Topic Exploration Report

This report summarises the results of a brief exploration to establish the quantity and quality of existing high-level evidence on the procedure of interest.

**Topic:** Daily online Image-Guided Radiotherapy (IGRT) for people undergoing radical prostate cancer treatment

**Topic proposer:** Jake Tanguay

**Report identifier:** RT10

**Topic exploration report number:** TER038

**Prepared by:** Cedar (Cardiff & Vale University Health Board)

**Report date:** 8 March 2019

**Purpose**

On behalf of Health Technology Wales, Cedar researchers conducted a rapid review of evidence on the implementation and use of daily online IGRT for people undergoing radical prostate cancer treatment. This exploratory summary will inform the prioritisation of radiotherapy procedures to be introduced at Velindre Cancer Centre (VCC), alongside expert opinion and other considerations. It could also be used to clarify the scope of an evidence appraisal. Some of the background information and resource impact considerations was submitted by clinical teams at VCC.

**Background**

The main objective of radiotherapy treatment is to destroy tumours without harming the healthy tissues which surround them. Imaging in radiotherapy is used to establish accurate diagnoses and staging by evaluating the growth rate and malignant potential of a tumour. Imaging is also used to accurately identify the specific location of the margins of a tumour to inform treatment planning. Radiotherapy procedures are therefore improved when there is an increased certainty in the anatomical location of the tumour margins, and in the precision of treatment delivery. The primary outcome measure is a reduction in the Planning Treatment Volume (PTV). This refers to the volume of the anatomical area of the tumour being targeted for treatment, and includes both the Clinical Target Volume (CTV) and an additional safety margin. The size of this safety margin (indicated by the CTV to PTV ratio), depends on positional uncertainties.

IGRT can be scheduled weekly or daily with fiducial markers (FM) and/or cone-beam computed tomography (CBCT). The goal of treatment is to accurately target the cancer cells and to minimise the risk of harm to surrounding healthy tissues [1]. However, the use of FM is associated with downsides such as the risk of sepsis, increase in staff time and costs [2].
**Proposed PICO**

<table>
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<tr>
<th><strong>Population</strong></th>
<th>Patients with prostate cancer who require radical radiotherapy (not palliative)</th>
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<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td><em>Daily online</em> image-guided radiotherapy (IGRT)</td>
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<tr>
<td><strong>Comparator</strong></td>
<td>Weekly IGRT</td>
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</table>
| **Outcome measures** | Reduction in Planning Target Volume (PTV)  
Proportion of patients who require revision of their treatment plan  
Costs of:  
- Initial implementation (including capital costs and training where relevant)  
- Ongoing service provision (e.g. staff time for treatment planning and delivery; consumables; maintenance of equipment)  
Patients' QoL  
Incidence of sepsis  
Adverse events (e.g. urinary toxicity, diarrhoea, fatigue) |

**Summary of findings**

It is not clear from the background and the costs table provided by the topic referer what is the current and proposed change in practice. Thus, evidence for weekly and daily IGRT, as well as CBCT and FM, was provided.

**Clinical evidence**

Two randomised controlled studies (RCTs; De Crevoisier et al. (2018) and Tondel, H. (2018)) and 11 more observational/comparative studies were identified. De Crevoisier et al. (2018) looked at daily vs. weekly IGRT with both CBCT and FM whereas Tondel et al. (2018) evaluated weekly offline orthogonal portal imaging with FM and daily IGRT with CBCT and FM.

The evidence from RCTs suggests that daily IGRT with CBCT and FM showed no advantage with respect to patient-reported side effects at the end of radiotherapy as compared to weekly offline portal imaging with FM (Tondel et al. 2018). However, De Crevoisier et al. (2018) reported that compared with weekly control, daily IGRT in prostate cancer significantly improves biochemical progression-free and clinical progression-free interval, and rectal toxicity.

Mixed comparators in RCTs and other publications do not allow comparison of results between studies. Also, full papers were not available for all evidence identified. Based on topic exploration, the high-quality evidence for clinical effectiveness is limited.
Economic evidence

The topic exploration identified 2 economic evaluations (Perrier et al. (2013); Pommier et al. (2012)).

Perrier et al. (2013) evaluated the data derived from the randomised controlled study (de Crevoisier et al. 2016) comparing the daily or weekly IGRT with CBCT or FM. The analysis includes detailed information about required staff time, room occupation time and mean cost per treatment fraction, according to IGRT modality and control frequency. Also, cost-sensitivities of CBCT- and FM-based IGRT with daily or weekly control were assessed. The costs of weekly imaging frequency were lower than daily frequency for both CBCT and FM.

Pommier et al. (2012) randomly assessed the additional costs of daily versus weekly IGRT using CBCT or FM. We were unable to access the full text of this publication. Based on the abstract, the average additional cost per patient was higher in case of daily than weekly IGRT for both CBCT and FM.

The economic evidence for this topic is very limited. Good levels of detail were provided for the topic for which full paper was available.

