East of England Radiotherapy Network:

Lung Protocol V4.0

Contents

1.0 Indications and patient population

This protocol covers treatment in the following situations:

a. Curative radiotherapy and chemotherapy given concurrently or sequentially for non-small cell lung cancer.

b. Curative radiotherapy alone for patients not suitable for chemotherapy for non-small cell lung cancer.

c. Adjuvant radiotherapy for non-small cell lung cancer.

d. Curative radiotherapy and chemotherapy given concurrently or sequentially for small cell lung cancer.

e. Prophylactic cranial radiotherapy for small cell lung cancer.

f. Palliative thoracic radiotherapy for mesothelioma, small cell and non-small cell lung cancer.

Please note: Stereotactic Ablative Radiotherapy (SABR) for localised lung cancer will be covered in a separate network protocol.

1.1 Curative treatment eligibility

1.1.a Inclusion criteria

- Patients should be of performance status of 0 to 2.
- Localised/locally advanced lung cancer without evidence of distal metastasis.

1.1.b Exclusion criteria

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

1.1.c Essential Pre-Radiotherapy investigations for curative patients

- FDG-PET-CT scan, ideally within six weeks of commencement of treatment to rule out any distal metastasis.
- CT brain with contrast for stage II disease and MRI brain for stage III disease at the earliest opportunity to rule out brain metastasis.
- Ideally full staging with EBUS or mediastinoscopy to determine the status of the mediastinal nodes (non-small cell lung cancer only).
- Ideally full lung function tests.
- For patients with ILD advice and input should be sought from their ILD team.

2.0 Localisation

- Depending on local practice, a limited 4D scan (or inspired/expired scan) plus a 3D scan with contrast should be acquired for patients undergoing radical treatment.
- The area of interest for the 4D scan should be indicated by the clinician or radiographers.
- Optionally, only a full length 4D scan may be acquired.
- A standard 3D scan may suffice for palliative treatments.
- Gating or breath hold should be considered for motion management if available.
- Patients are suitable for 4D CT if:
    - They are able to maintain the required position for one scan (4D) or 2 scans (4D + 3D with contrast)
    - Their regular breathing pattern can be maintained.
    - There is no atelectasis.

Localisation	Notes	
Position	Supine	
Arm/ leg/ head/ thorax position	Ideally arms above head.	Must be a comfortable and reproducible position
Immobilisation and supports	Winged chest board with optional vac bag Head and neck thermoplastic mask can be considered for apical tumour with arms down.	Elbows positioned to avoid collision with gantry or imaging arms during CBCT and treatment
	Leg and ankle immobilisation	Used as appropriate
Organ pre-requisites	N/A	
Contrast	With intravenous contrast if appropriate, and renal function is acceptable and venous access possible.	3D scan
CT acquisition	Slice thickness:	2.0 mm – 3.0 mm
	Scanning limits: whole lung	upper limit – angle of jaw
		Lower limit – to include relevant organs at risk such as liver and spleen.
	Scanning limits: area of interest	limited 4D scan based on tumour limits recorded during whole lung scan

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/week	Chemo/ comments
Curative/adjuvant/neoadjuvant radiotherapy for non-small cell lung cancer (with or without chemotherapy, given concurrently or sequentially)	55Gy/20#	5#	Platinum Doublet
	60-66Gy/30-33#	5#	
	60Gy/15#	5#	For N0 peripheral tumour away from mediastinum not suitable for SABR. To be used without concurrent chemotherapy.
	50-55Gy/20#	5#	Adjuvant radiotherapy alone
	60-66Gy/30-33#	5#	
	45Gy/25#	5#	For Pancoast tumours prior to surgery, with or without chemotherapy
Curative radiotherapy for small cell lung cancer with or without, chemotherapy, given concurrently or sequentially	45Gy/30#	2# per day	Cisplatin/Carboplatin – Etoposide
	66Gy/33#	5#	Cisplatin/Carboplatin – Etoposide
	40Gy/15#	5#	Cisplatin/Carboplatin – Etoposide
Palliative thoracic radiotherapy for small cell, non-small cell lung cancer, and mesothelioma	39Gy/13#	5#	
	36Gy/12#	5#	
	30Gy/10#	5#	
	20Gy/5#	5#	
	17Gy/2#	1#	
	10Gy/1#	1#	
	8Gy/1#	1#	
Prophylactic cranial radiotherapy (PCI) for small cell lung cancer	20Gy/5#	5#	
	25Gy/10#	5#	

