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Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Commissioning Policy: CP01

Brachytherapy for the Treatment of Localised Prostate Cancer

Interim Policy until 31st March 2021

Version 5.0

Document information	
Document purpose	Interim Policy
Document name	Brachytherapy for the treatment of localised prostate cancer
Author	Welsh Health Specialised Services Committee
Publication date	Interim Policy until March 2021
Commissioning Team	Cancer & Blood
Target audience	Chief Executives, Medical Directors, Directors of Finance, Radiographers, Oncologists, Medical Physics, Urologists, Cancer Services
Description	NHS Wales routinely commission this specialised service in accordance with the criteria described in this policy
Document No	CP01
Review Date	March 2021

Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) commission brachytherapy for people with localised prostate cancer in accordance with the criteria outlined in this document until 31st March 2021.

In creating this document WHSSC has reviewed this clinical condition and the options for its treatment. It has considered the place of brachytherapy for localised prostate cancer in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy.

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy.

1. Introduction

This policy has been developed for the planning and delivery of brachytherapy for localised prostate cancer for people resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) until 31st March 2021 and applies to residents of all seven Health Boards in Wales.

1.1 Plain Language Summary

The prostate is a gland. It is usually the size and shape of a walnut and grows bigger as you get older. It sits underneath the bladder and surrounds the urethra, which is the tube that carries urine (wee) out of the body. The prostate's main job is to help make semen – the fluid that carries sperm.

Prostate cancer can develop when cells in the prostate start to grow in an uncontrolled way. Some prostate cancer grows too slowly to cause any problems or affect how long you live. Because of this, many people with prostate cancer will never need any treatment. But some prostate cancer grows quickly and is more likely to spread. This is more likely to cause problems and needs treatment to stop it spreading.

Prostate cancer that is contained inside the prostate (called localised prostate cancer or early prostate cancer) does not usually cause any symptoms. But some people might have some urinary problems. These can be mild and happen over many years and may be a sign of a benign prostate problem rather than prostate cancer.

Most people with early prostate cancer do not have any signs or symptoms. One reason for this is the way the cancer grows. Early symptoms tend to occur if the cancer grows near the tube you urinate through (the urethra) and presses against it. Since prostate cancer usually starts to grow in a different part (usually the outer part) of the prostate, early prostate cancer does not often press on the urethra and cause symptoms.

If prostate cancer breaks out of the prostate it is described as locally advanced prostate cancer. If it spreads to other parts of the body it is described as advanced prostate cancer.

There are a variety of treatment options for prostate cancer, including:

- Active Surveillance: monitoring slow-growing localised prostate cancer, rather than treating it straight away. The aim is to avoid or delay unnecessary treatment and its side effects.
- Surgery may be a treatment option for people with localised prostate cancer.
- External beam radiotherapy uses high energy X-ray beams to treat prostate cancer.

- Low dose rate brachytherapy involves implanting tiny radioactive seeds into your prostate gland. Radiation from the seeds destroys cancer cells in the prostate. High dose-rate brachytherapy is a type of internal radiotherapy used to treat prostate cancer. You may have brachytherapy on its own or together with external beam radiotherapy.

1.2 Aims and Objectives

This policy aims to define the commissioning position of WHSSC on the use of brachytherapy for people with for localised prostate cancer.

The objectives of this policy are to:

- ensure commissioning for the use of brachytherapy is evidence based
- ensure equitable access to brachytherapy for people with for localised prostate cancer
- define criteria for people with prostate cancer to access treatment
- improve outcomes for people with prostate cancer.

1.3 Epidemiology

Prostate cancer is the most commonly occurring cancer for men in Wales with 2760 cases reported for 2016 with highest incidence observed in men aged 70 – 80. Over the last decade prostate cancer incidence has increased by 4% and is projected to rise significantly by around 12% by 2035. It account for around 12% of cancer associated deaths in men (the second most common cause). 88% of prostate cancer patients in Wales present with non metastatic disease and may be potentially eligible for curative treatment.

Using figures from the UK Prostate Cancer National Audit[1] it is possible to estimate the potential likely demand for brachytherapy. In England 9% of patients receiving radiotherapy for prostate cancer receive brachytherapy. If a similar proportion of Welsh patients were to receive brachytherapy that would equate to 57 patients (9% of the total number of patients receiving radiotherapy in Wales of 631).

1.4 Current Treatment

Non-metastatic prostate cancer may be managed using a number of different treatment options all given with curative intent. These include external beam radiotherapy, surgery and brachytherapy. All options are generally thought to be equally efficacious from a disease control perspective (i.e. cure rate) but each has its own distinctive profile with regard to logistics of delivery, short and long term side effects.

