to advise on reconstructive techniques in managing these conditions and may have personal operative experience. If the breast specialist does not have the prerequisite experience the Breast Unit must work in collaboration with a plastic surgeon with expertise in breast substitution. Local relapse within the conservatively treated breast will usually be managed by mastectomy.

CONTRALATERAL PRIMARY BREAST CANCER

Previous breast cancer increases the risk of a contralateral second cancer four-fold. Women who develop their first cancer below the age of 40 years may be at much higher risk. The optimal timing of mammography of the contralateral breast is currently unknown. Annual mammography is currently recommended. Tamoxifen decreases the risk of contralateral cancer and may slow the appearance the second primary breast cancer.

LOCALLY ADVANCED PRIMARY BREAST CANCER

Overall survival is poor although improvement may be achieved by systemic therapy. Achievement of local control of disease and symptomatic relief is of great importance. Treatment of locally advanced breast cancer must be by a multidisciplinary approach. Local control is usually gained by combined treatments that may include radical surgery and/or radiotherapy and systemic treatment.

REGIONAL RECURRENCE

Regional recurrence reflects both primary treatment failure and natural disease aggression. The majority of women with breast cancer do not develop symptomatic regional recurrence. Formal axillary clearance at the time of primary surgery reduces the

axillary recurrence rate to less than 1%. Patients who develop axillary recurrence should have axillary clearance if this is technically feasible. Radiotherapy should be considered if the lesion is unresectable.

METASTATIC BREAST CANCER

In metastatic breast cancer the metastases should preferably be proven by biopsy in patients with solitary lesions or those in whom there is a long interval between primary treatment and recurrence.

When metastases are proven all patients should be considered for eligibility into approved clinical trials.

Radiation therapy should be considered for patients with skeletal metastases and/or impending fractures, those with cerebral metastases, potential spinal cord compression or other localised deposits. Surgical treatment should be considered for recurrent chest wall disease and for solitary metastatic lesions. Orthopaedic surgeons have a crucial role in the management of metastatic bone disease and should be consulted with a view to preventing and treating pathological fractures.⁵⁷ Orthopaedic referral is always indicated when plain radiographs show genuine erosion of weight-bearing bone. In steroid hormone receptor-positive cases, endocrine therapy is recommended and can be expected to bring about a favourable response in approximately 75% of cases if both ER and PgR are positive. Multiple sequential trials of hormonal therapy are appropriate for these patients.

If the disease progresses or if the patient is ER and PgR-negative and is a candidate for chemotherapy based on general performance status and ability to tolerate potential side-effects, a trial of chemotherapy, preferably in a prospective study should be considered. A variety of newer agents including the taxanes and the evolution of high-dose chemotherapy for metastatic disease require further evaluation.

Following the symptomatic presentation of distant metastases, average life expectancy is around 2 years but virtually all patients will ultimately die from breast cancer. The aim of treatment is to palliate symptoms and to maintain the best possible quality of life. Systemic treatments (endocrine or cytotoxic) give some prolongation of life in many patients

The specialist breast surgeon should help in the

management of women with advanced disease. The surgeon should have a good understanding of the natural history of breast cancer and should take a joint role with the other oncologists when assessing patients with recurrent disease.

A variety of treatments may be appropriate depending on the site of metastases, the likely benefit versus toxicity and the preferences of the patient. These include systemic anti-cancer therapies, palliative measures such as radiotherapy for bone metastases, and bone stabilisation. A patient with recurrent breast cancer should remain under the care of the Breast Unit. Treatment must be according to protocols agreed within the Unit.

As the disease progresses the focus of care shifts to a more predominant role for the non-surgical oncologists within the Breast Unit. A patient with metastatic breast cancer requires considerable supportive care including relief of nausea and pain and acknowledgement of her psychological, social and spiritual well-being.

The involvement of the palliative care team in the hospital and the community should be sought.