4.0 Target volumes

- Standard target volume nomenclature should be used: https://www.aapm.org/pubs/reports/RPT_263.pdf

4.1 Curative radiotherapy

GTV/ITV – The primary tumour should be contoured on the maximal intensity projection on the 4D-CT dataset using lung window setting. The target volume should be visually confirmed on all respiratory phases on axial, coronal and sagittal views, by playing a cine-movie of the dataset representing different phases of the respiratory cycle.

- For locally advanced disease with mediastinal lymph node involvement, the GTV node is best outlined using the 3D scan with contrast enhancement, and its motion can be checked against the 4D-scan.

CTV – ITV should be expanded by 0-8 mm to create the CTV to include microscopic spread. It can be edited to account for anatomical barriers if appropriate.

PTV - If CTV is determined using 4DCT scan, active breathing control or gating **AND** daily CBCT are applied during treatment, then PTV is formed by expanding the CTV/ITV by 5-10mm isotropically. Otherwise, if active motion is not accounted for, PTV is formed by expanding the CTV by 7-15 mm isotropically.

4.2 Adjuvant radiotherapy

CTV – Areas of positive surgical margin at risk of local recurrence should be identified in conjunction with the operating thoracic surgeon and radiologist.

PTV - CTV + 5-10 mm isotropically if the CTV is outlined on a 4D dataset, otherwise PTV is formed by expanding CTV 7-15 mm isotropically.

4.3 Palliative radiotherapy

- Ideally palliative radiotherapy should be planned on a 3D dataset and delivered conformally if more than 10# used.

- **GTV -** The primary tumour should be contoured on the planning 3D-CT scan, with contrast if appropriate, using lung window setting and the involved lymph nodes on the mediastinal window setting.

- **PTV =** GTV + 7-20 mm isotropically.

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 canal/spinal cord	The spinal canal should be contoured according to its inner limits using bone windowing. It should be outlined on slices which include or are within 20mm of the PTV in the superior and inferior directions. Alternatively the spinal cord can be contoured with a PRV margin depending on the local protocol (3-5mm)
Lung-GTV	Each lung should be contoured separately on lung windowing. Contour the whole lung, from the apex to the diaphragm including all inflated and collapsed lung. Exclude the proximal bronchial tree and trachea. Combine the left and right lung and subtract the GTV from their combination by Boolean operation.
Brachial plexus	The brachial plexus originates at the spinal nerve root foraminae C5, C6, C7, C8 and T1 and terminates at the medial limit of the second rib. Identify and outline the vertebral bodies of C5, T1 and T2. On the coronal view, identify and outline the anterior and middle scalene muscles. Use a 5mm diameter paint brush to extend from the neural foramina to the space between the anterior and middle scalene. On slices in which the neural foramina is not visible, outline the space between the anterior and middle scalene muscles. C8, T1 and the main trunk of the brachial plexus can be contoured using the subclavian and axillary vessels as a surrogate for identifying the location of the brachial plexus. This neurovascular complex will be contoured starting proximally at C7 and following along the route of the subclavian artery ending after the neurovascular structures cross the second rib.
Oesophagus	The oesophagus should be contoured on the mediastinal windowing to include all muscle layers out to the fatty adventitia. Contour from the lower edge of the cricoid cartilage to the gastro-oesophageal junction.
Heart + A_Pulm	The whole heart should be outlined on mediastinal windowing to the extent of the pericardial sac. The cranial border is at the cranial aspect of the pulmonary artery (best viewed in the coronal section), and the caudal extent at the apex of the heart where the left ventricle blends with the diaphragm. Both pulmonary arteries should be fully contoured above the main bronchus.

