Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

This report summarises the existing evidence on the technology of interest in this Bevan exemplar application.

Topic:	**Extreme hypo fractionation combined with biodegradable rectal spacer insertion for prostate cancer radiotherapy**
Topic exploration report number:	TER133

Aim of Search

Cedar researchers searched for evidence on the use of extreme hypofractionated radiotherapy (eHFRT) with biodegradable rectal spacer insertion for the treatment of prostate cancer.

Summary of Findings

There is no published evidence relating to the specific combination of interventions addressed by this topic.

NICE Guidelines on prostate cancer diagnosis and management (NICE 2019) suggest that eHFRT is cost saving compared with conventional fractionation. However, clinically the evidence suggests that eHFRT may be slightly more or less effective than conventional fractionation (moderate hypofractionated radiotherapy - mHFRT). Nevertheless, the evidence was considered to have potentially serious or very serious limitations. Accordingly, due to the lack of good quality evidence, no recommendations were made on the use of eHFRT.

One systematic review by Koontz et al. (2015) reported that eHFRT shows promising biochemical control rates ranging from two to five years in more than 90% of the low-risk patients.

Another systematic review by Di Franco et al. (2017) reported renal and urinary toxicity from extreme hypofractionated stereotactic body radiotherapy from ten investigated studies. Mean percentage of acute, grade 2 toxicity was between 16% and 24% and late grade 2 toxicity was between 7% and 13%. No grade 3 toxicity were reported.

One UK based study conducted in six patients (King et al. 2018) reported that rectal spacer use resulted in a significant reduction of rectal doses when undergoing stereotactic body radiotherapy. The study indicated that rectal spacer insertion was well tolerated in all patients and allowed more patients to achieve both target volume objectives and organ at risk (OAR) constraints.

There are a number of clinical trials currently registered which are investigating the use of eHFRT (see Ongoing research). However, none include rectal spacers as part of their treatment protocols.

Key Sources of Evidence

Di Franco R, Borzillo V, Ravo V, et al. (2017). Rectal/urinary toxicity after hypofractionated vs conventional radiotherapy in low/intermediate risk localized prostate cancer: systematic review and meta analysis. Oncotarget. 8(10): 17383.

King RB, Osman SO, Fairmichael C, et al. (2018). Efficacy of a rectal spacer with prostate SABR—first UK experience. The British journal of radiology. 91(xxxx): 20170672.

Koontz BF, Bossi A, Cozzarini C, et al. (2015). A systematic review of hypofractionation for primary management of prostate cancer. European urology. 68(4): 683-91.

Areas of Uncertainty

There is a lack of evidence relating to the combination of eHFRT and biodegradable rectal spacers.

The evidence relating to the use of extreme hypofractionation also appears to be limited; however, based on the findings of this high-level search, it is possible that studies reporting evidence on hypofractionation included extreme hypofractionation. A full systematic search of the literature would be required to determine whether this is the case and identify all the relevant evidence relating to the use of extreme hypofractionation.

Brief literature search results

Resource	Results
UK guidelines and guidance	
Healthcare Improvement Scotland	We did not identify any relevant information from this source.
NICE	• NICE. (2019). Prostate cancer: diagnosis and management [NG131]. Online: National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng131 [Accessed 08.08.2019].
Guidelines International Network	• Guideline Clearing Report – The role of IMRT in prostate cancer. Program in Evidence-based Care. NGC:008830
Secondary literature and economic evaluations	
ECRI	We did not identify any relevant information from this source.
Cochrane library	We did not identify any relevant information from this source.
Medline	• Di Franco R, Borzillo V, Ravo V, et al. (2017). Rectal/urinary toxicity after hypofractionated vs conventional radiotherapy in low/intermediate risk localized prostate cancer: systematic review and meta analysis. Oncotarget. 8(10): 17383. • Levy JF, Khairnar R, Louie AV, et al. (2019). Evaluating the Cost-Effectiveness of Hydrogel Rectal Spacer in Prostate Cancer Radiation Therapy. Practical radiation oncology. 9(2): e172-e9. • Koontz BF, Bossi A, Cozzarini C, et al. (2015). A systematic review of hypofractionation for primary management of prostate cancer. European urology. 68(4): 683-91.
Primary studies	
Medline	• Bauman G, Chen J, Rodrigues G, et al. (2017). Extreme hypofractionation for high-risk prostate cancer: Dosimetric correlations with rectal bleeding. Practical radiation oncology. 7(6): e457-e62. • Gunnlaugsson A, Kjellén E, Hagberg O, et al. (2014). Change in prostate volume during extreme hypo-fractionation analysed with MRI. Radiation Oncology. 9(1): 22. • Ha B, Cho KH, Lee KH, et al. (2019). Long-term results of a phase II study of hypofractionated proton therapy for prostate cancer: moderate versus extreme hypofractionation. Radiation Oncology. 14(1): 4. • Jiang P, Krockenberger K, Vonthein R, et al. (2017). Hypo-fractionated SBRT for localized prostate cancer: a German bi-center single treatment group feasibility trial. Radiation Oncology. 12(1): 138. • King RB, Osman SO, Fairmichael C, et al. (2018). Efficacy of a rectal spacer with prostate SABR—first UK experience. The British journal of radiology. 91(xxxx): 20170672. • Mancosu P, Clemente S, Landoni V, et al. (2016). SBRT for prostate cancer: challenges and features from a physicist prospective. Physica Medica. 32(3): 479-84. • Murthy V, Gupta M, Mulye G, et al. (2018). Early results of extreme hypofractionation using stereotactic body radiation therapy for high-risk, very high-risk and node-positive prostate cancer. Clinical Oncology. 30(7): 442-7. • Nicosia L, Mazzola R, Rigo M, et al. (2019). Moderate versus extreme hypofractionated radiotherapy: a toxicity comparative analysis in low-and favorable intermediate-risk prostate cancer patients. Journal of cancer research and clinical oncology. 145(10): 2547-54.

	• Ricco A, Hanlon A, Lanciano R. (2017). Propensity score matched comparison of intensity modulated radiation therapy vs stereotactic body radiation therapy for localized prostate cancer: a survival analysis from the national cancer database. Frontiers in Oncology. 7: 185.
Cochrane library	• Pinkawa M. (2016). Rectal spacers to minimise morbidity in radiotherapy for prostate cancer. Radiotherapy and oncology. 119: S8-.
Ongoing secondary research	
Clinicaltrials.gov	• NCT01913717 – Short-term High Precision Radiotherapy for Early Prostate Cancer with Concomitant Boost on the Dominant Lesion • NCT01764646 - Hypofractionated Radiation Therapy in Prostate Cancer • NCT02313298 - Stereotactic Body Radiotherapy for Organ Confined Prostate Cancer • NCT02976402 - Stereotactic Hypofractionated Accelerated Radiotherapy Post Prostatectomy (SHARP) • NCT01434290 - Radiation Therapy in Treating Patients with Prostate Cancer

Date of search:	08 August 2019
Concepts used:	Prostate Cancer, Hypofractionated Radiotherapy, Extreme Hypofractionated Radiotherapy, eHFRT