East of England Radiotherapy Network:

Bladder Protocol V4.0

Contents

1.0 Indications and patient population

The majority (90% +) of bladder cancers are transitional cell carcinomas.

Squamous carcinomas comprise <5% of urothelial carcinomas in the UK. Rare types include adenocarcinomas and small cell carcinoma of the bladder. Management of these will be on an individual basis following MDT discussion, but radiotherapy for localised disease remains a treatment option.

1.1 This protocol covers treatment in the following situations:

a. Radical, curative intent radiotherapy for muscle invasive bladder cancer, with or without concurrent chemotherapy or carbogen/ nicotinamide radiosensitisation

b. Radical, curative intent radiotherapy for muscle invasive bladder cancer with pelvic nodal involvement

c. High dose palliative radiotherapy for locally advanced muscle invasive bladder cancer, or for patients with muscle invasive bladder cancer who are not suitable for radical treatment due to co-morbidities/ poor performance status

d. Palliative radiotherapy for bladder tumours

1.2 Curative treatment eligibility

1.2.1 Inclusion criteria

- Histological confirmation of muscle invasive bladder cancer, pT2a at least
- Localised bladder cancer with no evidence of metastases
- Adequate performance status, WHO PS 0-2

1.2.2 Exclusion criteria

- Non-muscle invasive bladder cancer (unless high suspicion of muscle involvement on imaging and further TURBT for confirmation not possible)
- Nodal or metastatic disease (pelvic nodal radiotherapy can be considered for low volume pelvic node involvement in selected patients)
- Poor PS
- Contra-indications to pelvic radiotherapy, e.g., prior radiotherapy treatment, significant inflammatory bowel disease

1.2.3 Essential Pre-Radiotherapy investigations for curative patients

- CT urogram/ CT chest or CT chest/abdo/pelvis with contrast
- Consider MRI bladder
- Consider FDG-PET if indeterminate findings on CT/MRI, or high risk of metastatic disease
- Cystoscopy and TURBT
- Bloods including FBC, U+Es, LFTs

- If hydronephrosis present, consider need for stenting or nephrostomy pre treatment
- Review and consideration of neo-adjuvant chemotherapy prior to radiotherapy
- Review and consideration of radiosensitisation with concurrent chemotherapy or carbogen/ nicotinamide
- MDT/ SMDT discussion

Consideration of surgical options with Urology team and patient, and decision documented for radiotherapy treatment.

2.0 Localisation

Localisation	Notes	
Position		Supine
Arm position		Arms at side with hands on chest
Immobilisation and supports		Knee wedge and ankle stocks
Organ pre-requisites	Patient asked to void immediately before scan and not to drink for 30 mins prior to scan	Empty bladder
	Consider ultrasound bladder scan	
	If catheterised, leave on free drainage	
Contrast		Not required. Use of contrast for pelvic nodes dependent on department protocol
CT acquisition	Slice thickness:	2 - 3mm
	Scanning limits	Superior - top of L4 (top of L3 if treating nodes)
	Scanning limits	Inferior - 5cm below ischium

Bowel preparation may be given prior to radiotherapy planning scan to ensure empty rectum. Individual department protocols may vary but an example would be movicol one sachet daily for 3 days prior with a micolette enema on day of scan.

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/week	Chemo/ comments
a. Radical, curative intent radiotherapy for muscle invasive bladder cancer	52.5-55/20	5	Radiosensitisation with 5-FU and Mitomycin C, or weekly gemcitabine chemotherapy Or carbogen and nicotinamide (BCON) Or radiotherapy alone Ideally adaptive planning, 'plan of the day'
	64/32*	5	
b. Radical, curative intent radiotherapy for muscle invasive bladder cancer with pelvic nodal involvement	64/32 to bladder	5	Can be given with radiosensitisation as above IMPART trial used 60Gy/32# to involved nodes and 52Gy/32# to adjuvant nodes Only for selected patients
	54-60/32 to involved nodes	5	
	50-54/32 to adjuvant nodes	5	
	55/20 to bladder with 44-47 to pelvic nodes	5	It is recommended that dose constraints from 20# prostate and nodal treatment are used for this regime
c. High dose palliative radiotherapy	30/5	1	Ideally adaptive planning, 'plan of the day'
d. Palliative radiotherapy	30-36/ 5-6	1	Ideally adaptive planning, 'plan of the day,' or CT based plan
	21/3	3	CT based plan
	20/5	5	
	6-8/1	1	AP-PA, for patients unfit for 21Gy/3#

