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1. INTRODUCTION AND TRIAL SUMMARY

PEARLS TRIAL SUMMARY

PROTOCOL TITLE  
PEARLS: A phase II/III trial of Primary radiothErapy for Androgen sensitive prostate cancer patients with Lymph nodeS

TRIAL POPULATION  
Men receiving radical radiotherapy for node positive prostate cancer.

TARGET DISEASE  
Histologically confirmed adenocarcinoma of the prostate with either
- any T stage, N1, M0 or
- any T stage, N1, M1a (limited to para-aortic region) or
- any T stage, N0, M1a (limited to para-aortic region) confirmed on PSMA-PET/CT imaging (stage IV disease).

TRIAL OBJECTIVES  
Phase II: To determine whether moderately fractionated extended field intensity modulated radiotherapy (IMRT) is safe in node positive prostate cancer
Phase III: To determine whether extended field IMRT improves metastasis free survival (MFS) compared to standard field IMRT in patients with N1 M0 disease.

TRIAL DESIGN  
Multi-stage randomised controlled trial.

RECRUITMENT TARGET  
893 (150 phase II, 743 phase III)

TRIAL TREATMENT  
Participants will be stratified by extent of lymph node disease into two cohorts: pelvic nodes or para-aortic +/- pelvic nodes and randomised to receive either:
- Control arm – standard field IMRT: 60 Gray (Gy) to the prostate (and 44Gy to the pelvis with integrated boost of 51Gy to the involved lymph nodes in 20 fractions for patients with pelvic-node disease only)
- Experimental arm – extended field IMRT: 60Gy to prostate and 44Gy to pelvis and para-aortic region with integrated boost of 51Gy to the involved lymph nodes in 20 fractions.

PRIMARY ENDPOINT  
Phase II: Acute lower gastrointestinal (GI) RTOG grade ≥2 toxicity at week 18 from start of radiotherapy.
Phase III: Metastasis free survival (MFS) in patients with N1 M0 disease.

SECONDARY ENDPOINTS  
Phase II
- Acute toxicity RTOG, CTCAE v5 GI, genitourinary (GU), blood/bone marrow (FBC) up to 18 week follow up.
- Ability to deliver 44Gy in 20 fractions to the pelvic and para-aortic lymph nodes with an integrated boost to the involved lymph nodes of 51Gy in 20 fractions within organ at risk dose constraints using the varying radiotherapy planning techniques and delivery systems at participating centres.
PEARLS RADIOTHERAPY PLANNING AND DELIVERY GUIDELINES

- Patient Reported Outcomes (EPIC-26, IPSS, PRO-CTCAE, EQ-5D-5L) at end of radiotherapy and week 18 follow-up and month 6, 12, 18, 24.
- Late RTOG and CTCAE v5 GI, GU at 6, 12, 18 and 24 months.

Phase III
- Acute toxicity RTOG, CTCAE v5 GI, GU, FBC at 18 week follow up.
- Late RTOG and CTCAE v5 GI, GU, FBC at 6, 12, 18 and 24 months and then annually for 5 years (excluding FBC after 24 months).
- Patient Reported Outcomes (EPIC-26, IPSS, PRO-CTCAE, EQ-5D-5L) at end of radiotherapy, week 18, and month 6, 12, 18, 24 and 60.
- Biochemical progression (Phoenix definition: 2ng/ml increase in PSA over the nadir achieved after completion of radiotherapy treatment)
- Failure free survival (FFS).
- Time to and pattern of failure within radiotherapy field.
- Time to distant progression, time to and pattern of progression.
- Overall survival.

EXPLORATORY ENDPOINTS
- Out of radiotherapy field MFS (para-aortic cohort only).
- Time to first symptomatic skeletal events.
- Time to castration resistance.
- Dosimetric and volumetric assessment of prostate, seminal vesicles, lymph nodes and organs at risk.

FOLLOW UP
Participants will be followed up at weeks 6, 8, 12, 18 and 6 monthly until year 5 from the start of radiotherapy.
Long-term data capture will be pursued through routine data sources.
1.1. TRIAL SCHEMA

Eligible patient group: Histologically confirmed adenocarcinoma of the prostate with T any N1 M0, T any N1 M1a or T any N0 M1a on PSMA-PET imaging (stage IV disease); on LHRHa +/- androgen receptor targeted therapy or completed early docetaxel chemotherapy and suitable for radiotherapy with no CTCAE Grade 2 unresolved toxicities.

RANDOMISATION (1:1)
stratified by extent of nodal disease
(pelvic nodes vs para-aortic +/- pelvic nodes)

STANDARD FIELD RADIOTHERAPY
IMRT to prostate +/- pelvis*
(boost to involved lymph nodes)
CONTROL ARM

EXTENDED FIELD RADIOTHERAPY
IMRT to prostate, pelvis and para-aortic nodes
(boost to involved lymph nodes)
EXPERIMENTAL ARM

IMRT treatment
20 fractions over 4 weeks

Toxicity assessments: Clinician (RTOG, CTCAE) weekly during radiotherapy and at week 6, 8, 12, 18 and 6 monthly until 24 months then annually to year 5.

Patient reported outcomes: Patient (EPIC-26, IPSS, PRO-CTCAE, EQ5D5L) at end of RT, week 18 and 6 monthly until 24 months and then at 5 years.

Efficacy assessments: disease/vital status 6 monthly from 30 months until year 5 and annually thereafter utilising routine data for long term outcomes.

Translational sub studies: Imaging biomarker, Immune cell repertoire, Gut microbiota.

Phase II primary endpoint: Acute lower gastrointestinal (GI) RTOG grade ≥2 toxicity at week 18 from start of radiotherapy.

Phase III primary endpoint: Metastases free survival (MFS) in patients with N1 M0 disease.

Acute toxicity (week 18 GI toxicity) stop/continue review

* Standard field size in the control group is defined by extent of nodal disease: participants with pelvic lymph node disease receive IMRT to the prostate + pelvic lymph nodes; participants with para-aortic node disease receive IMRT to the prostate
All patients will receive inverse-planned prostate IMRT delivered in 20 fractions with daily online image-guided radiotherapy (IGRT). Various IMRT delivery techniques are allowed, (static field, VMAT, helical tomotherapy), but rotational IMRT (i.e. VMAT or Tomotherapy) for pelvic +/- para-aortic lymph node treatments is recommended due to superior bowel sparing. All techniques will be referred to as IMRT in this document, unless specifically detailed.