5.1 Constraints

Structure name	Constraint	Optimal	Mandatory
For 55Gy/20#			
Lung-GTV	V18Gy	<30%	<35%
Lung D_{mean}		<15Gy	<20Gy
Contralateral lung	V5Gy	<60%	
Brachial plexus	D0.1cc		<55Gy
Oesophagus	D0.1cc		<105%
Spinal canal	D0.1cc	<40Gy	<44Gy
Spinal cord + PRV	D0.1cc	<40Gy	<44Gy
Heart + A_Pulm	D100%	< 36Gy	
	D67%	<44Gy	
	D33%	< 57Gy	
For 60-66Gy/30-33#			
Lung-GTV	V20Gy		<35%
Dmean		<18Gy	<20Gy
Contralateral lung	V5Gy	<60%	
Brachial plexus	D0.1cc		<65Gy
Oesophagus	D0.1cc		<65Gy
Spinal canal	D0.1cc	<46Gy	<50Gy
Spinal cord + PRV	D0.1cc	<46Gy	<50Gy
Heart + A_Pulm	D100% D67% D33%	<44Gy <52Gy <59Gy	
For 45Gy/30#			
Lung-GTV	V20Gy		<35%
Contralateral lung	V5Gy	<60%	
Oesophagus	D0.1cc		<105%
Spinal canal	D0.1cc		<40Gy
Heart + A_Pulm	V45Gy V22.5Gy	<30% <50%	
For 60Gy/ 15#			
Lung-GTV	V17.4Gy		<35%
Contralateral lung	V5Gy		<60%
Spinal Canal	Max point		35Gy
Oesophagus	Max point 5.0cc 10.0cc		50Gy <48Gy <45Gy
Brachial plexus	Max point		50Gy
Heart	Max point 10.0cc		63Gy <57Gy

Structure name	Constraint	Optimal	Mandatory
Trachea	Max point 10.0cc		63Gy <57Gy
Great vessel	Max point 10.0cc		63Gy <57Gy
Stomach	Max point 5.0cc 10.0cc		50Gy <48Gy <45Gy
Spinal canal + 5mm	Max		<38Gy
Cardiac vessels	Max		<63Gy
Chestwall	Max		<63Gy
Skin	Max		<50Gy
For 40Gy/ 15#			
Lung-GTV	V20	Aim for <25% in high-risk patients*	<30%
Oesophagus			
Spinal cord			<40Gy
Heart	V40Gy	<30%	

* Patients with two or more co-existing risk factors:

1) Significant lung volume loss (previous pneumonectomy, atelectasis, effusion)

2) Concomitant chemotherapy

3) Poor respiratory function and/or moderate/severe COPD and/or restrictive lung disease

6.0 Planning process/ technique

- IMRT/VMAT/Helical Arc Therapy/3D conformal planning
- Plan should be created using energy up to 10MV
- Radical/Palliative treatment plans should be optimised as per local techniques, taking into account the lack of scattering due to air within the PTV.
- Plan is normalised to an ICRU reference point or the median PTV dose.
- Robustness checks should be conducted to account for expected tissue motion with IMRT plans.

Palliative Treatment

- 3D-conformal planning/IMRT to cover site of symptomatic mass(es).

- Plan is normalised to ICRU reference point or the median PTV dose. Reference point should be placed away from high- or low-density areas.
- Heterogeneity correction may be considered for parallel-opposed fields using 5# or less, and without wedge or MLC optimisation.

PTV coverage

- For IMRT/VMAT/Helical Arc Therapy plans, at least 95% of PTV_{air} should receive at least 90% of the prescribed dose, whilst at least 95%-98% of PTV_{tissue} should receive at least 95% of the prescribed dose. No more than 2% of the PTV should receive a dose above 105% of the prescribed dose and no more than 0.1cc should receive more than 107% of the dose.
- For centres which do not routinely separate PTVair and PTV tissue, the following constraint should apply. D99%≥90% (Optimal Constraint), D95%≥95% (Mandatory Constraint), Dmax<105% (Optimal Constraint). Aim for a CTV coverage of V100% > 95% prescribed dose.
- For 3D-CRT plans, aim for 95% of the PTV receiving 95% of the prescribed dose and no more than 5% (or 2cc) of the PTV receiving a dose above 107% of the prescribed dose.