Economic impact

Based on information provided by the topic referrer, there is no need to purchase any additional equipment or organise the training for staff. The majority of staff are capable of planning the treatment for patients with prostate cancer. The intervention will not save time in the other parts of a patient’s pathway.

The proposed intervention would only benefit prostate patients with a radical intern and excluding those undergoing high-dose palliative radiotherapy. Thus, for the cohort of 300 patients per year, it is estimated that an additional 5 mins per each fraction (n=20) will be required. The additional time required (500 hours for all patients for all fractions) is estimated to incur the cost of £23,410 (there is no information where the cost per hour came from or why it was doubled). Also, 10% of patients would require an adaptive investigation requiring 4 hours per patient. The cost of adding 120 hours per annum (300 patients*0.1*4hours) for re-planning by physicists would incur the cost of £2,809.20 (there is no information where the cost per hour came from).

In summary, the total intervention cost, compared to the standard care in VCC now, would incur the cost of **£26,219.20** (£23,410 + £2,809.20) per annum.
Prioritisation criteria

**Clinical impact** (Potential for the technology to have an impact on patient-related health outcomes):
The high-quality evidence for this topic is limited - only two relevant RCTs were found. The intervention has the potential to improve clinical outcomes, however, more comparable data is required.

**Budget impact** (Impact of the technology on health care spending):
Based on the costs and savings provided by the topic referrer, the change in treatment will incur cost of £26,219.20 per annum for all patients.

**Population impact** (The size of the population that would be affected by the technology):
The topic proposer estimated that 300 patients will benefit from the change which accounts for approximately 11.8% ((300/2552)*100%) of all prostate patients in Wales (based on the data provided by Welsh Cancer Intelligence and Surveillance Unit, the incidence of prostate cancer in 2015 was 2552 patients).

**Equity** (The technology has the potential to introduce, increase, or decrease equity in health status):
No equity issues identified.

Questions for researcher

Based on the sources you have identified, is your impression that the evidence is likely to:

- favour implementation of the procedure?
- favour standard care?
- be inconclusive?

The evidence identified is inconclusive. There is no guidance or systematic review which would summarise the information for this topic and only two relevant RCTs are available. It is likely that the limited evidence identified will give inconclusive results.

Questions for topic proposer

- What source of information was used to provide the cost of physician time (£23.41 per hour)? Why some costs are doubled? Are there any additional costs included?
- How was the number of eligible patients calculated? Does the number of patients is likely to increase in coming years?
- Your proposal mentioned the Calypso system and potential savings. Can you explain how the Calypso system would decrease the time needed for treatment?
- What is the cost of implantation of fiducial markers and was it taken into account when completing the form?
- The change in practice requires additional 620 hours per annum of clinicians’ time. Will it affect (e.g. delay) the treatment of other VCC patients?
Sources of evidence


- Tondel, H. et al. 2018. Radiotherapy for prostate cancer - Does daily image guidance with tighter margins improve patient reported outcomes compared to weekly orthogonal verified irradiation? Results from a randomized controlled trial. Radiotherapy and Oncology 126, pp. 229 - 235. (NCT01550237)

References


## Appendix - Brief literature search results

<table>
<thead>
<tr>
<th>Resource</th>
<th>Results</th>
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<tbody>
<tr>
<td><strong>UK guidelines and guidance</strong></td>
<td><strong>NICE CG175 Prostate cancer: diagnosis and management (January 2014)</strong></td>
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</tbody>
</table>
| e.g. NICE; Healthcare Improvement Scotland; Guidelines International Network; SIGN | HIS - no evidence identified  
GIN - no evidence identified  
SIGN - no evidence identified |

**Secondary literature and economic evaluations**

| e.g. Cochrane library; Medline; systematic reviews, meta-analyses, economic evaluations | Economic evaluation:  

**Primary studies**

| Medline; RCTs; observational studies | RCTs:  
• Tondel, H. et al. 2018. Radiotherapy for prostate cancer - Does daily image guidance with tighter margins improve patient reported outcomes compared to weekly orthogonal verified irradiation? Results from a randomized controlled trial. *Radiotherapy and Oncology* 126, pp. 229 - 235. (NCT01550237)  

Other studies:  

<table>
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<th>Cochrane trials database</th>
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<tr>
<td>Ongoing secondary research</td>
<td></td>
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<tr>
<td>Clinicaltrials.gov</td>
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</tr>
<tr>
<td>1. NCT02034955 Prostatectomy Adaptive Radiation Therapy (ART) - Active, not recruiting</td>
<td></td>
</tr>
<tr>
<td>2. NCT01550237 Curative Image Guided Radiotherapy for Prostate Cancer (RIC) - Active, not recruiting (randomised controlled trial)</td>
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<td>Topic referrer</td>
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<tr>
<td></td>
<td>1 Prostatic Neoplasms/ (114788)</td>
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<td>3 Radiotherapy, Image-Guided/ (2454)</td>
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