BREAST CANCER
CLINICAL GUIDELINES

Date: August 2010
Review Date: April 2011

Breast NSSG on behalf of NECN

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INTRODUCTION

Terms of Reference

This document provides regional guidelines for the management of breast cancer and is designed to complement existing national guidelines e.g. National Institute for Health and Clinical Excellence (NICE) and British Association of Surgical Oncologists (BASO). This guideline does not override the individual responsibility of healthcare professionals in making decisions appropriate to the circumstances of the individual patient. It is not anticipated that the guidelines will cover all clinical situations in all patients, but where unusual circumstances exist, it is expected that such treatments would be discussed in the appropriate MDT.

These guidelines takes into account NICE clinical guidelines, CG80 and 81 (NICE February 2009), and have been reviewed and revised, following TSSG discussion, in August 2010.

The guidelines will be reviewed on an annual basis. Where new treatments are introduced between revisions they will be added as an addendum to the current guideline.

Facts and Figures

- More than 40,000 breast cancers are diagnosed each year in the UK (1)
- Breast cancer causes around 13,000 deaths per annum the UK (1)
- One woman in 9 will develop breast cancer at some time during her lifetime.
- Eight of ten breast cancers occur after the menopause.
- Screening may reduce the chance of dying from breast cancer. It provides women with more choices in the planning of their surgical treatment.
- Nine out of ten breast lumps are not cancer.
- The number of deaths from breast cancer in England peaked in the late 1980’s and since then has been falling faster than in any other country (2)
- Between five and ten per cent of women with breast cancer have an inherited predisposition.

Public Health and Prevention

Environmental factors including obesity (BMI>32), moderate amounts of alcohol, nulliparity, and hormone replacement therapy have been associated with an increased risk of developing breast cancer. Caffeine, dairy products and smoking are not known to cause breast cancer. In 88,000 women in the Nurses’ Health Study, there was an inverse association between breast cancer risk and the intake of low-fat dairy products. A healthy lifestyle involving regular physical activity, avoidance of high calorie diets and promotion of breastfeeding can lead to prevention of some cases of breast cancer.
SCREENING

General Population Screening

The National Breast Screening programme is well established. The aim of the screening programme is to produce a 30% reduction in mortality from breast cancer. The screening programme has an independent national quality assurance programme, run regionally by the Quality Assurance Reference Centre (QARC).

- All women aged 50 to 70 are currently invited for three yearly mammographic screening, although this is scheduled to expand to the age group 47 to 73 over the next few years.
- Women over 70 are informed that they may request mammography although they are not routinely invited in the national screening programme.
- The chance of finding a cancer by mammography screening is 1 in 200 as outlined below:

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>All clear</td>
<td>186</td>
</tr>
<tr>
<td>Recall for assessment</td>
<td>14</td>
</tr>
<tr>
<td>Needle biopsy</td>
<td>5</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
</tr>
</tbody>
</table>

Screening recommendations for women previously treated with radiotherapy for Hodgkin’s Disease

*DofH Expert Advisory Group recommendations for screening women treated for Hodgkins disease < 35 years and 8 years post treatment which included XRT to any breast tissue

- <25 years No imaging
- 25-29 years Annual MRI
- 30-50 years If fatty breasts annual mammography; if dense breasts annual mammography +/- or MRI
- >50 years NHS Breast Screening – 3 yrly mammography
Management of Patients with a Family History indicating increased risk of Breast Cancer

NICE guidance on familial breast cancer stratifies women into three groups: near population risk, raised risk and high risk.

<table>
<thead>
<tr>
<th>Group</th>
<th>Near population risk</th>
<th>Raised risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>10-year risk of less than 3% for women aged 40–49 years and a lifetime risk of less than 17%</td>
<td>10-year risk of 3–8% for women aged 40–49 years or a lifetime risk of 17% or greater but less than 30%</td>
<td>10-year risk of greater than 8% for women aged 40–49 years or a lifetime risk of 30% or greater</td>
</tr>
</tbody>
</table>

Management

In primary care – Reassurance, advice on avoiding risk factors.

In secondary care – The Breast screening unit.

In tertiary care – Specialist geneticist referral.

Referral pathways

1. **Northern half of the network (old Northern Cancer Network)**

In the Northern half of the network, both Primary Care and Secondary Care may refer directly to the Northern Genetics Service.

Women who meet the following criteria should be offered referral to secondary care (cancer screening unit):

- one first-degree female relative diagnosed with breast cancer at younger than age 40 years, or
- one first-degree male relative diagnosed with breast cancer at any age, or
- one first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years

or

- two first-degree relatives, or one first-degree and one second-degree relative, diagnosed with breast cancer at any age, or
- one first-degree or second-degree relative diagnosed with breast cancer at any age and one first-degree or second-degree relative diagnosed with ovarian cancer at any age (one of these should be a first-degree relative)

or

- three first-degree or second-degree relatives diagnosed with breast cancer at any age.

Women who meet the following referral criteria should be offered a referral to tertiary care (Northern Genetics Service):

- At least the following female breast cancers only in the family:
  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative), **or**
- three first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative), or
- four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative).

or

- Families containing one relative with ovarian cancer at any age and, on the same side of the family:
  - one first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, or
  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, or
  - another ovarian cancer at any age.

or

- Families containing bilateral cancer (each breast cancer has the same count value as one relative):
  - one first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years, or
  - one first-degree or second-degree relative diagnosed with bilateral breast cancer and one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years.

or

- Families containing male breast cancer at any age and on the same side of the family, at least:
  - one first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, or
  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

or

- A formal risk assessment has given risk estimates of:
  - a 20% or greater chance of a BRCA1, BRCA2 or TP53 mutation being harboured in the family, or
  - a greater than 8% chance of developing breast cancer age 40–49 years, or
  - a 30% or greater lifetime risk of developing breast cancer.

Clinicians should seek further advice from a specialist genetics service for families containing any of the following, in addition to breast cancers:

- Jewish ancestry
- sarcoma in a relative younger than age 45 years
- glioma or childhood adrenal cortical carcinomas
- complicated patterns of multiple cancers at a young age
- very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family).
2. Southern half of the network (old Cancer Care Alliance Network)
In the Southern half of the network, family history triage is undertaken by the Macmillan Cancer Family History Service at James Cook University Hospital, Middlesbrough. Primary Care and Secondary Care may refer directly to this service using the following referral guideline:

Refer women with any of the following:

- one first degree relative diagnosed with breast cancer below 40 years of age.
- two or more relatives diagnosed with breast cancer at any age.
- one first degree relative with ovarian cancer and one or more with breast or colorectal cancer.
- a paternal family history of breast cancer.
- a male first degree relative with breast cancer
- a family history of bilateral breast cancer
- a family history of breast cancer in addition to ovarian adenocarcinoma, sarcoma below 45, glioma or childhood adrenal carcinoma
- a family history of breast cancer with Jewish ancestry

Those patients who have been treated for a personal history of breast cancer should have annual mammographic follow up for five years. Mammographic surveillance is inappropriate in women with advanced incurable disease. (See Follow-Up Guidelines)

Management of Patients with a Family History Indicating Increased Risk of Breast Cancer: North of England Cancer Network Implementation of NICE guidelines

1. Mammographic screening should not start below the age of 40.

Exceptions:

- Women under 35 who were previously told that screening would start at 35 for example those with lymphoma treated with mantle radiotherapy (*see below). Some may prefer to start screening when they turn 40.
- Those who have had breast cancer.
- BRCA1/BRCA2 or P53 gene mutation carriers.

The latest NICE guidance (CG41 2006) suggest certain people may benefit from MRI surveillance. Breast MRI for FH patients will be arranged via the genetics service.

From 30–39 years:

- to women at a 10-year risk of greater than 8%.

From 40–49 years:

- to women at a 10-year risk of greater than 20%, or
- to women at a 10-year risk of greater than 12% where mammography has shown a dense breast pattern.

A 10-year risk of 8% aged 30–39 and a 10-year risk of 12% aged 40–49 years would be fulfilled by women with the following family histories:

- 2 close relatives diagnosed with an average age under 30 years*
- 3 close relatives diagnosed with an average age under 40 years*
- 4 close relatives diagnosed with an average age under 50 years.*

*All relatives must be on the same side of the family and one must be a mother or sister of the woman.

A genetic test would usually be required to determine a 10-year risk of 20% or greater in women aged 40–49 years.

The following interpretation of the NICE guidance is envisaged:

1. Standard (population) risk families should be reassured at Primary Care level. Occasionally Primary Care may seek advice regarding these families from the Northern Genetics Service or Macmillan Cancer Family History Service. Further clarification and reassurance may be provided by these services to the patient/Primary Care Team. In exceptional circumstances such patients may be seen in by the Northern Genetics Service or Macmillan Cancer Family History Service (for example high anxiety not resolved by Primary Care reassurance).

2. In the Northern half of the network, women assessed to be at raised or high risk according to the NICE guidelines should be referred to the Northern Genetics Service with a letter and a completed information collection sheet. In the Southern half of the network, women who fulfil the referral criteria listed above should be referred to the Macmillan Cancer Family History Service, who will send an information collection sheet to the patient. For most patients the information provided is verified by the service undertaking triage, the outcome of which is generally:

   a. Reassurance. This is the appropriate course of action for those at standard risk and includes those with a non-significant family history and also those that are at moderate risk but are currently too young for annual mammography.
   
   b. Referral to screening services. This is appropriate for those at moderate risk.
   
   c. Clinical Genetics appointment for those thought to be at high risk.

3. The NICE guidelines recommend a multi-disciplinary clinic for those at high risk of inherited predisposition to breast cancer. This will be a “virtual clinic” in that all specialists may not necessarily be at one clinic. Those at high risk will be seen by Genetics and will undergo radiological assessment with mammography once they are an appropriate age. There may also be surgical assessment
depending on how service provision is organised in any particular area. For patients considering prophylactic mastectomy there should be genetic assessment, surgical assessment and plastic surgical assessment. The NICE guidelines stipulate that Psychology services should also be available. This has a cost implication and is not currently available in the NECN.

4. Follow up for increased and high risk women from the age of 50 should be in the NHS breast screening programme.

Self-awareness/self-examination should be recommended to all women but particularly moderate and high risk women. If a woman finds a lump it is important:

   a. that she has rapid access to assessment. Some women are either too anxious or are phobic about self-examination in which case it is appropriate for Primary Care to provide an annual examination. There may be some circumstances where this happens in secondary care.

   b. BRCA1 and BRCA2 gene carriers, P53 gene carriers and other rare predisposition syndrome gene carriers should be followed up annually in Genetics by appointment or review letter whichever the patient prefers.

   c. Women opting for prophylactic mastectomy should be registered on a regional database.
Pathway for patients with suspected Breast Cancer

Triple assessment - One Stop - Breast Clinic

Clinical Examination
Imaging +/- Biopsies

Is cancer confirmed or still suspected?
Yes
No

Results discussed with patient

Discharge or follow up as per protocol

Holistic and rehabilitation assessment. Proposed treatment plan/further treatment outlined.

Alert Teenage and Young Adult (TYA) MDT if patient 16 to 24 years

Max Time in days

2ww referral received in secondary care

2ww referral received in secondary care

Relevant verbal and written information provided

Provide ongoing psychological support & assessment

Allocate Breast Care Nurse/ Key Worker

Inform patient’s GP of Serious Diagnosis

See TYA pathway

See Breast Rehabilitation pathway

Decision to treat date

First Treatment

Earliest Clinically Appropriate Date (ECAD) for commencement of subsequent treatment

Initial MDT discussion of investigation results, treatment & rehabilitation plan plus consideration for clinical trials

Histology/scan results available

Further investigations carried out

Further diagnostics?

No

Agree proposed treatment plan, follow up or discharge with patient

Yes

Primary Endocrine Therapy

Primary Chemotherapy

Surgery +/- reconstruction

Supportive Palliative Care

Patient assessed

MDT discussion to review histology & staging results also consider for clinical trials

Further investigations required?

Yes

Further investigations as required

Yes

Is adjuvant treatment required?

