GenesisCare Prostate Radiotherapy Protocol
UK

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1. Introduction and Purpose

This document defines GenesisCare UK (GenesisCare) recommended radiotherapy protocol for the treatment of the prostate gland (+-) seminal vesicles, pelvic lymph nodes and prostate bed.

2. Terms and Definitions

- Low/Intermediate risk – T1c T2a-c T3, PSA<15, Gleason ≤7.
- Low risk (D'Amico) T1-T2a, Gleason <=6, PSA <10 ng/ml
- Intermediate risk (D’Amico) T2b, Gleason 7, PSA 10-20 ng/ml
- High risk (D’Amico) T2c, Gleason >=8, PSA >20 ng/ml
- Hypofractionation: Low risk of seminal vesicle involvement T1b/c or T2a/b and with PSA + ((Gleason score -6) x10) <15
- Hypofractionation: Intermediate/high risk of seminal vesicle involvement
- Clinical stages T1b/c or T2a/b, and with PSA + ((Gleason score -6) x10) >15
- T2c or T3a. Intermediate Risk, small volume (non CHHiP eligible).
- High Risk T3A, MRI T3b; PSA>20; Gleason 8-10 (any)
- Prostate bed: high risk features for prostate bed + nodes. include: Grade group 3 or higher at formal histology, presence of extracapsular extension or seminal vesicle invasion at formal histology, rising PSA despite negative margins
- Palliative prostate radiotherapy

3. Scope

This protocol applies to all prostate radiotherapy treatments undertaken in GenesisCare centres.

4. Responsibilities

The Urology Clinical Reference Group are responsible for writing this Clinical Protocol. The Head of Physics and Head of Radiotherapy are responsible for implementing this procedure and subsequent local policies and procedures. Radiographers that are entitled and competent are responsible:

For ensuring the accurate and safe delivery of radiotherapy treatments.

**Note: Cone Beam CT is the GenesisCare gold standard of treatment delivery.**
5. Policy Treatment Considerations

5.1. **MR Linac SBRT**

5.2. **Hypofractionation (CHHiP)**
- A Scripted CHHiP protocol has been produced by GenesisCare available at the clinician's request which will automate the production of PTVs, planning structures and optimiser objectives.

5.3. **HDR/LDR**
- A 15Gy single # HDR prostate boost may be delivered in high risk cases (Not currently offered at GenesisCare) in combination with 46Gy in 23 fractions to the whole pelvis.
- A low dose brachytherapy boost delivering 110Gy to the prostate (not currently offered at GenesisCare) may be delivered in high risk cases (ASCENDE-RT trial, Journal of Clinical Oncology 2015 33:7_suppl, 3-3), in combination with 46Gy in 23 fractions to the whole pelvis or 36Gy/12# or 37.5/15# to the prostate.
- HDR/LDR boost can be delivered before or after EBRT

5.4. **Locally advanced PC**
- Treatment of the prostate/seminal vesicles with or without pelvic lymph nodes as determined by local clinician decision.
- Prostate cancer with small volume Oligometastatic disease in the pelvis, encompassable within a radical dose.
- Patients of good performance status with small volume synchronous oligometastases geographically close to the prostate and therefore encompassable within a high dose field. This could include obturator or external iliac lymph nodes, bone lesions within the bony pelvis around the prostate.
- Radiotherapy to the prostate in low volume metastatic disease.
- This includes patients where irradiation of the primary is indicated despite the presence of extra-pelvic metastases as based on STAMPEDE and CHAARTED data.

5.5. **Palliative Prostate Radiotherapy is indicated when radical treatment is inappropriate.**
- Elderly frail with local symptoms or hormone resistant disease.
- Metastatic with local symptoms.
5.6. **Post-prostatectomy salvage radiotherapy**

- This includes treatment to the prostate bed alone or with the inclusion of pelvic nodal irradiation.

- Salvage radiotherapy (SRT) is the administration of radiotherapy to the prostatic bed and possibly the surrounding tissues, including lymph nodes, in patients with PSA recurrence after surgery but no evidence of distant metastatic disease. Biochemical recurrence after surgery is defined as a detectable PSA level of $\geq 0.2$ ng/mL with a second confirmatory level of $>0.2$ ng/mL.

(Ref [https://www.practicalradonc.org/article/S1879-8500(19)30120-1/fulltext](https://www.practicalradonc.org/article/S1879-8500(19)30120-1/fulltext))

6. **Patient Selection**

6.1. **Consent**

As per GenesisCare Consent Policy (QR-POL-045).