Radiotherapy treatment can commence on any day of the week, except Monday.

2. TRIAL ARMS

Participants allocated to control or experimental arm will have:
- One radiotherapy plan generated to deliver all 20 fractions in a single phase IMRT technique with a comfortably full bladder and empty rectum; radiotherapy will be given in 5 fractions per week with daily online IGRT.

2.1. Lymph node boost volume

A suitable lymph node boost volume is defined as:
- On the staging PMSA PET-CT, nodes are identified as suspicious for disease if they visually display increased tracer uptake with SUV more than the background soft tissues with the index of suspicion increasing with the increase in SUV.

3. PROCEDURES BEFORE PLANNING

3.1. Staging MRI Imaging

Staging multi-parametric MRI examination with DWI pre-biopsy is optimal, however, MRI after biopsy and/or starting androgen deprivation therapy (ADT) is acceptable, with less than 2 months ADT duration desirable.

3.2. Nuclear medicine Imaging

PSMA PET-CT scan for staging is needed to fulfil the eligibility criteria for PEARLS. PSMA PET-CT scan after biopsy is acceptable. For PSMA PET-CT staging after ADT started, less than 4 weeks of ADT is desirable.
3.3. Androgen Deprivation Therapy (ADT) and other systemic therapies

A LHRH antagonist or LHRH agonist with flare cover is recommended. Total hormone therapy duration of 2-3 years is recommended in the pelvic node cohort of the trial patient population, ADT duration must be specified at registration. In the para-aortic cohort, total duration of hormone therapy for the experimental arm is recommended for 2-3 years in the trial patient population and at least 3 years in the control arm and should be specified at registration.

Radiotherapy treatment should commence as soon as possible and ideally within 8 weeks after randomisation and ideally within 12-24 weeks of starting hormone therapy if no additional systemic therapy has been prescribed. Radiotherapy treatment should start at least 6 weeks after the last docetaxel dose, but not more than 18 weeks after the last docetaxel dose. If patients are on androgen receptor targeted therapy, radiotherapy treatment should commence ideally between cycles 3 to 7 of the androgen receptor targeted therapy.

3.4. Fiducial markers

The use of fiducial markers is allowed, but not mandatory. If used:

- At least three fiducial markers will be placed under transrectal ultrasound guidance, using either transperineal or transrectal approach. Antibiotic cover should be administered if fiducial placement is done transrectally. The physician will place seeds such that they are visible (and not superimposed) on orthogonal imaging (where used) and ideally are separated by 2 cm or more. It is recommended that three seeds for kV imaging and at least two seeds for CBCT or CT imaging are usable for tracking during treatment.
- To allow fiducial stabilisation and resolution of swelling, leaving 7 days between insertion and imaging for radiotherapy planning is recommended.

3.5. Rectal spacer

The use of a rectal spacer is not permitted within the trial.

4. PLANNING SCANS FOR EXTERNAL BEAM RADIOTHERAPY

4.1. Patient Preparation and Positioning

4.1.1. Bowel preparation

Ideally a patient’s rectum should be empty of both flatus and faeces, bowel preparation is strongly recommended to reduce rectal diameter for all patients receiving radiotherapy. The
use of micro-enemas or alternative bowel preparation regimes, at planning and at least for the initial part of treatment, is advocated but not mandated.

4.1.2. Bladder preparation
It is recommended that patients have a comfortably filled bladder (150-250ml) for planning and treatment delivery. Patients should be asked to empty their bladder and then drink enough water (e.g. 325ml) to ensure a reasonably filled bladder on the planning scan and before each fraction of radiotherapy.

Ideally bladder volume at planning is > 150 ml. If below 150 ml, proceed with planning, encourage good hydration and monitor bladder filling during treatment on CBCT. If the bladder volume is consistently below that seen at planning and despite increasing oral fluids, please review bowel volumes on CBCT within PTV. On review, if the bowel volume within the PTV is more than on the planning CT and the initial plan mandatory bowel dose constraints are close to tolerance, consider replanning.

4.1.3. Immobilisation and skin markers
All patients will have their planning CT scan and radiotherapy treatment in the supine position. The use of knee and foot support is recommended, indexed to the treatment couch.

Arms must be displaced out of the radiotherapy field using local departmental immobilisation protocol. For patients having prostate +/- pelvic lymph node radiotherapy, placing arms across chest is common. For patients having para-aortic radiotherapy, arms must be displaced sufficiently to avoid the volume which extends to L2. Options include getting patients to cross their arms over their body, holding their shoulders or a hand support positioned very superiorly. Alternatively, patients could be positioned with arms above head, supported by a vac bag or chest-board. If adopting the second approach, consider the patient height and maximum linac couch travel possible.

For patients having prostate +/- pelvic lymph node radiotherapy, 3 pelvic tattoos, 2 lateral and 1 anterior are standard. For patients having para-aortic radiotherapy, in addition to 3 pelvic tattoos, tattoos at the level of xiphisternum or L2 are recommended.

4.2. Planning Scans
4.2.1. Planning CT scan
Planning CT scans will be performed in the treatment position. CT slices of ≤3.0 mm are mandated. Recommended scanning levels for prostate +/- pelvic lymph node patients are from the L2/L3 interspace to 2 cm below ischial tuberosity. For those patients randomised to
prostate, pelvic and para-aortic radiotherapy, extend the superior scanning level to the top of T12.

Patients who are randomised to pelvic +/- para-aortic node radiotherapy may be scanned with IV contrast to aid delineation as per department protocol. In addition, those with limited intra-abdominal fat may be considered for oral contrast administration.

All patients should have their rectal diameter reviewed either using a short series scan localised in-line with the prostate or on the completed CT planning scan. If the anterior/posterior diameter of the rectum is >4 cm at any level adjacent to the prostate the patient should be rescanned with additional bowel preparation. For patients who have a rectal AP diameter >4 cm despite re-scanning, acquire CBCT at fraction 1 to confirm similar rectal size.

4.2.2. PSMA PET-CT fusion
To aid in contouring of the lymph node boost sites, consider fusion (using bone) of the planning CT with the diagnostic PSMA PET-CT scan.

