NHS England

# Clinical Commissioning Policy Proposition:

# Radiotherapy after primary surgery for breast cancer

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# Clinical Commissioning Policy Proposition: Radiotherapy after primary surgery for breast cancer

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## Plain Language Summary

The policy proposition aims to confirm NHS England's commissioning approach to radiotherapy for patients with breast cancer after primary surgery.

NHS England currently commissions radiotherapy after primary surgery for breast cancer, but does not specify how the dose of radiation should be delivered. The dose can be split into a number of fractions delivered on separate days. There is currently variation in how many fractions patients with breast cancer receive after surgery.

NICE issued pathway guidance in the treatment of 'early and locally advanced breast cancer: adjuvant therapy' in September 2013. In this guidance, 15 fractions of radiotherapy (excluding boost) are recommended and are known to be highly effective in the majority of patients. This acknowledges the additional need beyond 15 fractions for boosts to the tumour bed (when required) and those patients that may present with clinical presentations which will require, after discussion with MDT and the patient, treatment outside the pathway.

Delivering the dose of radiation in no more than 15 fractions, rather than conventional schedules of up to 25 fractions, will prevent unnecessary travel, discomfort and inconvenience for many patients with no compromise to clinical effectiveness.

NHS England has concluded that there is sufficient evidence to support a proposal to routine commission of 15 fractions of radiotherapy for patients with breast cancer after primary surgery as standard treatment.

## 1. Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission 15 fractions of radiotherapy (excluding boost) after primary surgery for breast cancer.

This document also describes the proposed criteria for commissioning, proposed governance arrangements and proposed funding mechanisms.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether 15 fractions for patients with breast cancer after primary surgery will be routinely commissioned is planned to be made by NHS England by June 2016 following a recommendation from the Clinical Priorities Advisory Group.

## 2. Proposed Intervention and Clinical Indication

External beam radiotherapy (EBRT) is a component of standard practice in the treatment of breast cancer.

NICE issued pathway guidance in the treatment of 'early and locally advanced breast cancer: adjuvant therapy' in September 2013, recommending the use of EBRT at a total dose of 40 Gy in 15 fractions as standard practice for patients with breast cancer after primary surgery (including breast conserving surgery or mastectomy).

40 Gy in 15 fractions (excluding boost) is recommended for the majority of patients following primary surgery (breast conserving surgery or mastectomy) for breast cancer. Delivering the dose of radiation in no more than 15 fractions, rather than conventional schedules of up to 25 fractions, will prevent unnecessary travel, discomfort and inconvenience for many patients with no compromise to clinical effectiveness.

## 3. Definitions

External beam radiotherapy (EBRT) is delivered by a linear accelerator (linac), which focuses high-energy radiation beams onto the area requiring treatment. External beam radiotherapy is completely painless.

The radiation dose is split into a number of fractions delivered on separate days.

The fractionation schedule describes the number of fractions of the treatment.

## 4. Aim and Objectives

This policy proposition aims to define NHS England's commissioning position on radiotherapy fractionation schedules after primary surgery for breast cancer as part of the treatment pathway for patients with breast cancer.

The objective is to ensure evidence based commissioning with the aim of improving outcomes for patients with breast cancer.

## 5. Epidemiology and Needs Assessment

Breast cancer is a common cancer in the UK accounting for 30% of cancer in women. In 2011, 41,523 women were diagnosed with breast cancer in England and 9,702 women died of breast cancer (Cancer Research UK).

There are higher age standardised prevalence rates in Dorset and South East London, which both have 10 year prevalence rates at over 450 per 100,000 against the national average of around 420 (NCIN, 2006).

40% of patients whose cancer is cured received radiotherapy. In 2013, around 31,000 patients with breast cancer received radiotherapy as part of their treatment (RTDS).

In the first quarter of 2015, 88% of breast radiotherapy episodes received no more 15 fractions as the core treatment (RTDS).

## 6. Evidence Base

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commission of 15 fractions of radiotherapy for patients with breast cancer after primary surgery as standard treatment.

This evidence review looked at effectiveness and safety of use of 15 fractions as the core schedule (excluding boost) compared to other fractionation regimes in breast cancer.