6.2. **Inclusion Criteria**

- MDT confirmed diagnosis
- For MR Linac see appendix 1 for details

6.3. **Re-irradiation**

Re-irradiation should only be undertaken with caution and after appropriate consideration of the previous dose delivered, time since irradiation and careful assessment of the previous radiotherapy plan and dose.

6.4. **Scheduling of Patients**

A 7-day planning pathway is available at GenesisCare pending clinician availability.

Radical cases may start any weekday excluding Friday. Palliative cases can start any day.

Refer to Clinical Advisory Team (CAT) referral (RT-POL-136) criteria.
7. Patient Positioning and Localisation

<table>
<thead>
<tr>
<th>Immobilisation Device</th>
<th>Set-Up</th>
<th>Suggested Practice</th>
<th>Localisation</th>
<th>Tattoo/refen ce mark Location</th>
<th>Bladder/recta l status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head on scoop &amp; rectangle; arms on chest; Combi-fix</td>
<td>Supine, head to gantry; Hands on chest</td>
<td>Mandatory AP/ Lat Mosaiq set-up photograp h (Tattoo location visible. All CT wire removed); Clothing &amp; jewellery removed as necessary</td>
<td>Prostate/Bladder only: L4/5 vertebrae to 3cm inf to ischial tuberosities Primary+Nodes: L1/2 vertebrae to 3cm inf to ischial tuberosities</td>
<td>Anteriorly on m/l at approx. 5cm Sup to BOP (male) or at planner discretion depending on patient size Left &amp; Right Lat rotation tattoos at approx. HATT 10-12cm</td>
<td>Bladder comfortably full Rectum, Empty</td>
</tr>
</tbody>
</table>

8. Pre-treatment Imaging

MRI CT fusion is recommended where possible for planning radical prostate radiotherapy. Patients who have had a rectal spacer placed pre radiotherapy should have a planning MRI scan to facilitate visualisation of the rectal spacer. Contrast is required when pelvic nodal irradiation is planned and or at the doctor’s request.

9. Definition of Target and OAR

Target Volumes

9.1. GTV:

- The GTV is the prostate only in the CHHiP protocol.

9.2. CTVmrl

- The Clinical target Volume for the MR Linac (CTVmrl) are further defined in appendix 1 but reproduced here for easy reference:

  Volume and dose prescription are implemented according to the ICRU 83 regulations [Report 83, 2010]. Target definition is dependent on the risk assessment, in particular to the risk of seminal vesicle invasion. ‘Low risk’ patients are defined as patients with cT1c-T2a prostate cancer, a Gleason score <7 and a PSA <10 µg/L. ‘High risk’ patients have cT3-4 prostate cancer, or a Gleason score >7 or a PSA >20 µg/L, and ‘intermediate risk’ patients are
patients not included in the other two groups [EAU guidelines 2013, Heidenreich].

9.3. **Clinical target volume (CTV) definitions:**
- The urethral planning organ at risk volume (PRV): urethra plus 3mm; the area of integrated radiation sparing
- For ‘low risk’ patients: CTV = prostate minus the urethral PRV (see below)
- For ‘intermediate and high risk’ patients: CTV = prostate plus the base of the seminal vesicles (=2cm) plus any visible tumour extension seen on MRI minus the urethral PRV (see below).

9.4. **CTVp:**
- Clinical Target Volume (CTVp) defined as prostate gland (+/-) the seminal vesicles.

9.5. **CTVn:**
- The CTVn includes the Pelvic nodes below the bifurcation of the common iliac vessels to include the internal iliacs, obturator, presacral and external iliac nodes.

9.6. **CTVn+:**
- The CTVn+ includes the clinical or radiological involved lymph nodes to be boosted.

9.7. **CTV Prostate Bed**
- The CTV Prostate Bed is defined as:
  - Superior border: Base of seminal vesicle or if removed at estimated position from pre-op scans if available.
  - Inferior border: 5mm above penile bulb.
  - Anterior border: Caudal (<2cm above anastomosis) – Posterior border of pubic symphysis. Cranial (>2cm above anastomosis) – Posterior 1/3rd of bladder wall.
  - Below anastomosis: Posterior third of bladder wall.
  - **Posterior border:** Anterior rectal wall.
  - **Lateral border:** Medial border obturator internus and levator ani muscles.

9.8. **CTV Prostate bed + SVs**
- The CTV Prostate bed + SVs is defined as per prostate bed only but extending superiorly to include tips of seminal vesicles or if absent, estimated position of seminal vesicles from pre-op
imaging if available. This is at the discretion of the referring clinician.

9.9. CTV Prostate (Palliative):
- In palliative cases the CTV is defined as the prostate and any extra-prostatic extension.