5. ORGANS AT RISK AND TARGET VOLUME DEFINITIONS FOR EXTERNAL BEAM PLANNING

5.1. Organs at Risk (OAR)
Organ at risk (OAR) structures to be outlined, and naming convention, for PEARLS include:

<table>
<thead>
<tr>
<th>Volume</th>
<th>Naming convention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>Rectum</td>
</tr>
<tr>
<td>Bladder</td>
<td>Bladder</td>
</tr>
<tr>
<td>Urethra</td>
<td>Urethra</td>
</tr>
<tr>
<td>Right femoral head</td>
<td>FemurHead_R</td>
</tr>
<tr>
<td>Left femoral head</td>
<td>FemurHead_L</td>
</tr>
<tr>
<td>Penile bulb</td>
<td>PenileBulb</td>
</tr>
<tr>
<td>Bowel</td>
<td>Bowel</td>
</tr>
<tr>
<td>For para-aortic irradiation in addition:</td>
<td></td>
</tr>
<tr>
<td>Duodenum</td>
<td>Duodenum</td>
</tr>
<tr>
<td>Right kidney</td>
<td>Kidney_R</td>
</tr>
<tr>
<td>Left kidney</td>
<td>Kidney_L</td>
</tr>
<tr>
<td>Right ureter</td>
<td>Ureter_R</td>
</tr>
</tbody>
</table>
5.1.1. OAR definitions

**Bladder:** The bladder should be contoured in entirety from base to dome. The lateral extent is the outer bladder wall.

**Rectum:** The rectum should be contoured to the outer boundary of the external rectal wall, including rectal contents. Contour from the rectosigmoid flexure, approximately at the level of the S3 vertebral body, the rectosigmoid flexure is best visualized on sagittal viewing planes. The caudal border is at the anorectal junction where the perirectal fat can no longer be seen, coinciding with the insertion of the levator muscles and the pubo-rectalis sling; these structures are best visualised on coronal viewing planes.

**Bowel:** The bowel encompasses the small (duodenum, jejunum and ileum) and large bowel (caecum, ascending, transverse, descending, and sigmoid colon) structures in one contour, adhering closely to the outer boundary of the external bowel wall, including bowel contents. The superior extent of outlining should be 2 cm beyond the superior extent of CTVpsv or CTVn, whichever is most superior to the recto-sigmoid junction. Ensure small bowel in the lower pelvis caudal to the recto-sigmoid junction is included.

**Duodenum:** The duodenal contour extends from the pylorus to the duodenojejunal junction/ligament of Treitz. The majority of the structure is fixed to the retroperitoneum and follows a C-shaped course around the head of the pancreas. The contour follows four anatomical sections:
1) 5 cm in length and anterolateral to the body of the L1 vertebra
2) 7-10 cm descending adjacent to the L1-3 vertebral bodies
3) 6-8 cm in length, turning medially and crossing the L3 vertebral body. The aorta and inferior vena cava are posterior; the superior mesenteric artery and vein lie anteriorly
4) 5 cm in length and ascending from the L3 vertebral body to the cranial border of the L2 vertebral body
The contour adheres closely to the outer boundary of the external wall and includes duodenal contents. Take care to distinguish the duodenum from the head of the pancreas as the structures are in close proximity.

**Right and Left femoral heads:** Each femoral head should be contoured separately. The femoral heads are outlined to the bottom of the curvature of their heads (femoral necks are not included). Contour on bone windows.

**Right and left ureter:** Each ureter should be contoured separately. The cranial border is at the medial aspect of the kidney. The abdominal parts of the ureter are retroperitoneal and lie anterior to the psoas muscle. The ureters continue to run caudally over the pelvic brim at the bifurcation of the common iliac arteries.
At the level of the ischial spine, the ureter turns anterior and medial to enter the posterolateral wall of the urinary bladder, before opening into the urinary bladder at the ureteric orifice. The structure should be contoured to include all fibromuscular layers.

**Urethra:** The urethra extends from the internal urethral orifice at the bladder neck and continues caudally to the external urethral orifice. Outline the structure only if it is visible on the planning scan. Outline the urethra or catheter from the inferior to superior end of the prostate PTV; use the MRI to locate the structure.

**Penile bulb:** The penile bulb is the portion of the bulbous spongiosum of the penis immediately caudal to the genito-urinary diaphragm. The structure is bright on T2 weighted MRI. On CT, the structure is posterior to the urethra and has a round shape. The structure is normally 9-10 mm in the cranial-caudal direction. The contour should not continue into the shaft of the penis.

**Right and Left kidney:** Each kidney should be contoured separately from the upper to the lower pole. The kidney is easily distinguished from surrounding adipose tissue and is located at the level of the T12 and L3 vertebral bodies. The structure excludes cysts, pararenal fat, and the adrenal gland and is the outer contour excluding renal pelvis

**Spinal cord:** The spinal cord is contoured as the true spinal cord, not the spinal canal. The cranial border is at the level of the tip of the dens of the C2 vertebra, where the structure meets the brainstem. The caudal border is where the spinal cord thickens into the conus medullaris at the level of L1-2 vertebral bodies i.e. the cranial border of the cauda equina. Contour down to L2.

### 5.2. Target Volume Definition

Volumes will be defined according to ICRU reports 50, 62 and 83 \(^{(2,3,4)}\). Outlining should be carried out with the aid of the diagnostic MRI (if available) and PSMA PET-CT scan and PEARLS outlining protocol. For all arms, the prostate target and lymph node volumes are outlined in the same way.

Use the exact nomenclature below.