***55Gy/20# is the preferred radical fractionation, as recommended by the RCR Bladder Consensus Guidance (published 2023).**

4.0 Target volumes

- Use standard nomenclature as per AAPM 263
- https://www.aapm.org/pubs/reports/RPT_263.pdf
- Target volumes should match agreed naming conventions unless there are operational reasons for use of other naming. PTV ProKnow nomenclature should be used for NHSE ProKnow Collections and Scorecard Templates for upload.

4.1 Curative radiotherapy GTV/CTV

- **GTV**

  Bladder GTV is not normally outlined unless in a trial setting

- **CTV**

  Encompasses the visible bladder tumour, the whole bladder, and any extravesical spread. Should include 1.5cm of prostatic urethra in males or 1cm of urethra in females, if tumour is at base of bladder or distant CIS is present

4.2 Curative and high dose palliative radiotherapy PTV

- **PTV**

  CTV to PTV expansion will be done to create 3 PTVs, with the most appropriate to be used as an adaptive 'plan of the day'

  PTV small, medium, and large can all be produced from a single planning scan with an empty bladder (as per HYBRID trial)

  Exact margins used will depend on individual department protocols (based on internal audits), but the following table is a guide, with HYBRID trial margins in bold:

CTV to PTV expansion (cm)					
	Laterally	**Anteriorly**	**Posteriorly**	**Superiorly**	**Inferiorly**
PTV Small	**0.5**-0.8	**0.5**-0.8	**0.5**-0.8	**0.5**-0.8	**0.5**-0.8
PTV Medium	**0.5**-1.0	**1.5**	**1.0**	1.2-**1.5**	**0.5**-1.0
PTV Large	**0.8**-1.5	**2.0**	**1.2**-1.5	1.5-**2.5**	**0.8**-1.5

4.3 Nodal radiotherapy GTV/ CTV

- **CTV bladder**

  Encompasses the visible bladder tumour, the whole bladder, and any extravesical spread. Should include 1.5cm of prostatic urethra in males or 1cm of urethra in females, if tumour is at base of bladder or distant CIS is present

- **GTV nodes**

  Involved nodes should be identified from diagnostic imaging and contoured separately

- **CTV nodes**

Nodes are contoured using vessels as a surrogate, outlined superiorly from lower border of L5, with inferior border at the top of the femoral heads (stop at external iliac). Vessels are expanded by 7mm in x and y directions, then adjusted to edit out bone and muscle. From inferior border of L5 to the inferior border of S3, the expanded vessel contour is joined along the anterior surface of the sacrum using a 12mm rollerball. Then use 18mm rollerball to connect internal and external iliac volumes along the inner bony pelvis (edit off muscle). Use 18mm rollerball along inner obturator and stop 1cm above top of symphysis pubis, again editing off muscle.

This LN CTV is finally edited by growing bowel/ rectum by 3mm (to produce bowel/ rectal PRV) and excluding this expanded bowel/ rectum. If expanded bowel/ rectum covers vessels, these need to be added back in to the final LN CTV.