9.10. CTV Prostate – CHHiP:
- CTV1 – CHHiP (Low risk):
  - The CTV1 is prostate and base of seminal vesicles (proximal 2cm) with 5mm margin.
- CTV1 – CHHiP (Intermediate/high risk):
  - CTV1 is the prostate and seminal vesicles with 5mm margin for Group 2.
- CTV2 – CHHiP:
  - CTV2 is the prostate only + 5mm.
- CTV3 – CHHiP:
  - CTV3 is the prostate only.

9.11. ITV:
- The ITV is not applicable.

9.12. PTV Prostate:
- The PTV is defined as the CTVp + 7mm uniformly.
- Also acceptable: PTV66: CTV66 (Prostate/SV + 10mm)
- PTV74: CTV74 (Prostate only + 5mm) can be accepted if a 2nd dose level of PTV/SV + 10mm is used

9.13. PTVmrl:
- The PTV for the MR linac (PTVmrl) are further defined in appendix 1 but reproduced here for easy reference:
- The combination of MR-guided soft-tissue setup and online MR-imaging during treatment in combination with “gated” treatment (i.e. beam-on only when the target is in the predetermined position) enables the application of small uncertainty margins.
- PTV = CTV + 3 mm (in all external directions, i.e. excluding the urethral PRV).
9.14. **PTV Prostate Bed:**

- The PTV Prostate bed is defined as the CTV Prostate bed + 10mm uniformly.
- (0.7–1.0cm posterior margin depending on rectal area which should be defined on each CT planning slice -LCA guidance).

9.15. **PTVs1-3 (CHHiP):**

- PTVs 1-3 Add 5mm to the relevant CTV except for adding a 0mm margin posteriorly or posterior-inferiorly (towards the rectum) for PTV2+3 (with spacer, a 5mm can be maintained posteriorly and posterior-inferiorly).
- Also acceptable: PTV48 (1cm around prostate/SV) and PTV60 (5mm around prostate).

9.16. **Recommended modifications to margins**

- Lymph node volumes should follow vessels as defined by contrast CT using asymmetric manual expansions to nodes along tissue planes as defined in table below from Taylor et al Clinical Oncology 2007; 19: 542-550.

<table>
<thead>
<tr>
<th>Lymph node group</th>
<th>Recommended margins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Iliac</td>
<td>7mm margin around vessels; extend posterior and lateral borders to psoas and vertebral body</td>
</tr>
<tr>
<td>External Iliac</td>
<td>7mm margin around vessels; extend anterior border by additional 10-mm anterolaterally along iliopsoas muscle to include lateral external iliac nodes</td>
</tr>
<tr>
<td>Obturator</td>
<td>Join external and internal iliac regions with 18-mm wide strip along pelvic sidewall</td>
</tr>
<tr>
<td>Internal Iliac</td>
<td>7-mm margin around vessels; extend lateral borders to pelvic sidewall</td>
</tr>
<tr>
<td>Presacral</td>
<td>10-mm strip over anterior sacrum</td>
</tr>
</tbody>
</table>

Also include any visible nodes

Contouring Atlases available below:

- [https://www.rtog.org/LinkClick.aspx?fileticket=glmTGKHTmr0%3d&tabid=234](https://www.rtog.org/LinkClick.aspx?fileticket=glmTGKHTmr0%3d&tabid=234) (LNs)
- [https://www.rtog.org/LinkClick.aspx?fileticket=glmTGKHTmr0%3d&tabid=234](https://www.rtog.org/LinkClick.aspx?fileticket=glmTGKHTmr0%3d&tabid=234) (Postop +ve apex margin)
- [https://www.rtog.org/LinkClick.aspx?fileticket=_znZLMP1yco%3d&tabid=232](https://www.rtog.org/LinkClick.aspx?fileticket=_znZLMP1yco%3d&tabid=232) (Postop +ve SV)
9.17. **Nodal PTVs**

- Prostate + Nodes – Nodal PTV margin = 10mm
- Prostate Bed + Nodes – Nodal PTV margin = 7-10mm
- Involved Nodes (N+) margin = 5-10mm

9.18. **Organs at Risk (OAR)**

- Organs at risk are to be outlined as per GenesisCare UK Anatomy Atlas (PHY-MAN-102).

9.19. **OAR 1- Rectum**

- The rectum should be outlined from the anus (Usually at the level of the ischial tuberosities or 1cm below the lower margin of the PTV (whichever is more inferior) to the recto-sigmoid junction. The recto-sigmoid junction can usually be identified on the CT slice where the bowel turns anteriorly and laterally. This will give a length of 10-12cm in most cases. Any additional bowel in the volume should be outlined separately.

9.20. **OAR 2 – Bladder**

- The whole bladder should be outlined from base to dome.

