Anal Cancer Radiotherapy Treatment Protocol

1) Purpose/Scope

This protocol covers treatment in the following situations:

- Curative radiotherapy (± concomitant chemotherapy) for good prognosis T1N0 tumours; adjuvant radiotherapy (± concomitant chemotherapy) for surgically excised tumours with a margin smaller than 1mm.
- Curative radiotherapy and concomitant chemotherapy for early tumours with standard risk (T1 N0 with poor prognostic factors or T2 N0).
- Curative radiotherapy and concomitant chemotherapy for locally advanced tumours with high risk (T3/4 Nany or Tany N+ve).
- Palliative radiotherapy for patients with anal cancer and poor performance status.
- Tumours arising from an area of 5cm around the anal verge will be considered as anal cancer. Tumours arising outside this area will be referred to the skin cancer multidisciplinary team.

2) Indications for treatment

2.1 Inclusion Criteria

- Localised squamous cell carcinoma of the anus with no evidence of distant metastases (para-aortic nodal involvement could be considered for treatment with radical intent, at the discretion of the treating oncologist).
- Performance status of 0-1 on the ECOG scale, exceptionally 2.

2.2 Exclusion Criteria

- Inadequate cardiovascular, respiratory, renal, or hepatic function for safe delivery of radiotherapy and concomitant chemotherapy. Patients unfit for concurrent chemoradiotherapy could be considered for radiotherapy alone at the discretion of the treating oncologist.
- Inadequate immobilisation for safe delivery of radiotherapy.
- Anal cancer with adenocarcinoma histology type.

3) Pre-treatment Information required

- History and clinical examination, performance status, HIV status.
- Full blood count, urea and electrolytes, liver function tests.

- Testing for mutations in the DPYD gene to assess risk of toxicity with fluoropyrimidines.
- CT scan of chest, abdomen, and pelvis.
- For nodes identified on PET/CT, MDT discussion is recommended to determine which nodes should be included in the high dose volume.
- All female patients should have a per vaginal examination by the treating oncologist or be referred to the gynaecologist for examination.

3.1 Investigations for curative patients

- Whole body PET/CT in ≥T2 tumours or Tany N+ve.
- Consider biopsy/FNA of any suspicious inguinal nodes.
- MRI pelvis.
- Consider Examination under anaesthesia.

3.2 Optimisation prior to curative radiotherapy treatment

- Patients who are HIV-positive should be discussed with the infectious diseases team and standard CRT considered for those appropriate i.e. low viral load, on HAART, CD4 count >200 cells/mm3 and no other co-morbidities.
- Consider discussing with HIV physicians regarding potential interactions between chemotherapy and anti-retroviral medications.
- Indications for a de-functioning colostomy include tumours infiltrating into the posterior vagina and those with significant faecal incontinence due to sphincter dysfunction (secondary to tumour infiltration).
- It can be considered in those with significant pain or minor incontinence and tumours at risk of mechanical obstruction. The decision to proceed with a de-functioning colostomy is at the discretion of the MDT team with an awareness of the local reversal rate bearing in mind the poor reversal rate observed in ACT II once a stoma has been formed.

4) Consent

For radiotherapy consent see the RCR Radiotherapy consent form for anal cancer (November 2023 version 3) and for chemotherapy consent see the CRUK colorectal cancer SACT forms (July 2022).

5) Localisation

- Position – Supine, consider prone if bolus to anus required.
- Bolus - Clinician to decide, based on examination / imaging if tumour is adequately bolused by buttock cheeks. If there is not 5mm of tissue around the whole GTV, suggest using wax bolus sheet / gauze.
- For excised tumours - Mark scar with wire.
- Immobilisation and supports – Pillow under head, arms on chest, knees supported and ankles on foot-stocks.

- Organ pre-requisites - Comfortably full bladder, ideally aim for >250ml.
- Intravenous contrast, consider oral contrast to delineate small bowel.
- Consider radio-opaque marker at anal verge or distal point of macroscopic disease.
- CT acquistion - Slice thickness: 2-3mm, superior scanning limit top of L3, inferior scanning limit 7cm inferior to anal marker.

6) Volume Definition

6.1 Target volumes

- Use standard nomenclature as per AAPM 263
- https://www.aapm.org/pubs/reports/RPT_263.pdf
- Please refer to the RCR national guidance for VMAT or IMRT in anal cancer (2024) for illustrations of contouring.