Clinic attendance to assess progress should be at the Breast Unit in order to ensure continuity of care by one team and to minimise travel problems. This should be supported by a clinical nurse specialist.

PALLIATIVE AND TERMINAL CARE

Centres offering breast cancer treatment should ensure that there are adequate terminal care facilities to support the primary care team.

Palliative care services should be involved at an early stage rather than at a late stage in the patient's care. The expertise of palliative care specialists is at present sought too late in the disease process.

Early involvement of these specialists ensures huge gains in the quality of life of women with breast cancer.

Training and Continuing Education

SURGICAL TRAINING

All consultant surgeons treating patients with breast cancer should have developed a special expertise in the treatment of breast diseases and all surgeons who treat patients with breast disease will be expected to have specific training during their formal surgical training programme. The level of training required for a consultant surgeon with a special interest in breast disease depends to some extent on whether the consultant will practice in a Unit in which some 50% of the surgeon's time is devoted to this disease or in a Unit where the consultant will practice almost exclusively in breast diseases. The training requirements for each may differ somewhat.

For a general surgeon expecting to work as a consultant in a hospital in which some 50% of the consultant's time is involved in breast diseases, the following training would be appropriate:-

- (a) one year in higher training working 50% of the time for a consultant with a special interest in breast diseases in a Breast Unit.
- (b) an additional six months full-time in a Reference Breast Unit.
- (c) one month in a Medical Oncology service and one month in a Radiotherapy Unit.
- (d) one month in a Palliative Care Unit.

For a surgeon expecting to work as a consultant practising almost exclusively in breast diseases, the following training is considered appropriate:-

- (a) one year of training spending 50% of time with a consultant with a special interest in breast disease in a Breast Unit.
- (b) one year of training in a Reference Breast Unit.
- (c) a flexible year of research related to breast disease.
- (d) at least one month each in a Medical Oncology and Radiotherapy Unit.
- (e) at least one month in a Palliative Care Unit.

Breast Units are encouraged to support clinical research and to participate in multicentre studies aimed at improving treatments for breast cancer. There is evidence to suggest that patients treated in centres actively involved in research have improved outcomes.⁵⁸

Personnel must be given sufficient encouragement and time to update knowledge and skills.

Continuing postgraduate education in breast disease may be measured on a points system. Annual study days for surgeons in breast disease may be part of future continuing education.

AN ESTIMATE OF THE SURGICAL WORKLOAD IN A BREAST UNIT

It is suggested that there should be a Breast Unit for a catchment population of 300,000. Up to 40 new symptomatic breast referrals may be seen each week. A minimum of 100 new primary breast cancer patients will be treated in a Unit. Not all the patients will require surgery, due to age, or advanced stage, but at least two cases per week may require breast cancer surgery. Some cases will require lengthier procedures, e.g. for extensive local disease or reconstruction.

Locoregional recurrence, mammographic lesions for diagnostic biopsy and symptomatic benign breast conditions may require surgery. These sessions should be carried out by a specialist at consultant level or by advanced trainees under specialist guidance.

STANDARDS AND AUDIT

Breast Units should be required to provide data on the number of patients treated and type of treatment received. Units should also be able to report the long-term outcome measures in treating women with breast cancer. This includes data on local and regional recurrence, long-term morbidity of the primary treatment such as lymphoedema, uncontrolled local recurrence, distant metastases and death.

There should be a nominated surgeon who is ultimately responsible for the accuracy of the data collected. Each Unit should be able to provide results of its audit on at least an annual basis.

