East of England Radiotherapy Network:

Oesophagogastric Protocol V5

Contents

1.0 Indications and patient population

This protocol covers treatment in the following situations:

a. Neo-adjuvant radiotherapy and concomitant chemotherapy – for adenocarcinoma or squamous cell carcinoma oesophagus/GOJ

b. Curative radiotherapy and concomitant chemotherapy for squamous cell carcinoma of the oesophagus/GOJ

c. Curative radiotherapy and concomitant chemotherapy for adenocarcinomas of the oesophagus/GOJ when surgical resection not possible or appropriate

d. Curative radiotherapy and concomitant chemotherapy for SqCC upper third (cervical) oesophagus

e. Curative radiotherapy to the oesophagus for patients not suitable for radiotherapy and concomitant chemotherapy

f. Adjuvant radiotherapy for macroscopic or microscopic positive resection margin where risk of local recurrence is thought to exceed risk of distant disease relapse

g. Palliative radiotherapy to the oesophagus or stomach

1.1 Curative treatment eligibility

1.1.a Inclusions

- Localised oesophageal cancer with no evidence of metastases.
- Usual maximum disease length 10cm extending no more than 2 cm into stomach. Disease length and extension into stomach can be adapted in individual circumstances where OAR constraints are met.
- Adequate performance status and functional reserve (ECOG 0-1, exceptionally 2)

1.1b Exclusions

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

1.1c Essential Pre-Radiotherapy investigations for curative patients

- Bloods – FBC, plus U&E, LFTs, Mg as indicated for chemotherapy.
- Endoscopy and biopsy +/- endoscopic ultrasound (EUS) if MDT advised.
- CT chest, abdomen, and pelvis (consider repeat imaging post-op for adjuvant RT)
- FDG-PET
- Dietetic support – ensure patient has had a dietetic consultation prior to commencing RT.
- Lung function – if indicated clinically (exercise tolerance limited by shortness of breath).
- Cardiac function tests if concern about cardiac morbidity.
- DPYD testing before chemotherapy as per NHS-E guidance.

2.0 Localisation

Localisation	Options	Notes
Position		Supine
Arm position	Upper 1/3:	Arms down
	Lower 2/3:	Arms up
Immobilisation and supports	Upper 1/3:	Orfit
	Lower 2/3:	Strongly consider use of vacbag
Organ pre-requisites	Upper 2/3:	No fasting required
	Lower 1/3:	Consider asking patient to fast for 2 hours and then drink 200mls of liquid 15 - 30 mins prior to CT and each treatment. This can be particularly helpful where there is significant obstruction, or tumour involves the stomach.
Contrast		IV contrast
CT acquisition	Slice thickness:	Maximum of 3mm thickness
	Upper 2/3:	3DCT contrast enhanced free breathing Base of skull to base of lungs
	Lower 1/3 and abdominal (GOJ) tumours:	3DCT contrast enhanced free breathing (or exhale breath hold for radical tumours) Consider 4DCT/contrast enhanced 4DCT for radical tumours. Consider use of abdominal compression where available/ appropriate. Lung apex to L4

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/ week	Planning technique/ further comment
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/ 5FU 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/ 5FU or carboplatin-paclitaxel**
	60-65/30	5	**Weekly cisplatin. Plan with input from H&N team**
e. Curative radiotherapy to the oesophagus for patients not suitable for radiotherapy and concomitant chemotherapy	55/20	5	
	50/16	5	**Only to be used for a tumour length of 5cms or less in patients with adequate lung function**
f. Adjuvant RT for macroscopic or microscopic positive resection margin where risk of local recurrence is thought to exceed risk of distant disease relapse	50/20	5	
g. Palliative radiotherapy to the oesophagus or stomach	40/15	5	
	30/10	5	
	27/6	2	
	20/5	5	
	8/1	1	
*** Cisplatin 60 mg/m^2 q3w + Capecitabine 625 mg/m^2 bd po d1-21, 2 cycles pre-RT and 2 cycles with RT. Alternatively 5FU infusion (1000 mg/m 2 per day for 4 days). Consider omitting 1st 2 cycles pre-RT for small volumes**			
***Carboplatin (AUC2) and paclitaxel (50 mg/m^2) weekly (x5)**			

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

See SCOPE 2 or PROTIEUS protocol for a full description of target volume definition.