9.21. **OAR 3 – Femoral Heads**

The femoral heads should be outlined as per GenesisCare UK Anatomy Atlas (PHY-MAN-102), excluding the femoral neck.

9.22. **OAR 4 – Bowel**

- The bowel is to be outlined when there is nodal involvement 2cm superior the PTV.

9.23. **OAR 5 – Penile Bulb**

- The penile bulb should be contoured using the fused diagnostic MRI to aid recognition.

9.24. **OAR for the MR Linac are further defined in appendix 1 but reproduced here for reference:**

OAR should be contoured following the male pelvis normal tissue RTOG consensus contouring guidelines:
[https://www.rtog.org/CoreLab/ContouringAtlases/MaleRTOGNormalPelvisAtlas.aspx](https://www.rtog.org/CoreLab/ContouringAtlases/MaleRTOGNormalPelvisAtlas.aspx)

- Urethra: delineate the prostatic urethra using MRI
- Bladder: delineate the outer contour of the bladder on MRI
9.25. Treatment Planning - Prostate Dose Prescription. (For a summary of doses please see appendix 2.)

9.25.1. **MR Linac: As per inclusion criteria.** PTV dose prescription: 36.25 Gy in 5 fractions

9.25.2. **Low/Intermediate risk:** T1c T2a-c T3, PSA<15, Gleason ≤7. (Level 1 Evidence):

   - PTVp - 60Gy/20# over 4 weeks (CHHiP eligible)

9.25.3. Intermediate risk:

   - PTVp 78Gy/39# over 7.5 weeks. Also acceptable: 74Gy in 37# over 7.5 weeks and 76Gy in 38# over 7.5 weeks and 78Gy in 37# over 7.5 weeks or 60Gy in 20# over 4 weeks.

9.25.4. **High Risk disease:** T3A, MRI T3b; PSA>20; Gleason 8-10 (one)

9.25.5. Two schedules are in use depending upon whether the entire treatment is to be with external beam or brachytherapy (HDR/LDR) boost will be used.

9.25.6. External Beam Only (78Gy/39# or in 37# or 76Gy/38# or 74Gy/37# or 60Gy in 20# if clinical decision is not to treat the pelvic nodes)

   - PTVn: 60-62Gy in 37-39#
   - PTVp: 74-78Gy in 37-39#
   - PTVn+: 65-74Gy in 37-39# over 7.5 weeks (evidence J. Fowler et al. IJROBP 56; 4; 2003)
   - In case of excess bowel, reduce LN to 55Gy and nodal boost to 60Gy (LCA guidance).

9.25.7. External Beam IMRT+HDR Brachytherapy Boost (Level 1 Evidence)

   - PTVp & n combined: 46Gy in 23# over 4.5 weeks
   - PTVn+: 56.6-58Gy in 23# (if radiologically involved nodes)
   - HDR Boost: 15Gy single dose to HDR PTV

NB: the tumour and organs at risk outlines may be outlined by competent members of the planning team for all non-clinical trial patients. Assessment and approval of this competency is delegated to the physics department.
• For node –ve disease, also acceptable is 37.5Gy/15# EBRT followed by 15Gy HDR boost.

9.25.8.  External Beam IMRT+ LDR Brachytherapy Boost
• PTVp & n combined: 46Gy in 23# over 4.5 weeks
• PTVn+: 56.6-58Gy in 23# (if radiologically involved nodes)
  LDR Boost: 110Gy
• For node –ve disease, also acceptable is 37.5Gy/15# or 36Gy/12# EBRT followed by 110Gy LDR boost.

9.26.  Synchronous oligometastases treated radically with radiotherapy to both prostate and nearby small volume metastases:


9.27.  Prostate bed radiotherapy

Three schedules are in use for adjuvant and salvage radiotherapy depending upon the risk of pelvic lymph node involvement.

9.27.1.  Prostate Bed Dose Prescription (Level 1 Evidence)
• 52.5Gy-55Gy 20# Low/High Risk opting not to treat nodes over 4 weeks
• 66Gy/33# over 6.5 weeks. Visible gross disease might be boosted to a dose of 71.6Gy in 33# (Royal Surrey protocol). Alternatively, a total dose of 70-74Gy in 35-37 fractions as a boost to the visible disease (Oxford protocol).