The physical structure, staffing needs, equipment facilities and the organisation and training requirements for a Breast Unit are outlined and discussed in detail in a report on the Development of Services for Symptomatic Breast Disease prepared by a Sub-Group of the National Cancer Forum.⁶¹

References

1. Farrow DC, Hunt WC., Samte JM., Geographic Variation in the Treatment of Localised Breast Cancer. *N Engl J Med* (1992); 326 (17): 1097-1101.
2. Austoker J, Mansel R. (1999) Guidelines for Referral of Patients with Breast Problems, 2nd Edition. NHS Screening Programme and Cancer Research Campaign.
3. Provision of breast Services in the UK - The Advantage of Specialist Breast Units. Report of a Working Party of the British Breast Group, September 1994.
4. Dawson C., Lancashire MJR., Reece-Smith H., et al. Breast Disease and the General Surgeon 1: Referral of Patient with Breast Problems. *Ann R Coll Surg Eng* 1993; 75: 7-86
5. Austoker J, Mansel RE., Baum M., et al. Guidelines for Referral of Patients with Breast Problems. NHSBSP Publications. 1995.
6. Gollidge J., Wiggins J.E., Callam M.J. Effect of Surgical Subspecialisation on Breast Cancer Outcome. *Br J Surg* 2000; 1420-5.
7. Quality Assurance Guidelines for Surgeons in breast Disease. NHSBSP Publications 1992. No. 20 1995; 21 (Suppl. A).
8. NHSBSP in association with the Royal College of Nursing. Draft Guidelines for Nurses in Breast Cancer Screening. NHSBSP Publications, 1993, No. 29.
9. NHSBSP Radiographers Quality Assurance Co-ordination Committee. Quality Assurance Guidelines for Radiographers NHSBSP Publication. 1994.
10. Quality Assurance Guidelines for Medical Physics Services in Mammography in the NHSBSP. NHSBSP Publication, 1995.
11. Commissioning and Routine Testing of Mammography X-ray Systems. 1P5F59, NHSBSP Publication, 1994.
12. Radiographic Quality Control Manual for Mammography. NHSBSP Publications 1993, No. 21.
13. Quality Assurance Guidelines for Radiologists. NHSBSP Publications, No. 15. Royal College of Radiologist, 1995.
14. The Royal College of Pathologists Working Group. Pathology Reporting in Breast Cancer Screening (2nd Edn). NHSBSP Publications, 1997.
15. Subgroup of the National Co-ordinating Committee for Breast Screening Pathology. Guidelines for Cytology Procedures and Reporting on Breast Cancer Screening Cytology. NHSBSP Publications, 1993. No. 2
16. Pathology Reporting in Breast Cancer Screening. NHSBSP Publications; 1995, No. 3. The Royal College of Pathologists Working Group.
17. Given-Wilson R., Layer G., Warren M., et al False Negative Mammography; Causes and Consequences. *Breast* 1997; 6:361-6.
18. Donegan WL., Evaluation of a Palpable Breast Mass. *N. Engl J Med* 1992; 327: 937-42.
19. Layfield LD., Glasgow GJ., Cramer H. Fine Needle Aspiration in the Management of Breast Mases. *Pathol Annu* 1989; 24: 23-62.
20. Cusick JD., Dotan J., Jaacks RD., Boyle WT. The Role of Tru-Cut Needle Biopsy in The Diagnosis of Carcinoma of the Breast. *Surg Gynaecol Obstet* 1990; 170:407-10.
21. McMahon AJ., Lufty AM., Matthew A. et al . Needle Core Biopsy of the Breast with a Spring Loaded Device. *Br J Surg* 1992 79:1042-45
22. Edeiken S. Mammography and Palpable Breast Cancer. *Cancer* 1988; 61:263-5.
23. McDermott E.W., (1997) Irish Guidelines for Surgeons in the Management of Breast Cancer. *Irish Medical Journal*, 90: 1; 6-10.
24. Joint Council for Clinical Oncology. Reducing Delays in Cancer Treatments: Some Targets. London: Royal College of Physicians and Royal College of Radiologists, 1993.
25. Winchester D.P., Cox J.D. (1998 Standards for Diagnosis and Management of Invasive Breast Cancer. *CA Cancer J. Clin.* 48; 83-107
26. Veronesi U., Luini A., Galimberti V., et al: Conservative Approaches for the Management of Stage I/II Carcinoma of the Breast. *Milan Cancer Institute Trials. World J. Surgery* 1994;18:70-75.
27. Arriagada R., Le MG., Rochard F., et al: Conservative Treatment Versus Mastectomy in Early Breast Cancer: Patterns of Failure with 15 Years of Follo-Up Data. *Institut Gustave-Roussy Breast Cancer Group. J Clin Oncol* (1996); 14:1558-1564.
28. Fisher B., Anderson S., Redmond C.K., et al: Reanalysis and Results after 12 Year of Follow-up in a Randomized Clinical Trial Comparing Total Mastectomy with Lumpectomy with or without Irradiation in the Treatment of Breast Cancer. *N Eng J Med* (1995);333:1456-1461
29. Jacobson J.A., Danforth D.N., Cowan K.H., et al: Ten-Year Results of a Comparison of Conservation with mastectomy in the Treatment of Stage I and II Breast Cancer. *E Engl J Med* (1995);332:907-911.
30. Van Dongen J.A., Bartelink H., Fentiman IS., et al: Randomized Clinical Trial to Assess the Value of Breast-Conserving Therapy in Stage I and II Breast Cancer: EORTC 10801 Trial. *J Natl Cancer Inst* (1992); 11:15-18
31. Blichert-Toft M., Rose C., Andereson J.A., et al: Danish Randomized Trial Comparing Breast Conservation Therapy with Mastectomy: Six Years of Life-Table Analysis. *J Natl Cancer Inst Monogr* (1992); 11:19-25.