4.4 Nodal radiotherapy PTV

- **PTV bladder**

  CTV to PTV margin 1.5-2cm

  Adaptive plan of the day not normally used if nodal volumes also treated

- **PTV nodes**

  Involved nodes - GTV to PTV margin 0.5-1cm

  Adjuvant nodes - CTV LN to PTV LN margin 0.5-0.7cm

4.5 Palliative radiotherapy

- **CTV**

  Encompasses the visible bladder tumour, the whole bladder, and any extravesical spread. Should include 1.5cm of prostatic urethra in males or 1cm of urethra in females, if tumour is at base of bladder or distant CIS is present

- **PTV** = CTV to PTV margin 1-2cm

5.0 Organs at risk

- Aim for the use of standard nomenclature as per Global Harmonization Group consensus guidelines: https://www.thegreenjournal.com/action/showPdf?pii=S0167-8140%2820%2930294-2

Structure name	Description
Rectum	Outline inferiorly from the lowest level of the ischial tuberosities, to the rectosigmoid junction (identified as the level where there is anterior inflection of the bowel, best seen on sagittal views); include the full circumference and rectal contents
Bowel	Small and large bowel (including sigmoid colon) are outlined as a single structure, as individual loops (not a 'bowel bag'); cranial extent should be 2cm beyond the superior extent of the PTV
Femur_ Head_L or _R	Outline to the bottom of the femoral head curvature, do not include femoral necks

5.1 Constraints

5.1.1 20# Schedule

Structure name	Constraint	Optimal	Mandatory
PTV_Sm / PTV_ Med/ PTV_Lar	D98%	≥95%	≥90%
	D50%	+/- 1%	
	D2%	≤105%	≤107%

Structure name	Constraint	Optimal	Mandatory
Rectum	25Gy		80%
	41.7Gy		60%
	50Gy		50%
	54.2Gy		30%
	58.3Gy		15%
Bowel	V37.5	116cc	139cc
	V41.7	104cc	127cc
	V45.8	91cc	115cc
	V50.0	73cc	98cc
	V54.2	23cc	40cc
	V58.3	0cc	10cc
	V61.7	0cc	0cc
Femur_ Head_L or _R	41.7Gy		50%
	46Gy		<2cm^3

Dose constraints are from standard arm of the RAIDER trial.

5.1.2 32# Schedule

Structure name	Constraint	Optimal	Mandatory
PTV_Sm / PTV_ Med/ PTV_Lar	D98%	≥95%	≥90%
	D50%	+/- 1%	
	D2%	≤105%	≤107%

Structure name	Constraint	Optimal	Mandatory
Rectum	30Gy		80%

	50Gy		60%
	60Gy		50%
	65Gy		30%
	70Gy		15%
	75Gy		5%
Bowel	V45	116cc	139cc
	V50	104cc	127cc
	V55	91cc	115cc
	V60	73cc	98cc
	V65	23cc	40cc
	V70	0cc	10cc
	V75	0cc	0cc
Femur_ Head_L or _R	50Gy		50%

Dose constraints are taken from the RAIDER trial protocol.

5.1.3 32# Schedule, bladder, and nodes

Structure name	Constraint	Optimal	Mandatory
PTV_Sm / PTV_ Med/ PTV_Lar	D98%	≥95%	≥90%
	D50%	+/- 1%	
	D2%	≤105%	≤107%
PTVn	D98%	≥95%	
PTVn	D2%	≤105%	≤107%

Structure name	Constraint	Optimal	Mandatory
Rectum	30Gy		80%
	50Gy		60%
	60Gy		50%
	65Gy		30%
	70Gy		15%
	75Gy		5%
Bowel	V45	139cc	209cc
	V50	122cc	183cc
	V55		105cc
	V60		84cc
	V65		26cc
Femur_ Head_L or _R	50Gy		50%

Dose constraints are taken from the IMPART trial protocol.

