OESOPHAGUS

RADIOTHERAPY TREATMENT CLINICAL GUIDELINES

Contents:

1). SCOPE OF THE GUIDELINES

To summarise the planning and treatment of patients with oesophageal cancer receiving radiotherapy treatment with curative / palliative intent for use in Radiotherapy Centres within the South West Radiotherapy Network.

2). SELECTION CRITERIA / INDICATIONS FOR TREATMENT

2.1). Situations Covered Within This Protocol:

- Neo-adjuvant radiotherapy and concomitant chemotherapy – for adenocarcinoma or squamous cell carcinoma oesophagus/GOJ
- Curative radiotherapy and concomitant chemotherapy for squamous cell carcinoma of the oesophagus/GOJ
- Curative radiotherapy and concomitant chemotherapy for adenocarcinomas of the oesophagus/GOJ when surgical resection not possible or appropriate
- Curative radiotherapy alone to the oesophagus for patients not suitable for concomitant chemotherapy
- Adjuvant radiotherapy for macroscopic or microscopic positive resection margin where risk of local recurrence is thought to exceed risk of distant disease relapse
- Palliative Radiotherapy to the oesophagus

2.2). Inclusion criteria:

- Localised oesophageal Cancer with no evidence of metastases (palliative patients may be treated in the presence of metastases).
- Discussion in Multi-Disciplinary Meeting (to include Oesophago-Gastric Surgeon and Clinical Oncologist in the case of 2.1.1 to 2.1.5)
- Usual maximum primary disease length 10cm extending no more than 2cm into stomach.
- Disease length and extension into stomach can be adapted in individual circumstances where OAR constraints are met.
- Adequate performance status (ECOG 0-1) and functional reserve. Can also consider ECOG 2 for 2.1.6.

2.3). Exclusion criteria:

- Inadequate cardiovascular and / or respiratory function for safe delivery of radiotherapy +/- concomitant chemotherapy
- Not suitable for immobilisation required to deliver radiotherapy

3). PRE-TREATMENT INFORMATION REQUIRED

3.1). For radical / neoadjuvant treatments:

- Bloods – FBC, renal function, LFT, Mg, DYPD testing if treatment to include fluoropyrimidine based chemotherapy
- Endoscopy and biopsy + Endoscopic Ultrasound (unless MDT deem unnecessary e.g.: in impassable tumours / palliative treatment)
- CT chest, abdomen and pelvis (consider repeating imaging post op in adjuvant treatment)
- FDG-PET (ideally within 6 weeks of commencing RT)
- Dietetic support – ensure dietetic consult prior to commencing RT, consider placement of RIG / PEG if grade 3 dysphagia prior to treatment (or tumour >8cm)
- Lung function if indicated clinically (exercise tolerance limited by shortness of breath)
- ECG +/- Cardiac function tests if concern regarding cardiac morbidity

3.2). For palliative treatments:

- Bloods – FBC, renal function, LFT, Mg, DYPD testing if treatment to include fluoropyrimidine based chemotherapy
- Endoscopy and biopsy
- CT chest, abdomen and pelvis

4). CONSENT

- Ensure discussion of individualised benefits and toxicities & provide patient with information sheet / booklet.
- By IR(ME)R Practitioner at new patient / planning clinic and using Royal College of Radiologists (RCR) Site Specific Consent form, or
- By Entitled IR(ME)R Operator under delegated authority at new patient / planning clinic also using RCR site specific consent form
- Clinicians should be encouraged to use the standardised RCR Oesophageal Consent Form – please click here to access

5). LOCALISATION

Patients will be scanned as per local protocol and taking into consideration the following recommendations:

Localisation	Notes	
Position	Upper 1/3:	Supine
	Lower 2/3:	Supine
Arm/ leg/ head/ thorax position	Upper 1/3:	Arms down
	Lower 2/3:	Arms up
Immobilisation and supports	Upper 1/3:	Thermoplastic immobilisation head and neck shell
	Lower 2/3:	Upper body immobilisation as per local protocol
Organ pre-requisites	Upper 1/3:	No fasting required
	Lower 2/3:	Consider 2 hours fast and then drink 200mls of liquid 30 mins prior to CT.**
Contrast	Upper 1/3	IV contrast *** +/- oral contrast**
	Lower 2/3	IV contrast *** +/- oral contrast**
CT acquisition	Slice thickness:	Maximum of 3mm
	Scanning limits Upper 1/3:	Base of skull to L4 (ensure lung bases is covered)
	Scanning limits lower 2/3:	Lung apex to L4

*Where available consider 4DCT planning scan and/or abdominal compression or other methods of respiratory motion control for lower thoracic oesophageal and abdominal (GOJ) tumours.

