NHS England



# Clinical Commissioning Policy Proposition: Proton Beam Therapy for Cancer of the Prostate

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**Prepared by NHS England Specialised Services Clinical Reference Group for Radiotherapy**

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# 1 Executive Summary

## Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

## Plain Language Summary

This policy proposition aims to set out the NHS England Commissioning position on the use of Proton Beam Therapy for Cancer of the Prostate.

A cancer arising on the prostate gland (Prostate Cancer) is a common cancer in men, and can be cured by treatment targeted at the prostate alone when it has not spread to other parts of the body. Radiotherapy with photons (X-Rays) is one of the most effective treatments for localised Prostate Cancer and does so with very low rates of late side effects when delivered with the most modern techniques.

Proton Beam Therapy uses charged particles called protons instead of photons (X-Rays). This has some theoretical advantages over conventional radiotherapy in certain groups of patients, such as young children due to an increased ability to deliver the radiation dose preferentially to the cancer target compared to surrounding healthy tissues and the rest of the patient. It is expensive however compared to conventional radiotherapy. In certain clinical situations there is sufficient evidence of improved clinical outcomes to justify that expense. In other situations such as in the treatment of Prostate Cancer, despite being used extensively in other countries,

particularly in the USA, there has been no evidence to suggest significant improved clinical outcomes in terms of either better cancer control or reduced late side effects.

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of Proton Beam Therapy for localised Prostate Cancer.

## 2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission Proton Beam Therapy for Prostatic Cancer.

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 Proton Beam Therapy for Prostatic Cancer will be routinely commissioned is planned to be made by NHS England by June 2016 following a recommendation from the Clinical Priorities Advisory Group.

## 3 Proposed Intervention and Clinical Indication

Radiotherapy is a highly effective therapy for localised Cancer of the Prostate. There are a series of localised treatment options including active monitoring, radical prostatectomy (surgery to remove the prostate), conventional radiotherapy and brachytherapy (where small radioactive seeds or implants are placed into the prostate gland). Proton Beam Radiotherapy is a new potential alternative to conventional radiotherapy. It is available in some other countries.

NHS England will not routinely commission Proton Beam Radiotherapy for localised Cancer as there is insufficient evidence of any improved clinical outcomes or cost effectiveness when compared to high quality conventional radiotherapy

## 4 Definitions

**Cancer of the Prostate**: is the most common cancer in men. Where the cancer is only in the prostate gland and has not spread into the surrounding tissues or to other parts of the body, it is also called localised prostate cancer.

**Proton Beam Radiotherapy (PBT):** is the use of high-energy proton beams used instead of conventional X-Rays to treat cancer. It is capable of being precisely targeted using imaging to match a high dose treatment volume to the shape and position of the tumour area within the body. Because of its characteristic properties to stop at a precise depth in tissue with no dose beyond that point, it can deliver treatment with significantly reduced volumes of unnecessarily irradiated normal tissues. It is given in a number of daily treatments, or fractions, over several weeks.

PBT is significantly more expensive that conventional radiotherapy and currently is only commissioned by the NHS for certain rare cancers especially those in children and skull base or spinal cancers where there is sufficient evidence of improved outcomes to justify it.

**Intensity Modulated Radiotherapy (IMRT):** IMRT is an advanced form of conventional radiotherapy given from outside the body to target tumours inside the body. It uses many small beams of varying strength to shape the dose of radiation to match the tumour and is very precise. By doing this it allows a reduction of radiation dose to healthy surrounding tissues and so reduces late side effects of treatment.

**Image Guided Radiotherapy (IGRT):** IGRT is the way radiotherapy is targeted precisely within the body. Images from different types of scan such as CT and MRI are used to plan where the tumour and surrounding normal health tissues are situated and are used to assist in delivering the treatment. Imaging devices mounted on the radiotherapy equipment can also match the plan to the position of the patient and tumour each day during treatment to ensure the treatment is delivered accurately.

PSA: One of the best indicators of disease activity in patients with prostate cancer is the measurement of a protein produced by the prostate called Prostate Specific Antigen (PSA) in the blood. Where this biochemical level remains low after treatment it correlates with local control of the disease. Where it rises this is known as biochemical failure and is a marker of local progression of the disease.



## 5 Aims and Objectives

This policy proposition considered: The NHS England commissioning position on the use of Proton Beam Therapy for Cancer of the Prostate

The objectives were to: set out the NHS England commissioning position on the use of Proton Beam Therapy for Cancer of the Prostate

## 6 Epidemiology and Needs Assessment

Prostate cancer is the most common cancer in men affecting 1 in 12 men, and makes up 26% of all male cancer diagnoses in England. In 2011, 35,567 men were diagnosed with prostate cancer, with a corresponding Age Standardised Rate (ASR) of 106.7 per 100,000 population (95% Confidence Interval 105.6-107.8). There were 9,123 deaths from prostate cancer in 2011 in England, translating to a mortality rate of 23.8 per 100,000 population (95% Confidence Interval 23.3-24.4) (ONS, 2014).

Prostate cancer is predominantly a disease of older men (aged 65–79 years) but around 25% of cases occur in men below the age of 65. Increased incidence and mortality is observed in men of black African or Caribbean family origin compared with white Caucasian men (NICE, 2014).