9.28.  High lymph node risk- positive nodes on histology at prostatectomy or presence of high-risk features at prostatectomy
• 66Gy in 33# PTVp over 6.5 weeks
• 52-55Gy in 33# PTVn (RADICALS)
• 58-70Gy in 33# PTVn+ (MVH protocol, AUA 2013, EUA 2016)
- Boost to visible tumour/enlarged node recurrence up to 71.6Gy in 33\# (Royal Surrey protocol). Alternatively, a total dose to 70-74Gy in 35-37 fractions as a boost to the visible disease (Oxford protocol)

### 9.29. Palliative Radiotherapy

Aim for local disease control where either there is evidence of metastatic disease or a patient is judged not fit for radical treatment

- IMRT – 36Gy in 6\#, treated 1 fraction per week over 6 weeks or 55Gy in 20\# daily schedule (STAMPEDE) 60Gy in 20\# over 4 weeks also considered appropriate
- AP PA Fields/3D CRT – 21Gy in 3\# MPD/Target mean dose alternate days over 1 week.
- AP PA Fields/3D CRT – 8-10Gy in 1\# or 20Gy in 5 \# MPD/Target mean

### 9.30. Delivery Technique

The standard technique will typically employ VMAT.

### 9.31. Dose Targets and Constraints

#### 9.31.1. Minimum Target Coverage

- As per PHY-POL-007: V95>99% is optimal and V95\%>98\% is acceptable if required to meet OAR constraints.

#### 9.31.2. Max dose

- The maximum 2cc dose to the PTV should be ≤107.

#### 9.31.3. OAR Dose Constraints

### Prostate

<table>
<thead>
<tr>
<th>Organ at Risk</th>
<th>Dose (Gy)</th>
<th>78Gy/39# Mandatory/optimal Volume (%)</th>
<th>60Gy 20# Volume (%)</th>
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<tbody>
<tr>
<td>Rectum</td>
<td>30</td>
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<td></td>
<td>40</td>
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<td>Penile Bulb</td>
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|                  | 50 |    | 50 |
|                  | 60 |    | 10 |

### Prostate Bed/Prostate with HDR Boost

<table>
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<tr>
<th>Organ at Risk</th>
<th>Dose (Gy)</th>
<th>52Gy Volume (%)</th>
<th>20#</th>
<th>66Gy Volume (%)</th>
<th>33#</th>
<th>Prostate with HDR Boost 46Gy Volume (%)</th>
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<tbody>
<tr>
<td>Rectum</td>
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</table>

### CHHiP trial Constraints

<table>
<thead>
<tr>
<th>Organ at Risk</th>
<th>Dose for 2Gy/# Prescribed Dose</th>
<th>Dose for 3Gy/# Prescribed Dose</th>
<th>% of prescription dose</th>
<th>Max Vol (% or cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>30</td>
<td>24.6</td>
<td>41</td>
<td>80%</td>
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<td>50</td>
<td>40.8</td>
<td>68</td>
<td>60%</td>
</tr>
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<td></td>
<td>60</td>
<td>48.6</td>
<td>81</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>52.8</td>
<td>88</td>
<td>30%</td>
</tr>
</tbody>
</table>

|                  | 50 |    | 50 |
|                  | 60 |    | 50 |
9.32. MR Linac Dose constraints OAR

Rectum and anal canal:

- $D_{105\%} (38.1 \text{ Gy}) \leq 0.1 \text{ cc}$
- $D_{100\%} (36.25 \text{ Gy}) \leq 1 \text{ cc}$
- $D_{95\%} (34.4 \text{ Gy}) \leq 5 \text{ cc}$
- $D_{90\%} (32.6 \text{ Gy}) \leq 10 \text{ cc}$

Bladder: (because of daily adaption, bladder is chosen instead of bladder wall)

- $D_{102\%} (37.0 \text{ Gy}) \leq 0.1 \text{ cc}$
- $D_{100\%} (36.25 \text{ Gy}) \leq 1 \text{ cc}$
- $D_{90\%} (32.62 \text{ Gy}) \leq 15 \text{ cc}$

Femoral heads:

- $D_2 \leq 50\%$ of the prescribed PTV dose (18.1 Gy)

Penile bulb

- $D_{\text{mean}} \leq 75\%$ of the prescribed PTV dose (27.2 Gy)

9.33. Plan Approval

9.33.1. Plan approval should be by a Clinical Oncologist, or where agreed and documented by the oncologist, by competent members of physics staff who may perform the plan approval for all radical prostate plans as long as:

a) the consultant has electronically approved the prescription;
b) the consultant has signed The GTV and CTV, OARs are approved by either the consultant or a competent member of physics staff;
c) all PTV and OAR constraints are met and distribution is within current ICRU guidelines; and

d) assessment and approval of this competency is delegated to the physics department.

4.31.2 For the MR Linac, daily adaptive plans are approved by the attending clinician.

10. Pre-treatment Quality Assurance

10.1. All complex IMRT/VMAT plans undergo a fluence delivery check on the linac (e.g. using MapCheck2 or ArcCheck). For guidance on this process see RT189 and MapCheck/ArcCheck manuals. This check is usually carried out prior to commencing treatment and always before a fifth of the treatment has occurred (e.g. before fraction 5 on a 25# treatment).