No

Appropriate After Care

Chemotherapy

Endocrine Therapy

Radiotherapy

Biological Agent
CRITERIA FOR URGENT BREAST CLINIC REFERRAL (UNDER 2 WEEK RULE)

Symptoms and warning signs that are suspicious and warrant urgent investigation:

- **Lump**
  - any new discrete lump
  - new lump in pre-existing nodularity
  - asymmetrical nodularity that persists at review after menstruation

- **Pain**
  - if associated with a lump
  - unilateral persistent pain in post-menopausal women

- **Other potential signs of cancer**
  - ulceration
  - skin nodule
  - skin distortion
  - breast abscess or inflammation not settling after one course of antibiotics
  - nipple discharge especially if age >50, or bloodstained
  - nipple eczema unresponsive to topical steroids
  - recent (<3month) nipple inversion

- **Physical Examination**
  - An appropriate examination should be performed prior to referral
  - The aspiration of a lump in a patient with a history of multiple cysts should only be performed by a General Practitioner who has the necessary skills. Aspiration of solid lumps should not be attempted as it may affect imaging and delay diagnosis or even lead to mis-diagnosis.

**Priority for Referral**

Following the Government's Health Service Circular (HSC 242/98), all patients with symptoms deemed to be suspicious by their GP will, if the letter is faxed or e-mailed, be seen within 14 days of the decision for referral (3). The guidance for the GPs determining which symptoms are suspicious is outlined in the booklet by Austoker et al (4). Such referrals must be considered as urgent and offered the next available appointment by the local breast clinic. The guidance for GPs should be directed by the Hospital and must be clear and easy to follow; an example of the recommended guidance is listed in Appendix 1.

**Two weeks for all breast clinic referrals**

In line with new targets all referrals to symptomatic breast clinics will be seen within 2 weeks from the end of 2009.
## Referral Pathways

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<tr>
<th>PCT Referral Pathways</th>
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<th>Designated MDT</th>
<th>Named Lead/ Contact</th>
<th>Screening Centres</th>
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</thead>
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<tr>
<td>Redcar &amp; Cleveland Middlesbrough</td>
<td>South Tees Hospitals NHS FT</td>
<td>James Cook University Hospital</td>
<td>Mr R Bryan 01642 850850</td>
<td></td>
</tr>
<tr>
<td>Stockton on Tees and Hartlepool</td>
<td>North Tees &amp; Hartlepool NHS FT</td>
<td>University Hospital of North Tees</td>
<td>Mr VJ Kurup 01642 617617</td>
<td>Yes</td>
</tr>
<tr>
<td>Newcastle</td>
<td>Newcastle Upon Tyne Hospitals NHS FT</td>
<td>RVI Queen Victoria Road Newcastle upon Tyne NE1 4LP</td>
<td>Mr R Bliss 0191 2336161</td>
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<tr>
<td>Northumbria</td>
<td>Northumbria Health Care NHS FT</td>
<td>North Tyneside General Hospital Wansbeck General Hospital</td>
<td>Mr M Carr 0844 8118111</td>
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<tr>
<td>Gateshead</td>
<td>Gateshead Health NHS FT</td>
<td>Queen Elizabeth Hospital</td>
<td>Mr K Clark 0191 482000</td>
<td>Yes</td>
</tr>
<tr>
<td>Sunderland Easington</td>
<td>City Hospitals Sunderland NHS Foundation Trust</td>
<td>Sunderland Royal Hospital</td>
<td>Mr O Iwuchukwu 0191 5656256</td>
<td></td>
</tr>
<tr>
<td>South Tyneside</td>
<td>South Tyneside NHS FT</td>
<td>South Tyneside District Hospital</td>
<td>Ms B Weber 0191 4041000</td>
<td></td>
</tr>
<tr>
<td>North Durham -</td>
<td>County Durham and Darlington NHS FT</td>
<td>University Hospital of North Durham</td>
<td>Mr K Callanan 0191 3332333</td>
<td></td>
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<tr>
<td>South Durham (Darlington and Bishop Auckland)</td>
<td>County Durham and Darlington NHS FT</td>
<td>Darlington Memorial Hospital</td>
<td>Mr R Brookstein 01325 380100</td>
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<tr>
<td>NHS Cumbria</td>
<td>North Cumbria University Hospital NHS Trust</td>
<td>Cumberland Infirmary</td>
<td>Mr M Williams 01228 523444</td>
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<tr>
<td>Hambleton and Richmond (Screening Patients)</td>
<td>South Tees Foundation Trust</td>
<td>Friarage</td>
<td>Mr R Bryan</td>
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HOSPITAL INVESTIGATION AND ASSESSMENT OF BREAST CANCER \(^{(5,6)}\)

Triple assessment increases the accuracy and reduces overall cost of diagnosis when compared with selective use of the component tests. The three tests when used in experienced hands can result in a positive predictive value of 99\% \(^{(7)}\), thus minimising the need for open biopsy \(^{(8)}\). This reduces surgical time and minimises anxiety induced by delay. At least 90\% of women with breast cancer should be diagnosed pre-operatively.

Triple assessment comprising clinical examination, imaging (mammography /ultrasound) and biopsy, is recommended for women with suspected breast cancer at a single visit.

- Biopsy by needle core biopsy and/or FNA. Needle core biopsy is the investigation of choice where malignancy is suspected.
- Local anaesthetic may be appropriate for some patients.
- All facilities and staff needed to provide this service should be in close proximity to the diagnostic clinic.
- The results of triple assessment should be given to the patient within five working days.

The following investigations are recommended for different breast symptoms once clinical examination has taken place:

**Breast Lump:** Triple assessment:

**Breast Pain:** Unilateral persistent mastalgia without palpable abnormality: clinical examination only.

- Localised areas of painful nodularity: mammography (if > 35 years old) and/or ultrasound

- All focal lesions: FNA

**Nipple discharge:** clinical examination and imaging as indicated.

**Nipple retraction:** clinical examination and imaging as indicated.

**Change in skin contour:** triple assessment

When a diagnosis of cancer is made, the only other routine investigations recommended prior to surgery are a chest x-ray, full blood count and biochemistry (bone & liver).

See further information on perioperative staging later.
COMMUNICATING THE DIAGNOSIS

Informing the Patient

- The patient should be informed of the diagnosis by a Consultant or an appropriately experienced member of the MDT\(^9\).
- Facilities should be available for the patient to be informed of the diagnosis during a private uninterrupted consultation.
- A trained breast CNS should be available during the consultation and should be available to provide additional counselling if required\(^{10}\).
- Opportunity to contact the breast CNS for further counselling (confidential phone numbers, address and contact cards etc) should be offered and follow up arrangements fully understood.
- Patients should be given time, information and support to make a fully informed decisions about their treatment. This should include discussion with the surgeon, in liaison with the breast CNS, of suitable treatment options. The offered options and the decisions for therapy as indicated by the discussions held at the multi-disciplinary team (MDT) should be recorded in the patient record\(^{11,12}\).
- Details of available therapy should not necessarily be discussed at the diagnostic visit, especially if in the “one-stop” setting. Where necessary, arrangements should be made for a subsequent “treatment planning” visit.
- Patients should be given the opportunity for a close friend or relative to be present during the consultation and the subsequent journey home.
- Written information concerning breast cancer treatment should be available and offered to all patients\(^{13}\).
- A prognosis should not be offered before adequate staging information is available.

Informing the Primary Care Team

- The GP should be informed of the diagnosis on the same day as the patient or by noon the day following, preferably by fax, using a serious diagnosis proforma.
- The general practitioner should be made aware of the information which has been given to the patient and, if possible, an outline of the planned treatment.
- If the diagnosis is made as in inpatient, the Primary Care Team should be informed prior to discharge from hospital
- Hospital nursing staff should ensure that relevant community nurses are also informed
- Major alterations to the management plan should be communicated to the General Practitioner by telephone, fax or letter within one working day. Similarly, if alterations are made by the general practitioner, these should be communicated to the hospital within two working days. A patient held record, where available, would be a supplementary means of such communication.
CANCER WAITING TIMES TARGETS 2009/10

The cancer standards stipulate a maximum of 31 days from decision to treat to first definitive treatment, and 62 days from 2 week referral to definitive treatment. From December 2009 all referrals to symptomatic breast clinics will be subject to the 2 week rule.

As announced in the Department of Health Cancer Reform Strategy (2007), the 31 day standard has been extended to cover all cancer treatments. This applies to all surgery and drug treatments from December 2008, and to radiotherapy treatments from December 2010.

⇒ Decision to Treat
The decision to treat date is the date of the consultation in which the patient and clinician agree the treatment plan for first treatment. If the first treatment requires an admission (e.g. Surgery) this date is recorded on hospital PAS systems, as the "Date of decision to admit" (used for calculation of waiting list statistics).

⇒ First Definitive Treatment
The first definitive treatment is normally the first intervention which is intended to remove or shrink the tumour. Where there is no definitive anti cancer treatment almost all patients will be offered a palliative intervention (e.g. stenting) or palliative care (e.g. Symptom control) which should be recorded for these purposes.

⇒ Subsequent Treatment
The 31 day standard for subsequent treatment begins at either a second “decision to treat date” or an “earliest clinically appropriate date” (ECAD) for the patient to undergo the next event in their care pathway.

⇒ Breach Reasons
Detailed reports on breaches are recorded and should include how long the patient waited, reason for the breach in the target and action put in place to prevent further breaches.
IMAGING GUIDELINES

Imaging in all patients should be carried out to the standards set by the National Breast Screening Programme.

Planning should be in progress to move to digital mammography.

Breast Screening Population

1. Screening

All screening mammograms are read by two trained film readers, one of whom must be a radiologist or consultant practitioner.

Cases judged to be technically adequate, with no suspicious clinical findings and showing no signs of malignancy are entered as “routine recall”. Technically inadequate films can be sent for repeat by one reader.

All other cases are submitted for consensus or arbitration before the final outcome is decided.

Individual judgement is needed in every case but in general, the guidelines for recall for assessment are:

1.1 Well defined masses, either solitary or multiple. These are not recalled for assessment except where a solitary lesion develops between screens.

1.2 The following abnormalities are to be recalled for assessment:
   - Ill defined or stellate masses.
   - Areas of stromal deformity not accounted for by previous surgery.
   - Indeterminate or suspicious clustered micro-calcification.
   - Asymmetric densities.

1.3 Clinical recall. Women who declare a new breast lump, deformity/nipple retraction or blood stained discharge are to be recalled for assessment. An exception is made for those women who have recently been investigated for the same complaint and whose screening mammograms are normal.

2. Assessment practice

Assessment should follow NHSBS guideline 49, 2010.

2.1 Clinical examination of the breast by the assessing Radiologist is mandatory if a mammographic or ultrasonic abnormality is confirmed. In this context the term ‘Radiologist’ includes the Consultant Radiographer.

2.2 Mammographic imaging. Further views, including repeat oblique or cranio-caudal films may be taken as may spot compression and/or
magnification views of the lesion as decided by the assessing Radiologist.

2.3 Ultrasound of the abnormal quadrant as a minimum, preferably of the whole breast.

2.4 Pre-treatment ultrasound evaluation of the axilla should be performed in all patients suspected of having invasive breast cancer. Morphologically abnormal lymph nodes should be sampled by FNA or core biopsy according to locally agreed protocols.

3. **Needle biopsy**

3.1 Cysts may be aspirated to confirm the diagnosis or at the patient’s request.

3.2 Wide Bore Needle (WBN) biopsy is the preferred test for most lesions, whether radiologically benign or malignant and ultrasound guidance should be used whenever possible.

3.3 Fine Needle Aspiration Cytology may be taken in addition or where WBN is technically not possible.

3.4 Specimen radiographs should be taken whenever WBN is performed for assessment of microcalcification. A copy of the radiograph should accompany the specimens to the laboratory.

3.5 Vacuum assisted Core Biopsy is now available in many units and may be used as first line sampling for microcalcification. It may also be used:

   - following a B1/B3/B4 result at 14 gauge core biopsy
   - diagnostic excision of papillary lesions and radial scars / complex sclerosing lesions without atypia that have been diagnosed at core biopsy.

4. **Breast Care Nurse (BCN)**

The BCN should be available to provide support and information to women in the clinic as appropriate to their needs. Women must be introduced to the BCN if they are being referred to a surgeon.

5. **Results**

A result letter is sent to the woman and her GP. Wherever possible this should be written by the assessing Radiologist.