6.2 Curative radiotherapy for good prognosis, T1 N0 tumours

- **GTV**_A = Includes the gross primary anal tumour volume.
- **CTV**_A = GTV_A + 10mm. Following this, manually enlarge to ensure coverage of entire anal canal including outer border, from the anorectal junction (approximately 4cm superiorly from anal verge identified by the radio-opaque marker) to the anal verge including the internal and external anal sphincters. Edit to exclude bone and muscle.
- **PTV**_A = CTV_A + 10mm.

6.3 Curative radiotherapy for early, standard risk (T1/2N0) tumours

- **GTV**_A = Includes the gross primary anal tumour volume.
- **CTV**_A = GTV_A + 10mm. Following this, manually enlarge to ensure coverage of entire anal canal including outer border from the ano-rectal junction (approximately 4cm superiorly from anal verge identified by the radio-opaque marker) to the anal verge including the internal and external anal sphincters. Edit to exclude bone and muscle.
- **CTV**_E = Elective nodal areas should include bilateral inguinal femoral, external iliac, internal iliac, obturators and presacral lymph nodes. For the mesorectal nodal area, if there is no gross disease, either primary tumour or nodal disease, within the mesorectum, only the lower 50 mm of the mesorectum is included in the CTV_E. Note: In the unusual event of gross tumour infiltration into the ischiorectal fossa (defined by cancer >5 mm outside the levators, puborectalis muscles, external anal sphincter or anal verge clinically or by diagnostic imaging) please follow the guidance used for inclusion of the ischiorectal fossa as per locally advanced tumours.
- **PTV**_A = CTVA + 10mm.
- **PTV**_E = CTV_E + 5mm.

6.4 Curative radiotherapy for locally advanced, high risk (T3/4 Nany or Tany N+ve) tumours

- **GTV**_A = Includes the gross primary anal tumour volume.
- **GTV**_N = Includes involved nodes <3cm.
- **GTV**_N3 = Includes involved nodes >3cm.
- **CTV**_A = GTV_A + 15mm. Following this, manually enlarge to ensure coverage of entire anal canal including outer border from the ano-rectal junction (approximately 4cm superiorly from anal verge identified by the radio-opaque marker) to the anal verge including the internal and external anal sphincters. If no bone or muscle involvement, edit to exclude bone and muscle, if bone or muscle involvement only edit structure free from infiltration.
- **CTV**_N = GTV_N + 5mm.
- **CTV**_N3 = GTV_N3 + 5mm
- **CTV**_E = Elective nodal areas should include bilateral inguinal femoral, external iliac, internal iliac, obturators and presacral lymph nodes. For the mesorectal nodal area, if there is no gross disease, either primary tumour or nodal disease, within the mesorectum, only the lower 50 mm of the mesorectum is included in the CTV_E. Note: In the unusual event of gross tumour infiltration into the ischiorectal fossa (defined by cancer >5 mm outside the levators, puborectalis muscles, external anal sphincter or anal verge clinically or by diagnostic imaging) please follow the guidance used for inclusion of the ischiorectal fossa as per locally advanced tumours.
- **PTV**_A = CTVA + 10mm.
- **PTV**_N = CTV_N +5mm
- **PTV**_N3 = CTV_N3 +5mm
- **PTV**_E = CTV_E + 5mm.

6.5 Palliative radiotherapy

- IMRT/opposed fields to cover all macroscopic disease or symptomatic disease; consider contouring GTV and adding 10-20mm circumferential margins to guide field placement.

7) 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

- **Bowel_Small** - Contouring should include all individual small bowel loops to at least 20mm above the superior extent of both PTVs.
- **Genitals** - Delineation of the male genitalia should include the penis and scrotum. In women it should include the clitoris, labia majora and minora.

An additional avoidance structure avoiding inguinal creases can be utilised at clinician's request.

- **Bladder** - Entire bladder including outer bladder wall.
- **Femur_Head_L or _R** - To be contoured separately on each side. To include the ball of the femur, trochanters, and proximal shaft to the level of the bottom of ischial tuberosities.

8) Dose and Fractionation

8.1 Curative radiotherapy for good prognosis, T1 N0 tumours

- Gross anal disease (PTV_A)= 50.4 Gy in 28# (1.8 Gy/#) in 5.5 weeks.