10.2. For the MR Linac, daily adaptive plan quality assurance is carried out with the patient on the couch prior to treatment.

11. Pre-treatment Verification

11.1. Treatment verification is to be undertaken day 1 prior to treatment.

11.2. MR Linac treatment verification is undertaken daily.

12. Treatment IGRT

12.1. Image Guidance is to be performed using daily CBCT.


13. Image Assessment

13.1. As per Radiotherapy Imaging Policy (RT-POL-028), Clip-box to include the surrounding bony anatomy not including the femur.

13.2. Perform Bony match then match to prostate.

13.3. Review rotations + translations are in tolerance.

13.4. Ensure the CTV remains within the 95% Isodose.

13.5. Review bladder/rectal filling/gas.

13.6. Assess position of seminal vesicles if part of CTV.
13.7. Review skin contour, if >1cm difference in tissue discuss with planning.

13.8. Try to ensure the patient’s legs (femoral head/neck) are in a similar position to planning CT; this can alter consistently on treatment if the patient was tense and “clenching” at CT.

14. Treatment delivery

As per Radiotherapy treatment Policy (RT-POL-014), weekly radiographer-led on-treatment reviews are documented on MOSAIQ. Radiographer-led end of treatment reviews documented on MOSAIQ.

15. Stereotactic Radiotherapy

15.1. Stereotactic radiotherapy on a standard linear accelerator (non-MR Linac) is currently unavailable pending review.

15.2. Stereotactic radiotherapy is a potential treatment option for patients who fulfil the PACE trial entry criteria (outlined below) who are accepting of the lack of randomised outcome data.

15.3. Inclusion criteria:

- Low to intermediate risk disease and selected high risk disease
- T1-3a disease
- Gleason 3+3, 3+4, 4+3 and selected 4+4
- PSA<20
- PS 0-2
- Prostate volume ≤90cc
- Inclusion of patients to treatment under PACE trial parameters should be agreed by the MDT

15.4. Dose Prescription 36.25Gy in 5 fractions on alternate days over 2 weeks (7.25Gy x 5) prescribed to PTV

- GTV = prostate gland
- CTV = prostate gland (low risk patients)
- Prostate gland and proximal 1 cm seminal vesicles (Intermediate risk patients)
- Prostate gland and proximal 2 cm seminal vesicles (high risk patients)
- PTV = CTV+5mm margin all directions except posteriorly 3mm edited off rectum if fiducial markers used or 5mm in all direction if soft tissue matching
• Dose constraints as per PACE trial

16. Evaluation

This Protocol will be monitored by Clinical Reference Group, Head of Medical Physics, Head of Radiotherapy and Chief Medical Officer.

17. References

• B.R. Prestidge et al (2016): x
• H.M. Sandler
• Search for articles by this author Affiliations - Cedars-Sinai, Los Angeles, CA
• PACE TRIAL: https://www.clinicaltrials.gov/ct2/show/NCT01584258.

18. Appendix

• Appendix 1: Stereotactic MR-guided Adaptive Radiation Therapy for Localised Prostate Cancer.
• Appendix 2: Dose List for Prostate Cancer
## Revision History

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>Revised By (Position Title)</th>
<th>Description of change</th>
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<tr>
<td>1.0</td>
<td>April 2018</td>
<td>Chief Medical Officer</td>
<td>New Protocol</td>
</tr>
<tr>
<td>2.0</td>
<td>July 2020</td>
<td>Philip Camilleri – Urology Clinical Reference Group Lead</td>
<td>Updates to include MRL, updates to doses and reformatted to new format</td>
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<tr>
<td>2.1</td>
<td>August 2020</td>
<td>Mark Bowler – Head of Radiotherapy</td>
<td>Addition of Nodal PTV margins and removal of references to SpaceOAR and replaced with spacers.</td>
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Appendix 1 Stereotactic MR-guided Adaptive Radiation Therapy for Localised Prostate Cancer.

Stereotactic radiotherapy is a treatment option for patients who fulfil the entry criteria (outlined below) who are accepting of the lack of randomized outcome data. Long term outcome and toxicity data from non-randomised series does support the safety and efficacy of this therapy.

**Population (base)**

Patients with localized prostate cancer with a clinical stage T1-3b, with a maximal volume of 90 cc on transrectal ultrasound (TRUS) and no suspicious lymph nodes observed on either a diagnostic MRI or CT scan and no signs of distant metastases on radiological staging are eligible. All patients will be discussed in a multidisciplinary team meeting (MDT).