Guidance regarding the agreed management in specific clinical situations is given below:

5.1 The results of all core biopsies should be discussed at an MDT before the result is given to the woman wherever possible.
5.2 Where the imaging features are of benign microcalcification, but no calcification is obtained at WBN and the Pathology result is B1, the preferred outcome is immediate repeat WBN (14G or 11G.)

5.3 The finding of atypical ductal hyperplasia (ADH) on a WBN biopsy is abnormal and requires referral for excision biopsy or VACB.

5.4 The decision to place a woman on early recall (EC) should be confirmed by MDT discussion. EC is not an alternative to full assessment and should only be used in circumstances that make full assessment impossible.

5.5 If an early recall is felt necessary, interval should be 6 months for a mass lesion and 12 months for calcifications.

5.6 The management of B3 lesions should be decided by MDT discussion with the pathologist and decisions made on a case by case basis

6. Surgical Referral

Women should be referred for surgical excision of a lesion in the following circumstances:

6.1 Where the results of triple assessment indicate that malignancy is present or has not been excluded. Specifically this means lesions yielding WBN result of B4 or B5. Lesions yielding lower Pathology scores should also be referred when there is a high degree of Radiological concern (R4 or R5).

6.2 Where the woman wishes to have the lesion excised irrespective of the Radiology/Pathology findings.

6.3 The referral sent to the surgeon should include details of lesion type/size, distance from the nipple and presence/absence of axillary lymphadenopathy.

6.4 Lesions likely to benign at surgical excision can be considered for vacuum-assisted excision and this should be discussed at the MDT.

Clinical policy for symptomatic breast radiology

Imaging.

For patients aged less than 35 years, the first line imaging is by ultrasound. For women aged 35 and over first line imaging test is by two-view mammography. Mammography in men over 35 should be used when there is no clear clinical or ultrasonic evidence of gynaecomastia. Where the patient complains of a focal abnormality or where one is detected on the mammograms further views should be obtained as requested by the radiologist

Where malignancy is suspected:
- Measure lesion size and distance from the nipple-areola complex
- Look for additional tumour foci
- Scan the axilla looking for abnormal nodes following local protocols for biopsy criteria.

Report writing
The report should include a description of the abnormal findings, a measurement of the size of any significant abnormal findings and, in the case of suspected malignancy, the distance from the edge of the lesion to the nipple-areola complex.

There should be a conclusion that includes a 1-5 score for each side and imaging modality.

Additional investigations
Vacuum-assisted core biopsy (VACB). This is a second-line test to be used when the 14G core biopsy has not given a definitive diagnosis and following MDT discussion or discussion between radiologists. (See screening / assessment clinical policy.)

MRI scans
The routine use of MRI is not recommended but should be considered in the following circumstances:

- If there is discrepancy regarding the extent of disease from the clinical examination, mammography and ultrasound assessment for planning treatment.
- If breast density precludes accurate mammographic assessment.
- To assess tumour size if breast conserving surgery is being considered for invasive lobular cancer.
NECN GUIDELINES FOR PATHOLOGY REPORTING

Following the diagnosis of breast cancer a tumour should be staged according to the pT and pN categories of TNM classification (see appendix 1). The breast multidisciplinary team must include a pathologist or pathologists with a special interest and expertise in breast pathology and cytology, with designated time for breast cancer work. The pathology services must be organised according to the NHSBSP guidelines and include the RCPath minimum dataset - link to both sets of guidelines as follows:-

http://www.cancerscreening.nhs.uk/breastscreen/publications/nhsbsp58.html
http://www.cancerscreening.nhs.uk/breastscreen/publications/qa-08.html

Histopathology Standards:

Histopathology procedures and reporting should be as described in the NHSBSP document “Pathology Reporting in Breast Cancer Screening”. The recording of the data for symptomatic patients must be same as that for the screening patients.

Histopathology departments and surgeons must have access to specimen radiography. Specimen radiograph must accompany the specimen.

Histopathology laboratories should work towards nationally defined accreditation standards. It is desirable that Pathologists reporting breast cancer routinely should participate in the EQA National scheme.

It is the responsibility of the operating surgeon to ensure that the specimen is orientated and marked for the pathologist as agreed locally. Ideally nodal levels should be labelled and sent separately. There should be agreement between surgeons and pathologists in each unit on how specimens are oriented and labelled and considering the requirement for a specimen X-ray where appropriate.
SURGICAL TREATMENT OF BREAST CANCER

- Surgical treatment of breast cancer, especially reconstructive surgery, should be carried out by surgeons with a special interest and training in breast disease (see the BASO 1998 guidelines for recommendations for Surgical Training). Breast surgeons must work in Breast Units that provide necessary expertise and facilities for multidisciplinary approach (14).

- In patients where breast conserving surgery is considered unwise and mastectomy is to be carried out, or where a patient requests mastectomy but with minimal cosmetic disruption, an opportunity should be provided before mastectomy for the patient to discuss the possibilities for breast reconstruction with an oncoplastic surgeon if this is oncologically appropriate. If reconstruction is needed and the MDT concerned do not have the relevant expertise the patient will be referred to another MDT within the Network.

- Multidisciplinary case review and planning (MDM) should be the standard for all patients with newly diagnosed breast cancer (15). Patients with recurrent or metastatic disease should be discussed where uncontrolled local disease is present, or at the discretion of MDT members.

- Consultants and other core members of the multidisciplinary team within the breast unit should have contractual time for attendance at multidisciplinary meetings in a planned programmed activity.

- The conclusions of the MDM should be recorded in all the patient records, irrespective of the number of hospitals that the patients attend for the management of their breast cancer. This should be supported by the appropriate clerical requirements. The MDM should be minuted with an attendance record; the minutes should be made available to all core members of the MDM.

- The number of therapeutic procedures should be recorded. 90% of patients having conservation surgery should have three or less therapeutic operations.

- It is the responsibility of the operating surgeon to ensure that the specimen is orientated and marked for the pathologist as agreed locally. Ideally nodal levels should be labelled and sent separately. There should be agreement between surgeons and pathologists in each unit on how specimens are oriented and labelled and considering the requirement for a specimen X-ray where appropriate.

- A diagnostic or therapeutic axillary procedure should be performed in all patients with an invasive cancer unless the MDT has specifically advised against this.

- Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided
needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique. SLNB should only be performed by a team that is validated in the use of the technique, as identified in the New Start training programme.

Management of In situ breast cancer

1) Ductal carcinoma in situ (DCIS)
Up to 20% of screen detected cancers and 1-2% of symptomatic cancers fall into this group. DCIS is a direct precursor of invasive breast cancer. Fine needle aspiration is inadequate for distinguishing DCIS from invasive cancer. A core biopsy is necessary for cases with microcalcifications with mammographic appearance of DCIS. Vacuum assisted devices are also available e.g. mammotome.

The risk of recurrence following surgery is influenced by grade, size, patient’s age and resection margin. These factors form part of the Van Nuy’s prognostic index. The resection margin in the greatest predictor of recurrence.

Surgical management:

- **Multifocal or extensive (>40mm) DCIS**: simple mastectomy. Consider SLNB.

- **Small (<40mm), non-central, unifocal lesions**: taking into consideration the patient body habitus and with regard to the resulting cosmetic appearances, the aim is complete local excision.

- **Margins**: remain a contentious issue and there are no clear guidelines available. The Surgical guidelines for the management of breast cancer (Association of Breast Surgery at BASO 2009) state: “Units should have local guidelines regarding acceptable margin width for DCIS and individual cases should be discussed at the treatment MDT meeting. If, after MDT meeting discussion, the margin of excision is deemed to be inadequate then further surgery to obtain clear margins should be recommended”.

Follow-up specimen mammography is needed to confirm complete excision of all suspicious calcifications, particularly if they are extensive or approach the edge of the surgical specimen.

Adjuvant treatment for DCIS:

- Optimum adjuvant treatment of DCIS is still uncertain. The ultimate goal is to identify lesions that are more likely to recur locally, and thus, might be better treated with further adjuvant therapies. Over treatment of lesions unlikely to recur should be avoided.

Adjuvant Tamoxifen for DCIS:

- The UKCCCR DCIS trial showed no significant benefit from Tamoxifen\(^{16}\). The (US) NSABP B24 suggested a small reduction in the risk of recurrence (9.3% vs 6%, absolute benefit 3.3%) although this was in patients without rigorous control of excision margins. No survival advantage was demonstrated.
The current evidence does not support the use of adjuvant endocrine therapy for DCIS outside a clinical trial. However patients who enter the IBISII trial will be randomised between tamoxifen and arimidex.

**Lobular carcinoma in situ (LCIS)**

This is an uncommon condition, invisible on mammography and often detected coincidentally during histological evaluation of breast tissue. It acts as a marker for increased risk of developing either ductal or lobular breast cancer in the future which is 5-10 times the standard population risk. Invasive cancers may occur either in the ipsilateral or contralateral breast. Invasive cancers are likely to be visible on mammography thus annual mammographic screening for 5 years or until the patient enters the NHS BSP (whichever is later) is recommended.

Recent recommendations point out that pleomorphic LCIS should be treated in the same manner as DCIS and clear margins of excision are required.

**Radiotherapy for non-invasive lesions is discussed in the main Radiotherapy section of this guideline.**
SURGICAL TREATMENT OF INVASIVE BREAST CANCER

Small unifocal invasive cancers with no palpable nodes.

- Surgery may be wide local excision or total mastectomy, according to patients’ preference, and the size and location of the primary tumour. Co-morbidities may restrict the treatment choices available to the patient and must be considered in treatment planning.

- The maximum size of cancers undergoing breast conserving surgery cannot precisely be regulated, however patient habitus, resulting cosmetic appearances and adequacy of resection margins should be taken into account. For the majority of patients a primary cancer greater than 4cm will probably not be best managed by breast conserving surgery. In those patients undergoing breast conserving surgery the margins must be clearly marked, preferably by a method agreed by the surgeon, radiologist and pathologist.

- There are good data from randomised controlled trials supporting the view that surgical margin status is a strong predictor of long term local recurrence rates, although the trend towards smaller resection margins does not appear to confer a higher local recurrence rate, especially if adjuvant therapy is planned.

- Resection margins remain a contentious for invasive breast cancer. The Surgical guidelines for the management of breast cancer (Association of Breast Surgery at BASO 2009) state: “Units should have local guidelines regarding acceptable margin width for DCIS and individual cases should be discussed at the treatment MDT meeting. If, after MDT meeting discussion, the margin of excision is deemed to be inadequate then further surgery to obtain clear margins should be recommended”.

- The indication for diagnostic vs. therapeutic axillary surgery should be discussed in the MDT meeting prior to operation. In rare cases of invasive cancer, there will be a recommendation for no axillary surgery, e.g. in a patient with advanced disease undergoing mastectomy for local control.

- Sentinel Lymph Node Biopsy is the standard of care for staging the axilla. Pre-operative axillary ultrasound gives additional pre-operative axillary staging information.

The following are not suitable for SNB.
  - Proven histologically malignant axillary lymphadenopathy
  - Locally advanced or inflammatory breast cancer
  - Pregnancy

- A negative SLNB should identify those patients without axillary node involvement, thus obviating the need for a more morbid ALND. The risk of arm morbidity, particularly lymphedema, is significantly lower after SLNB than ALND. A recent systemic review, performed by the ASCO expert guidelines
panel, included 69 eligible trials of SLNB in early stage breast cancer, representing 8059 patients\(^{(18)}\). The SLN was identified using radiocolloid, blue dye, or both. Overall, 95 percent had a SLN successfully identified. The false negative rate overall was 7.3 percent.

- Further axillary treatment should be offered to those who:
  - Have macrometastases or micrometastases in a sentinel lymph node
  - Have a preoperative ultrasound guided needle biopsy with histologically proven metastatic cancer.

The preferred technique is axillary lymph node dissection (ALND) because it gives additional staging information. Where further surgery is deemed inappropriate following MDT discussion, radiotherapy to the lymph node drainage areas may be considered.

**Level of dissection** — ALND extent can be defined by either the number of axillary LNs resected or their anatomic location. Axillary LNs are divided into three levels based upon their relationship to the pectoralis minor muscle:

- **Level I** — inferior and lateral to the pectoralis minor muscle
- **Level II** — posterior to the pectoralis minor and below the axillary vein
- **Level III (infraclavicular)** — medial to the pectoralis minor and against the chest wall.