7.0 Peer Review/ Contour QA

- All target volume delineation for radical plans should be prospectively peer reviewed by either another thoracic oncologist, or a thoracic radiologist.
- 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 should be mandatory for radical treatment. Consider 4D/gated cone beam CT if tumour motion as per local protocol.	Soft tissue match to PTV where possible Use bony or surrogate anatomy if soft tissue match is unclear	If available, 6DoF couch used with professional judgement of patient stability/immobilisation, match including rotations
	MV pre-treatment image or 2D kV imaging daily if CBCT	Stable bony anatomy	

	unavailable		

9.0 Side effects

All patients undergoing thoracic radiotherapy should complete the standardised consent form available on the Royal College of Radiologists' website.

https://www.rcr.ac.uk/clinical-oncology/service-delivery/national-radiotherapy-consent-forms

NB Consider all patients receiving radical radiotherapy for prophylactic treatment of pneumocystis jiroveci pneumonia (PJP) during or after their treatment if they are thought to be at risk, for example: lymphocyte count 0.6x109/L and/or for a minimum of six weeks post radiotherapy as per RCR lung consensus statements https://www.rcr.ac.uk/system/files/publication/field_publication_files/bfco205-radiotherapy-for-lung-cancer-rcr-consensus-statements.pdf.

9.1 Possible early or short-term side effects

Expected (50- 100%)	Initial management (if appropriate)
Mild tiredness	
Mild soreness when swallowing	Soluble paracetamol. Lidocaine hydrocortisone mouth wash.
Skin soreness, redness and itching in the treatment area	Topical application of water-soluble emollient or patient's own moisturising cream (providing it is Sodium Lauryl Sulphate free). 1% hydrocortisone topical application.
Temporary hair loss in treatment area	
Common (10- 50%)	**Initial management (if appropriate)**
Moderate to severe fatigue	
Mild lung inflammation – which can cause mild breathlessness, cough or changes on x-ray	Prednisolone at 40mg od reducing dose with PPI cover.

9.1 Possible early or short-term side effects	
Moderate to severe soreness when swallowing	PPI if there is evidence of reflux. Sulcrafate/Peptac. Xylocaine pump/spray. Oromorph prn. Support from nutritional team for supplement. Placement of RIG/NG tube if advised by the nutritional team.
Mild nausea	Metoclopramide Ondansetron Domperidone
Less common (Less than 10%)	**Initial management (if appropriate)**
Shortness of breath or cough	Prednisolone at 40mg od reducing dose with PPI cover. If severe symptoms should be admitted and treated with oxygen support and intravenous methylprednisolone.
Moderate to severe nausea or vomiting	Metoclopramide Ondansetron Domperidone
Risk of infection	
Lhermitte's sign	
Rare (Less than 1%)	**Initial management (if appropriate)**
Coughing-up blood	
Severe redness and skin soreness	Topical application of water-soluble emollient or patient's own moisturising cream (providing it is Sodium Lauryl Sulphate free). 1% hydrocortisone topical application.
Hospitalisation to help manage symptoms	
Difficulty swallowing	Support from nutritional team for supplement.

9.1 Possible early or short-term side effects	
	Placement of RIG/NG tube if advised by the nutritional team.
Risk to life	

9.2 Possible late or long-term side effects	
Expected (50- 100%)	**Initial management (if appropriate)**
Lung fibrosis	
Common (10- 50%)	**Initial management (if appropriate)**
Worsening of shortness of breath and cough	Prednisolone at 40mg od reducing dose with PPI cover.
Long-term irritation of the oesophagus	Prednisolone at 40mg od reducing dose with PPI cover.
Less common (Less than 10%)	**Initial management (if appropriate)**
Long-term shortness of breath or cough	Home oxygen.
Long-term irritation of the oesophagus	
Oesophageal stricture	
Risk of damage to the heart	
More prone to bone fractures in the radiotherapy treatment area	
Rare (Less than 1%)	**Initial management (if appropriate)**
Chronic lung infections	
Risk of organ damage	
Risk of damage to the nerves to the arms/ hands	
A different cancer in the treatment area	

9.2 Possible late or long-term side effects	
Hypothyroidism	
Hyposplenism	Additional vaccinations. Prophylactic antibiotics.
Risk to life	

10.0 Follow up guidance

The East of England Lung Cancer Network Cancer Group issued Patient Initiated Follow Up (PIFU) Guidelines in July 2022. The following is a summary of this guidance. The EofE Lung Cancer Network Cancer Group state that 'Clinicians should always use their clinical judgment to determine if an individual patient is suitable for PIFU. These consensus recommendations have been produced as guidance for follow-up pathways and are based on available evidence. Where little evidence existed, expert consensus was agreed.' It is agreed within the EofE RTN that these guidelines can be used at the clinician's discretion.