### 5.3. GTV and CTV Definition:

**Prostate +/- pelvic nodes**

<table>
<thead>
<tr>
<th>Volume</th>
<th>Structure</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTVp</td>
<td>Prostate</td>
<td>Prostate, plus proximal 1 cm of seminal vesicles (see Figure 1) and any extraprostatic extension (periprostatic fat, seminal vesicle or base of bladder).</td>
</tr>
<tr>
<td>CTVpsv</td>
<td>Prostate and seminal vesicles</td>
<td>CTVp and any remaining seminal vesicle</td>
</tr>
</tbody>
</table>
VESSEL  Pelvic vessel  Common iliac, left- and right-sided external iliac, internal iliac and obturator vessels

CTVn  Pelvic lymph nodes  Pelvic nodal volume and CTVnb

GTVnb  Lymph node boost volume  Pelvic radiologically defined on PSMA PET-CT pathological residual lymph node volume

CTVnb  Lymph node boost volume  GTVnb + 3 mm

Figure 1: Schematic illustration (sagittal plane) of the 1 cm proximal seminal vesicle CTV inclusion for CTVp (except for T3b patients when if the extent of involved seminal vesicle is greater than the proximal 1 cm, the involved volume of the seminal vesicles will be included as CTVp)

**Prostate, pelvic and para-aortic**

<table>
<thead>
<tr>
<th>Volume</th>
<th>Structure</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTVp</td>
<td>Prostate</td>
<td>Prostate, plus proximal 1 cm of seminal vesicles (see Figure 1) and any extraprostatic extension (periprostatic fat, seminal vesicle or base of bladder).</td>
</tr>
<tr>
<td>CTVpsv</td>
<td>Prostate and seminal vesicles</td>
<td>CTVp and any remaining seminal vesicle</td>
</tr>
<tr>
<td>VESSEL</td>
<td>Pelvic and retroperitoneal vessel</td>
<td>Aorta, inferior vena cava, common iliac, left- and right-sided external iliac, internal iliac and obturator vessels</td>
</tr>
</tbody>
</table>
5.4. Clinical Target Volumes and Planning Target Volumes

Prostate, prostate + pelvic, prostate +/- para-aortic node IMRT (with or without intra-prostatic fiducials)

<table>
<thead>
<tr>
<th>Arm</th>
<th>Site</th>
<th>Structure name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Prostate SV</td>
<td>CTVpsv</td>
<td>Prostate and seminal vesicles CTVpsv plus 8 mm</td>
</tr>
<tr>
<td></td>
<td>Prostate</td>
<td>CTVp, PTVp_6000</td>
<td>Prostate, proximal 1 cm of SV or in T3b disease the involved SV * CTVp plus 4 mm</td>
</tr>
<tr>
<td>PP</td>
<td>Prostate SV</td>
<td>CTVpsv</td>
<td>Prostate and seminal vesicles CTVpsv plus 8 mm</td>
</tr>
<tr>
<td></td>
<td>Prostate</td>
<td>CTVp, PTVp_6000</td>
<td>Prostate, proximal 1 cm of SV or in T3b disease the involved SV * CTVp plus 4 mm</td>
</tr>
<tr>
<td></td>
<td>Pelvic LN</td>
<td>CTVn, PTVn_4400</td>
<td>Pelvic nodes + CTVnb CTVn plus 5 mm</td>
</tr>
<tr>
<td></td>
<td>LN boost</td>
<td>GTVnb1, GTVnb2, CTVnb_5100, PTVnb</td>
<td>LN boost volume(s) GTVnb1 + 3 mm, GTVnb2 + 3 mm margin + ..... All volumes form CTVnb CTVnb plus 5 mm</td>
</tr>
<tr>
<td>PPP</td>
<td>Prostate SV</td>
<td>CTVpsv</td>
<td>Prostate and seminal vesicles CTVpsv plus 8 mm</td>
</tr>
<tr>
<td></td>
<td>Prostate</td>
<td>CTVp, PTVp_6000</td>
<td>Prostate, proximal 1 cm of SV or in T3b disease the involved SV * CTVp plus 4 mm</td>
</tr>
<tr>
<td></td>
<td>Pelvic and para-aortic LN</td>
<td>CTVn, PTVn_4400</td>
<td>Pelvic and para-aortic lymph nodes + CTVnb CTVn plus 5 mm</td>
</tr>
<tr>
<td></td>
<td>LN boost</td>
<td>GTVnb1, GTVnb2, CTVnb_5100, PTVnb</td>
<td>LN boost volume(s) GTVnb1 + 3 mm, GTVnb2 + 3 mm margin + ..... All volumes form CTVnb CTVnb plus 5 mm</td>
</tr>
</tbody>
</table>

- P = prostate; SV = seminal vesicles; PP = prostate and pelvic LN; PPP = prostate, pelvic and para-aortic LN
*for T3b disease, extend CTVp to the most distal extent of the SV determined by the involved SV volume or proximal 1 cm

6. EXTERNAL BEAM RADIOThERAPY PLANnING GUIDELINES

6.1. Radiotherapy Technique

This trial simultaneously treats multiple dose-level PTV structures in a single phase. Therefore, an IMRT or VMAT planning technique must be used to obtain the prescription doses for adjacent PTVs. Rotational IMRT (i.e. VMAT or Tomotherapy) is recommended for nodal treatments due to superior bowel sparing. Pelvic and/or para-aortic lymph node treatments are randomly allocated to patients in the trial dependent upon diagnostic PSMA PET-CT findings.

6.2. Isocentre Placement

As per standard practice, except for patients randomised to para-aortic lymph node radiotherapy on Elekta c-arm linacs. Please see section 7.3.

6.3. Prescribed Dose and Fractionation

In all arms, treat the patient in 20 fractions. In all arms, treat the prostate to 60 Gy and the seminal vesicles to 47 Gy, with prostate and pelvic arm and prostate, pelvic and para-aortic arm also simultaneously treating the pelvic +/- para-aortic lymph nodes to 44 Gy in 20 fractions and PSMA PET-CT-involved lymph nodes to 51 Gy in 20 fractions.

6.4. Definition of PTVs for Dose Reporting with their Dose Constraints

<table>
<thead>
<tr>
<th>Planning Target Volumes</th>
<th>Dose to PTV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTVpsv_4700</td>
<td>Report dose to PTVpsv_4700–PTVp_6000</td>
</tr>
<tr>
<td></td>
<td>$D_{50%} \geq 47.0$ Gy (median**); $D_{98%} \geq 44.65$ Gy (95%)</td>
</tr>
<tr>
<td>PTVp_6000</td>
<td>Report dose to PTVp_6000</td>
</tr>
<tr>
<td></td>
<td>$D_{50%} = 60$ Gy (median**); $D_{98%} \geq 57.0$ Gy (95%), $D_{2%} \leq 64.2$ Gy (107%)</td>
</tr>
<tr>
<td>PTVn_4400</td>
<td>Report dose to PTVn_4400 minus (PTVpsv_4700 and PTVnb_5100)</td>
</tr>
<tr>
<td></td>
<td>$D_{50%} = 44$ Gy (median**); $D_{98%} \geq 41.8$ Gy (95%), $D_{2%} \leq 47.1$ Gy (107%)</td>
</tr>
<tr>
<td>PTVnb_5100</td>
<td>Report dose to PTVnb_5100</td>
</tr>
<tr>
<td></td>
<td>$\dagger D_{50%} = 51.0$ Gy (median**), $D_{2%} \leq 54.0$ Gy</td>
</tr>
</tbody>
</table>