**Summary:**
There is level 1 evidence that hypo-fractionated radiotherapy (HFRT), with 40 Gy delivered in 15 fractions over 3 weeks:
- has equivalent relapse rates as conventionally fractionated radiotherapy (CFRT), with 50 Gy over 25 fractions;
- have better distance relapse rates and survival rates than CFRT;
- reduces the risk of skin reactions and changes in breast appearance;
- in direct care delivery cost comparison, the cost of 15 fraction was less than that of 25 fractions.

None of the trials directly compare 15 fractions with other HFRT regimes. Hence, it is difficult to form an opinion about comparative efficacy of various hypofraction regimes.

**Detailed summary:**

Efficacy
Whole breast radiotherapy is used following either breast conserving therapy or a mastectomy with an intention to improve survival and reduce recurrences. The clinical efficacy of such treatments is measured in terms of the relapse rates, survival rates and toxicity rates. For the purpose of comparison, these rates are mapped to Cox proportional hazard regression model, which allows two fractional regimes to be compared with a hazard ratio (HR). With CFRT placed in the denominator, a HR less than 1 favours HFRT. Majority of evidence base is from the following large randomised control trials comparing

different HFRT regimes with CFRT:
• START pilot (comparing 39 Gy in 13 fractions and 42.9 Gy in 13 fractions over 5 weeks)
• START A (comparing 41.6 Gy in 13 fractions and 39 Gy in 13 fractions over 5 weeks)
• START B randomised control trial (comparing HFRT 40 Gy in 15 fractions over 3 weeks with CFRT 50 Gy in 25 fractions over 5 weeks)
• Whelan et al, 2002 (comparing 42.5 Gy in 16 fractions over 5 weeks)
• UK FAST (30 Gy and 28.5 Gy in 5 fractions over 5 weeks).
Haviland et al, 2013 publication on START B randomised control trial (RCT) with 10-years follow-up results provides most relevant evidence for 15 fractions. Data from four large RCTs and six smaller 6 smaller RCTs (< 500 participants), have been combined in two meta-analyses (James et al., 2010; Zhou et al, 2015).
All these trials are non-blinded, with the exception of the photo assessors used to determine any change in breast appearance. The study population was largely women with early stage, node negative, operable invasive breast cancer. Whelan et al, 2002 only included women treated with lumpectomy. Clinical equipoise was not maintained in most trials as patients could receive additional boost treatment, at the discretion of treating clinician. During the START B trial 43% of the patients received a 10 Gy boost over 5 fractions. This was evenly distributed over the control and trial arms.

**Clinical effectiveness:**
This was reported in terms of relapse rates and overall survival rates.
Relapse rates:
Relapse rates are reported as local (relapse in the breast or chest wall) and distance (relapse in non-irradiated organs). After 10 years, START B found no statistically significant difference for local relapse rates between HFRT and CFRT but found the distance relapse rates were lower with HFRT. This equivalence of local relapse rates was found in all RCTs and meta-analysis on the four large RCTs. The START A trial found that distance relapse rates were equivalent between HFRT and CFRT.

**Survival rates:**
The START B trial reported a significant improvement in the overall survival rate of HFRT (40 Gy in 15 fractions) with a HR 0.80 (p=0.042) after 10 years (Haviland et al., 2013). The other large RCTs (START Pilot, START A and Whelan et al, 2002) report similar survival rates compared to CFRT (50 Gy over 25 fractions). A meta-analysis of all four key RCTs comparing all hypofractionation schedules compared to CFRT found no statistically significant improvement in overall survival rates at 5 years, HR 0.89 (p=0.16), (James et al., 2010).

**Safety outcomes:**
Acute and late toxicities are measured by looking for change in breast appearance, skin reddening (telangiectasia) and oedema on the breast or arm. Late toxicities also include rates of rib fractures, lung fibrosis and ischaemic heart disease.

