LONDON CANCER
NORTH AND EAST

London Cancer

Guidelines for referral, investigation and management of Anal Carcinoma

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1.0 TNM Classification

Primary Tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumour more than 5 cm in greatest dimension
T4	Tumour any size directly invades other organs e.g. vagina, urethra, bladder (involvement of the rectal wall, perirectal skin, subcutaneous tissue or sphincter muscle(s) alone is not classified as T4)

Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in perirectal lymph node(s)
N2	Metastasis in unilateral internal iliac and/or unilateral inguinal lymph nodes(s)
N3	Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes

2.0 Pre-treatment assessment

- History and examination.
- Proctoscopy, EUA and biopsy. Histopathology results should be available.
- Staging CT chest, abdomen and pelvis. PET-CT may be performed
- MRI pelvis
- Ultrasound guided biopsy of suspicious or enlarged inguinal nodes
- Blood tests - FBC, U+E, LFTs.
- Any other investigations considered necessary – this may include HIV testing
- All patients should be discussed at the Anal Cancer MDT Meeting and the management strategy agreed.
- Patients should be given information sheets at their clinic attendance and afforded the opportunity to discuss the treatment options in full.
- Patients may require additional support and should be referred to other healthcare professionals as appropriate e.g. to dietician, counsellor or stoma nurse.
- Infertility and potential fertility preservation strategies should be discussed with all male patients and with all female patients of child-bearing age. Effective contraception should also be discussed with all patients due to have pelvic radiotherapy.
- Informed consent is required for all patients
- The Radiotherapy Management Plan should be devised as per the local guidelines

3.0 Radiotherapy Planning

3.1 Patient Positioning and Image Acquisition

- Patients with anal margin tumours may be scanned and treated prone with the use of a "belly-board" to enable accurate positioning of bolus. In all other patients, and those with margin tumours but where patient mobility or body habitus precludes prone treatment, the patient may be scanned and treated supine.
- In patients with anal margin tumours or extension of tumour onto the perianal, perineal or gluteal skin, bolus should be applied by the treating clinician at planning to ensure adequate dose to this area.
- If possible, an anal marker should be placed at scanning to define the clinical position of the anal margin. In patients who are to be treated supine, this should be taped to the approximate position for scanning.
- Bowel preparation is not usually possible for anal cancer patients. Bladder preparation should be followed such that the bladder is comfortably full for planning and treatment.
- Intravenous contrast is required for all patients receiving radical treatment.
- Patients will be scanned from 2cm superior to the top of L5 to 7cm below the anal marker with 3mm slices.

Patients may be treated in a 2-phase technique (in line with the ACT II trial protocol) but it anticipated that most will be treated with an IMRT solution with an integrated phase II.

3.2 Conventional Planning Volumes

GTV

- Visible tumour as seen on CT and PET-CT, taking into account the data from clinical examination and MRI.
- Positive nodes on PET or biopsy should be defined as separate nodal GTVs.

PTV

- Phase I: Includes GTV and all areas at risk of microscopic disease (inguinofemoral nodes and pelvic nodes). Always allow a minimum 3cm margin around any GTV in all directions. Field borders should be defined on the posterior beam, using the same isocentre as the phase II volume will have.
- Field Borders:
    - Superior border: the more superior of (i) 2cm above the inferior aspect of the Sacro-Iliac Joints or (ii) 3cm above superior limit of macroscopic disease including involved lymph nodes 2 cm above inferior aspect of SI joints
    - Lateral borders: approximately mid-point of femoral neck (to cover inguinal nodal area)
    - Inferior border: 3cm below anal verge or 3cm below inferior extent of tumor for anal margin tumors. Be mindful that the inferior border of the phase 2 will be more than 3cm below the GTV and the phase I inferior border should match or exceed this.
- Phase II: PTV = GTV(s) + 3 cm

3.3 IMRT planning volumes

GTV

- Visible tumour as seen on CT and PET-CT, taking into account the data from clinical examination and MRI.
- Positive nodes on PET or biopsy should be defined as separate nodal GTVs.

Gross CTV

- GTV (anal primary and involved nodes) + 2cm, trimmed to barriers of spread

Mesorectal CTV

- The entire mesorectum from the peritoneal reflection cranially to at least 3cm below the GTV caudally. The cranial extent of this CTV may be amended in low, early, node-negative disease.

Pelvic Vessels

- Delineate the external and internal iliac vessels bilaterally from the bifurcation of the common iliac vessels to the proximal femoral artery

Nodal CTV

- Pelvic Vessels + 0.7cm, trimmed to patterns of spread and amended to include any obvious nodal regions (paying particular attention to the inguinal regions)
- In node positive patients, the Nodal CTV should match the nodal portions of the Gross CTV.

Presacral CTV

- The pre-sacral nodal territory up to the L5/S1 interspace for patients with T3/4 disease or any involved mesorectal lymph nodes
- The nodal territory can be abbreviated to 2cm above the inferior aspect of the sacro-iliac joints in patients with T1/2 tumours with no mesorectal lymph node involvement.

CTV1

- Merges Gross CTV, Mesorectal CTV, Nodal CTV and Pre-sacral CTV into one structure. This should be checked again for coverage of patterns of spread and trimmed from barriers to spread.

PTV1

- CTV1 + 0.5cm posteriorly and laterally and 1.0cm in all other directions.

PTV2

- Gross CTV + 0.5cm posteriorly and laterally and 1.0cm in all other directions.
- It must be ensured that the PTV1 and 2 inferior and lateral extents are compared and it is ensured that the PTV2 volume matches or is within the PTV1 volume.