5.1.4 36Gy/6# Schedule

Structure name	Constraint	Optimal	Mandatory
PTV_Sm / PTV_ Med/ PTV_Lar	D98%	≥95%	≥90%
	D50%	+/- 1%	
	D2%	≤105%	≤107%

Structure name	Constraint	Optimal	Mandatory

Rectum	17Gy	50%	80%
	28Gy	20%	60%
	33Gy	15%	50%
	36Gy	5%	30%
Bowel	V25	139cc	208cc
	V28	122cc	183cc
	V31	105cc	157cc
	V33	84cc	126cc
	V36	26cc	39cc
Femur_ Head_L or _R	28Gy		50%

Dose constraints are taken from the HYBRID trial.

6.0 Planning process/ technique

- IMRT/VMAT for curative and high dose palliative treatments using adaptive plan of the day technique
- IMRT/ VMAT for curative bladder and nodal radiotherapy
- Simple field arrangements for single fraction palliative RT
- IMRT/VMAT/3D CRT for other palliative fractionations

7.0 Peer Review/ Contour QA

- Prospective peer review should ideally occur for difficult cases e.g. extensive extravesical spread, hip replacements affecting image quality
- If contoured as per department protocol, requirement for peer review is determined by individual centres
- A description of the peer review process including changes made should be saved in the patient record
- The peer review process and outcomes should be audited
- Planning notes are recommended for all radical cases, and any palliative cases that do not conform to department protocol

8.0 Target verification

Modality	Frequency	Match point	Additional information
CBCT	Daily, pre treatment Post treatment CBCT recommended to assess intra-fraction bladder filling on 1#	Bladder: choose plan that covers bladder PTV by minimum 3mm allowing for intra-fraction filling	For all radical and high dose palliative, adaptive 'plan of the day'
CBCT	Daily, pre treatment	Bladder	For all palliative treatments except single fraction

kV/ kV	Daily, pre treatment	Bone	For all palliative treatments if CBCT not possible
kV/ kV	Daily, pre treatment	Bone	Single fraction AP-PA

For adaptive planning, monitor throughout treatment and document the plan used for each fraction. If the large plan is required frequently, reassessment is recommended to ensure dose constraints are being met, and coverage of PTV is adequate.

9.0 Side effects

9.1 Possible early or short-term side effects	
Expected (50% - 100%)	**Initial management (if appropriate)**
Fatigue	Advice on rest and exercise
Urinary symptoms: Frequency; urgency; cystitis	Tamsulosin Solifenicin NSAIDS
Bowel symptoms: Diarrhoea	Loperamide
Common (10% – 50%)	**Initial management (if appropriate)**
Urinary symptoms: urinary hesitancy	
Bowel symptoms: frequency; urgency	Proctosedyl/ Scheriproct suppositories
Vaginal discomfort or discharge	
Less common (Less than 10%)	**Initial management (if appropriate)**
Hair loss in the treatment area	
Skin irritation and colour changes in treatment area	Topical application of water-soluble emollient or patient's own moisturising cream (providing it is Sodium Lauryl Sulphate free). 1% hydrocortisone topical application.
Bowel symptoms: rectal pain/ discomfort	
Bowel symptoms: feeling of not completely emptying bowels	
Bleeding from bladder or bowel	
Rare (Less than 1%)	**Initial management (if appropriate)**
Urinary symptoms: retention	
Urinary symptoms: incontinence	

9.2 Possible late or long – term side effects	
Expected (50% - 100%)	**Initial management (if appropriate)**
Infertility	Advise accordingly for infertility
Early menopause	Consider HRT
Common (10 – 50%)	**Initial management (if appropriate)**
Urinary symptoms: frequency; urgency	Tamsulosin Solifenicin Cystoscopy/ urology review
Urinary symptoms: reduced bladder capacity	
Changes in ejaculate	
Inability to achieve adequate erections	Sildenafil/ Tadalafil Erectile Dysfunction Clinic referral
Shrinkage or scarring of the vagina	Topical HRT Use of vaginal dilators
Loss of orgasm	
Less common (Less than 10%)	**Initial management (if appropriate)**
Urinary symptoms: cystitis; incontinence; incomplete emptying of bladder	
Urinary stricture	
Bleeding from bladder or bowel	
Bowel symptoms: frequency; urgency; diarrhoea	Dietary advice Loperamide
Inflammation of the rectum	
Intermittent abdominal discomfort	
Rare (Less than 1%)	**Initial management (if appropriate)**
Pelvis/ hip bone thinning and/or fracture	Analgesia There is no evidence for the use of calcium/ vitamin D/ bisphosphonates
Bowel/ bladder damage: perforation; fistula; bowel obstruction; severe bleeding	Sigmoidoscopy/ surgical review
A different cancer in the treatment area	