[1] National Prostate Cancer Audit

Patients are counselled at the time of diagnosis regarding the pros and cons of each treatment choice. Invariably patients will have a preferred treatment option and this together with the patients' disease characteristics, baseline fitness (and co- morbidities) guide treatment selection.

1.5 Proposed Treatment

Brachytherapy is delivered using radioactive isotopes (usually Iodine 125 or Iridium 192) either as a permanent radioactive seed implant (LDR, Low Dose Rate Brachytherapy) or as a temporary implant with the radioactive source being removed at the end of the procedure (HDR, High Dose Rate Brachytherapy).

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the evidence of brachytherapy for patients with localised prostate cancer. We have concluded that there is enough evidence to fund the use of brachytherapy, within the criteria set out in section 2.1.

1.7 Relationship with other documents

This document should be read in conjunction with the following documents:

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Prostate Cancer: diagnosis and management. Nice Guideline NG131. 9 May 2019.

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of brachytherapy for people with localised prostate cancer in accordance with the criteria identified in this policy.

2.1 Inclusion Criteria

WHSSC will fund brachytherapy to treat localised prostate cancer for:

- low risk patients or patients with 1 intermediate risk factor only: brachytherapy (LDR or HDR) as monotherapy may be offered;
- patients with intermediate or high risk localised prostate cancer: brachytherapy (LDR or HDR) may be offered (in combination with EBRT).

The risk groups for prostate cancer are defined in table 1.

Table 1: Prostate cancer risk stratification

Level of Risk	PSA		Gleason Score		Clinical Stage
Low Risk	<10 ng/ml	and	s6	and	T1 to T2a
Intermediate Risk	10-20 ng/ml	or	7	or	T2b
High Risk[i]	>20 ng/ml	or	8-10	or	≥T2c
Abbreviations: PSA, Prostate-Specific Antigen					
[i] High-risk localised prostate cancer is also included in the definition of locally advanced prostate cancer.					

Source: NICE guideline NG131[2]

2.2 Exclusion Criteria

Brachytherapy alone should not be offered to people with high risk localised prostate cancer.

2.3 Continuation of Treatment

Brachytherapy is administered as a single, one-off treatment.

2.4 Acceptance Criteria

The service outlined in this specification is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

[2] Overview | Prostate cancer: diagnosis and management | Guidance | NICE

2.5 Patient Pathway (Annex i)

- Referral from secondary care urology surgeon to the Early Prostate Cancer Supra Regional MDT (at University Hospital Wales (UHW) for South Wales patients).
- Patients suitable for brachytherapy will be referred to the brachytherapy centre.
- Follow up at brachytherapy centre and discharge back to local urology services.
- EBRT delivered locally by each health board for its patients.

2.6 Designated Centres

- Velindre Cancer Centre
  Velindre Road
  Whitchurch
  Cardiff
  CF14 2TL

- The Christie NHS Foundation Trust
  Wilmslow Road
  Manchester.
  M20 4BX

- Queen Elizabeth Hospital
  University Hospitals Birmingham NHS Foundation Trust
  Mindelsohn Way
  Edgbaston, Birmingham
  B15 2GW

2.7 Exceptions

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If the patient wishes to be referred to a provider outside of the agreed pathway, and IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

2.8 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties.

2.9 Responsibilities

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinician considering treatment should:

- discuss all the alternative treatment with the patient;
- advise the patient of any side effects and risks of the potential treatment
- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Evidence

WHSSC is committed to regularly reviewing and updating all of its commissioning policies based upon the best available evidence of both clinical and cost effectiveness.

3.1 HDR monotherapy for low to intermediate risk disease

In a systematic review of the literature published in 2017, 15 publications were identified comprising of 3546 patients. The authors combined the data to look at clinical outcomes (biochemical disease control) and toxicity data. A variety of dose and fractionation schedules were described, including 19.0 Gy as a single fraction to 54.0 Gy in nine fractions. Biochemical control rates ranged from 66 to 100% in low-risk, 63 to 98% in intermediate-risk and 81-93% in high-risk patients. Late grade 3 genitourinary and gastrointestinal toxicity was 0-16% and 0-2%, respectively. The reported potency preservation rates ranged from 60 to 90%. These clinical outcomes compare very favourably to those reported for both surgery and external beam radiotherapy. The authors concluded "that high biochemical control and low complication rates are reported with HDR monotherapy. It is a safe and effective local treatment modality for organ-confined prostate cancer".