32. Brar HS., Sisley JF., Johnson RH. Value of Preoperative Bone and Liver Scans and Alkaline Phosphatase in the Evaluation of Breast Cancer Patients. *Am J Surg* 1993; 165: 221-3.
33. Bishop HM., Blamey RW., Morris AH., et al. Bone Scanning: Its Lack of Value in the Follow Up Of Patients with Breast Cancer. *Br J Surg* 1979; 66: 7524.
34. NIH Consensus. Treatment of Early-Stage Breast Cancer. *JAMA* 1991; 265: 391-5.
35. Falch CM. Singletary SE., Bland KI. Clinical Decision Making in Early Breast Cancer. *Ann Surg* 1993; 217: 207-25.
36. Donegan WL. Prognostic Factor: Stage and Receptor Status in Breast Cancer. *Cancer* 1992; 72: 1755-64.
37. Fentiman IS., Mansel RE. The Axilla; Not a No Go Zone. *Lancet* 1991; 337:221-3.
38. Davies GC., Millis RR., Hayward JL. Assessment of Axillary Lymph Node Status. *Ann Surg* 1982; 196: 642-4.
39. Veronesi U., Rilke F., Luini A., et al. Distribution of Axillary Node Metastases by Level of Invasion: An Analysis of 539 Cases. *Cancer* 1987; 59: 682-7.
40. Danforth DN., Findlay PA., McDonald HD., et al. Complete Axillary Lymph Node Dissection for Stage 1-11 Carcinoma of the Breast. *J Clin Oncol* 1986; 4: 655-62.
41. Kinne DW. Controversies in Primary Breast Cancer Management. *Am J Surg* 1993; 166: 502-8
42. Rosen PP., Leslet MT., Kinne DW., et al. Discontinuous or 'Skip' metastases in Breast Carcinoma. Analysis of 1228 Axillary Dissections. *Ann Surg* 1983; 197: 276-83.
43. Reynolds JV., McDermott E.W.M., Mercer P.M., Murphy D., Cross S., O'Higgins N.J. Audit of Complete Axillary Dissection in Early Breast Cancer. *Eur J Cancer* 1994;30A.2:148-149.
44. Cabanes PA., Salmon RJ., Vilcoq JR., et al. Value of Axillary Dissection in Addition to Lumpectomy and Radiotherapy in Early Breast Cancer. *Lancet* 1992; 339:1245-48.
45. Krag D., Waver D., Ashikag T., et al: The Sentinel Node in Breast Cancer – A Multicenter Validation Study. *N Eng J Med* (1998);339:941-6
46. Frykberg ER., Bland KI. Overview of the Biology and Management of Ductal Carcinoma In-Situ of the Breast. *Cancer* 1994; 74:350-61.
47. Silverstein MJ., Cohan BF., Gierson Ed., Furmanski M., Gamagami P., Coburn W.J., et al. Ductal Carcinoma In Situ. 227 Cases Without Microinvasion. *Eur J Cancer* . 1992; 28:630-4
48. Lenington W.J. Jensen R.A., Dalton L.W. Page DL. Ductal Carcinoma In Situ of the Breast. Heterogeneity of Individual Lesions. *Cancer* 1994; 73: 118-24.