**Changes in skin and breast appearance:**
START B reported in both their 5 year and 10 year follow up that the risk of skin toxicities and change in breast appearance was lower in HFRT than in CFRT. In particular the hazard ratios for breast shrinkage, telangiectasia and breast oedema all favoured HFRT. Other toxicities demonstrated no differences between HFRT and CFRT. Other HFRT regimes also demonstrated reduced toxicity levels. For example, START A gave evidence

for reduced rates of skin toxicities in the 39 Gy arm, but not the 41.6 Gy arm. A meta-analysis of 7 RCTs, comparing fractions of 2.5-3.0 Gy, found a HR for 0.50 (p=0.02) for grade 2/3 skin toxicity.

**Other toxicities:**
In both the START A and START B trials, there was no statistically significant difference in the rates of rib fracture, lung fibrosis and ischaemic heart disease after 10 years. However, experts have raised concerns about the long term risks, following HFRT. Appelt et al, 2012 mathematically modelled long term risk of mortality from radiation induced heart disease. 40 Gy /15 fractions, 39 Gy /13 fractions and 42.6 Gy / 16 fractions appear to have more favourable radiation doses to the heart, than 50 Gy /25 fractions.

**Cost effectiveness:**
Three studies reviewed in meta-analysis (Zhou et al., 2015) and Rajagopalan et al, 2015 have compared the total costs of 16 fractions HFRT to those of CFRT. They have all concluded that HFRT to be 10% to 30% lower cost than CFRT, depending on assumptions and specifics of the healthcare. None of the studies were based on the UK healthcare system.

## 7. Proposed Criteria for Commissioning

NHS England commissions radiotherapy after primary surgery for breast cancer.

40 Gy in 15 fractions (excluding boost) is recommended for the majority of patients following primary surgery (breast conserving surgery or mastectomy) for breast cancer. At least 80% of patients for whom radiotherapy is indicated as part of treatment for breast cancer should receive no more than 15 fractions (excluding any boost).

Exclusion criteria: under certain clinical conditions, other fractionation schedules may be appropriate.

Reasons for all individual treatments exceeding 15 fractions must be recorded by the trust. Providers should be aware that NHSE may wish to audit any significant variation in the rates of treatment courses exceeding 15 fractions.

## 8. Proposed Patient Pathway

The service specifications for radiotherapy (B01/S/a) describe the detail of the care pathways for this service.

Radiotherapy is part of an overall cancer management and treatment pathway. Decisions on the overall treatment plan should relate back to an MDT discussion and decision.

Radiotherapy in the NHS in England is delivered by 50 centres; all centres provide radiotherapy for breast cancer. If EBRT is indicated, the patient is referred to a clinical oncologist for assessment, treatment planning and delivery of radiation fractions. Each fraction of radiation is delivered on one visit, usually on an outpatient basis.

## 9. Proposed Governance Arrangements

The service specifications for radiotherapy (B01/S/a) describes the governance arrangements for this service.

In particular, it is imperative that the radiotherapy service is compliant with the Ionising Radiation (Medical Exposure) Regulations (IR(ME)R) 2000.

Clinical Governance systems and policies should be in place and integrated into organisational governance with clear lines of accountability and responsibility for all clinical governance functions and Providers should produce annual Clinical Governance reports as part of NHS Clinical Governance reporting system.

## 10. Proposed Mechanism for Funding

Radiotherapy planning and delivery is a national tariff service covered by payment by results and referenced in the radiotherapy service specification. It should be funded via the relevant local specialised commissioning team.

## 11. Proposed Audit Requirements

Radiotherapy providers must submit their activity to the national Radiotherapy Dataset (RTDS) on a monthly basis. Reasons for all individual treatments exceeding 15 fractions must be recorded by the trust. Providers should be aware that NHSE may wish to audit any significant variation in the rates of treatment courses exceeding 15 fractions.

The Quality System and its treatment protocols will be subject to regular clinical and management audit.

See radiotherapy service specifications B01/S/a for the most up to date audit requirements.

## 12. Documents That Have Informed This Policy Proposition

Clinical commissioning policy statement: radiotherapy after primary surgery for breast cancer (B01/PS/d), NICE pathway: early and locally advanced breast cancer: adjuvant therapy, and NICE clinical guideline 80: ealry and locally advanced breast cancer: diagonis and treatment.

## 13. Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it continues to be routinely commissioned (expected by June 2016).