** For tumours involving the stomach or where there is significant obstruction, consider asking patient to fast for 2 hours and then drink 200mls of water 30 minutes prior to CT. Ensure the same process is followed prior to each treatment delivery.

*** Unless palliative in which case intravenous contrast not deemed necessary

6). VOLUME DEFINITION

Advise standard nomenclature followed as per AAPM 263: please click here to access.

6.1). Curative radiotherapy GTV / CTV (see SCOPE2 protocol for full description of target volume definition)

6.1.1). GTV

Primary tumour (GTVp) and involved nodes (GTVn), as defined by diagnostic imaging, should be contoured on a contrast-enhanced 3D RT planning CT, acquired in addition to optional 4DCT (for distal oesophageal). The entire oesophageal wall should be included circumferentially, including adjacent to nodal disease distant to primary. The GTV should encompass the disease as defined on any of the above imaging modalities used (i.e. CT, EUS and/or PET), even if it is only apparent on a single modality.

6.1.2). CTV (as per SCOPE2 protocol)

CTV_A = GTVp + 20mm sup-inf (manually grown along direction of oesophagus) and GTVn + 10mm sup-inf. Grown (CTV_B) to include a circumferential margin of 1cm into adjacent mediastinum where there may be microscopic disease. CTV_C = CTV_A + 0.5cm circumferentially. CTV_B is then edited off uninvolved structures such as bone, lung, heart, great vessels with a minimum 5mm margin (as guided by CTV_C) from GTVp.
For lower third tumours with nodes below the diaphragm which will not be adjacent to the oesophagus, the nodes are contoured separately and a 5mm circumferential margin added. The final CTV (CTV_B) is edited manually to a maximum of 20mm inferior to GTV to include the nodal regions along the lesser curve of the stomach, the left gastric region and the coeliac region (if these lie within 20mm inferior of GTV or GTV_N). The final CTV should be 1 cm inferior to the lowest node or 2 cm inferior to GTVp (whichever is the most inferior).

6.1.3). ITV using 4DCT (derived using principles similar to those detailed in the SCOPE2 Protocol and summarised below)

From the 4DCT data sets, identify the extreme phases of motion (MaxIn and MaxEx). It is recommended that the dataset that best represents the time weighted average is used as the reference (Ref) dataset of the 4DCT phases (if contrast-enhanced). Alternatively, a 3DCT can be obtained for the reference image. It is recommended that the reference dataset is also outlined. The CTV is contoured on the Ref, MaxIn and MaxEx phases. The ITV is defined as the composite of these CTV volumes combined with each other.
The ITV is reviewed and expanded as necessary on each CT slice for the duration of the respiratory cycle to ensure the CTV is covered on each slice.
Planning is undertaken either on the reference 3D dataset or the reference dataset of the 4D scan (ensuring that all OARs are included).

6.1.4). PTV

CTV is grown by 10mm sup inf and 5mm circumferentially for proximal and mid 1/3 oesophageal tumours. CTV is grown by 10mm superiorly, 15mm inferiorly and 5mm circumferentially for lower 1/3 oesophageal tumours. If using 4DCT then ITV is grown by 5mm isotropically.

6.2). Adjuvant RT CTV

The location of tumour bed is identified by fusing planning CT with pre-op diagnostic CT/PET-CT and identifying site of original tumour and locations at highest risk of relapse using information from the surgeon and histopathology results. The CTV (tumour bed) is the area defined by vertebra/large vessels posteriorly, lungs laterally, heart/vessels/liver anteriorly. It is strongly recommended to liaise with the surgeon at the time of contour placement including the use of screen sharing or sharing screen shots. PTV margins would be as for 6.1.4.

6.3). Palliative RT

For simple treatments, GTV may be contoured as a guide and fields placed using Virtual Simulation to ensure adequate coverage. Consider formal contouring as previous for 3D conformal / VMAT treatment.

6.4). Brachytherapy

Brachytherapy can be considered as either primary therapy or a boost to external beam treatment for patients not suitable for radical radiotherapy whose prognosis is in excess of 3 months.

It may also be considered as palliative re-irradiation after previous radical external beam therapy. Regionally this service is offered in Bristol and Exeter. Discussion with relevant clinicians is encouraged.

