London Cancer
Clinical Radiotherapy Guidelines for Carcinoma of the Bladder

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1. Introduction

These guidelines are intended to direct the treatment of patients with invasive bladder cancer with radiotherapy. They have been developed from guidelines already in existence at Barts Health NHS Trust, University College London Hospitals NHS Foundation Trust, Royal Free London NHS Foundation Trust, Princess Alexander Hospital, North Middlesex Hospital and Barking, Havering and Redbridge University Hospitals NHS Trust. They should be read and used in conjunction with other guidelines covering the investigation and surgical and chemotherapeutic management of bladder cancer. They also do not remove the need to follow the Local Rules and Work Instructions that have been developed at individual radiotherapy departments.

1.1. Cancer definition

Transitional cell carcinoma of the bladder

1.2. Stages

T (primary staging)
- Tis  Carcinoma in situ
- T1  Tumour invades subepithelial connective tissue
- T2a  Tumour invades superficial muscle
- T2b  Tumour invades deep muscle
- T3  Tumour invades perivesical tissue
- T4  Tumour extends to other organs

N (lymph nodes)
- N0  No regional lymph node metastasis
- N1  Metastasis in a single lymph node 2cm less in greatest diameter
- N2  Metastasis in a single lymph node more than 2cm but less than 5cm in dimension, or multiple nodes
- N3  Metastasis in lymph node more than 5cm in diameter

M (distant disease)
- M0  No distant disease
- M1  Distant disease

1.3. Indications

- Curative treatment
- T2-T4a N0 M0 (UICC/TNM 2002)

1.4. Intent

Radical treatment

1.5. Timing of radiotherapy

- Radiotherapy to start within 4 weeks from time of decision to treat. Bladder cancers fall into Category 2 patients
• In event of patient receiving neo-adjuvant chemotherapy. Radiotherapy should start 3-4 weeks post chemotherapy

2. Chemotherapy and EBRT/IMRT

Chemotherapy Neoadjuvant situation
• Gemcitabine/cisplatin
• Gemcitabine/carboplatin

Chemotherapy Regime for concurrent chemo-radiotherapy
• Week 1 day 1-5  5 Fluouracil and Mitomycin
• Week 4  days 22-26  5 Fluouracil

Radiotherapy Dose schedules
• 64Gy/32 fractions over 6½ weeks
• 55Gy/20 fractions over 4 weeks. Consider in elderly, frail or advanced stage

2.1. Essential investigations prior to radiotherapy and chemotherapy (info required for planning)

The following investigations should have been performed and the results available before radiotherapy planning commences:
• Clinical history
• Baseline clinical examination and PS
• TURBT notes and histology
• Results of staging investigations. CT Scan +/- MRI/PET
• FBC, U/E. HB>12
• Creatinine clearance (in case of platinum based chemotherapy)

2.2. Information for patients

Patients should be given an appropriate patient information leaflet about bladder radiotherapy, and have access to a urology nurse or other specialist practitioner. In the case of patients receiving neo-adjuvant or concurrent chemo-radiotherapy appropriate patient information should be given.

2.3. Consent

All patients must have given written informed consent before chemotherapy and radiotherapy planning commences. Consent should be taken by a practitioner who is familiar with bladder radiotherapy planning and administration

2.4. Trials

TOUCAN
Vandetanib in non-cisplatin fit patients with urothelial cancers - A randomised phase II Trial of carboplatin and gemcitabine +/- vandetanib in first line treatment Of advanced Urothelial cell Cancer in patients who are not suitable to receive cisplatin

TUXEDO
Phase I/II feasibility study of cetuximab with 5FU and mitomycin C or cisplatin with concurrent radiotherapy in muscle invasive bladder cancer

3. Radiotherapy treatment planning

3.1. Position/immobilisation

- Patients should be planned and treated in the supine position.
- Empty bladder, bowel preparation if needed
- Arms folded across chest
- Immobilisation system or knee and ankle support

3.2. Image acquisition

Scanning

Patients are 3D-planned using data from a CT planning scan. The patient should be scanned in the treatment position (see above). It is recommended that the scan boundaries are:

- Top of sacroiliac joints.
- 5cm below ischial tuberosities

Volume delineation and nomenclature

Volume

GTV: - Defined by clinical and radiological staging. To encompass the whole bladder and any perivesical disease

PTV = GTV +1.5-2cm margin

Organs at Risk

Femoral heads and the rectum should be outlined as Organs at risk

<table>
<thead>
<tr>
<th>DVH constraints for OAR</th>
<th>Normal Tissue Dose Constraints</th>
<th>Dose (Gy)</th>
<th>Max Vol (% or cc)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Dose for 2Gy/# Prescribed Dose</td>
<td>Rectum</td>
<td>Femoral Heads</td>
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Per CHIPP protocol
Planning technique

3D planning using CT data

3.3. **Treatment technique**

Beam arrangement
- 3 or 4 field conformal plan
  - Or
- Inverse planned IMRT

3.4. **Treatment verification**

- Ultrasound of the bladder prior to treatment to assess the bladder is empty can be employed.
- Inter and Intra-fraction volume changes lead to shape changes rather than three dimensional vector displacement of a stable volume

**Linac Verification**
- Cone Beam CT will be taken on day 1-3 and once weekly from then on to review patient set-up and radiation dose to organs at risk and to ensure adequate coverage of the bladder.
- Weekly cone beam
- In patients displaying significant random error or treated with a small margin consider cone beaming daily.

3.5. **On treatment review definition**

On treatment review clinic
- Weekly review by on treatment review specialist
- Weekly FBC
- HB >12
- Acute toxicity documented. RTOG toxicity sheet completed weekly

3.6. **Schedule gap category for management of unscheduled interruptions**

- Radiotherapy to start within 4 weeks from time of decision to treat. Bladder cancers fall into Category 2 patients
- In event of patient receiving neo-adjuvant chemotherapy. Radiotherapy should start 3-4 weeks post chemotherapy

3.7. **Side effects radiotherapy**

Toxicity

All toxicities should be explained to the patient at the time of consent being taken.

**Acute Toxicity**
- Tiredness
• Cystitis – urinary frequency, dysuria
• Looseness of bowel motion

Late Toxicity
• Bladder shrinkage
• Urinary Incontinence
• Increased bowel frequency and urgency
• Rectal bleeding
• Impotence
• Vaginal stenosis
• Infertility

Follow up
• 4-6 Weeks Post treatment follow up.
• Cystoscopy at 3 months

3.8. Palliative Radiotherapy

Indications
• T4 or node positive
• Metastatic disease

Dose schedules
• 21 Gy in 3 fractions alternate days will require 3 or 4 field conformal plan
• 30-36Gy in 5-6 fractions treated weekly will require 3 or 4 field conformal plan
• 20 Gy in 5 fractions daily parallel opposed fields to MPD
• 8Gy single fraction parallel opposed fields to MPD
4. References