The possibility of breast reconstruction should be discussed. The data in studies are inconclusive as to the perceived benefits from reconstructive surgery following mastectomy or breast conserving surgery\(^{(20)}\).

**Larger tumours or with palpable nodes**

- Mastectomy and axillary node clearance to level 2 or 3 is currently the standard treatment.

- In selected patients sentinel node biopsy is an acceptable alternative to axillary dissection.

- The possibility of immediate or delayed breast reconstruction should be discussed unless this is deemed inappropriate by the MDT, usually on the basis of risk of inadequate excision in the case of immediate reconstruction or risk of recurrence and/or death in the case of delayed reconstruction.

- If considered of doubtful operability, or where downstaging to enable breast conservation is desired, patients may be eligible for pre-operative systemic treatment with either chemo- or hormone therapy. Where possible this should be in a clinical trial.

- The Clinical Trials units at NCCC and JCUH have a portfolio of clinical trials including neoadjuvant treatment of breast cancer. Further information may be
Complications of Surgery:

1. Breast conserving surgery. Patients should be warned that the cosmetic results may not be ideal. The primary aim of therapy is to remove the cancer with a low risk of recurrent disease. Oncoplastic techniques, such as reduction mammoplasty, may allow larger tumours to be removed whilst preserving the breast in suitable ladies. Similarly, central breast tumours may be considered for breast conserving surgery. The axillary incision can lead to tethering of the axillary skin leading to restrictive movement in the shoulder. All patients prior to breast cancer surgery should be seen pre-operatively by the Physiotherapist and instructed in the post operative exercises; this should continue post-operatively. Damage to the intercosto-brachial nerve results in hypoasthesia in the upper inner arm which may not fully recover. All patients should be warned of lymphoedema and facilities should exist for treatment of this condition at Cancer Unit level.

2. Mastectomy. Patients should be warned of the likely cosmetic appearance following this surgery; this should include practical information about the timing and type of prosthesis available. A small number of patients with large breasts or who are obese may require scar revision subsequently.

3. All types of surgery. Axillary seroma formation, wound haematoma and infection are possibilities and should be explained.

4. Lymphoedema: is a swelling of the arm due to poor lymphatic drainage, which can be caused by surgery, radiotherapy, or lymphatic obstruction from tumour. Venous obstruction can also cause a similar clinical picture. Acute lymphoedema should therefore trigger appropriate investigations.

Lymphoedema is common in patients who have had an axillary dissection (2–10%). The combination of axillary irradiation therapy with axillary dissection increases the risk of arm oedema to 13–18%. Axillary recurrence following adequate axillary surgery is so infrequent (0–2%) that routine axillary radiotherapy is not generally indicated.

Lymphoedema can affect quality of life and activities of daily living depending on severity. It can lead to reduced movement due to arm weight, pain, cosmetic disfigurement and reduced wound healing. A difference of more than 2 cm between the affected and normal arms is considered clinically significant.

Prior to axillary surgery patients should be warned of the risk of lymphoedema and given appropriate preventative advice. This includes avoidance of venepuncture on the affected side. Any signs of infection in the “at risk” arm should be treated promptly with antibiotics. Patients should be taught exercises following surgery. Prevention of lymphoedema must be highlighted and reinforced throughout the patient journey and supported with written advice.
Treatment of lymphoedema involves physiotherapy, massage and compression bandaging. Patients should be able to access a local lymphoedema clinic and all units are encouraged to develop links with such a clinic or set up their own service.

**Cosmetic Breast Reconstruction:**

In the presence of both invasive and non-invasive cancer, immediate reconstruction must be discussed in the MDT meeting prior to the procedure.

*Immediate* reconstruction following mastectomy is suitable for patients not likely to require adjuvant radiotherapy:

- Patients with small tumours with likely clear margins and negative nodes who request a mastectomy
- DCIS
- Small but centrally placed lesions
- Prophylactic mastectomy

*Delayed* breast reconstruction is suitable for the following categories of patients:

- Patients who were at high risk of local recurrence but have been disease free for a period of time, generally regarded as 2 to 5 years

*To minimise the risk of loco-regional recurrence* in patients undergoing reconstruction, patients should be advised against reconstruction according to the following criteria:

- High local recurrence risk such as with extensive lymph node involvement
- Extensive skin infiltration
- Disease attached to the chest wall
- Active cancer at any site

**Pre and Peri-operative Staging**

**Minimum**

- Chest x-ray, full blood count and liver biochemistry should be the minimum baseline investigation for proven invasive breast cancer and should performed before surgery in all patients.

**For higher risk Cancers**

Gerber et al. studied the frequency of distant metastases in a series of more than 1000 patients with early breast cancer[21]. Approximately 3% of patients were found to have metastases. The overwhelming majority of patients had one of the following risk factors:

- Primary tumour > 5cm
- 4 or more involved axillary nodes
It is recommended that patients meeting these criteria should have additional staging in the form of a CT scan of chest and abdomen and bone scan.

Less than 1 in 800 patients without a risk factor have metastases and these patients should not be fully staged unless there is clinical suspicion.

Patients undergoing neoadjuvant therapy with either chemotherapy or hormones should be fully staged before treatment if they have a tumour > 5cm in diameter or palpable axillary lymphadenopathy.
RADIOThERAPY FOR BREAST CANCER

Adjuvant Radiotherapy for Invasive Breast Cancer
(For non invasive breast cancer, see below)

Introduction

Ideally should begin within 6 weeks of completion of surgery or chemotherapy dependant on wound healing, shoulder mobility and the timing of chemotherapy. Delays of >8 weeks may be detrimental. A recent meta-analysis of 15,000 patients confirmed that delay in starting radiotherapy was associated with a significant increase in local relapse rate. This increase was seen when radiotherapy was delayed beyond 8 weeks following surgery corresponding to an increase in local recurrence rate from 5.8% to 9.1% at 5 years (22).

Anthracycline, capecitabine and taxane chemotherapy are radiosensitizers, therefore a gap of at least 3 weeks is recommended before commencing adjuvant radiotherapy. CMF has been given concurrently with radiotherapy. However, the incidence of acute radiotherapy side effects is increased although there is no evidence of an increase in long term side effects. In the absence of long term cardiac toxicity data on Herceptin and radiotherapy, at present adjuvant Herceptin is to be started after completion of radiotherapy and not concomitantly. This is in accordance with NICE guidelines. There is data from the American Intergroup trial N9831 suggesting that herceptin given concurrently with radiotherapy does not result in increased cardiac or other toxicity and hence, if confirmed, this policy may require review.

All patients should receive adjuvant breast radiotherapy after breast conserving surgery (23). The EBCCTG radiotherapy overview (24) found that:-

1. ¾ of local recurrence occurred in the first 5 years.
2. Local recurrence was reduced by 2/3 by radiotherapy after wide local excision in node negative (reduced from 30% to 10%) and node positive breast cancers (reduced from 45% to 15%) at 15 years.
3. There was a 5% survival benefit from radiotherapy in node negative and 7% in node positive breast cancer after breast conserving surgery at 15 years.
4. Local recurrence was reduced by 2/3 by radiotherapy after mastectomy in node negative (reduced from 8% to 3%) and node positive breast cancers (reduced from 30% to 8%) at 15 years. Survival benefit of 5% was seen only in node positive breast cancer after mastectomy.
5. There was an excess mortality from heart disease (rate ratio 1.27, SE 0.07, 2p=0.0001) and lung cancer (rate ratio 1.78, SE 0.22, 2p=0.0004).

Post Breast Conserving Surgery

No subgroup of tumours has been identified which does not benefit from lower local recurrence rates following radiotherapy. However, elderly patients with good prognostic features are at low risk of recurrence. According to the CALGB trial in patients aged >70 with T1N0 ER+ve breast cancer, the five year recurrence rate following breast conserving surgery was 4% without radiotherapy versus 1% with radiotherapy(25). Patients with early breast cancer should be considered for the
PRIME II study. The PRIME II trial is currently looking at radiotherapy versus observation in patients aged >65, with grade I or 2, <3cm in diameter, ER positive, node negative tumours.

Indications for radiotherapy to lymph node drainage areas are as for post mastectomy (see below).

**Post mastectomy**

**High Risk**
The following patients should be offered adjuvant chest wall radiotherapy post-mastectomy:-
- all T3 (>5cm) breast cancers
- all T4 breast cancers (involving chest wall or skin)
- breast cancers with 4 or more positive lymph nodes in the axilla.
- margin<3mm
- Indications for axillary and/or supraclavicular fossa radiotherapy (see below)

**Intermediate risk**
Relative indications for adjuvant chest wall radiotherapy post-mastectomy include 2 or more of the following factors: age<40 years, grade 3, 3+ nodes positive or lymphovascular invasion (LVI).

Locoregional failure rates following mastectomy without RT are 5 to 15 percent for women with 1 to 3 positive nodes, and these women should be offered entry into the SUPREMO study. Eligibility criteria include N1 disease or T2 tumours which are G3 and/or have evidence of LVI.

**Indications for radiotherapy to lymph node drainage areas:**

1. **Axilla**
   - Positive node(s) in patients who have not had an axillary node dissection and don’t wish to have further surgery.
   Relative indication:-
   - >1mm extracapsular or perinodal infiltration
   - SCF node involvement
   - Apical node involved

2. **Supraclavicular fossa**
   - Four or more positive nodes
   - Apical node involved
   - SCF node involvement
   Relative indications:-
   - After neo-adjuvant chemotherapy for inflammatory or locally advanced breast cancer
   - 1-3 positive nodes and other poor prognostic factors (eg T3, grade 3 +/- LVI)
These apply to patients treated surgically by either mastectomy or breast conserving surgery.

**Patients unsuitable for surgery:**

A small group of patients are unsuitable for primary surgery resulting from medical incapacity, infirmity or where there is high risk from general anaesthetic (preferably as assessed by the anaesthetist). Hormone therapy is the mainstay of treatment provided the tumour is hormone receptor positive. In one study of 113 patients, hormonal therapy with Tamoxifen provided local control for a median time of 2.5 to 3 years \(^{(27)}\). Letrozole has been proven to be superior compared to tamoxifen in terms of time to progression \(^{(28)}\). Radiotherapy may be considered appropriate if the tumour is ER –ve, or upon progression on hormonal therapy. Some patients with fungating, bleeding or painful tumours who require a faster response can also be offered primary radiotherapy.

**NECN recommendation for palliative radiotherapy for locally advanced breast cancer:-**

Dose 40 Gy in 15 fractions over 3 weeks by tangential fields.

**Alternative fractionation:-**

Dose 32Gy in 4 fractions delivered once a week over 4 weeks. There is no published data on this fractionation regime but it has been used previously at the NCCT in a limited number of frail patients who would not be able to cope with daily travel.

**Radiotherapy technique**

The breast/chest wall, and axilla if indicated, are treated by isocentric tangential fields. It is not possible to completely exclude the axilla with this technique, but the superior and lateral field borders can be positioned to include the axilla when required or, conversely, to exclude most of the axilla.

If indicated a supraclavicular fossa field is matched on to cover the apex of the axilla and supraclavicular fossa nodes.

The chest wall may be treated by electrons in suitable patients.

Treatment is 3D planned to achieve as nearly as possible dose homogeneity to within +7%/-5% (prescribed according to ICRU 50/62).

The recommended prescribed dose is **40 Gy in 15 fractions over 3 weeks**.

In certain situations 50Gy in 25 fractions over 5 weeks may be preferred. The indications are all relative rather than absolute:

- For patients in whom >2cm lung is included on any slice.
- Patients requiring axillary and/or SCF node irradiation.
- Suboptimal Dose distribution. Dose homogeneity of +7%/-5% as recommended by ICRU 50/62 is the ultimate aim but cannot be routinely achieved. An improved technique is being introduced with the aim of achieving a dose distribution of +10%/-5% in most patients.
- Following breast reconstruction.