3.2 High dose rate brachytherapy plus external beam radiation therapy intermediate to high risk disease

The safety and feasibility of combining high dose rate brachytherapy with external beam radiotherapy were initially shown in the multicentre RTOG 0321 study. In this trial patients with high-risk prostate cancer (T1c to T3b) were treated with EBRT (45 Gy in 25 fractions) plus HDR brachytherapy (19 Gy in two fractions). At a median follow-up of 2.5 years, 125 patients were evaluable; the rate of late grade ≥3 gastrointestinal or genitourinary toxicity was acceptably low (2.6 percent at 18 months).

The efficacy of HDR brachytherapy plus EBRT has been compared with EBRT alone in two small randomised trials:

- In one trial, 104 men with clinical T2 or T3 prostate cancer were randomly assigned to EBRT alone (66 Gy in 2 Gy fractions) or EBRT (40 Gy) preceded by a single, transperineal, temporary implantation of iridium-192 brachytherapy (35 Gy) given over 48 hours. At a median follow-up of eight years, the rate of biochemical or clinical failure was significantly lower in the brachytherapy plus EBRT group (29 versus 61 percent). The improvement in biochemical control was maintained at a median follow-up of 14 years (HR 0.53, 95% CI 0.31-0.88). However, there was no statistically significant difference in overall survival, even with prolonged follow-up.
- In another trial, 218 patients were randomly assigned to EBRT alone (55 Gy in 20 fractions over four weeks) or EBRT (35.75 Gy in 13 fractions over 2.5 weeks) plus HDR brachytherapy (17 Gy

divided into two fractions over 24 hours). In a secondary report with follow-up extending up to 10 years, RFS (Relapse-free survival) was significantly longer with the combined treatment a median time to relapse of 116 months compared to 74 months for EBRT alone. The 5-, 7- and 10-year estimates are 75%, 66% and 46% for EBRT + HDR-BTb (HDR-Brachytherapy boost) compared to 61%, 48% and 39% for EBRT alone (log rank p = 0.04). However there was no improvement in overall survival.

The interpretation of these trials is complicated by the variable dose and fractionation schedules used with the EBRT plus HDR brachytherapy combination, as well as the small sample size.

3.3 References

- N. Tselis, P. Hoskin, D. Baltas et al. High Dose Rate Brachytherapy as Monotherapy for Localised Prostate Cancer: Review of the Current Status. Clinical Oncology 29 (2017) 401-411.

- H Tharmalingham et al Radiotherapy and Oncology 133:S337 · April 2019.

- Hsu IC, Bae K, Shinohara K, Pouliot J, et al. Phase II trial of combined high-dose-rate brachytherapy and external beam radiotherapy for adenocarcinoma of the prostate: preliminary results of RTOG 0321. Int J Radiat Oncol Biol Phys. 2010;78(3):751. Epub 2010 Mar 6.

- Dayes IS, Parpia S, Gilbert J, et al. Long-Term Results of a Randomized Trial Comparing Iridium Implant Plus External Beam Radiation Therapy With External Beam Radiation Therapy Alone in Node-Negative Locally Advanced Cancer of the Prostate. Int J Radiat Oncol Biol Phys. 2017;99(1):90. Epub 2017 May 17.

- Hoskin PJ, Rojas AM, Bownes PJ et al. Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer. Radiother Oncol. 2012 May;103(2):217-22. Epub 2012 Feb 16.

3.4 Date of Review

This document is scheduled for review in March 2021.

4. Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

5. Putting Things Right:

5.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5.2 Individual Patient Funding Request (IPFR)