** For median doses, values within 1% of the stated figure are acceptable.
† The median dose may be reduced (44 Gy $\leq D_{50\%} \leq 51$ Gy) if PTVnb near bowel/duodenum
6.5. Normal Tissue Dose Constraints for Organs at Risk

The nomenclature used in Section 5.1 Organs at Risk (OAR) should be used for planning in all benchmark and clinical cases. Failure to do so may result in plan having to be resubmitted. Note that OARs have both optimal dose constraints that should be the aim in planning and mandatory constraints that must be achieved for the plan to be acceptable. When reporting, ensure that the entire OAR volume, including any overlap with the PTVs, has been included.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Dose for 20# [Gy]</th>
<th>Maximum Volume</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Optimal</td>
<td>Mandatory</td>
<td></td>
</tr>
<tr>
<td>Rectum*</td>
<td>24</td>
<td>70 %</td>
<td>80 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32</td>
<td>51 %</td>
<td>65 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>38 %</td>
<td>50 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>27 %</td>
<td>35 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>-</td>
<td>30 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>-</td>
<td>15 %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>1 %</td>
<td>3 %</td>
<td></td>
</tr>
</tbody>
</table>

D\text{mean} \leq 35 \text{ Gy}

| Bladder          | 40               | 50 %           | -              |
|                  | 48               | 25 %           | 50 %           |
|                  | 60               | 5 %            | 35 %           |

| Bowel\^\# (standard) | 36               | 78 cm\text{\textsuperscript{3}} | 158 cm\text{\textsuperscript{3}} |
|                    | 40               | 17 cm\text{\textsuperscript{3}} | 70 cm\text{\textsuperscript{3}} |
|                    | 44\^\#          | 14 cm\text{\textsuperscript{3}} | 28 cm\text{\textsuperscript{3}} |
|                    | 48\^\#          | 0.5 cm\text{\textsuperscript{3}} | 6 cm\text{\textsuperscript{3}} |
|                    | 52\^\#          | < 0.01 cm\text{\textsuperscript{3}} |

| Bowel\^\# (only for prostate, pelvic and para-aortic RT, if not able to meet the standard bowel constraints) | 36               | 78 cm\text{\textsuperscript{3}} | 158 cm\text{\textsuperscript{3}} |
|                                                                                     | 40               | 40 cm\text{\textsuperscript{3}} | 110 cm\text{\textsuperscript{3}} |
|                                                                                     | 44\^\#          | 28 cm\text{\textsuperscript{3}} | 70 cm\text{\textsuperscript{3}} |
|                                                                                     | 48\^\#          | 0.5 cm\text{\textsuperscript{3}} | 6 cm\text{\textsuperscript{3}} |
|                                                                                     | 52\^\#          | < 0.01 cm\text{\textsuperscript{3}} |

| Duodenum          | 46\^\#          | 4 cm\text{\textsuperscript{3}} |
|                  | 51\^\#          | 0.5 cm\text{\textsuperscript{3}} |

| Penile bulb       | 22               | 50 %           | -              |
|                  | 48               | 10 %           | -              |

| Left Femoral Head | 40               | 5 %            | 50 %           |
| Right Femoral Head| 40               | 5 %            | 50 %           |

| Left Kidney       | 18               | 25 %\^\*\*    |
| Right Kidney      | 18               | 25 %\^\*\*    |

| Spinal cord       |                  | Dmax<36 Gy\^\*\* |

*The rectal mean dose of 35 Gy should not compromise the coverage of PTVp\_6000 or PTVpsv\_4700. If D\text{3\%} \leq 60 \text{ Gy} and D\text{mean} \leq 35 \text{ Gy} the rectal NTCP for rectal bleeding and faecal incontinence do not exceed 6 %.*
If the mandatory dose constraints are not achieved and the plan is optimal for prostate and pelvic radiotherapy, the coverage of PTVn_4400 should be reduced to achieve the dose constraints. If the mandatory dose constraints are not achieved and the plan is optimal for prostate, pelvic and para-aortic radiotherapy, the adjusted bowel mandatory dose constraints can be used.

If the adjusted mandatory dose constraints (adapted from Phase 1/2 Dose-Escalation Study of the Use of Intensity Modulated Radiation Therapy to Treat the Prostate and Pelvic Nodes in Patients with Prostate Cancer Ferreira M et al. IJROBP 2017) are not achieved and the plan is optimal for prostate, pelvic and para-aortic radiotherapy, the coverage of PTVn_4400 should be reduced to achieve the dose constraints.

Coverage of PTVnb may be compromised if adjacent to bowel.

From RTOG 0937 protocol

7. RADIOThERAPY DELIVERY AND ON-TREAT CONSIDERATIONS

It is important to ensure that patients follow the bladder/bowel preparation instructions they used at the planning CT scan appointment.

The IGRT employed may vary depending on the patient’s treatment site. Volumetric imaging for IGRT is mandated for patients receiving prostate and pelvic +/- para-aortic lymph node radiotherapy. IGRT considerations for prostate only, prostate + pelvic lymph nodes and prostate + pelvic lymph nodes + para-aortic lymph nodes are discussed below.

7.1. Prostate only IGRT

All patients will have daily image-guided radiotherapy with initial alignment to tattoos. Volumetric verification using CBCT or MVCT is recommended, either matching to soft-tissue or implanted fiducial markers. Ultrasound and MRI guided RT is also accepted. 2D imaging is only permissible if prostate fiducial markers are used (a minimum of 2 fiducial markers is allowed but 3 fiducials are recommended).

All measured shifts should be applied online.

If at fraction 1, any shift value is greater than 10 mm; check the bone match, rectal and bladder filling and if correctable re-position and re-image. If the set-up error cannot be effectively resolved do not commence treatment until the images have been reviewed by a locally assigned responsible person (e.g. PI, senior radiographer, IGRT lead, physicist). In rare occasions, a re-scan and replan may be required.