The indication for using 50Gy/25f should be specified on the prescription.
Tumour bed boost with electrons

A breast boost is not routinely recommended but should be considered in those at above average risk of local recurrence in the region of the tumour bed. It has been demonstrated in an EORTC trial to reduce local recurrence rates following breast conserving surgery in selected patients \(^{(29)}\). All patients in the EORTC trial had microscopically complete excision margins. The greatest benefit was seen in those <40 years old (10% vs 20%), a modest benefit in those between 40 and 50 (5% vs 10%) and no benefit in women over 50 years old (3% vs 4%). However, cosmetic appearance was poorer after boost. At 3 years, 86% of patients in the no-boost group had an excellent or good result, compared to 71% in the boost group \((p = 0.0001)\).

A 2007 update of the EORTC trial \((J\ Clin\ Oncol\ 2007\ 25-22:3259-67)\) no longer suggests a statistically significant interaction by age group, but the absolute reduction at 10 years was largest in the under 40s. The authors suggested increasing the age for boost to 60.

The NCCC policy has been to use boosts for those with margins <5mm. An audit of local recurrence rates in women <40 years at NCCT \((2008)\) found a low recurrence rate of 5%.

The NECN recommendation is that a boost is given to the following groups:
- Women under the age of 40
- Women >40 years old with a resection margin of <3mm

Other factors should be considered in patients who do not fall into the above groups. They represent relative indications for a breast boost and should not be considered in isolation. These factors include
- Lymphovascular invasion
- Grade 3
- ER/PR negative
- Presence of extensive in-situ carcinoma (>25%)
- T3

It is preferable that the boost is planned using information from the pathology report, surgical notes and pre-operative mammograms. Surgical clips in the tumour bed, where present, aid localisation. Electron energy is prescribed to ensure that 90% of the prescribed dose reaches the surface of pectoralis major. Study of the planning CT scan improves accuracy in deciding the electron energy and a method of planning the boost on the planning scan is being developed. The electron mark-up is currently done clinically, with the aim to cover the at risk area with a 1.5cm to 2cm margin.

Dose for boost = 10Gy in 5 fractions in one week.

Unwanted side effects of radiotherapy

Immediate side effects during adjuvant breast irradiation include fatigue and skin erythema or desquamation. To prevent this from happening, patients should be advised to avoid deodorant on the treated side, wear loose clothing and pat skin dry after washing to minimize friction and epithelial loss.
During radiotherapy skin reaction is managed with aqueous cream and if symptomatic with 1% hydrocortisone cream unless there is evidence of moist desquamation. Moist desquamation should be managed with barrier dressings including geliperm and colloid dressings during radiotherapy. After the completion of radiotherapy, flamazine ointment can be used if there is moist skin desquamation.

**NCI CTCAE Version 3.0 for Radiation Acute Skin Reaction**

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Asymptomatic mild redness of skin, commonly seen in the 2nd week of breast radiotherapy</td>
<td>Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate oedema. May be seen in the third week of breast radiotherapy</td>
<td>Moist desquamation other than skin folds and creases; bleeding induced by minor abrasions. Rarely seen with breast radiotherapy.</td>
<td>Skin necrosis ulceration of full thickness dermis; spontaneous bleeding from involved site. Never seen with breast radiotherapy.</td>
</tr>
</tbody>
</table>

**Radiation pneumonitis:** is a clinical syndrome of cough, fever and/or shortness of breath accompanied by radiographic changes consistent with a non-infectious infiltrate. It usually comes on six weeks after radiotherapy and resolves completely by six months. In a retrospective analysis of 1624 women treated with conservative surgery and adjuvant breast irradiation at a single institution, the overall incidence of symptomatic radiation pneumonitis was only 1% at a median follow-up of 77 months, although this increased to 3% with the addition of a supraclavicular field(30). Administering concomitant chemotherapy with SCF irradiation lead to radiation pneumonitis in 8.8%. One study of 140 patients found no case of radiation pneumonitis in patients in whom less than 3.35 cm lung was measured at the central axis of the simulation film, with all cases of radiation pneumonitis occurring in patients with more than 4 cm of lung irradiated, suggesting that the central lung depth is a guide to risk (31).

The NECN recommendation is that the central lung depth be kept to <3cm in all patients receiving tangential field radiotherapy.

**Lymphoedema:** is a swelling of the arm due to poor lymphatic drainage, which can be caused by surgery, radiotherapy, or lymphatic obstruction from tumour. Venous obstruction can also cause a similar clinical picture. Acute lymphoedema should therefore trigger appropriate investigations.
Mild lymphoedema is common in patients who have had an axillary dissection (2–10%). The combination of axillary irradiation therapy with axillary dissection (level 2) increases the risk of arm oedema to 13–18%. Axillary recurrence following adequate axillary surgery is so infrequent (0–2%) that routine axillary radiotherapy is not generally indicated (see indications above).

Lymphoedema can affect quality of life and activities of daily living depending on severity. It can lead to reduced movement due to arm weight, pain, cosmetic disfigurement and reduced wound healing. A difference of more than 2 cm between the affected and normal arms is considered clinically significant.

Patients with axillary surgery are told following surgery to avoid venepuncture on the affected side. Any signs of infection in the at risk arm should be treated promptly with antibiotics. Patients should be taught exercises following surgery.

Treatment of lymphoedema involves skin care, simple lymphatic drainage, exercise and compression hosiery/bandaging. Patients should be able to access a local lymphoedema clinic and all units are encouraged to develop links with such a clinic or set up their own service.

**Brachial plexus injury:** No cases of this injury were recorded in the recently reported START trials or in the RCR survey of patients treated by 50 Gy in 25 fractions and therefore the expected incidence in patients treated according to this guideline is expected to be exceedingly low or absent.

**Cardiac toxicity:** An increased risk of cardiac deaths was noted 10-15 years following older techniques for breast irradiation. This risk should be much reduced for patients with modern techniques and should approach a maximum of < 0.5% (32). Whilst every care should be taken whilst planning to avoid the heart, including the use of MLC shielding, priority should be given to coverage of the tumour bed, especially in high risk cancers.

The indications for radiotherapy may need to be modified in individual patients in the light of their perceived individual risk of any of the above late effects. For example previous radiotherapy or pregnancy would be absolute and radiation sensitivity syndromes relative contraindications to conservative surgery with radiotherapy rather than mastectomy.

**Adjuvant Radiotherapy for DCIS**

- Three large randomised trials (NSABP-B17, EORTC and UKCCCR DCIS) have shown that adjuvant radiotherapy reduces the risk of local recurrence and the development of ipsilateral invasive cancer by around 50%, although no effect was seen on survival.

- NSABP-B17 has reported 12 year data on adjuvant radiotherapy. Radiotherapy reduced local recurrence from 32% to 16%. Around half of the recurrences were invasive.
- EORTC trial 10853 has reported 10-year follow-up, and found that the group receiving RT had significantly fewer invasive (8 versus 13 percent) and noninvasive (5 versus 14 percent) recurrences as compared to surgery alone.

- In the UKCCCR study, the hazard ratio with adjuvant radiotherapy was 0.36 and 0.45 for DCIS and invasive cancer respectively (16). All patients had complete surgical excision of the lesion confirmed by specimen radiography and histology (unlike NSABP and the EORTC studies).

- From the Silverstein data, there is a subgroup of patients that would have a very low risk of recurrence despite omission of radiotherapy.

The NECN recommendations for adjuvant radiotherapy in DCIS

The following are indications to consider adjuvant radiotherapy:-

- Margin<2mm following local excision and if further surgery not possible
- Margin<1mm if patient has had a mastectomy
- All high grade DCIS following breast conserving surgery
- All DCIS with comedo necrosis following breast conserving surgery

Electron boost may be used in DCIS if the MDT feels that there is risk of residual disease after surgical resection that cannot be improved by further surgery, although the evidence for this is weak.
ENDOCRINE THERAPY FOR INVASIVE BREAST CANCER

Oestrogen and Progesterone receptor status should be identified in all patients with invasive breast cancer. No decisions on systemic hormone therapies should be made until the test result is known.

The EBCCTG overview confirms that five years of tamoxifen in the adjuvant setting reduces the risk of death by 31% per annum in receptor positive breast cancer \( ^{33} \). ER and/or PR positivity are strong predictive factors for benefit from hormonal therapy. Hormone treatments should not be offered to ER and PR negative patients \( ^{34} \). ER status is determined using the Allred Quickscore, ranging from zero to eight.

The Allred Quickscore:

<table>
<thead>
<tr>
<th>Score for proportion</th>
<th>Score for intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0=no stain</td>
<td>0=no stain</td>
</tr>
<tr>
<td>1=&lt;1%</td>
<td>1=weak stain</td>
</tr>
<tr>
<td>2=1-10%</td>
<td>2=moderate stain</td>
</tr>
<tr>
<td>3=11-33%</td>
<td>3=strong stain</td>
</tr>
<tr>
<td>4=34-66%</td>
<td></td>
</tr>
<tr>
<td>5=67-100% nuclei staining</td>
<td></td>
</tr>
</tbody>
</table>

Summed to give a maximum out of 8. Quickscore zero to two are deemed receptor negative, and Quickscore three to eight are deemed receptor positive.

**Hormone Treatment Recommendations**

- Always consider the current NCRN Trial Portfolio when considering anti-endocrine therapies.
- All ER and/or PR +ve patients should be offered endocrine treatment unless there is a contraindication to its use. Based on current evidence the optimal duration of endocrine treatment is 5 years.
- **Tamoxifen for 5 years is the standard of care for all premenopausal women.**
- **AROMATASE INHIBITORS ARE ONLY EFFECTIVE IN POST MENOPAUSAL WOMEN.**
- **Letrozole for 5 years is the standard of care for all postmenopausal women.** NICE guidance CG 80 recommends initial treatment with an aromatase inhibitor for all post menopausal women, except those with low risk of recurrence. Following review of the most recent randomised clinical trials, including BIG 1-98, the NECN guideline treatment of choice is letrozole.
  - The NICE guidance on aromatase inhibitors recommends use of each aromatase inhibitor within its license taking and taking recurrence risk into account:
    - Letrozole for a further 4 years after completion of 4-5 years Tamoxifen in node positive patients.
    - Letrozole, in addition, is licensed for Neoadjuvant treatment.
  - Both chemotherapy and tamoxifen can induce temporary amenorrhoea, and therefore if patients are being considered for switch therapy to an aromatase
inhibitor, they must have gone through the menopause before starting chemotherapy as standard assays of E2 are unreliable in this setting.

- In those node positive patients who were premenopausal prior to the start of tamoxifen but who now appear to be postmenopausal following systemic therapy the question of extended endocrine treatment with an AI may arise. Where this is felt to be clinically appropriate an MDT discussion is recommended. Menopausal status should be assessed 2 months after stopping tamoxifen using estimation of FSH and oestradiol. A sensitive oestradiol measurement is more accurate than standard serum oestradiol but is not available locally.

- Where a high risk patient remains premenopausal after 5 years of tamoxifen, extended tamoxifen should only be considered after a full discussion of the risks and benefits of continuing therapy with the patient.

Sequencing of Chemotherapy and Endocrine therapy

- Endocrine therapy should never be started until receptor status is known.
- Endocrine therapy should not, ideally, be started until the patient has been discussed in an MDM and the possibility of clinical trials has been considered.
- Endocrine therapy should be deferred/interrupted in patients receiving chemotherapy because of trial data suggesting a survival advantage when Tamoxifen was given in sequence compared to concurrently.
- Don’t forget to start Endocrine Therapy after chemotherapy has finished, usually 3-4 weeks after the last injection.

Complications of Endocrine Therapy

These are well documented and each Unit should have written information for patients for whom endocrine therapy is proposed.

In summary:

1. Bone loss: bone mineral density should be assessed with a baseline dual energy X-ray absorptometry (DEXA) scan in the following patients:
   - Those starting aromatise inhibitors
   - Those having a treatment-induced menopause
   - Those starting ovarian ablation/suppression therapy

   The future screening and treatment of these patients with bisphosphonates should be offered according to the “Guidance for the management of breast cancer treatment-induced bone loss: A consensus position statement from a UK expert group (2008), see appendix 2.

2. Menopausal symptoms: the following may be helpful for some patients with distressing symptoms:
   - Oil of Evening Primrose
   - Auricular acupuncture
   - Selective serotonin re-uptake inhibitor antidepressants, paroxetine and fluoxetine may be offered for relieving hot flushes, except in those taking tamoxifen in whom they may reduce the effectiveness of tamoxifen.
Clonidine, venlafaxine and gabapentin should only be offered after patients have been fully informed of the significant side effects.