10.0 References

NICE Guideline NG2 - Bladder Cancer: diagnosis and management (Feb 2015) https://www.nice.org.uk/guidance/ng2

The American Association of Physicists in Medicine. (2018). Standardizing Nomenclatures in Radiation Oncology. Available at https://www.aapm.org/pubs/reports/RPT_263.pdf (Accessed: 29th July 2021).

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Hafeez et al. *Protocol for tumour-focused dose-escalated adaptive radiotherapy for the radical treatment of bladder cancer in a multicentre phase II randomised controlled trial (RAIDER): radiotherapy planning and delivery guidance.* http://dx.doi.org/10.1136/bmjopen-2020-041005

HYBRID: A multicentre randomised Phase II study of Hypofractionated Bladder Radiotherapy with or without Image Guided Adaptive Planning - Protocol Version 3.1.

Tan et al. The Intensity-Modulated Pelvic Node and Bladder Radiotherapy (IMPART) Trial: A Phase II Single-Centre Prospective Study. Clin Onc 32 (2020) 93-100.

Proknow Technical Oversight Group (PTOG), IPEM - PTV nomenclature - 31st January 2024 Version 1.0

Addenbrooke's Radiotherapy Clinical Protocol - Radiotherapy Treatment for urothelial bladder cancer (Rev 9, March 2018)

Colchester Radiotherapy Clinical Protocol - Bladder Cancer (Rev 5, Dec 2019)

Ipswich Hospital Guidelines for Bladder Radiotherapy (Issue 4)

Norfolk and Norwich University Hospital - Radiotherapy for Bladder Cancer (V8, Aug 2019)

Peterborough City Hospital - Bladder Cancer Radiotherapy Treatment (Rev 13, Nov 2020)

Southend Bladder Planning Summary

11.0 Members of the protocol drafting committee

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12.0 Amendment History

A record of changes in this document

Date	Updated version number	Previous version number	Page Number/ Section (updated version)	Details
30.11.21	V1.0			New Document
1.12.22	V2.0	V1.0	Updated version	Updated document issued with changes as outlined below:
			Pg 4	Removal of reference to RAIDER trial in localisation table
			Pg 5	Preferred dose/ fractionation 55Gy/20# added
			Pg 6	Removal of reference to RAIDER trial
24.07.23	V2.1	V2.0	Pg7	OAR guidance updated to include GHG consensus guidelines
04.12.23	V3	V2.1	Pg4	CT scan thickness changed to 2-3mm
			Section 3	20Gy/5# added to palliative RT
			Section 3b	55Gy/20# to bladder with 44-47Gy to pelvic nodes added as dose option
			Section 5	OAR nomenclature updated
			Section 9.1	Skin reaction updated to reflect update RCR consent forms
27.03.24	V3.1	V3.0	Pg5	#s per week for 30-36Gy corrected
26.02.24	V4	V3.1	Section 4	Target volume/ ProKnow statement added
			Section 5	Statement re: ProKnow nomenclature added as agreed by EofE RTN ProKnow Group
			Section 2	Use of contrast for pelvic nodes updated to 'dependent on department protocol'
			Section 9	Side effect information updated as per RCR consent form
			Section 10	References updated
			Section 11	Protocol committee members updated