8.2 Curative radiotherapy for early, standard risk (T1/2N0) tumours

- Elective (PTV_E) = 40 Gy in 28 # (1.43 Gy/#) in 5.5 weeks.
- Gross anal disease (PTV_A) = 50.4 Gy in 28# (1.8 Gy per #) in 5.5 w

8.3 Curative radiotherapy for locally advanced, high risk (T3/4 Nany or Tany N+ve) tumours

- Elective (PTV_E) = 40 Gy in 28# (1.43 Gy /#) in 5.5 weeks.
- Gross nodal disease <3 cm (PTV_N) = 50.4 Gy in 28# (1.8 Gy /#) in 5.5 weeks.
- Gross nodal disease >3 cm (PTV_N3) = 53.2 Gy in 28# (1.9 Gy /#) in 5.5 weeks.
- Gross anal disease (PTV_A) = 53.2 Gy in 28# (1.9 Gy /#) in 5.5 weeks.

8.4 Palliative radiotherapy

- There are no good-quality trials evaluating different dose fractionation schedules for palliative treatment. An appropriate regime should be chosen after considering the patients likely prognosis, disease burden, symptoms and performance status. Doses of 20-30Gy in 5-10 fractions can be considered.

9) Concurrent chemotherapy

For good prognosis T1N0 tumours or surgically excised tumours with a margin smaller than 1mm, consider curative/adjuvant radiotherapy with or without concurrent chemotherapy.

Concurrent chemotherapy should be prescribed in all other patients that are considered fit for standard treatment. Acceptable regimens are:

- Mitomycin 12 mg/m2 day 1 with 5FU 1,000 mg/m2 days 1–4 and days 29–32.
- Mitomycin 12 mg/m2 day 1 with capecitabine 825 mg/m2 twice daily on days of external beam radiotherapy (XRT).

Dose reductions due to patient co-morbidities, dihydropyrimidine dehydrogenase (DPD) status, performance status and/or age are at the discretion of the treating team.

10) Plan evaluation

Organ	OAR / target	Optimal constraint	Mandatory constraints
PTV	D99%	>90%	>90%
	D95%	>95%	>95%
	D50%	Between 99% and 101%	Between 97% and 101%
	D5%	<105%	<107%
	D2%	<107%	<110%
Lower-dose PTVs	D99%	>90% of prescribed dose	>90% of prescribed dose
	D95%	>95% of prescribed dose	>95% of prescribed dose
	D50%	<110%	<125%
Small bowel	D200 cc	<30 Gy	<35 Gy
	D150 cc	<35 Gy	<40 Gy
	D20 cc	<45 Gy	<50 Gy
	D5 cc	<50 Gy	<55 Gy
Femoral heads	D50%	<30 Gy	<45 Gy
	D35%	<40 Gy	<50 Gy
	D5%	<50 Gy	<55 Gy
Genitalia	D50%	<20 Gy	<35 Gy
	D35%	<30 Gy	<40 Gy
	D5%	<40 Gy	<55 Gy
Bladder	D50%	<35 Gy	<45 Gy
	D35%	<40 Gy	<50 Gy
	D5%	<50 Gy	<58 Gy

11) Verification

Modality	Frequency	Match point	Additional information
KV planar/MV planar/ CBCT	Daily online imaging. Minimum CBCT performed days 1-5 and weekly thereafter as minimum. Online kV/MV images to be performed on other days.	Bone match to PTV	Any deviation from this and 5mm CTV to PTV margins may not be appropriate.

12) On-treatment review

Weekly review by member of the multi-disciplinary team.

13) Follow up

There is currently no robust evidence on optimal follow up and investigations. Imaging follow-up policies are therefore variable based on existing departmental practices and predicted risk of recurrence in individual patients. The following is a suggested follow-up protocol that could be considered.

- Follow up; At 6 weeks post end of treatment, 3-monthly (Years 1-2), 6-monthly (Year 3) then annually (year 4-5) with MRI (pelvis) at 3 and 6 months and CT (Chest, abdo, pelvis) at 12, 24 and 36 months.

14) Late effects

The Macmillan Radiotherapy Late Effects Service is aimed at providing physical and emotional support to people living with long term effects because of their radiotherapy treatment. The service is funded by charity Macmillan Cancer Support and the NHS Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Alliance.

Late effects following radiotherapy treatment for cancer can show themselves in many ways depending on the type of treatment you received, and the area of the body treated. These effects can develop from three months or many years after radiotherapy treatment has been given. The service is for people who have finished all their cancer treatment (excluding long term hormones).

For more information: **Late Effects**

References:

Document Approval

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