Radiotherapy Treatment

- The clinician must approve, sign and date treatment images, plan and associated documentation.
- Patients should routinely receive oral ciprofloxacin 250mg b.d. prophylaxis commencing on fraction 6 of radiotherapy.

4.0 Policy and Radiation Prescription

4.1 CURATIVE TREATMENT

Conventional 2-phase technique

PHASE 1

30.6 Gy in 17 # over 3 weeks and 2 days

PHASE 2

19.8 Gy in 11# over 2 weeks and 1 day
For bulky tumours, consider dose escalation to 23.6Gy in 13# over 2 weeks and 3 days

TOTAL DOSE

50.4 Gy in 28# over 5 weeks and 3 days
Consider 54 Gy in 30# for bulky tumours

IMRT

These doses are the equivalent of a radical treatment dose of 54.6Gy in 1.8Gy fractions for a/b of 2Gy; and 35GY in 1.8Gy fractions. They therefore represent a slight dose increase in the radical dose from ACT2 style dosing and a correction for overall treatment time for the elective volume.

PTV1 = PTV53.2
53.2Gy in 28 daily fractions over 5 weeks and 3 days (1.9Gy/fration)
Dose should be prescribed to the mean dose of PTV 53.2

PTV2 – PTV39.2
39.2Gy in 28 daily fractions over 5 weeks and 3 days (1.4Gy per fraction)
90% of the dose to the 39.2 dose level = 37.24Gy which equates to the 70% isodose with reference to 53.2Gy

4.2 CHEMOTHERAPY

All patients receiving concurrent chemotherapy should have a peripherally inserted central catheter (PICC line).

Radiotherapy to start no sooner than 2 hours after start of 5FU infusion

- For patients < 70 years old and no other significant co-morbidities:
    - Mitomycin C 12 mg/m2 iv bolus (max 20mg) on day 1
    - 5-Fluorouracil 1000 mg/m2 continuous infusion days 1-4 and days 29-32.
    - In selected patients where platinum therapy may be beneficial, Cisplatin 60mg/m2 may be substituted for the mitomycin and delivered in weeks 1 and 5.

- For patients >70 years or those with significant co-morbidities:
    - Mitomycin C 10 mg iv bolus on day 1

- 5-Fluorouracil 750 mg/m2 continuous infusion days 1-4 and days 29-32

Consider reducing 5FU dose if diarrhoea is severe at Week 5.

4.3 PALLIATIVE TREATMENT FOR SYMPTOMATIC CONTROL (IF WIDESPREAD METASTATIC DISEASE)

- 30Gy in 10# over 2 weeks +/- chemotherapy (Mitomycin C/5FU)

Or

- 20Gy in 5# over 1 week

Or

- 8Gy in 1# single fraction

5.0 CRITICAL ORGANS AND TOLERANCE DOSES

- Normal tissues outlined include bladder, femoral heads, pelvic bones, genitalia and small bowel.
- Bladder should be outlined from base to dome, excluding the CTV.
- Any small bowel within 2cm of PTV should be outlined separately.
- Genitalia should be delineated throughout the volume for both males and females.

Bladder	
V30	80%
V40	40%
V50	0%
Small Bowel	
V30	40%
V40	30%
V50	0%
Genitalia	
V30	45%
V40	10%
V48	0%
Pelvic Bones	
V15	45%
V20	30%
V50	0%
Femoral Heads	
V45	5%
V55	0%

6.0 Clinical Assessment during Radiotherapy

- Set up on machine to be seen if requested by clinician. On treatment imaging, including daily kilovoltage imaging should follow standard departmental protocols. Cone-Beam CT may be used fractions 1-3 and then weekly to assess soft tissue reproducibility not evident on kilovoltage imaging.
- Weekly review at on-treatment clinic to inspect perineum and natal cleft.

7.0 Toxicity

- Skin reaction
  - For dry desquamation severe erythema apply aqueous cream
  - For moist desquamation, apply appropriate dressing e.g mepitel
- Pain control
  - lignocaine gel (not anusol) topically
  - oral analgesia
  - consider topical morphine
- Diarrhoea/proctitis
  - loperamide, codeine phosphate
- Admit to ward for symptom control if problems with pain control or hygiene, as gaps in treatment significantly increase risk of recurrence.
- Reinforce motivation as regime is difficult to tolerate both physically and psychologically. Refer to counsellor if necessary.

8.0 Gaps in Radiotherapy Treatment

Gaps should therefore be avoided when possible.
Consider weekend treatment if bank holidays or unscheduled breaks in treatment occur as per the departmental policy

9.0 Follow-up

- Follow up 4-6 weeks after treatment completion
- 2-3 monthly follow up in the first year with Digital Rectal Examination
- MRI at 6 monthly intervals for 3 years in high-risk disease. Low-risk disease may require only one baseline post-treatment MRI.
- If evidence of persistent disease then requires EUA and biopsy +/- salvage surgery

10.0 Side Effects of Radiotherapy Treatment

Acute radiation reaction (settles 4-6 weeks after completing treatment)

Common effects -

- Diarrhoea
- Proctitis
- Lethargy
- Desquamation
- Urinary frequency

Late radiation reaction (side effects occurring after 6 months)

Possible effects

- Anal dysfunction
- Persistent proctitis
- Change in bowel habit
- Telangiectasia
- Vaginal fibrosis
- Infertility