NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Intensity modulated radiotherapy for treatment of breast cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of intensity modulated radiotherapy for the treatment of breast cancer.

Background

Breast cancer is the most common cancer found in women. In 2004 there were more than 44,000 women diagnosed with breast cancer in the UK. This corresponds to approximately 30% of all newly diagnosed cancers in women each year. In 2005, 12,400 women died of breast cancer in the UK. It is the second most common cause of cancer related deaths in women. Breast cancer can also occur in men with about 300 men diagnosed in the UK every year. The management of breast cancer in men is the same as in women although men are more likely to present with a more advanced stage of the disease.

Prognosis of breast cancer depends on the stage at which it is diagnosed. Breast cancer is classified according to the size of the primary tumour, the extent of spread to regional lymph nodes and whether there are distant metastases (known as the TNM [tumour, node, metastasis] classification), and may be grouped into four stages. Stage 0 describes ductal carcinoma in situ (DCIS), characterised by the presence of malignant cells in the breast ducts but with no evidence of invasion of the periductal connective tissues. Stages I to II are used to describe early breast cancer (or operable breast cancer) that has spread locally at the time of diagnosis and may or may not have spread to regional lymph nodes. Stage III denotes locally advanced (inoperable) disease and stage IV denotes metastatic disease.

Between 16 and 20% of women initially presenting with breast cancer have locally advanced disease with distant metastases, leaving around 80% of new diagnoses with early disease. Approximately 20-30% of women diagnosed with early or localised breast cancer will eventually relapse and develop metastatic breast cancer.

Treatment for early disease can be divided into primary treatment, which is surgical (removal of the tumour), and adjuvant treatment, which may include radiotherapy and/or cytotoxic chemotherapy after removal of the primary cancer by surgery. Many women may also receive hormone therapy alongside cytotoxic chemotherapy regimens. Adjuvant therapy is prescribed with the intention of eradicating clinically undetectable disease that could not be removed by surgery and reducing local recurrence.

Adjuvant radiotherapy is delivered to the breast and chest wall and also to lymph nodes. The British Association of Surgical Oncology (BASO) recommends radiotherapy to the breast and chest wall for women with DCIS or invasive breast disease following breast conserving surgery and axillary radiotherapy for node positive disease in women who have not undergone axillary lymph node clearance. Radiotherapy may also be considered following mastectomy for invasive disease. The Scottish Intercollegiate Guideline Network (SIGN) recommends supraclavicular radiotherapy for women with 4 or more positive axillary lymph nodes.

Currently radiotherapy is delivered using 3-dimensional conformal radiotherapy (3D CRT). It is delivered by non-modulated beams, which can be shaped geometrically to avoid irradiating normal surrounding tissue. Side effects of radiation include acute skin toxicity, lumpiness of the breast, poor appearance, pain and swelling of the arm.

The technology

Intensity modulated radiotherapy (IMRT) is the term applied to any radiotherapy where the beam of radiation is not uniform across the field to be irradiated, but consists of beamlets of varying intensity. IMRT is delivered by attaching a multileaf collimator (MLC) to a linear accelerator or by using compensators which are designed and constructed for individual patients. The modulation of the radiation beam in IMRT allows precise delivery to cancerous tissue while sparing surrounding normal tissue from exposure. It is therefore suitable for the delivery of radiation to locations where diseased tissue is located close to vital structures and decreases the side-effects of radiation.

IMRT systems available in the UK include the following models:

Manufacturer	Model
Elekta	Axesse Precise Treatment System Synergy Synergy Platform
Varian	Clinac Trilogy
Siemens	Artiste Primus Oncor Impression Oncor Avant-garde Oncor Expression Simtec
TomoTherapy	Hi-Art

The system requires essential software that allows the physician to determine the dose and distribution of radiation. IMRT makes use of ‘inverse planning’ where the clinician determines the dose and distribution of radiation and

computer software works backwards from this to determine the direction and intensity of the beams required to achieve this. IMRT can also be delivered using 'forward planning'.

Systems that combine the ability to simultaneously image can improve the accuracy of targeting of radiation by compensating for movement of body structures. Imaging also allows verification of the actual dose delivered and allows for compensation for any deviation from planned dose in subsequent sessions.

Quality assurance (QA) is an important component of IMRT. It consists of checks on the precision of the equipment and verification that the prescribed dose and dose distribution have been planned and are being delivered. For some cancers QA is less time consuming as the QA procedure can be standardised for the class of tumour, but for unusual or complex cancers it needs to be individualised.

Intervention	Intensity modulated radiotherapy
Population(s)	People with breast cancer for whom radiotherapy is appropriate.
Standard comparators	3-dimensional conformal radiotherapy (conventional radiotherapy)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

	This should include costs for specialist staff and quality assurance.
Other considerations	If evidence allows, the appraisal will seek to identify subgroups of individuals for whom the technology is particularly clinically and cost-effective. Such subgroups could be based on the type of surgery (mastectomy or breast conserving), stage of cancer or need for lymph node irradiation.
Related NICE recommendations	Related Technology Appraisals: TA 30 Guidance on the use of taxanes for the treatment of breast cancer, September 2001 TA 34 Guidance on the use of trastuzumab for the treatment of advanced breast cancer, March 2002 TA 54 Guidance on the use of vinorelbine for the treatment of advanced breast cancer, December 2002 TA 62 Guidance on the use of capecitabine for the treatment of locally advanced or metastatic breast cancer, May 2003 TA 107 Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer, August 2006 TA 108 Paclitaxel for the adjuvant treatment of early node-positive breast cancer, September 2006 TA 109 Docetaxel for the adjuvant treatment of early node-positive breast cancer, September 2006 TA 112 Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer, November 2006 TA 116 Gemcitabine for the treatment of metastatic breast cancer, January 2007 TA 147 Bevacizumab for the first-line treatment of metastatic breast cancer (terminated appraisal), June 2008 Related Guidelines: Cancer service guidance. Improving outcomes in breast cancer, August 2002

	CG 41 Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of CG14), October 2006 Guidelines in development Breast cancer (advanced): diagnosis and treatment, Expected February 2009 Breast cancer (early & locally advanced): diagnosis and treatment, Expected February 2009 Related Interventional Procedures: IPG089 Interstitial laser therapy for breast cancer, September 2004 IPG147 Endoscopic axillary lymph node retrieval for breast cancer, December 2005