**Inclusion criteria**

- Age of 18 years or older
- WHO performance score 0-2
- Biopsy proven adenocarcinoma of the prostate
- Gleason ≥ 6
- Prostate volume ≤ 90 cc on TRUS
- T-stage: cT1c-T3b (on MRI and/or endorectal ultrasound)
- All patients should be able to undergo MRI scans
- No evidence of lymph node or distant metastases on radiological staging
- The multidisciplinary team advised external beam radiotherapy treatment
- IPSS (International Prostate Symptoms Score) ≤19
- Previous TURP is allowed provided there is at least 8 weeks interval with radiotherapy
- The administration of concomitant hormonal therapy is allowed
- Ability to provide written informed consent.

**Exclusion criteria**

- Previous irradiation in the pelvic region
- Contra-indications for MRI
- As no safety data for 0.35 Tesla MRI scanners are available on electronic devices such as pacemakers or implanted defibrillators, deep brain stimulators, cochlear implants, this constitutes an
absolute contraindication for this study, even for devices that have been considered safe for MRI scans with higher magnetic field strengths

- Patients who have a metallic foreign body in their eye, or who have an aneurysm clip in their brain, cannot have an MRI scan since the magnetic field may dislodge the metal
- Patients with severe claustrophobia may not be able to tolerate an MRI scan
- Patients with a hip prosthesis will not be eligible for the MRI scan

TREATMENT

Radiotherapy treatment schedule
The treatment consists of a short course of radiotherapy with 5 fractions of 7.25 Gy per fraction delivered on the prostate with a simultaneous integrated sparing (SIS) of the urethra with a dose of 32.5 Gy in 5 fractions (6.5 Gy per fraction). Treatment is delivered on alternate days within a maximum overall treatment duration of 14 days.

Treatment preparation
In preparation for treatment delivery, all patients will undergo a planning-MRI scan (MRIdian) and a planning-CT scan. Patients will be simulated and treated in supine position. The CT scan slice thickness will be 2 mm. The superior limit of the CT scan will be at least at L1 and inferior limit will be half-way the femur. The planning-CT will be fused with the planning-MRI scan. If a diagnostic MRI scan is performed, including T1 and T2 sequences, these scans can be co-registered to assist in target definition. The fusion will be centred on the area of interest, i.e. the prostate. All patients will be treated using online MR-guided gated radiotherapy with adaptation of treatment plans immediately prior to each treatment delivery (SMART). Patients will be instructed to have a full bladder and if possible, an empty bowel prior to the planning CT and MRI scan and prior to each treatment fraction. In order to achieve this with some reproducibility patients are instructed to empty their bladder two hours before treatment, followed by intake of 500cc of water. In case of constipation, mild laxatives will be prescribed. No rectal balloons or routine pre-treatment enemas will be used.

Definitions of target volumes and organs at risk
Volume and dose prescription are implemented according to the ICRU 83 regulations [Report 83, 2010]. Target definition is dependent on the risk assessment, in particular to the risk of seminal vesicle invasion. ‘Low risk’ patients are defined as patients with cT1c-T2a prostate cancer, a Gleason
score <7 and a PSA <10 µg/L. ‘High risk’ patients have cT3-4 prostate cancer, or a Gleason score >7 or a PSA >20 µg/L, and ‘intermediate risk’ patients are patients not included in the other two groups (EAU guidelines 2013, Heidenreich).

Clinical target volume (CTV) definitions:
The urethral planning organ at risk volume (PRV): urethra plus 3mm; the area of integrated radiation sparing.

For ‘low risk’ patients: CTV = prostate minus the urethral PRV (see below)
For ‘intermediate and high risk’ patients: CTV = prostate plus the base of the seminal vesicles (=2cm) plus any visible tumour extension seen on MRI minus the urethral PRV (see below)

Planning target volume (PTV) margins:
The combination of MR-guided soft-tissue setup and online MR-imaging during treatment in combination with “gated” treatment (i.e. beam-on only when the target is in the predetermined position) enables the application of small uncertainty margins.

PTV = CTV + 3 mm (in all external directions, i.e. excluding the urethral PRV).

Organs at risk (OAR) definitions:
OAR should be contoured following the male pelvis normal tissue RTOG consensus contouring guidelines:
[https://www.rtog.org/CoreLab/ContouringAtlases/MaleRTOGNormalPelvisAtlas.aspx]
Urethra: delineate the prostatic urethra using MRI
Bladder: delineate the outer contour of the bladder on MRI
Rectum and anus: delineate the full circumference of the rectum and anus until 4 cm above the PTV
Penile bulb: delineate the full penile bulb
Femoral heads: delineate both femoral heads

Radiation technique
Radiation therapy will be delivered using online MR-guided gated radiotherapy with adaptation of treatment plans immediately prior to each treatment delivery. Treatment technique consists of static field intensity modulated radiotherapy fields from three Cobalt-sources in the MRIdian.
Standard plans will consist of 10 beam groups (30 beams) with a maximum of 10 segments from each beam.