- **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**.** 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.

- **CTV** is defined using principles established in the SCOPE clinical trial radiotherapy protocol.
    - CTV = GTVp + 20mm sup-inf (manually grown along direction of oesophagus) and GTVn + 10mm sup-inf. Then edited to include adjacent mediastinum where there may be microscopic disease with a minimum 5mm margin 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.

4.2 Adjuvant radiotherapy CTV

- **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 tumour bed is the area defined by vertebra/large vessels posteriorly, lungs laterally, heart/vessels/liver anteriorly.

4.3 Curative/ adjuvant radiotherapy ITV/ PTV

ITV using 4DCT - ITV should be derived using principles similar to those detailed in the SCOPE2 protocol which is summarised here.

- 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). In cases where one of the extreme phases of motion (MaxIn or MaxEx) will be used for treatment delivery (e.g., Exhale Breath-Hold) then this must be labelled as the reference dataset. Otherwise, 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 and with the CTV from the contrast-enhanced CT.
    - 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).

- **PTV**
    - PTV = CTV + 10mm minimum sup/inf, CTV + 5mm minimum circumferentially (upper and mid-3rd).
    - PTV (tumours of lower 3rd/OGJ) = CTV + 10mm minimum superiorly, 15 mm minimum inferiorly, 5mm minimum circumferentially.
    - PTV using 4DCT = ITV + 5mm minimum isotropically.

4.4 Palliative radiotherapy

- For simple treatments, contour GTV and add margin to PTV of 10mm axially and 10-20mm sup-inf. Consider formal contouring as previous for 3D conformal or IMRT/VMAT treatments.

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
Spinal Cord	The spinal cord (rather than canal) should be outlined on slices which include or are within 20mm of the PTV in the superior and inferior directions.
SpinalCord_PRV	A Planning Risk Volume (PRV) is created to account for positioning error using an appropriate margin, usually 5 mm. i.e. 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 vessel's 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 RCR guidance (to be published 2021)

5.1 Constraints

For use with the following doses:

41.4Gy in 23 fractions with concomitant chemotherapy

45-50Gy in 25 fractions with concomitant chemotherapy

50-55Gy in 20 fractions

Structure name	Constraint	Optimal	Mandatory
PTV/ PTV_Eval*	D98% 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
SpinalCord_PRV	D0.1 cc	< 40Gy	< 42Gy
Heart	Dmean V25Gy V30Gy V40Gy	< 25Gy < 50% < 45% < 30%	<30Gy -
Lungs (Combined lungs)	Dmean V20Gy V5Gy	< 17Gy < 20% <60%	<19Gy ≤25%
Stomach_excl_PTV (Stomach excluding PTV_5000)	V50Gy	< 16cc	< 25cc
Liver	Dmean V30Gy	≤ 28Gy < 30%	≤30Gy <60%
Individual kidneys	V20Gy	< 25%	≤30%
Spleen	Mean dose	< 10Gy	

* PTV_Eval is used as necessary and may be cropped from lung as required for each clinical case and as defined locally.

6.0 Planning process/ technique

- IMRT/VMAT/ Helical Arc Therapy for curative treatments.
- Consider 3D Conformal for palliative (and curative if still achieving optimal dose-distribution constraints)
- Simple field arrangements (e.g. parallel opposed) may be more appropriate for palliative RT.

7.0 Peer Review/ Contour QA

- All curative and adjuvant volumes should be prospectively peer reviewed before the start of treatment.
- 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.

8.0 Target verification

Modality	Frequency	Match point	Additional information
kV planar/ MV planar/ CBCT	Daily CBCT. Daily kV images if CBCT not possible	Bone match to PTV	Soft tissue match as required

9.0 Side effects

9.1 Possible early or short-term side effects	
Expected (50% - 100%)	**Initial management (if appropriate)**
Tiredness	Rest when required Light exercise
Skin soreness, itching and colour changes in treatment area	E45 cream, hydrocortisone cream, patient's current moisturiser as long as it is Sodium Lauryl Sulphate (SLS) free.
Increased saliva or mucous production	Saline nebulisers
Loss of appetite/ weight loss	Dietitian review for all patients Assess cause of weight loss e.g. insufficient intake due to pain/ vomiting/ inadequate training in enteral use and manage as appropriate Dietary supplements if the above have been addressed – Fresubin/ Fortisip/ Ensure.
Inflammation of the oesophagus/ pain and/ or difficulty swallowing	Gaviscon Omeprazole/ lansoprazole Mucaine (oxetacaine and antacid) Soluble paracetamol/ Co-Codamol Morphine/ oxycodone Transdermal opiate patches Steroids
Indigestion or heartburn	Dietary advice, lansoprazole
Nausea or vomiting	Antiemetics