49. Silverstein J.J., Poller D.N. Waisman J.R., et al. Prognostic Classification of Ductal Carcinoma-In-Situ. *Lancet* 1995; 345:1154-7.
50. Fisher B., Costantino J., Redmond C., et al. (1993) Lumpectomy Compared with Lumpectomy and Radiation Therapy for the Treatment of Intraductal Breast Cancer. *N. Eng. J. Med.* 328; 1581-1586.
51. Julien J-P, Bijker N., Fentiman I.S., Peterse J.L., Delledonne V., Ronanet P., Avril A., Sylvester R., Migurlet F., Bartelink H., van Dongen J.A. (2000) Radiotherapy in Breast Conserving Treatment for Ductal Carcinoma in Situ: First Results of EORTC Randomised Phase III Trial 10853. *Lancet*, 355; 528-533
52. Silverstein J.J., Gierson E.D., Waisman J.R., Senofsky G.M., Coburn W.J., Gamagami P. Axillary Lymph Node Dissection for T1a Breast Carcinoma. Is it Indicated? *Cancer* 1994; 73:664-7.
53. Anderson J.A. Lobular Carcinoma In Situ: A Long Term Follow-Up of 52 Cases. *Acta Pathol Microbiol Scand* 1974; 82:1298-303.
54. Goldhirsch A., Glick J.H., Gelber R.D., Senn H-J (1998). Meeting Highlights: International Consensus Panel on the Treatment of Primary Breast Cancer. *J. Natl. Cancer Institut.* 90: 21;1601-08.
55. Early Breast Cancer Trialist Collaborative Group. Polychemotherapy for Early Breast Cancer: An Overview of the Randomised Trials (1998). *The Lancet* 352ii; 930-942.
56. Winchester D.P., Cox J.D. (1998) Standards for Diagnosis and Management of Invasive Breast Cancer. *CA Cancer J. Clin.* 48:83-107.
57. The Guidelines for the Management of Metastatic Bone Disease in Breast Cancer in the United Kingdom. British Association of Surgical Oncology (1999). *European Journal of Surgical Oncology* 25, 1; 4-23
58. Stiller CA. Survival in Patients with Breast Cancer: Those in Clinical Trials Do Better. *Br Med J* (1989); 299: 105-9.
59. BASO Breast Surgeons Group. The Training of a Surgeon with an Interest in Breast Disease. *Eur J Surg Oncol* 1996; 22 (Suppl.A): 24.
60. Blichert-Toft M., Smola M.G., Cataliotti L., O'Higgins N. on behalf of the European Society of Surgical Oncology. Principles and Guidelines for Surgeons in the Management of Symptomatic Breast Cancer. *Eur J Surg Oncol* (1997); 23:101-9.
61. O'Higgins N., O'Keefe B., O'Doherty A. Development of Services for Symptomatic Breast Disease. Report to the National Cancer Forum. The Department of Health and Children (2000).





Royal College of Surgeons in Ireland

123 St. Stephen's Green, Dublin 2, Ireland

Tel: 353-1 402 2100. Fax: 353-1 402 2460. Web: www.resi.ie