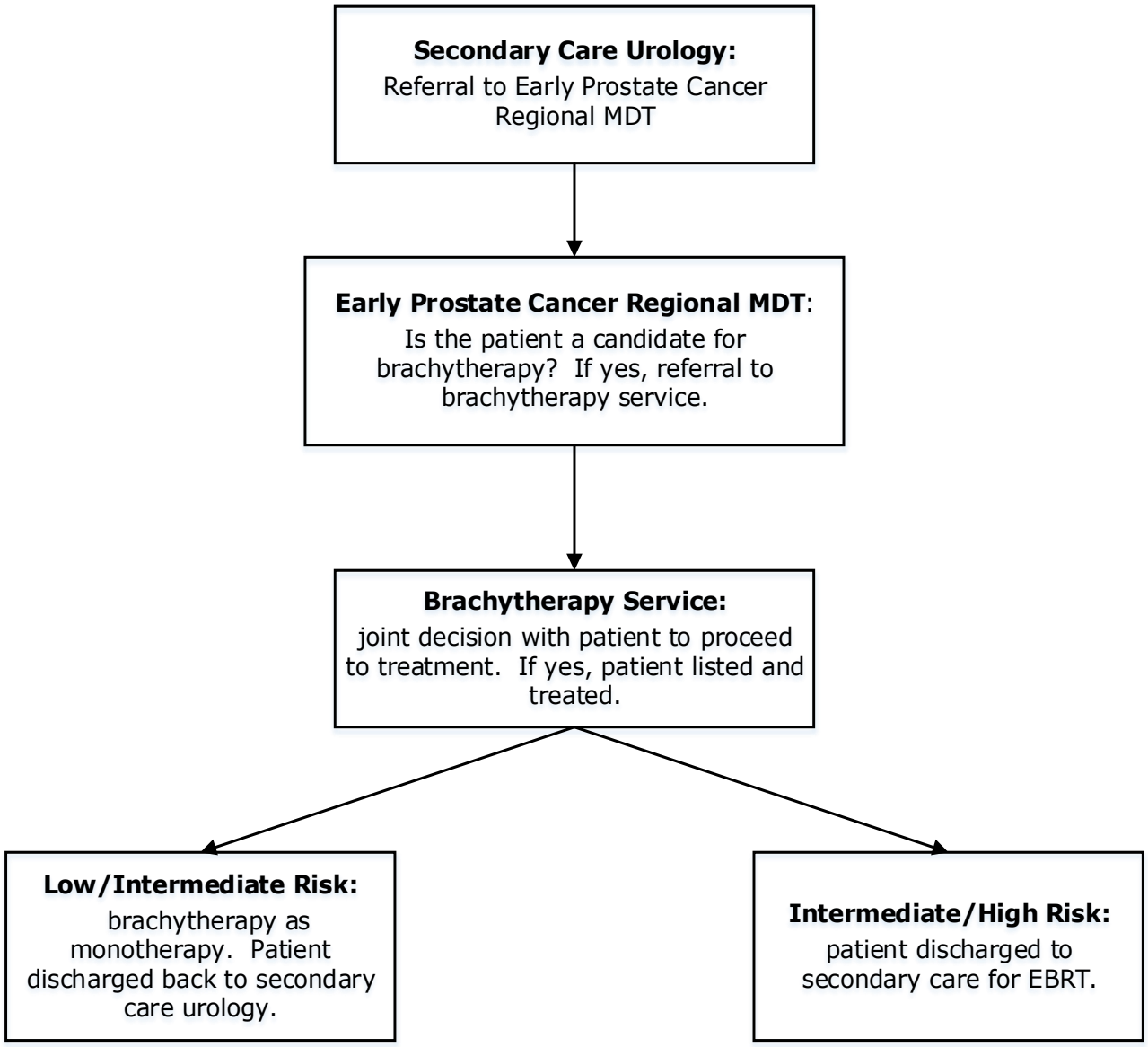
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, and IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

Annex i Patient Pathway



Annex ii Codes

Code Category	Code	Description
ICD-10	C61X	Malignant neoplasm of prostate
ICD-10	C79.8	Secondary malignant neoplasm of the other specified sites is assigned
OPCS 4	M70.6	Radioactive seed implantation into prostate
OPCS 4	X65.3	Delivery of a fraction of interstitial radiotherapy
OPCS 4	Y36.3	Radioactive seed implantation NOC

Annex iv Abbreviations and Glossary

Abbreviations

EBRT External beam radiotherapy

HDR **High Dose Radiotherapy**

IPFR Individual Patient Funding Request

LDR Low Dose Radiotherapy

NICE National Institute of Health and Care Excellence

PSA Prostate specific antigen

WHSSC Welsh Health Specialised Services

Glossary

Brachytherapy
A form of radiotherapy in which the radiation is given using either permanently implanted radioactive seeds (low dose rate) or temporarily inserted radioactive sources (high dose rate) directly into the prostate.

External beam radiotherapy (EBRT)
This is radiotherapy given by using ionising radiation (e.g. high energy X-rays) produced in a machine and directed at the tumour from outside the patient.

Gleason score
An internationally recognised grading system, based on examination of prostate tissue, where a pathologist allocates an overall cell abnormality score that can help predict prostate tumour behaviour. A low Gleason score (≤6) indicates a relatively favourable cancer, a high Gleason score (≥8) indicates a relatively aggressive cancer.

Gy (Gray)
Unit of radiotherapy dose

Individual Patient Funding Request (IPFR)
An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

Localised prostate cancer
Cancer which has been staged as T1 or T2 (confined to the prostate gland).

Prostate
A gland of the male reproductive system which produces fluid for semen.

Prostate Specific Antigen (PSA)
A protein produced by the prostate gland and identified in the blood. Men with prostate cancer tend to have higher levels of PSA in their blood (although most men with prostate cancer have normal PSA levels). PSA levels may also be increased by conditions other than cancer and levels tend to increase naturally with age.

Welsh Health Specialised Services Committee (WHSSC)
WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.