South West Wales Cancer Centre

Department of Radiotherapy: Quality System
Department of Radiotherapy Physics: Quality System

Radiotherapy Clinical Protocol: NSCL - Non-Small Cell Lung Cancer

QA Ref: RTQW4090

Version No: 5.0

Authorised by: [redacted]

Authorised on:

Radiotherapy clinical protocol: Non-Small Cell Lung Cancer

Date of change	Index number/Rev No	Details of Change
May 2018	RTQW4090/3.0	This is the result of the merger of RTQW4090 (Non-Small Cell Lung Cancer (NSCLC)) and RTQW4093 (Concurrent chemoradiotherapy in NSCLC). RTQW4093 has been withdrawn from the Quality System.
June 2021	RTQW4090/4.0	Addition of palliative doses 17Gy/2#/8d and 25Gy/5#/1w. Clarification of dose constraints, whilst splitting between NSCLC and SCLC protocols. Change in cranial border of Heart delineation
Jan 2026	RTQW4090/5.0	Dose Constraints removed and new reference added QFORM3.165, Responsibility section updated to reference separate document. Documents section also updated.

Objective

This protocol outlines investigations, staging system, radiotherapy technique and dose, fractionation and includes an outline of management including chemotherapy and follow up procedure for patients referred with non-small cell lung cancer for Radiotherapy (NSCLC).

Scope

Any patients referred to the south West Cancer Centre for non-small cell lung cancer.

Responsibility

Please see 'Radiotherapy Clinical Protocol Responsibilities' (RTQW4177)

Documentation

Booking and Scheduling Radiotherapy	RTQW1009
Prescribing Radiotherapy	RTQW3007
Oncologist/SpR/Locum IR(ME)R Entitlement form	RTQF3016
Ionising Radiation (Medical Exposure) Regulations 2017 in Radiotherapy and Radiotherapy Physics (Including IR(ME)(A)R 2024	RTQP5001
Procedure for making, amending or cancelling a patient referral to the South West Wales Cancer Centre (SWWCC) for Radiotherapy treatment	RTQP1001
Referral of emergency patients	RTQP1005
Medical exposures and pregnancy	RTQW3018
Common Terminology criteria for adverse events (CTCAE) version 5	

Method

Background to the Role of Radiotherapy

Radiotherapy is a local treatment used in lung cancer for palliative and potentially curative treatment. This can be either sole treatment or as part of treatment with other modalities such as chemotherapy **or** in a neo-adjuvant setting to downstage/downsize tumour bulk **or** after surgery for incomplete R1 or R2 resections.

Early lung cancer can be successfully treated with stereotactic radiotherapy and is an option for those patients not suitable for or unwilling to undergo radical resection.

Traditionally locally advanced lung cancers were treated with largely palliative intent, either with radiotherapy or chemotherapy, with poor outcome. Radical radiotherapy is increasingly used as a concurrent treatment with systemic chemotherapy in a curative setting.

Over the last two decades, a multi-modality treatment approach has been investigated in different settings, namely concurrent chemoradiotherapy vs sequential chemotherapy and radiotherapy and different dose/fraction radiotherapy schedules in unresectable stage III non-small cell lung cancer. Results have consistently shown superior overall survival, progression free survival with better local control and reduction of risk of death for concurrent chemoradiotherapy compared to sequential therapy. It has been adopted as a standard of care in many centres worldwide, including North America, Europe and UK centres. The main concern is the side effects of treatment, namely, acute oesophagitis and toxicity to normal lung. In a meta-analysis of concomitant versus sequential chemoradiotherapy in locally advanced non-small cell lung cancer there was an absolute benefit in overall survival of 4.5% at 5 years in favour of concomitant treatment which came at the expense of increased incidence of oesophagitis (grade 3-4 18% vs 4%). Otherwise, the treatment is well tolerated by patients who are selected carefully. The best chemotherapy regimen, dose and fractionation are not fully settled, but both Cisplatin + Etoposide and Cisplatin and Vinorelbine, are active and superior to any other regimens at the present time. Carboplatin can be used in patients, who are not suitable for cisplatin.

Current guidelines discourage pneumonectomy following neoadjuvant or upfront chemotherapy due to the increased morbidity hence radical radiotherapy or chemoradiotherapy is increasingly used in this setting.

Aim of Radical Radiotherapy

All patients with early stage disease not suitable for surgery or with unresectable, stage III (including multi station N2 disease) non-small cell lung cancer, should be considered for treatment, after MDT discussion and detailed discussion with the patient. This should be recorded in the radiotherapy notes for audit purposes.

Selected patients with N3 disease confirmed on PET imaging which is encompassable in a radical radiotherapy field may also be considered for radical dose radiotherapy. This will be delivered in conjunction with systemic therapy (either concurrent or sequential as consolidation thoracic radiotherapy) and considered on an individual patient basis after discussion with the consultant responsible for their care. All patients should be assessed by the Consultant Clinical Oncologist or nominated team member to confirm suitability for treatment.

All patients should be seen in the treatment review clinic once a week, by the Consultant Clinical Oncologist or nominated team member, and any side effects or modifications of the dose of chemoradiotherapy, or change in radiotherapy should be recorded. This includes a record of the dyspnoea score. The WHO dyspnoea score is to be used to assess the status of breathing initially, and the dyspnoea grading under CTCAE recorded at on treatment review and subsequent follow up assessments.