During the course of radiotherapy if a significant shift is required (> 10 mm), the shift should be implemented and the patient re-imaged after the shift. If the initial image was 2D it is recommended that the second image be volumetric (3D) to allow visualisation of OAR deformation. If shifts > 10 mm occur on more than 1 occasion, arrange an offline review by a locally assigned responsible person (e.g. PI, senior radiographer, IGRT lead, physicist).
7.2. Prostate and pelvis IGRT

All patients will have daily image-guided radiotherapy with initial alignment to tattoos. Volumetric verification using CBCT or MVCT is mandated, using bony anatomy and prostate soft tissue or fiducial markers to guide verification.

The CBCT length imaged should capture the prostate and as much of the nodal volume as practical. Set a standard pelvic bone ROI and perform the initial registration to bone. Record the isocentre shifts but do not apply the corrections. Rematch (using automatic function where available) to the prostate CTV or implanted fiducial markers. If the difference between the prostate and bone (nodal) match is ≤ 5 mm, apply the isocentre shift (based on prostate alignment) and continue treatment without further action. Please refer to section 7.4 with respect to management of differences between prostate and bone isocentre shifts.

All measured shifts should be applied online.

Please record shifts applied for each fraction in the IGRT Verification spreadsheet.

7.3. Prostate, pelvic and para-aortic IGRT

All patients will have daily image-guided radiotherapy with initial alignment to tattoos. Volumetric verification using CBCT or MVCT is mandated, using bony anatomy and prostate soft tissue or fiducial markers to guide verification.

The field length for this group of patients is approximately 35 cm, making IGRT considerations more complicated. The processes employed to image this extended volume will depend on the equipment available and may be guided by departments’ previous experience imaging gynaecological patients with para-aortic lymph node fields.

It is appreciated that daily capture of the entire volume is likely not possible, but effort should be made to optimise imaging to enable the greatest extent of the treatment volume to be visualised daily.

**ELEKTA:**
The M20 filter is specified as this produces a CBCT length of approximately 26 cm. This CBCT length will not cover the entire volume but should be positioned to capture the whole of the prostate gland up to the L3/L4 junction depending on patient height.

It is not recommended that the imaging centre be moved manually to achieve this coverage, instead careful consideration of isocentre position during the planning stages is required. It is recommended that the isocentre be placed 13 cm superior to the inferior prostate PTV border. With a symmetrical CBCT field this should facilitate visualisation of the prostate apex.
up to approximately L3/L4 on the resulting image. The position of L3/L4 is considered superior enough to characterise L2 position.

**Example of isocentre placement and resulting CBCT**
The example shown is of a patient having radiotherapy to their prostate bed, pelvis and para-aortic (up to L2/L3 vertebral interspace) lymph nodes but the premise is the same. Image A, the patient’s planning CT scan, shows the isocentre is positioned approximately 13 cm superior to the inferior PTV margin. Image B presents the patients on treatment CBCT, the resulting image includes the primary PTV and enough of the nodal PTV to confidently review para-aortic lymph node coverage.

Image matching should follow the process presented in section 7.2.

**Varian:**
The maximum single CBCT scan length is 17.5 cm. The CBCT centre should be shifted daily using the ‘offset CBCT’ function to enable visualisation of the entire prostate and as much of the vertebra as possible. As a minimum to include the sacral promontory.

For the first 3 fractions, the multiscan option should be utilised to visualise the superior extent of the field. Subsequently a multiscan should be acquired weekly as a minimum to check alignment of the para-aortic lymph nodes. If a patient’s set-up is complicated by pelvic rotation, multiscans can be acquired more frequently. If the multiscan option is not available,
kV imaging pairs can be utilised to visualise the L-spine adjacent to the para-aortic lymph node volume to compliment the standard CBCT data.

**Example of standard and multiscan CBCT**
The example shown is of a patient having radiotherapy to his prostate and extended pelvis up to L3/L4 vertebral interspace. Image A shows the standard CBCT with the imaging centre offset inferiorly to image the prostate CTV. Image B is the patient’s multiscan image, enabling the nodal volume to be visualised.

- Please refer to section 7.4 with respect to management of differences between prostate and bone isocentre shifts.

Please record shifts applied for each fraction in the IGRT Verification spreadsheet.

### 7.4. Management of differences between prostate and bone isocentre shifts

If the **difference between bone and prostate isocentre shifts is > 5 mm but ≤ 10 mm:**

Apply shifts from prostate match, treat and refer for offline radiographer review.

**Offline radiographer review:**
- Check the matched planning CT and CBCT.
  - Do vessels within the CTVn lie outside PTVn by more than 1 mm over at least 3 slices?
  - If so, try to determine cause of difference. • Did the patient tense their buttocks at planning CT and now relaxed? • Is rectal and/or bladder filling significantly different?

**ACTION**
• Instruct patient as appropriate (e.g. if bladder or rectal filling), aiming to reduce shift
• If this deviation occurs a second time refer to a locally assigned responsible person 
  (e.g. PI, senior radiographer, IGRT lead, physicist) for clinical and dosimetric review.

If the **difference between bone and prostate isocentre shifts is > 10 mm**: 
Stop, do not deliver radiotherapy.
Review the image for set-up issues influencing the mismatch between bone and prostate soft tissue. For example, is the patient’s rectal diameter large and pushing the prostate anteriorly or the patient’s bladder full and pushing the prostate inferiorly. If the identified factor is amenable to improvement, apply the appropriate intervention e.g., patient to evacuate rectum or empty bladder and re-setup.

If after re-setup the difference is < 10 mm follow the processes above. If the deviation is still > 10 mm do not treat and arrange offline review with a locally assigned responsible person (e.g. PI, senior radiographer, IGRT lead, physicist) to establish cause.

Please record shifts applied for each fraction and details of any intervention required in the IGRT Verification spreadsheet.

8. **TREATMENT SCHEDULING**

Treatment can start on any day of the week except Monday. The treatment course must not be delivered in less than 28 days. Unscheduled treatment interruptions up to 5 days are acceptable as per RCR guidance. If further delays have occurred (e.g. machine breakdown), record this and the reasons on the treatment CRF. Do not treat more than one fraction per day and 5 fractions per week.