6.5). Peer Review

- All curative and adjuvant volumes should be prospectively peer reviewed before the start of treatment. Ideally this would be prior to commencement of planning.
- A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.
- The peer review process and outcomes should be audited

7). ORGANS AT RISK

7.1). Contouring

Structure name	Description
Spinal canal	The spinal canal should be outlined on slices which include or are within 20mm of the PTV in the superior and inferior directions.
SpinalCanal_PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, this would usually be 5 mm, but can be reduced to 3mm at clinician's discretion. ie. CordPRV = SpinalCord + 5mm circumferentially
Lungs	The right (Lung_R) and left (Lung_L) lungs combined to obtain lung DVH. The trachea and bronchioles should **not** be included in this volume.
Heart	The whole heart should be outlined to the extent of the pericardial sac (if visible). The major blood vessels (superior to the organ) and the inferior vena cava (towards the inferior extent of the heart) are excluded. The superior extent is often difficult to define and may be simplified by identification of the vessels superior to the heart.
Liver	The whole liver is outlined if the level of its superior edge overlaps with the level of the inferior extent of the PTV.
Kidney_L and Kidney_R	Both kidneys should be outlined separately if the superior level of either kidney is coincident with, or overlaps with, the level of the inferior extent of the PTV.
Stomach	The whole stomach must be outlined if it is coincident with the PTV
Spleen	See the RCR "Incidental irradiation of the spleen" guidance (published 2021) – click here to access

A suitable reference should be used to maintain OAR contouring quality, such as Jabbour, S.K., et al., *Upper abdominal normal organ contouring guidelines and atlas: a Radiation Therapy Oncology Group consensus*. Pract Radiat Oncol, 2014. 4(2): p. 82-9.

7.2). Constraints

Structure name	Constraint	Optimal	Mandatory
PTV	V95% (47.5Gy) Dmedian	> 95% 100%	≥ 90% The median should be between 98-102% of the prescription dose
ICRU Maximum dose	D1.8cc		<107% of highest prescribed dose
SpinalCanal_PRV	D0.1 cc	< 40Gy	< 42Gy
Heart	Dmean V30Gy	< 25Gy < 45%	<30Gy -
Lungs (Combined lungs)	Dmean V20Gy	< 17Gy < 20%	<19Gy ≤25%
Stomach_excl_PTV	V50Gy	< 16cc	< 25cc
Liver	Dmean V30Gy	≤ 28Gy < 30%	≤30Gy
Individual kidneys	V20Gy	< 25%	≤30%
Spleen	Dmean	< 10Gy	<10Gy

Special consideration needs to be taken with GOJ tumours where there may be overlap of dose with the spleen, particularly where prognosis is > 1 year. The spleen is very radiosensitive and low dose RT may impact on splenic function. Patients with a dysfunctional spleen are at risk of overwhelming sepsis from encapsulated bacteria, which can potentially be life-threatening.

Where appropriate mean splenic dose and V10 should be considered and recorded. Aim to keep the spleen Dmean < 10Gy. If the mean splenic dose is >10Gy the patient should be considered at high risk for functional hypo-splenism and managed based on national guidelines from the British Committee for Standards in Haematology. This should include pneumococcal, haemophilus influenza type B conjugate vaccine, meningococcal conjugate vaccine at least 2 weeks prior to

starting RT. In addition, prophylactic antibiotics should be offered and started when RT starts and given a supply of emergency antibiotics.

8). DOSE AND FRACTIONATION

Classified as Category 1 in the RCR guidelines for management of gaps / interruptions on treatment.

Intent	Dose (Gy)/#	#/week	Chemo/ comments
a. Neo-adjuvant radiotherapy and concomitant chemotherapy	45/25	5	**Cisplatin- capecitabine/ 5FU or carboplatin-paclitaxel**
	41.4/23	5	**Carboplatin-paclitaxel**
b. Curative radiotherapy and concomitant chemotherapy for squamous cell carcinoma of the oesophagus/GOJ	50/25	5	**Cisplatin-capecitabine or carboplatin-paclitaxel**
c. Curative radiotherapy and concomitant chemotherapy for adenocarcinomas of the oesophagus/GOJ when surgical resection not possible or appropriate	50/25	5	**Cisplatin-capecitabine or carboplatin-paclitaxel**
d. Curative radiotherapy and concomitant chemotherapy for SqCC cervical (upper third) oesophagus	50/25	5	**Cisplatin-capecitabine or carboplatin-paclitaxel**
	60-65/30	5	**Weekly cisplatin. Plan with input from H&N team**
e. Curative radiotherapy alone to the oesophagus for patients not suitable for radiotherapy and concomitant chemotherapy	55/20 OR 60/30	5	
	50/16	5	**Only to be used for a tumour length of 5cms or less in patients with adequate lung function (used during COVID-19 pandemic to minimise attendance)**
f. Adjuvant RT for macroscopic or microscopic positive resection margin where risk of local recurrence is thought to exceed risk of distant disease relapse	45-50/25	5	**Cisplatin- capecitabine or carboplatin- paclitaxel**
g. Palliative radiotherapy to the oesophagus or stomach	40/15	5	**3D conformal planned / VMAT**
	30/10 or 20/5	5	**V sim**
	27/6	2	**V sim or conformal**
	6-8/1	1	**V Sim**