9.1 Possible early or short-term side effects	
Abdominal discomfort or bleeding	
Common (10-50%)	**Initial management (if appropriate)**
Hair loss in treatment area	N/A
Inflammation of lungs causing cough or shortness of breath	Codeine linctus Oral morphine
Feeding via tube into stomach/ small intestine	
Admission to hospital	May require placement of feeding tube at start of treatment or during to support nutrition and hydration
Sore mouth or throat	Oral analgesia as per the WHO Analgesic Ladder, lidocaine oral spray or solution
Less Common (Less than 10%)	**Initial management if appropriate**
Mouth ulcers	Benzydamine hydrochloride mouthwash, salt water, bicarbonate of soda mouthwash
Change in voice	
Rare (Less than 1%)	**Initial management (if appropriate)**
Risk of oesophageal fistula	
Pneumonia	

9.2 Possible late or long – term side effects	
Common (10 – 50%)	**Initial management (if appropriate)**
Ongoing fatigue	Assess for reversible causes (e.g. anaemia), exercise advice
Oesophageal stricture	May require endoscopic assessment and dilatation
Oesophageal dysmotility	Prokinetics
Fibrosis of underlying lung which can cause breathlessness, cough, or changes on x-ray	Steroids
Less common (Less than 10%)	**Initial management (if appropriate)**
Hypothyroidism	Thyroxine
Risk of damage to heart (depending on position of tumour)	
Skin changes in treatment area including altered colour, scarring and telangiectasia	
Rare (Less than 1%)	**Initial management (if appropriate)**
Oesophageal or gastric ulceration or perforation	
Oesophageal fistulation	
Long-term need for feeding via a tube	
Bleeding	
Myelitis	
Risk of rib fracture after an injury	N/A
Hyposplenism	May require additional vaccinations and prophylactic antibiotics
Long-term decline in kidney function	
A different cancer in the treatment area	N/A
Risk to life	N/A

10.0 References

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PROTIEUS: *A Randomised Phase 2 Trial Comparing Proton versus Photon-Based Neoadjuvant Chemoradiation, followed by Adjuvant Immunotherapy, in Oesophageal Cancer.* ISRCTN50098578, IRAS ID 329646.

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
22.1.21	V1.0			New Document
25.1.22	V2.0	V1.0	Updated version	Updated document issued with changes as outlined below:
25.1.22	V2.0	V1.0	5.1	Dose and fractionation added to dose constraints.
25.1.22	V2.0	V1.0	5.1	Spleen constraints changed from mandatory to optimal.
25.1.22	V2.0	V1.0	2.0	Lower CT scanning limits for upper oesophagus updated.
21.9.22	V2.1	V2.0	Pg 8/ 5.1	PTV D98% dose constraint added
01.02.23	V3.0	V2.1	Pg 3/ 2.0 Pg 4/3.0 Pg 7/ 5.0 Pg 9 / 6.0	Added recommended type of CT scans Drinking protocol for lower 2/3 oeso updated to give range of 15-30 mins prior to CT and treatment and clarified when drinking protocol is required. Removed palliative planning techniques from Table as information already in Section 6.0 GHG consensus guidelines added. Rephrased technique section to consider conformal and simple arrangements as sometimes a more complex treatment for palliative may be appropriate
12.02.24	V4	V3.0	P10	Skin reaction information updated
14.03.25	V5	V4	Section 2	Localisation table updated
			Section 3	Chemotherapy information updated
			Section 4	Target volume description updated to include reference to ProKnow
			Section 4.1	CTV information updated to include reference to PROTIEUS trial

			Section 4.3	Upper and mid-3rd added for clarity
			Section 5	V5 and PTV_Eval added to table
			Section 6	Planning process information updated
			Section 8	Verification information updated
			Section 10	Reference list updated to include PROTIEUS trial
			Section 11	Membership updated
			Author	Author of document updated