9. **DOCUMENTATION ON COMPLETION OF RADIOTHERAPY**

On completion of radiotherapy planning, all plans (including PSMA PET-CT images and PMSA PET-CT report, CT images, structures, plan and dose matrix), Plan Assessment Form* and IGRT Verification spreadsheet** should be exported, anonymised and sent to the RTTQA team electronically following the exporting data guidelines in section 10.9. Please discuss any concerns with the QA team.

* For Phase II only; for Phase III a screenshot of the clinical protocol from the treatment planning system, showing the PTV and OAR dose constraint data, may be sent as an alternative.
** For pelvic nodes treatment only
10. RADIOTHERAPY QUALITY ASSURANCE

10.1. Radiotherapy Quality Assurance Overview

Radiotherapy quality assurance (RTQA) includes pre-trial and on-trial components. RTQA will be streamlined where feasible with other prostate trials, e.g. PIVOTALboost – see section 10.6 for details.

RTQA documentation and data can be downloaded from the RTTQA website: http://www.rttrialsqa.org.uk

Please send all completed RTQA to the PEARLS RTQA contact at: pearls.rtqa@nhs.net

Pre-trial QA includes:
- Benchmark outlining case
- Benchmark planning case
- Facility questionnaire
- PET facility questionnaire

On-trial QA includes:
- Prospective and/or retrospective case reviews
- Review of staging PSMA PET-CT imaging and report
- Dosimetry site visit (subject to prior RTTQA dosimetry accreditation)

All outlining should be either performed by, or reviewed and approved by, the PI at the centre who has been through the pre-trial outlining QA. Since this is a clinical trial and the patient numbers may not be excessive we hope this approach will be acceptable. However, where this is not feasible, the PI should review and approve clinical outlines for the first cohort of PEARLS patients recruited by each additional clinician at that centre to encompass a combination of the following, after which (assuming these are satisfactory) they are also approved for PEARLS:
- 3 pelvic lymph nodes contours
- 3 para-aortic lymph nodes contours
- 3 nodal boost contours

Please notify the RTQA team of any additional clinicians who have been locally approved in this way. A form is available from the RTQA team to facilitate this.

Should the PI leave and be replaced, the new PI should complete the PEARLS benchmark outlining QA.
10.2. Pre-Trial Questionnaires

10.2.1. Facility Questionnaire

The Prostate Facility Questionnaire (FQ) collects information about the radiotherapy equipment, techniques and procedures used by a centre for the trial.

The questionnaire will be sent to each site by the RTQA team as it may be pre-filled with information provided from previous trials. If the FQ has been completed previously for another prostate trial, please update where necessary to reflect procedures and equipment for the PEARLS trial and re-submit.

10.2.2. PMSA PET-CT Facility Questionnaire

The PSMA PET-CT Facility Questionnaire collects information about the PET equipment, dose calibrators and transfer of data capability.

10.3. Benchmark Cases

An outlining and a planning benchmark case will be completed by all trial centres. QA will be streamlined for those centres who have completed RTQA accreditation for other prostate trials (see section 10.6 for details).

10.3.1. Downloading data from RTTQA website

Download the benchmark case DICOM datasets from the RTTQA website:
http://www.rttrialsqa.org.uk

- Log in
- Select ‘Downloads’ from the menu bar
- Open ‘Top Level Folders’ (see below) and select the ‘PEARLS prostate PA nodes’ folder
- Select files and choose ‘Download’ from the ‘Action’ column
10.3.2. Outlining Benchmark Case

All centres wishing to participate in the PEARLS trial will need to complete a contouring exercise for para-aortic lymph nodes. The PSMA PET-CT, planning MRI, planning CT and structure set, and a PDF file containing the PET report (file PEARLS_outlining_benchmark.zip) should be downloaded from the RTTQA website. Please import the DICOM data for Patient ID/Name = “PEARLS_outlining_benchmark” into your own outlining or treatment planning system (TPS). You will need to register the PSMA PET-CT to the planning CT.

Refer to outlining instructions in section 5, supplemented by the “PEARLS Pelvic Lymph Node, Extended Field and Nodal Boost Contouring” document. An outlining video to support the atlas is available on the RTTQA website.

Please contour the following structures on the planning CT, with the aid of the PSMA PET-CT scan for the nodal boost and with the MRI for the prostate if this is what you do locally. Please use the trial structure naming convention. Contouring requirements have been streamlined according to prior RTQA accreditation for both the site and the PI for the PIVOTALboost and PACE trials.

<table>
<thead>
<tr>
<th>Structure</th>
<th>PIVOTALboost RTQA approved</th>
<th>PACE RTQA approved</th>
<th>No RTQA approval in PACE or PIVOTALboost</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTVp</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>CTVpsv</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>CTVn</td>
<td>Yes, start contour at L5/S1 interspace to para-aortic region</td>
<td>Yes, including pelvis and para-aortic region</td>
<td>Yes, including pelvis and para-aortic region</td>
</tr>
<tr>
<td>GTVnb</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CTVnb</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rectum</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bladder</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bowel</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bowel_03</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Duodenum</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Duodenum_03</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>PenileBulb</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Kidney_R</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Kidney_L</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ureter_R</td>
<td>Optional</td>
<td>Optional</td>
<td>Optional</td>
</tr>
<tr>
<td>Ureter_L</td>
<td>Optional</td>
<td>Optional</td>
<td>Optional</td>
</tr>
<tr>
<td>SpinalCord</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Once outlines have been created, reviewed and accepted by the local PI, please export and return the DICOM CT and Structure data to the RTQA team (see section 10.9).
10.3.3. Planning Benchmark Case

All sites must complete and submit the PEARLS planning benchmark case for the prostate, pelvis and para-aortic LN arm. The CT images and pre-outlined structure set are available for download from the RTQA website.

Please import the CT images and structure set for Patient ID/Name = "PEARLS_planning_benchmark" into your own TPS. The CT has been delineated by the CI with the following structures, which should not be edited. No additional structures, e.g. for PTV/OAR overlaps, have been created; the individual centre should create these as needed.

- Target volumes: CTVp, CTVpsv, CTVn, GTVnb, CTVnb

You will need to create the PTVs.

This patient should be planned as a prostate, pelvic and para-aortic LN case with nodal boost. Please complete the PEARLS Plan Assessment form (PAF) and provide a copy of the TPS treatment planning report (for beam details).