* Cisplatin 60 mg/m^2 q3w + Capecitabine 625 mg/m^2 bd po d1-21: 2 cycles with RT (can consider 1-2 cycles prior to RT). Alternatively, 5FU infusion (1000 mg/m 2 per day for 4 days). Neoadjuvant chemotherapy with a platinum-based regimen can be considered.

*Carboplatin (AUC 2) and paclitaxel (50mg/m2) weekly x 5

9). PLANNING

IMRT/VMAT/ Heliac Arc Therapy for curative treatments using ICRU 83.

- PTV V95% Optimal >95%, Mandatory ≥90%
- Dmedian 98-102%
- D99% ≥95% of prescribed dose and D1% ≤107% of the prescribed dose

Conformal for high-dose palliative (40Gy/15#).

Simple field arrangements for palliative RT (for 30Gy in 10# cord dose should be calculated and be </= 100%).

10). VERIFICATION

Daily CBCT with online correction matching to PTV unless OAR priority match stated by clinician (daily kV images if CBCT not possible).

11). ON-TREATMENT REVIEW

Patients should be reviewed weekly whilst on treatment to assess for acute toxicity. Review may be with CCO / specialist trainee / Specialist Radiographer according to local departmental policy.

For radical patients bloods (FBC, U&E, Creatinine, LFT) and weight should be checked weekly and further dietetic input accessed for any patients losing weight.

End of Treatment Summary will be completed and provided to the patient and GP in the final week of treatment. This will include a record of radiotherapy treatment received and any anticipated side effects, any continuing medication or support requirements as well as anticipated follow up.

11.1). Management of acute toxicity

Side effect	Medication / Action advised (if appropriate)
Odynophagia	• Gaviscon • Omeprazole/ lansoprazole • Mucaine (oxetacaine and antacid) or Sucralfate • Soluble paracetamol/ Co-Codamol (consider laxatives if needed) • Morphine/ oxycodone • Transdermal opiate patches • Admit if necessary, for nutritional support

Side effect	Medication / Action advised (if appropriate)
Skin erythema	• Topical emollients
Secretions	• Saline nebulisers
Cough	• Simple linctus • Codeine linctus • Low dose liquid morphine
Weight loss	• Document current nutritional supplementation including volume and type of feed through RIG. • Establish cause of weight loss, insufficient intake due to: pain/ vomiting/ inadequate training in enteral use. • Dietary supplements prescription if the above have been addressed – Fresubin/ Fortisip/ Ensure. • Refer to dietician for further assessment

12). FOLLOW UP / LATE EFFECTS

Consider weekly follow up initially post treatment if toxicities require close monitoring.

Follow up in outpatients at 4-6 weeks to assess for acute toxicity resolution / nutritional status

CT scan at 12 weeks post completion of radical RT.

There is no evidence to guide frequency of subsequent follow up and therefore can be done according to local protocol. Discharge at 5 years if disease free.

12.1). Subacute / Long term side effects

Side effect	Medication advised (if appropriate)
Secretions	• Hyoscine patch • Carbocisteine • Saline nebulisers
Cough	• Simple linctus • Codeine linctus • Low dose liquid morphine sulphate
Dysphagia	• Consider stricture or recurrence • OGD +/- dilatation (consider placement of temporary stent to aid dilatation if needed) • Bx with caution given risk of perforation

Side effect	Medication advised (if appropriate)
Breathlessness	• Refer to specialist physiotherapy service if available
Vertebral Fragility Fracture	• Refer to fracture liaison service or rheumatologist • May need consideration for bisphosphonate treatment

13). REFERENCES

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14). CHANGE/GOVERNANCE PROCESS FOR THE REGIONAL SW RT ODN GUIDELINES

To access all available SW RT ODN Clinical Guidelines, please click here (SWAG CA website).