3. Abnormal or irregular vaginal bleeding should always be investigated fully because it may, very rarely, be a Tamoxifen-induced endometrial carcinoma.

4. Tamoxifen increases the risk of venous thromboembolic disease. Patients should be warned of this and advised on sensible precautions during e.g. long haul air travel.
Endocrine Therapy For Metastatic Disease

Endocrine therapy should be considered as first-line treatment for the majority of patients with hormone receptor positive disease, particularly where disease is confined to the bone. Where there is significant visceral disease chemotherapy, followed by endocrine therapy is likely to be the preferred option.

Pre-menopausal

- Tamoxifen is the first line hormonal therapy of choice for patients with receptor +ve metastatic breast cancer (who are not already taking adjuvant tamoxifen). Those patients who have not previously taken Tamoxifen or who have completed a 5 year course more than one year before are suitable for consideration of Tamoxifen.
- In women already taking Tamoxifen, consider ovarian suppression +/- an aromatase inhibitor.

Post-menopausal

- Aromatase inhibitors are the treatment of choice for post-menopausal women with ER +ve breast cancer (38). A change from a non-steroidal to a steroidal AI may give benefit in women who have previously received both a non-steroidal aromatase inhibitor and Tamoxifen.
- Progestagens may be considered in both pre and post menopausal women when antioestrogens have failed.

Hormone replacement therapy (HRT)

It is advised that every patient diagnosed with breast cancer should cease HRT. There are newer forms now becoming available which may be sufficiently selective to confer a reduced risk to patients with respect to recurrence of their breast cancer. There is currently an NCRN study looking at this.
CHEMOTHERAPY FOR INVASIVE BREAST CANCER

Adjuvant Chemotherapy

Chemotherapy should start within 31 days of the completion of surgery, or earliest clinically appropriate date. Hormone treatments should be interrupted or delayed until chemotherapy is complete.

Anthracycline containing polychemotherapy (e.g. FAC) reduces the annual risk of death by 38% for women under age 50, and by 20% for women aged 50 to 69 (39). The absolute benefit would be proportional to the individuals’ risk of recurrence and this can be estimated using the adjuvantonline tool available at www.adjuvantonline.com. This tool is to be used by health professionals familiar with the issues in the adjuvant treatment of breast cancer. The intention is that this tool be used to provide information that will then be helpful in shared decision making by the patient and the health professional.

For women < 70 years old, the St Gallen Consensus statement recommends that:

- All women with Node positive breast cancer and all women with Receptor negative breast cancer should be offered chemotherapy and so should be referred for an oncology opinion (40).

Some women, for example those age >35 with T1, N0, ER+ve Grade 1, HER2 -ve tumours are unlikely to benefit from chemotherapy and do not need to be referred.

HER2 positive breast cancer is a feature which increases (up to double) the risk of recurrence. All patients with HER2 positive breast cancer with tumour size >1cm should be referred to the medical/clinical oncologist for discussion of adjuvant chemotherapy followed by Herceptin (Trastuzumab).

Choice of Adjuvant Chemotherapy Regimen:

Choice of individual regimen requires an assessment of the risks and benefits for the individual patients.

Always consider entry to the NCRN adjuvant trials portfolio.

Node –negative patients who are suitable for adjuvant chemotherapy should receive an anthracycline containing regimen. Appropriate regimens are:

- EC X 6 (Epirubicin 90mg/m2 Cyclophosphamide 600mg/m2)
- FEC X 6 (5FU 600mg/m2 Epi 75mg/m2 Cyclo 600mg/m2)

Dose intensity should be maintained using secondary prophylaxis with G-CSF in event of neutropenic sepsis. Dose reductions are accepted both from the outset and in response to toxicity depending on performance status and clinical judgement of the treating physician.

In patients wishing to minimise the risk of alopecia, or who have a contra-indication to anthracyclines, classical CMF would be an alternative.
A taxane containing regimen should be considered in all node-positive patients and offered where clinically appropriate. The regimen of choice is **FEC-T (Docetaxel)**. **TC (Docetaxel + Cyclophosphamide)** is an accepted alternative in patients with cardiac co-morbidity.

A network-wide audit of FEC-T chemotherapy has shown rates of neutropenic sepsis rates in excess of 20% in unsupported patients. The use of primary prophylaxis with GCSF is therefore recommended with this regimen.

**Cardiac Monitoring & Anthracyclines** *(43)*

Transient ECG changes can occur during anthracycline therapy and are not in themselves an indication to discontinue treatment. There is, therefore, no absolute need for an ECG at baseline although is may be a useful marker of cardiac disease.

There is a risk of cardiomyopathy in patients with increasing cumulative exposure to anthracyclines and patients with any of the following risk factors should have a baseline assessment of LVEF by either echocardiogram or MUGA scan.

- Age above 65
- Hypertension requiring medication
- Heart failure
- Left ventricular hypertrophy
- Mediastinal irradiation
- Myocardial Infarction
- Planned cumulative doxorubicin dose > 360 mg/m² or epirubicin dose > 600 mg/m²
  - In these patients repeat assessment during chemotherapy is recommended
- Any other identified cardiac risk factor

**Adjuvant Tastuzumab (Herceptin)**

20 percent of breast cancers overexpress HER2, a cell surface tyrosine kinase receptor. The addition of Herceptin to adjuvant chemotherapy is recommended for women with HER2-overexpressing tumors that are >1 cm or N+.

Two North American Cooperative Group trials were initially designed as parallel clinical trials. In NSABP trial B-31, 1736 women with HER2-positive, node-positive (N+) breast cancer received AC x 4 followed by Paclitaxel (175 mg/m² over 3 hours) x 4; they were randomly assigned to no further therapy (group NSABP-1) or weekly trastuzumab (initial loading dose 4 mg/kg, then 2 mg/kg weekly for one year, NSABP-2), beginning with the first dose of paclitaxel *(39)*. The North Central Cancer Treatment Group (NCCTG)-coordinated Intergroup trial N-9831 tested the value of adding trastuzumab to sequential AC and paclitaxel. Combined analysis of both trials confirm a 49 percent reduction in the risk of disease recurrence and a 37 percent reduction in the risk of death (four-year OS 93 versus 89 percent) *(45)*. Similar figures were reported for the HERA trial *(46)*.
In the FinHer trial (47), women with N+ or high-risk node-negative breast cancer were randomly assigned to three courses of docetaxel or vinorelbine followed by FEC x 3. The 232 women with HER2-positive breast cancer were randomly assigned to receive nine weekly trastuzumab infusions after completing chemotherapy. DFS was significantly better among those who received trastuzumab (89 versus 78 percent, \( p = 0.01 \)), similar in magnitude as other studies using one year of Herceptin.

There was a higher incidence of cardiac toxicity in the patients that received adjuvant Herceptin. A recent meta-analysis of five randomised control trials of adjuvant Herceptin found a 7.2% increased risk of significant drop in cardiac function and 1.61% increased risk of symptomatic NYHA grade 3-4 heart failure following one year of Herceptin (48).

Management of cardiac events in trastuzumab-treated patients

1. **Baseline cardiac assessment prior to cytotoxic chemotherapy**
   - Medical history & physical examination including BP measurement
     - To detect pre-existing cardiac disease and risk factors.
     - 12-lead electrocardiogram (ECG), with echocardiogram if abnormal
   - LVEF measurement using Echo or radionucleotide multiple-uptake gated acquisition (MUGA) scan.

2. **Interventions at baseline**
   - Referral to a cardiologist
       - Recommended for patients with significant cardiac co-morbidity.
   - Modification of planned chemotherapy regimen
       - In patients with low or borderline LVEF
       - Prophylactic ACE inhibitor therapy may also be considered.
   - Initiation of ACE inhibitors to control hypertension
       - Hypertension is a potent modifiable risk factor for the development of heart failure during Trastuzumab treatment.
       - Blood pressure above 140/85 mmHg should be treated with an ACE inhibitor, with primary care supervision of dose and renal function
   - Lifestyle recommendations
       - Smoking cessation, healthy diet & alcohol intake, optimising weight

3. **Management of cardiac function during trastuzumab**
   - Assessment of LVEF prior to starting trastuzumab treatment
       - LVEF should be assessed after chemotherapy and before Trastuzumab.
       - Patients with an LVEF >= institution LLN should start Trastuzumab.
       - Patients with LVEF < institutional LLN should not start Trastuzumab but should be started on an ACE inhibitor and referred to a cardiologist. Repeat assessment of cardiac function should take place after 3 months.
       - Sharp falls in LVEF (> 0.10) during cytotoxic chemotherapy may indicate increased susceptibility to cardiac dysfunction on Trastuzumab. Prophylactic ACE inhibitor therapy may be considered for such patients.
   - Routine LVEF monitoring is recommended after 4 and 8 months.
       - Assessment at the end of treatment is recommended for patients requiring cardiovascular intervention during treatment.
Additional testing is required in patients who have LV dysfunction.

 Patients developing signs and symptoms of heart failure should have their trastuzumab treatment interrupted, receive an ACE inhibitor and be referred to a cardiologist.\textsuperscript{33,44,45}

If the LVEF falls to \( \leq 0.40 \), (representing biologically important LV systolic dysfunction) trastuzumab should be interrupted the patient should receive an ACE inhibitor and be referred to a cardiologist for treatment.\textsuperscript{33,44,45}

After Trastuzumab interruption and appropriate medical therapy, LVEF should be re-checked after 6–8 weeks. Trastuzumab may be re-initiated if the LVEF is restored to a level above the LLN.

If the LVEF falls to below the LLN but \( > 0.40 \), trastuzumab may be continued, but an ACE inhibitor should be initiated.

- If the patient is already on an ACE inhibitor, they should be referred to a cardiologist.
- LVEF assessment should be repeated after 6–8 weeks.

If the LVEF falls by 0.10 points or more but remains above the LLN, trastuzumab may be continued. Intervention with an ACE inhibitor is recommended in an attempt to reduce the risk of further LVEF decline of symptomatic CHF.

LVEF Monitoring should be repeated after 6–8 weeks.

**Traffic light system**

Navigation through these guidelines may be facilitated by the adoption of a traffic light system.

- A green light indicates LVEF above the LLN, no signs or symptoms of CHF and any trastuzumab-related LVEF fall being \( < 0.10 \).
- An amber light indicates LVEF between the LLN and 0.40, with no signs or symptoms of CHF, or a trastuzumab-related LVEF reduction of 0.1 or more.
- A red light indicates LVEF \( \leq 0.40 \) or symptoms and signs of cardiac failure.

Prior to chemotherapy, green indicates go. Red or amber indicates careful consideration of decision to start chemotherapy, with consideration of non-anthracycline-containing regimens. Both amber and red are indications for the initiation of ACE inhibitors, and referral to cardiology for the optimisation of cardiac function.

Post chemotherapy, green indicates go. Amber indicates defer until green. Red indicates that it is unlikely to be safe to start trastuzumab. Both amber and red are indications for the initiation of ACE inhibitors and referral to cardiology for the optimisation of cardiac function. It is recommended that LVEF is reassessed after 3 months, and that trastuzumab is not commenced unless LVEF is within normal limits at that point.

During trastuzumab, green is an indication to continue treatment. Amber is also an indication to continue chemotherapy, but patients should also be taking an ACE inhibitor. Patients who drop into the amber range while on an ACE inhibitor should be referred for a cardiology opinion. Red is an indication to interrupt trastuzumab, start on an ACE inhibitor (not already taking one) and refer for a cardiology opinion.
Patients whose trastuzumab is interrupted (i.e. red light) should not restart until LVEF is within the normal range (i.e. green light).

**Neo-Adjuvant Chemotherapy**

For patients with locally advanced disease or tumours where downstaging might facilitate conservative surgery, including inflammatory breast cancers, neo-adjuvant therapy, ideally in the context of a clinical trial should be considered.

The diagnosis must be established by core biopsy and ER, PR and HER-2 status should be ascertained.

If T3 or node positive, staging investigations including a CT scan of thorax and abdomen ± bone scan should take place before the commencement of neoadjuvant chemotherapy.