Data Export: Once the benchmark plan has been created, reviewed and accepted by the local PI, the export of the CT images, dose matrix, RT plan and structure set in DICOM format should be returned to the RTQA team (see section 10.9). Avoid re-anonymising as this causes problems and may delay your review.

Note that RTQA approval can be obtained when the benchmark cases have been approved. However, you cannot recruit your first patient (be “activated”) until you have returned your Facility Questionnaire and had it approved.

10.4. Review of staging PSMA PET-CT imaging and report

The PSMA PET-CT images (DICOM format and anonymised) and the PSMA PET-CT report (anonymised) must be submitted prospectively for RTQA review for the first two patients at each site randomised in the PEARLS trial.

10.5. Patient Case Reviews

The outlining and treatment planning for the first cohort of patients recruited by each trial centre will be subject to review by the RTQA team. This may be a prospective (i.e. pre-treatment) or timely retrospective review, to be advised by the RTQA team on a case-by-case basis – see table in section 10.6.4. Additional reviews may be requested by the RTQA team.

To ensure a short response time for prospective reviews please notify the RTQA team when a patient has been identified, and please allow 2 weeks between submitting data and the RT treatment start date to allow time for amendments. Please send outlining for review in
advance of RT treatment planning where possible to expedite the review. Failure to give the QA team sufficient notice of a case may result in delays in the case being reviewed. Should it not be possible to complete a review prior to the planned treatment start date, it is the PI’s responsibility to decide whether to start treatment as planned (prepared to re-plan for remaining treatment fractions if necessary) or to delay treatment start until review is complete.

For outlining reviews please send:
- PSMA PET-CT images (with DICOM registration object if used) and PET report
- Planning CT images
- DICOM structure set

For planning reviews please send:
- Planning CT images
- DICOM structure set
- DICOM dose matrix
- DICOM plan file
- Completed PAF
- Copy of TPS treatment plan report (for beam details)
- Patient-specific QA results (measured or calculated); may be sent following the review

See section 10.9 for data export instructions.

Note the following:
1. All retrospective reviews are “timely”: data to be submitted within a week of treatment start and review to be completed before another trial patient is treated.
2. The RTQA team will be in touch if a patient is recruited who needs a prospective review.

10.6. Streamlining of RTQA

Streamlining of RTQA is based on prior completion of RTQA for another NIHR-portfolio prostate trial (e.g. PIVOTALboost, PACE).

10.6.1. Facility Questionnaire (FQ)
If the prostate FQ has been completed previously, please check and amend any details which have changed or are different for the PEARLS trial; the RTQA team will provide a copy of your FQ with PEARLS-specific questions added.

10.6.2. Benchmark Outlining Case

Please see table in section 10.3.2 for streamlining of contouring QA for centres accredited for PIVOTALboost and PACE trials.

If both the centre and the PI have been approved for PIVOTALboost:
• Please complete para-aortic node contouring only (i.e. from L5/S1) on the outlining benchmark case

If both the centre and the PI have been approved for PACE but not PIVOTALboost:
• Please complete pelvic nodes and para-aortic node contouring (but not prostate) on the outlining benchmark case

If the centre is open for PIVOTALboost/PACE but the PI is different, the full contouring will be required.

10.6.3. Benchmark Planning Case
This is required for all sites.

10.6.4. Patient Case Reviews
Case review requirements, with streamlining for PIVOTALboost and PACE centres, are shown in the table below for each trial arm. However, you will be notified about the type of review required by the RTQA team when a suitable patient is randomised.

<table>
<thead>
<tr>
<th>Trial arm</th>
<th>Centre/PI in PIVOTALboost</th>
<th>Centre/PI in PACE but not PIVOTALboost</th>
<th>No prostate trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate-only (P)</td>
<td>N/A</td>
<td>N/A</td>
<td>Prospective a</td>
</tr>
<tr>
<td>Prostate and pelvic LN (PP)</td>
<td>N/A</td>
<td>Prospective b</td>
<td>Prospective b</td>
</tr>
<tr>
<td>Prostate, pelvic and para-aortic LN (PPP)</td>
<td>Prospective</td>
<td>Prospective</td>
<td>Prospective</td>
</tr>
<tr>
<td>Nodal boost (PP or PPP)</td>
<td>Prospective</td>
<td>Prospective</td>
<td>Prospective</td>
</tr>
</tbody>
</table>

a – if PP or PPP case not yet reviewed
b – if PPP case not yet reviewed

The RTQA team may request additional prospective or retrospective reviews as required.

10.7. Dosimetry Audit
All sites are required to have a recent dosimetry site visit by the RTTQA group. Sites which do not have this will be contacted individually by the RTTQA team to arrange an audit.

10.8. Ongoing Data Collection
Radiotherapy plan data and PSMA-PET will be collected (in DICOM format by electronic transfer) for all patients having radiotherapy within the trial. These data will be stored on a secure server by the sponsor. All patient data must be anonymised before transfer, and
should be re-identified with the trial number. The Plan Assessment Form and IGRT Verification spreadsheet (for pelvic/PA nodes patients only) should also be sent.

Plans should ideally be submitted once they have been approved by the PI and had an independent check. Data associated with any re-plans during radiotherapy treatment should also be submitted.

Please send the following data:
- PSMA PET-CT images and PET report
- Planning CT images
- DICOM structure set (ensure trial naming convention has been followed)
- DICOM dose matrix
- DICOM plan file

10.9. DICOM Data Export
DICOM data should be transferred to the RTTQA group via their central secure transfer service. Anonymised and encrypted data will pass through a firewall to a host server located in a secure NHS environment to which access is restricted to authorised users.

All NHS radiotherapy centres have a centre specific link and unique password to access the service – contact the RTQA team if you do not have this.

Instructions for use:
1. Data must be anonymised at source and should be encrypted using 7zip/WinZip or equivalent
2. All files for a single patient must be zipped into one file
3. Files must be labelled with the Trial Name and Trial ID, e.g. UKC022001
4. Follow unique centre link to the service
5. Insert unique centre password
6. Upload files
7. Email RTQA contact at pearls.rtqa@nhs.net to confirm data uploaded and share password to unzip data

11. REFERENCES


RCR The timely delivery of radical radiotherapy: guidelines for the management of unscheduled treatment interruptions; 4th edition; January 2019

PACE protocol version 10, 20th May 2019