**Treatment planning, dose calculation and set-up verification**

Radiation dose prescription will be performed according to the following specifications:

**PTV dose prescription: 36.25 Gy in 5 fractions** (PTV minus urethral PRV)

- $D_{95\%} \geq 95\%$ of the prescribed dose (95% of the PTV receives at least 95% of the prescribed dose)
- $D_{2\%} \leq 110\%$ of the prescribed dose (2% of the PTV receives a maximum dose of 110% of the prescribed dose)

**Urethral PRV dose prescription (SIS): 32.50 Gy in 5 fractions**

- $D_{98\%} \geq 95\%$ of the prescribed dose (98% of PRV receives at least 95% of PD, i.e. 30.9 Gy)
- Urethral PRV: $\leq 110\%$ of the prescribed dose (2% of PRV receives a maximum of 107% of PD, i.e. 35.8 Gy)

**Dose constraints OAR**

**Rectum and anal canal:**

- $D_{105\%} (38.1 \text{ Gy}) \leq 0.1 \text{ cc}$
- $D_{100\%} (36.25 \text{ Gy}) \leq 1 \text{ cc}$
- $D_{95\%} (34.4 \text{ Gy}) \leq 5 \text{ cc}$
- $D_{90\%} (32.6 \text{ Gy}) \leq 10 \text{ cc}$

**Bladder:** (because of daily adaption, bladder is chosen instead of bladder wall)

- $D_{102\%} (37.0 \text{ Gy}) \leq 0.1 \text{ cc}$
- $D_{100\%} (36.25 \text{ Gy}) \leq 1 \text{ cc}$
- $D_{90\%} (32.62 \text{ Gy}) \leq 15 \text{ cc}$

**Femoral heads:**

- $D_{2\%} \leq 50\%$ of the prescribed PTV dose (18.1 Gy)

**Penile bulb**

- $D_{\text{mean}} \leq 75\%$ of the prescribed PTV dose (27.2 Gy)
### BIOLOGICAL EQUIVALENT DOSES

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<th>Total dose (Gy)</th>
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Appendix 2 – Dose List for Prostate Cancer

Prostate: Low/Int risk:
- 55-60Gy in 20# over 4 weeks or
- 74Gy in 37 over 7.5 weeks or
- 78Gy in 37 fractions over 7.5 weeks

Prostate High risk including pelvic nodes:
- Prostate PTV to be treated to 74Gy in 37 or 78Gy in 39#
- Nodes to be treated to 55Gy-70Gy in 37-39Gy in 7.5-8 weeks
- Boost to node or gross disease outside the prostate 60Gy-74Gy in 37-39# in 7.5-8 weeks limited by dose to OARs

Prostate High risk without pelvic nodes:
- Prostate PTV to be treated to 60Gy in 20#
- See section – 4.26.8

Prostate bed:
- 52.5-55Gy in 20# in 4 weeks or
- 64- 66Gy in 32-33Gy in 6.5 weeks
- Boost to gross tumour recurrence in prostate bed up to 71.6Gy in 33# in 6.5 weeks or up to 74Gy in 37# in 7.5 weeks

Prostate bed and nodes:
- 66Gy in 33# over 6.5 weeks to the prostate bed. Boost to gross tumour recurrence in prostate bed up to 71.6Gy in 33# over 6.5 weeks or up to 74Gy in 37# in 7.5 weeks
- Nodal dose: 52-55Gy in 33# in 6.5 weeks. Boost to nodal masses 57Gy-71.6Gy in 33# in 6.5 weeks or up to 74Gy in 37# in 7.5 weeks.

Synchronous small volume metastases near prostate (prostate, nodes and metastases):
- Prostate: 74Gy in 37# in 7.5 weeks.
- Nodes: 55-70Gy in 37-39# in 7.5-8 weeks.
- Metastases treated to between 64-74Gy in 37-39# over 7.5-8 weeks depending on nearby OAR tolerances

Metastatic Prostate cancer (STAMPEDE):
- Dose to prostate: 55-60Gy in 20# over 4 weeks or 36Gy in 6 fractions treating once a week for 6 weeks
Palliative radiotherapy:

- 8-10Gy single #
- 21Gy in 3# treated on alternate days
- 20Gy in 5# treated daily
- 36Gy in 6# treated once a week for 6 weeks