FEC or EC for 4-6 cycles is the off trial standard treatment. There are no data on the benefits of post surgical chemotherapy in patients who have received neoadjuvant treatment, although sequences of chemotherapy (eg. Anthracycline followed by taxane) appear to be superior to anthracycline only combinations in this setting.

Patients who are ER positive should routinely be offered Tamoxifen after surgery.

In ER negative patients post surgical treatment should be discussed carefully on a case by case basis and may include Taxane monotherapy.

**Chemotherapy In Metastatic Disease**

Chemotherapy should be offered as first-line treatment for patients with advanced breast cancer whose disease is imminently life-threatening or requires early relief of symptoms because of significant visceral involvement, providing they have had an opportunity to discuss the likely side effects and are prepared to accept them. The alternative of endocrine therapy should always be considered in hormone receptor positive patients.

This should always be discussed with the appropriate breast oncologist, taking into account the patient’s wishes, prevailing NICE guidance and available clinical trial options. The following sequence of drugs may be considered in patients with metastatic disease, bearing in mind previous exposure in the adjuvant setting:-

1. Anthracycline
2. Taxane, 3 weekly docetaxel being the treatment of choice in the younger, fitter patient, weekly taxol being an alternative in others.
3. Capecitabine or Vinorelbine
4. Vinorelbine or Capecitabine
5. Others
6. Platinum-containing regimes for metastatic breast cancer

All suitable patients should be offered treatment within a clinical trial. Where none exists, a platinum-containing regime can be considered particularly in patients who have triple negative disease. If a taxane has not yet been used, the combination of carboplatin and paclitaxel should be considered. In the event of taxane therapy already being used, the
combination of choice is gemcitabine and carboplatin. As many patients in this setting are heavily pretreated, a weekly schedule is recommended. The same regime may be considered in patients who are not triple negative, after exhausting all other available therapies, only after a frank discussion about risks and likely response rates.

In all patients receiving palliative chemotherapy consideration should be given to criteria for assessing treatment response including method of assessment and assessment interval.

Patients should have adequate baseline assessment at a time that allows for realistic on-treatment documentation of response.

**Trastuzumab in metastatic disease**

In HER2 positive patients who relapse after completing adjuvant Trastuzumab, this may be reintroduced, where clinically appropriate, in the metastatic setting. For the best response rates Trastuzumab should be used in combination with chemotherapy, usually a taxane though vinorelbine may be an alternative in some patients.

It is recognised that, in a very small number of patients who would be suitable for trastuzumab, chemotherapy is not always appropriate, or may even be refused by the patient. In this setting single agent trastuzumab may be considered.

Treatment is not recommended beyond tumour progression with the exception of those patients responding to Trastuzumab in non-CNS sites and who relapse in brain and where the intention is to give radiotherapy. In this instance Trastuzumab should continue until either un-treatable CNS progression or progression in a systemic site.

**Further information on chemotherapy and its side effects and dose adjustments in organ failure can be found at:**
BISPHOSPHONATES FOR BONY SECONDARIES

Bisphosphonate therapy prevents skeletal complications from osteolytic bone involvement by inhibiting osteoclasts. In the seminal paper by Hortobagyi in 1996, the median time to the occurrence of the first skeletal complication was greater when IV pamidronate 90 mg was delivered 4 weekly compared to the placebo group (13.1 vs. 7.0 months, P=0.005)\(^{(53)}\). In 2001, Zoledronic acid (4 mg) via 15-minute intravenous infusion was published to be as effective and well tolerated as 90 mg of pamidronate given over 2 hours in the treatment of bone metastases in patients with metastatic breast cancer\(^{(54)}\). Similar results are available for oral clodronate and ibandronate\(^{(55)}\). Upper GI adverse events were higher with oral ibandronate and it should be stressed to the patient that she should drink a full glass of liquid with the tablet and remain upright for at least ½ an hour after taking the tablet.

**Serious complications from bisphosphonates**

An association has been noted between bisphosphonate therapy and development of the renal impairment due to a number of different mechanisms, including collapsing focal glomerulosclerosis. Because of the potential for renal toxicity, ASCO guidelines recommend that creatinine be monitored prior to each dose\(^{(56)}\). An increase of >44 micromol/L in serum creatinine, or an absolute level of >124 micromol/L among patients with normal baseline values should prompt temporary discontinuation. If renal function returns to baseline, therapy can be restarted cautiously.

Osteonecrosis of the jaw is an uncommon complication affecting usually the mandible. In one study, the incidence of ONJ was 1.5 percent among patients treated with these agents for 4 to 12 months, rising to 7.7 percent after treatment for 37 to 48 months.

The following variables were predictive for the development of osteonecrosis (or avascular necrosis) of the jaw:

- Dental extraction
- Sequential therapy with pamidronate/zoledronic acid
- Longer follow-up time
- Older age at diagnosis

Conservative debridement of necrotic bone, pain control, infection management, use of antimicrobial oral rinses, and withdrawal of bisphosphonates are preferable to aggressive surgical measures for treating this condition. The NECN recommends stopping bisphosphonates 3 weeks prior to and for 3 weeks after any dental procedure for patients on bisphosphonates.
BREAST CANCER FOLLOW UP

Although there is no evidence that routine follow up by a specialist increases long term survival, it is believed that many women welcome the reassurance of regular review whether this is by specialist or by GP. A recent randomised controlled trial suggested that an improved quality of life occurred when patients had access to a breast CNS for one year following surgery \(^{(57,58)}\).

The purpose of follow up is:

1. To identify salvageable local recurrence. The incidence of local recurrence after conservative surgery and radiotherapy is reported to be about 10% @ 5 years, rising at 1% per year\(^{(16)}\).
2. To detect and manage treatment-related toxicity.
3. To screen for new primary tumours.
4. Patient psychosocial support.
5. To assess treatment outcomes/audit.
6. Teaching of Trainees in all disciplines.

There is no evidence for the use of tumour markers in the follow up of asymptomatic patients and these are not recommended.

Northern network follow up protocol (as per NICE guidance)

After completion of definitive treatment
Low/moderate risk (T1-2, N0, M0)
6 monthly review year 1
annual review years 2,3,4,5
annual mammography for 5 years then discharge.

High risk (T3-4, N1,M0-1)
After active treatment including herceptin
6 monthly reviews year 1 and 2
annual review years 3,4,5.
Annual mammograms

If under 50 after 5 years continue 2 yearly mammos until screening age. Annual clinical exam can be continued until 50 if patient prefers.

Follow up can be by surgeon, oncologist or breast care nurse.

Clinical trial follow up requirements take precedence over these guidelines.

Patient information

- Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:
  - designated named healthcare professionals
  - dates for review of any adjuvant therapy
- details of surveillance mammography
- signs and symptoms to look for and seek advice on
- contact details for immediate referral to specialist care, and
- contact details for support services, for example support for patients with lymphoedema.

The NECN written care plan proforma is shown in appendix 3
THE BREAST CARE CLINICAL NURSE SPECIALIST (CNS)

The CNS is part of the multidisciplinary team and should be available for any patients undergoing treatment for breast cancer if they so wish. Patients should be aware of the CNS availability when attending a breast clinic.

- The CNS should be present at the time of diagnosis when any options for treatment are discussed.

- A suitable room with adequate privacy should be available at this time. The patient may be emotionally shocked and may not be able to assimilate the information given, the presence of a companion such as a partner or friend is encouraged.

- The CNS will initiate a plan of care and arrange further contact with the patient/family as needed, ensuring the patient is aware of how to contact the CNS.

- The CNS will assess each patient’s need for information and advice regarding their condition. This may include treatment choices, arm care and mobility, prosthetics, bra advice and treatment options as well as body image and psychosexual issues. The information may be written and/or verbal as desired by the patient.

- Support must be available both pre-and postoperatively and on subsequent outpatient visits to the hospital when patients may be receiving their results and further treatment may be discussed. The CNS should ensure a suitably trained nurse fits mastectomy patients with a temporary prosthesis prior to hospital discharge.

- The CNS will assess the patient for signs of anxiety and depression and refer to other health care professionals as appropriate.

- The CNS will establish links with the primary health care team (PHCT) and other relevant health care professionals to foster collaborative working and improve the patient journey.

- There must be an agreed programme of continuing education for the CNS, including IPR, nursing research and evidence of professional development plans. The CNS needs to be involved in the education of nursing staff on breast disease, both formally and informally, in the hospital setting and elsewhere.

- Ideally breast units need at least 2 CNSs to provide cross cover and it is mandatory that a CNS attends each multidisciplinary team meeting and is a core member of that team.

- The CNS is responsible for ensuring the details of the patient’s key worker are recorded in the medical notes.
PALLIATIVE CARE

1. The median survival of a patient with metastatic breast cancer is 24 months, with between 5 and 20% of patients surviving over 5 years depending on site of metastases. Therefore provision must be made for management of symptoms attributed to secondaries. The hospital team must have access to expertise in palliative care, in order to provide good symptom management advice during OP clinics when necessary, and in order to offer the best possible palliative care to in-patients. Palliative care services should work in liaison with the breast care team and the patient’s primary care team.

2. Lymphoedema treatment clinics use a combination of compression, massage and exercise to reduce and control lymphoedema, emphasising the importance of self-management to patients. This is a specialist treatment, and the swollen limb needs careful monitoring to avoid or treat skin damage, thrombosis and cellulitis, whilst monitoring for recurrent disease. Breast cancer units should have access to a local lymphoedema service. The lymphoedema service for breast cancer patients should be fully funded by the NHS, even if it does not take place on NHS premises.

The involvement of palliative care teams in the Hospital and the community should be sought (BASO Guidelines).

Palliative care provision:

Palliative care for breast cancer patients should be available as part of the NHS provision for their care: NCN cancer guidelines should specify this component of treatment, which can be purchased by PCTs via charities (eg local Hospices) or via Trusts. It is not acceptable to assume that a palliative care service funded by charitable means will have the capacity to respond to the needs of all patients referred by practitioners in the NHS. Breast Cancer Units should calculate their potential use of palliative care services, and include these costs in their negotiations with PCTs (see below)\(^{59,60}\).

The ideal provision of palliative care services might include:

- CNS in palliative care: ideally, available to attend the breast clinic for symptom management advice, patient and carer support. The palliative care nurse is thus introduced by and integrated as part of the breast care team.
- CNS in palliative care: available for ward consultations for in-patients with palliative care needs.
- CNS in palliative care: in community, for home visits to continue symptom review and psychological support, where needed.
- Consultant in palliative medicine: available to see breast cancer patients with more complex symptoms, either in combined breast clinic or via the consultant’s own OP clinic.
- Consultant in palliative medicine: availability to see patients with advanced disease on hospital wards or in their own homes, act as a resource to clinical nurse specialists, offer informal advice to breast care team.
- Attendance at breast cancer MDT, or liaison with breast care team following MDT, to discuss appropriate referrals.
Network wide guidelines exist for the management of certain core symptoms and situations in palliative care. These have been incorporated into a small A5 sized booklet and are distributed across the network. They are also available on the North of England cancer network website where other guidelines and links will be available.

www.cancernorth.nhs.uk

We also feel it can be helpful to give an explanation of some of the different terms often encountered when ‘palliative care’ is discussed.

Supportive Care

- “Umbrella” term for all services which help patient and family to cope with the condition and its treatment – from pre-diagnosis, through diagnosis and treatment, to cure, continuing illness or death and into bereavement
- Aims to help patient maximise benefits of treatment and to live as well as possible with the effects of the disease
- Should be given equal priority alongside diagnosis and treatment.

Supportive care includes:
- Self help and support
- User involvement
- Information giving
- Psychological support
- Symptom control
- Social support
- Rehabilitation
- Complementary therapies
- Spiritual support
- End of life and bereavement care

Palliative Care

- Part of, and embraces many elements of, supportive care.

Defined (NICE 2004) thus: “the active holistic care of patients with advanced progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with other treatments”.

Key features of palliative care

- Affirm life and regard dying as a normal process.
- Provide relief from pain and other distressing symptoms.
- Integrate the psychological and spiritual aspects of patient care.
- Offer a support system to help patients live as actively as possible until death.
- Offer a support system to help the family cope during the patient’s illness and in their own bereavement.