Follow-up Visit Number	Follow-up Time	Imaging Schedule	Clinic Follow-up With…
1	Within 6 weeks	CXR	Oncology / Surgeons
2	3 months	CT Chest (Initial Post Rx)	Respiratory (but CT to be requested in advance prior to OP)
3	6 months	CXR	Oncology
4	9 months	CXR	
5	12 months	CT Chest / Abdomen	
6	15 months	CXR	
7	18 months	CT Chest / Abdomen	
8	24 months	CT Chest / Abdomen	
9	30 months	CXR	
10	36 months	CT Chest / Abdomen	
11	48 months	CT Chest / Abdomen	
12	60 months	CT Chest / Abdomen (consider discharge to GP if clear)	

A full copy of the guidance is provided here:

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11.0 References

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4. Hall W., Guiou M., Lee N. et al, “Development and validation of a standardised method for contouring the Brachial Plexus: Preliminary Dosimetric Analysis Among Patients Treated with IMRT for Head and Neck Cancer”, International Journal of Radiation Oncology, Biology, Physics 2008; 72(5): 1362-1367

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10. Swanick, C.W., et al., Use of simultaneous radiation boost achieves high control rates in patients with non-small-cell lung cancer who are not candidates for surgery or conventional chemoradiation. Clin Lung Cancer, 2015. 16(2): p. 156-63.

11. East of England Lung Network Cancer Group. 2022. *Patient Initiated Follow Up (PIFU) Guidelines*. Cambridge: East of England Cancer Alliances (North and South)

12. The Royal College of Radiologists. Radiotherapy for lung cancer. RCR consensus statements. London: The Royal College of Radiologists, 2020

12.0 Members of the protocol drafting committee

Cambridge University Hospital NHS Foundation Trust: Rachel Kirby, Huiqi Yang, Kamal Thippu.

East Suffolk and North Essex NHS Foundation Trust: Hayley James, Dale Fowler, Kent Yip (Chair), John Sprunt, Louise Coley.

Mid and South Essex NHS Foundation Trust: Joanne Evans, Laura Doverty, Rafiqul Islam.

Norfolk and Norwich University Hospital NHS Foundation Trust: Pinelopi Gkogkou, Zacharias Tasigiannopoulos, Sam Cole, Natasa Solomou, Alex Martin.

North West Anglia NHS Foundation Trust: Sarah Treece, Jaak Joe, Mark Cowen

13.0 Amendment History

A record of changes in this document

Date	Updated version number	Previous version number	Page Number/Section (updated version)	Details
01.09.21	V1.0			New Document
01.02.22	V2.0	V1.0	Updated version	Updated document issued with changes as outlined below:
01.02.22	V2.0	V1.0	5.1	OAR constrains added for 60Gy/15#
01.02.22	V2.0	V1.0	5.1	Contralateral lung constraint changed to optimal from mandatory
01.02.22	V2.0	V1.0	5.1	Heart + A_Pulm changed to optimal from mandatory
01.02.22	V2.0	V1.0	10.0	References updated
01.02.23	V3.0	V2.0	5.0	Change of standard nomenclature to GHG consensus as advised by Network Oversight Group
			5.1	Constraints added for 40Gy/15#
			P9	Lung GTV and contralateral lung tolerances added for 60Gy/ 15#
			9.0	Statement added about management of PJP
			10.0	New section added – follow-up guidance
			11.0	References updated
26.03.24	V4.0	V3.0	Section 3.0	27Gy/ 6# removed from dose/ fractionation table 60Gy/ 15# - reference to Covid-19 removed 55Gy/ 20# removed for SCLC
			Pg 9	Correction – Lung GTV not lung PTV
			5.1	Constraints for D Mean re-ordered for clarity