Treatment for localised prostate cancer is one of the most common curative indications for conventional radiotherapy in the UK. Conventional radiotherapy with IMRT and IGRT is very precise and considered standard care. In 2014/15 15,710 treatment episodes were delivered in England. Current NICE guidance recommends 37 daily treatment fractions for prostate radiotherapy.

## 7 Evidence Base

**NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.**

A full evidence search was conducted in November 2014. A further search was conducted in March 2016. No further evidence relevant to the questions addressed in the original evidence review was found.

**Clinical effectiveness**

- A systematic review which covered a variety of potential indications for proton beam therapy included three randomised controlled trials of proton beam therapy for prostate cancer [1]:
    - The first trial randomised participants between proton beam therapy and photon treatment. There were no significant differences in overall survival, disease-specific survival, total recurrence-free survival or local control between the two arms.

    - The second trial randomised participants between two doses of proton beam therapy. Overall survival was similar for the two groups, but rates of biochemical failure were higher for the low dose group, and more of these patients subsequently required androgen deprivation [the use of drugs to reduce the circulating levels of male hormones in association with radiotherapy is now accepted as a standard of care in some patient groups to achieve best clinical outcomes] in association with radiotherapy for recurrence.
  - The third trial compared five different proton beam therapy fractionation and dose regimes. Rates of biochemical failure were similar in the five arms.

- The review also included three non-randomised studies
  - The first study reported quality-of-life data from men who had received either proton beam therapy or IMRT. There were no differences for most measures, but the men who received proton beam therapy had more rectal urgency and frequent bowel movements.
  - The second study compared men who had received IMRT, proton beam therapy and three-dimensional conformal [an older method of delivering radiotherapy that accurately shapes the radiotherapy dose to the tumour] photon radiotherapy. Each treatment had a different pattern of adverse effects, with none emerging as safer.
  - The third study reported no significant differences in further cancer treatment, urinary incontinence, erectile dysfunction or hip fracture in men who had received IMRTand proton beam therapy. Those who had proton beam therapy were more likely to experience gastrointestinal morbidity.
- We found one further controlled study which reported no differences in gastrointestinal or genitourinary late side effects between men treated with proton beam therapy and intensity-modulated photon radiotherapy.

**Cost effectiveness**

- A systematic review of the cost effectiveness of radiotherapy for prostate cancer included two analyses:

- The first reported a comparison of proton beam therapy andIMRT. The authors estimated that the incremental cost per quality-adjusted life year of proton beam therapy was US$63,578 (£42,400) for a man of 70 years and US$55,726 (£37,200) for a man of 60 years. These costs are above the thresholds for NHS treatment.
- The second study compared the cost effectiveness of proton beam therapy, stereotactic body radiotherapy and IMRT. Proton beam therapy was more expensive and produced lower quality of life than stereotactic body radiotherapy. Compared with IMRT, proton beam therapy had a cost per quality-adjusted life year of US$36,344,000 (£24,230,000).

**Activity and cost:** No cost or activity data were available.

**Equity:** No specific equity issues were identified.

**Summary and Conclusions**

Despite the high prevalence of the diagnosis, the evidence about the effectiveness of proton beam therapy for prostate cancer is far from conclusive:

Shipley et al's (1995) trial compares a higher radiation dose delivered with protons with a lower dose delivered with photons.[2] It indicates that more proton radiation does not improve outcomes but gives rise to more adverse effects.

Zeitman et al's (2010) trial is a comparison on two doses of proton beam therapy and therefore does not address the central uncertainty about the technique's effectiveness relative to other forms of radiotherapy. It suggests higher doses are more effective.[3]

Kim et al's (2013) trial was too small to reach useful conclusions and in any case was also a comparison of different proton beam therapy regimes.[4]

Hoppe et al ( 2014) reported slightly lower rates of side effects with proton beam therapy than intensity-modulated photon radiotherapy.[5] However, this study was an unrandomised comparison of two cohorts not assembled with this hypothesis in

mind, and was confounded by differences between the men in each cohort.

Gray et al's (2013) study had the same drawbacks as Hoppe et al's. It reported different patterns of adverse effects from different forms of radiotherapy, with no technique emerging as least toxic. [6]

Sheets et al (2012) indicated no significant differences in toxicity, apart from a higher risk of gastrointestinal adverse effects after proton beam therapy than after intensity-modulated photon radiotherapy.[7]

Fang et al's study indicates no advantages from proton beam therapy.[8]

The analyses of cost effectiveness are based on this insecure and inconclusive evidence of the relative effectiveness and safety of proton beam therapy. They do not indicate that the treatment is cost effective.

## 8 Proposed Criteria for Commissioning

Not Applicable

## 9 Proposed Patient Pathway

Not applicable

## 10 Proposed Governance Arrangements

Not applicable

## 11 Proposed Mechanism for Funding

Not applicable

## 12 Proposed Audit Requirements

Not applicable

## 13 Documents That Have Informed This Policy Proposition

There are no relevant UK documents. The American Society of Therapeutic Radiology has however issued an ASTRO Model Policy on Proton Beam Therapy in which Prostate Cancer treatment with proton beam therapy is not supported except

within trials or registration studies, as there is a need for more evidence.

https://www.**astro**.org

## 14 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 is routinely or non-routinely commissioned (expected by May 2016).

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