General Palliative Care is that care delivered by health professionals whose main role is not working with palliative care patients but who necessarily come across these patients in their work. This care is therefore delivered by a majority of healthcare professionals.
Specialist Palliative Care is delivered by professionals for whom the majority of their working role is in managing patients with palliative care needs. These professionals would therefore manage, or be advising in the care of, patients and their families whose needs are more complex, challenging, time consuming and refractory to usual input, and where this demand exceeds that which can reasonably be expected to be delivered by a professional whose main role is in another discipline.

End of Life Care

- An approach that enables the supportive and palliative care needs of both patient and family to be identified and met throughout the last phase of life and into bereavement.

Key features of end of life care

- Anticipation and management of deterioration in the patient's condition
- Advance care planning in accordance with patient preferences
- Patient choice about place of care and death
- Effective co-ordination of care across all teams and providers of care (in statutory, voluntary and independent sectors) who are involved in the care of patient and family

Care of the Dying

- Care of the patient and family in the last hours and days of life.
- Incorporates four key domains of care, physical, psychological, social and spiritual
- Supports the family through this phase and into bereavement.

References

- National Council for Palliative Care Palliative Care Explained (2007)
CLINICAL TRIALS

The Cancer Reform Strategy states that “in order to ensure that we build for the future of cancer services there is a need for increased support for research”. This statement underpins the need for promoting research to fill the gaps in the evidence and spreading good practice.

The NECN Research Networks will work with the Service Network to promote integration of research into routine practice.

Both NECN Research Networks will be meeting the performance based working proposals for the National Cancer Research Network (NCRN). This includes maintaining overall accrual and improving accrual into randomised controlled studies, (RCT’s) with the aim being to provide as wide reaching a portfolio as possible across the NECN. There is a need to ensure that the Networks portfolios are inclusive of trials for all disease groups and that there is an expansion of pre-malignancy and non-cancer screening trials. Both Networks believe it is important that patients within the NECN have equity of access to trials open.

- New initiatives to strengthen research into prevention of cancer are underway. The Research Networks will work with key stake holders and the Primary Care Research Networks to ensure that patients in the North East and Cumbria have access to these trials.
- The CRS states that there is funding for screening trials and the Research Networks will support the setting up and coordination of screening trials.
- The NCRN has an important role in identifying potential new therapies and making sure that clinical trials are undertaken in a timely manner. NCRN engages with Industry and NICE with the aim of maximising the impact of NCRN trials on subsequent NHS Practice. There will be further investment over the next 10 years into researching cures and treatments of the future. The Research Networks will ensure they maintain a wide reaching balanced portfolio and promote industry trials.
- Access to high quality information is a prerequisite for patients to be able to participate in decision making about their care and this includes research trials. All staff need to be aware of research portfolios so they can ensure they provide patients with relevant information.
- Reducing inequalities in equity of access to cancer trials.
- Promoting research proposals on cancer in equalities – encouraging more trials which include older people and ensuring that children and young adults are treated at centers where a complete portfolio of relevant trials is supported.
- NCRI will help fund research on data collected by the National Cancer Intelligence network (NCIN), facilitating a more informed analysis of cancer services.
- To ensure research is incorporated in World Class Commissioning for cancer.
- To work more closely with our Patient and Carer Group, particularly in relation to equity of access for patients to clinical trials. We hope they will be able to help us provide a patients perspective and help support us raise awareness.

The Cancer Reform Strategy supports the need for promoting integration of research into routine practice and the NECN Research Networks are keen to advance this concept.
AUDIT

Data on patients in the NHSBSP are collected as part of QA for the programme.

- Audit data should be collected on all patients with breast cancer.
- Measures should include basic demographics, treatment and outcomes.
- Individual Trusts retain the responsibility for data collection required to demonstrate adherence to prevalent cancer standards.
- Funding for collection of “BASO” data is not available from the NECN.

A network-wide audit will be agreed annually and the results discussed at the March NSSG meeting.
PATIENT SUPPORT GROUPS

BACUP
3 Bath Place,
Rivington St,
London
EC2A 3JR
Tel: 0171 696 9003 (Admin)
Tel: 0171 613 2121 (Info)
www.cancerbackup.org.uk

Cancerhelp
Cancer information Department
Cancer Research UK
P.O. Box 123
Lincoln’s Inn Fields
London WC2A 3PX
www.cancerhelp.co.uk

Cancer Relief Macmillan Fund
15-19 Britten St,
London
SW3 3TZ
Tel: 0171 351 7811
www.macmillan.org.uk

Cancerlink
17 Britannia St,
London
WC1X 9JN
Tel: 0171 833 2451
www.cancerlink.org


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## Appendix 1 – TNM Staging of Breast Cancer

### Staging of breast cancer

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tx</strong></td>
<td>Primary tumor cannot be assessed.</td>
</tr>
<tr>
<td><strong>T0</strong></td>
<td>No primary found.</td>
</tr>
<tr>
<td><strong>Tis</strong></td>
<td>In-situ ductal, lobular or Paget disease of the nipple only.</td>
</tr>
</tbody>
</table>
| **T1**           | T1mic: Microinvasion not larger than 0.1 cm in greatest dimension  
                   T1a: Tumor larger than 0.1 cm but not larger than 0.5 cm in greatest dimension  
                   T1b: Tumor larger than 0.5 cm but not larger than 1.0 cm in greatest dimension  
                   T1c: Tumor larger than 1.0 cm but not larger than 2.0 cm in greatest dimension |
| **T2**           | Tumor larger than 2.0 cm but not larger than 5.0 cm in greatest dimension |
| **T3**           | Tumor larger than 5.0 cm in greatest dimension |
| **T4**           | T4a: Extension to chest wall, not including pectoralis muscle  
                   T4b: Edema (including peau d’orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast  
                   T4c: Both T4a and T4b  
                   T4d: Inflammatory carcinoma |

<table>
<thead>
<tr>
<th>Pathologic classification (pN)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pNX</strong></td>
<td>Regional lymph nodes cannot be assessed (e.g., not removed for pathologic study or previously removed)</td>
</tr>
</tbody>
</table>
| **pN0**                       | No regional lymph node metastasis histologically, or only isolated tumor cells (ITC)  
                   (Note: ITCs are defined as single tumor cells or small cell clusters not larger than 0.2 mm) |
| **pN1**                       | pN1mi: Micrometastasis (larger than 0.2 mm but not larger than 2.0 mm)  
                   pN1a: Metastasis in one to three axillary lymph nodes  
                   pN1b: Metastasis in internal mammary nodes with microscopic disease detected by SLN dissection but not clinically apparent**  
                   pN1c: Metastasis in one to three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by SLN dissection but not clinically apparent. |
| **pN2**                       | pN2a: Metastasis in four to nine axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)  
                   pN2b: Metastasis in clinically apparent* internal mammary lymph nodes in the absence of axillary lymph node metastasis |
| pN3          | pN3a: Metastasis in ten or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm); or, metastasis to the infraclavicular lymph nodes  
               | pN3b: Metastasis in clinically apparent* ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph node(s); or, in more than three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent**  
               | pN3c: Metastasis in ipsilateral supraclavicular lymph nodes |

<table>
<thead>
<tr>
<th>AJCC Stage Groupings</th>
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</tr>
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<tbody>
<tr>
<td>Stage 0</td>
<td>Tis, N0, M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T0, N1, M0, T1*, N1, M0 , T2, N0, M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2, N1, M0, T3, N0, M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T0, N2, M0, T1, N2, M0, T2, N2, M0, T3, N1, M0, T3, N2, M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4, N0, M0, T4, N1, M0, T4, N2, M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>Any T, N3, M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T, Any N, M1</td>
</tr>
</tbody>
</table>
Appendix 2 – Algorithms for Management of Breast Cancer Treatment-Induced Bone Loss

Guidance for the management of breast cancer treatment-induced bone loss

[Diagram showing algorithms for managing bone loss with or without aromatase inhibitor use]
Algorithm 2b Postmenopausal adjacent treatment with aromatase inhibitors

- **High Risk**
- **Medium Risk**
- **Low Risk**

**Commencing aromatase inhibitor therapy**

- **All other patients**

**Measure BMD by axial DXA (spine and hip) within 3-6 months**

- **Low T-score < -2.0 or known vertebral fractures**
  - **Assess for secondary osteoporosis**
    - Calcium + vitamin D supplementation if clinically indicated
  - **Treat with bisphosphonates at osteoporosis doses and calcium + vitamin D supplementation**
  - **Repeat axial DXA after 24 months and/or monitor if deemed with biochemical markers after 6 months**

- **Low T-score < -1.0 but > -2.0**
  - **Lifestyle advice**
    - Calcium + vitamin D supplementation if clinically indicated

- **Both T-scores > -1.0**
  - **Lifestyle advice**
    - Measure patient
    - No further assessment unless clinically indicated

---

*Previous low trauma fracture, older age, family history, menopausal symptoms, cardiovascular disease, and other risk factors may also be used to identify and to risk stratify postmenopausal women who may benefit from a Claus or WHO BMD testing.*

*Bisphosphonates are available in oral and intravenous preparations, with long-term administration in a variety of disease settings.*

*Repeat BMD testing after 24 months of therapy to assess for changes.*

**Annual rate of bone loss of <0.5% at lumbar spine or total hip and/or T-score > -2.0**

- **Yes**
- **No**
Appendix 3 - Follow-Up Care After Treatment For Breast Cancer

This leaflet will explain your follow-up care. It is possible to transfer your follow-up care after your treatment has finished, please advise us if you wish to do so.

Follow-up appointments

You will be followed up in the clinic regularly for five years. During the first year, your appointments will be variable depending on your treatment. After the first year or when you finish treatment your appointments will be yearly. This appointment will include an examination by your team which will be your surgical, oncology or nurse team, a review of your medication and an opportunity to discuss any worries or concerns. If you have no further problems your care will be transferred to your general practitioner after five years of treatment.

If you are taking part in a clinical trial, or are under fifty years of age, your follow-up may be longer than five years.

Endocrine therapy/medication

If you are pre-menopausal you will usually be prescribed Tamoxifen tablets for five years. If you are post-menopausal you may be prescribed a different endocrine drug, i.e an aromatase inhibitor drug. Not everyone is suitable for this type of therapy and this will be discussed with you.

If you are prescribed an aromatase inhibitor drug i.e Anastrazole, Letrozole, Exemestane, (a type of hormone treatment sometimes used to treat post menopausal women with breast cancer) you will need to have a DEXA scan (a scan to check your bone mineral density) as these drugs can cause a reduction in bone thickness. This scan will be arranged by your hospital team or GP when you first start this medication and then may be repeated at two years and five years if necessary. You will be advised if you need further scans.

Your medication will be reviewed at your appointment but if you have any problems with your medication in between your appointment then contact your breast care nurse or GP.

Mammogram follow-up

An x-ray of your breasts (mammogram) will be carried out each year for five years. Your hospital team will arrange this. The breast unit will inform you of the results by letter within three weeks. After five years you will be offered mammograms on the National Breast Screening Programme every three years. Once you are over seventy years old you are still entitled to have a mammogram but you will have to organise this yourself by contacting your local breast screening unit or GP. Occasionally you may be offered other forms of radiology testing for example ultrasound or MRI, you will be advised if you require these tests.

If you are under fifty you may be discharged after 5 years or you may be reviewed yearly till you are fifty. Your hospital team will discuss this with you.
What symptoms do I need to look for between my appointments?

If you noticed any of the following symptoms then you should contact your breast care nurse, GP or hospital team for advice:

- If you develop any swelling in your arm/hand and are concerned you are developing lymphoedema
- Recent changes in the area of your surgery including rashes or spots that don’t go away
- New lumps at the site of your surgery
- New lumps in your armpits or neck
- New lumps or changes in the other breast or armpit

Any new or persistent changes in your general health that is unexplained and last for more than a few weeks, for example:

- Any new persistent shortness of breath or cough
- Any new persistent neck or back pains
- Any new persistent aches or pains

These symptoms may not be related to your previous breast problem but should be checked out if they are persistent.

Concern between appointments

If you have any other concerns or problems between your follow-up appointments contact your breast care nurse/key worker who will give you advice and if necessary bring your hospital appointment forward

Your breast care nurse/key worker is..........................................................

Contact number ..........................................................