Indications for radiotherapy/patient selection (Referral criteria)

Initial/diagnostic investigations

- **Bloods** FBC, U&E, LFT, bone profile
- **Radiology** CXR, CT (thorax + upper abdo with contrast)
- **Histology/Biopsy** i.e. CT guided biopsy, bronchoscopy, EBUS, EUS, Mediastinoscopy, VATS.

A patient may be treated without histology if Lung MDT concludes that highly likely to be malignant and unable to obtain tissue (i.e. procedure high risk for patient or tumour inaccessible)

- **Full Pulmonary Function Test (including gas transfer)**

  A patient may be treated without full lung function under certain circumstances (patient unable to tolerate or considered hazardous during coronavirus pandemic)

Staging investigations

- PET-CT for all patients potentially suitable for radical/curative treatment.
- Staging EBUS if indicated
- CT head with contrast if stage II and MRI head if stage III (patients with ≥ stage II disease are at increased risk of brain mets which if detected early may be amenable to surgical resection or SRS with improved outcomes)
- Bone scan as appropriate
- MRI for pancoast tumours unless contraindicated
- Request PDL1 for all patients being considered for concurrent Chemo/RT
- Any other investigation as appropriate

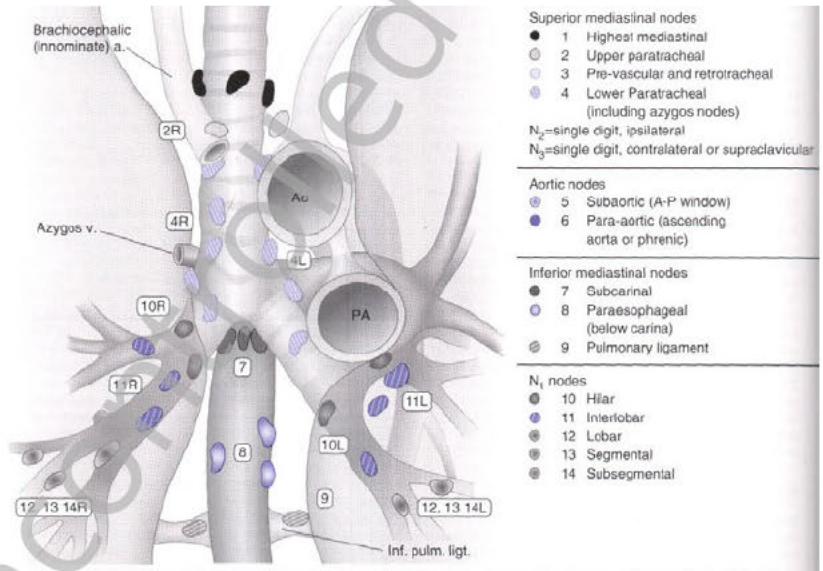
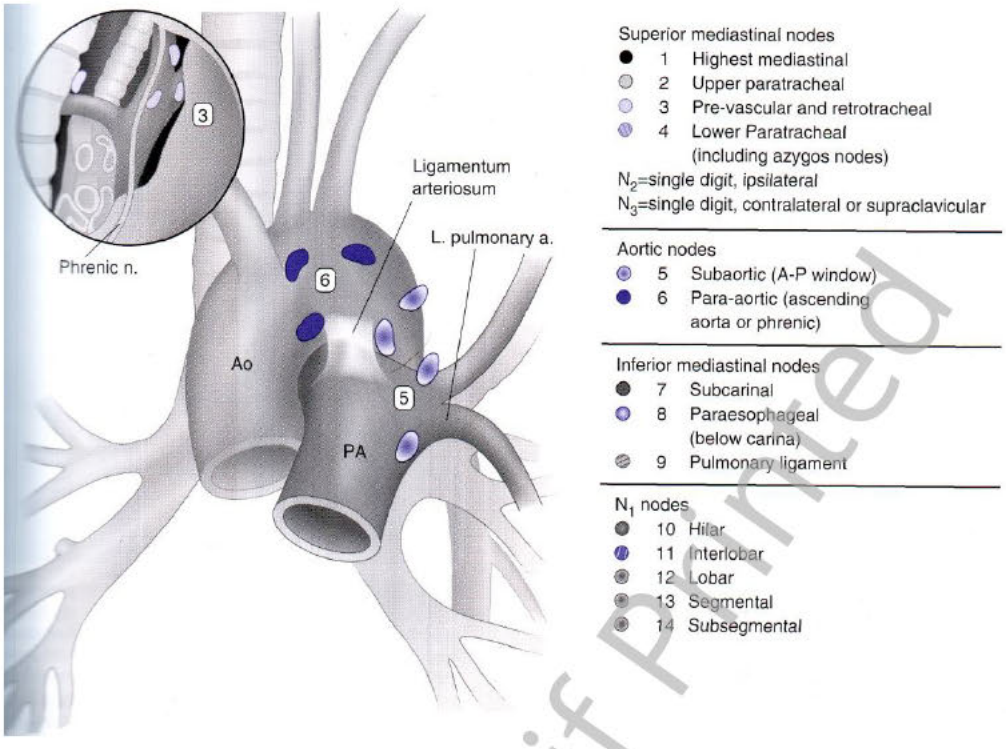


Figure 44.2 Mediastinal lymph node maps. a, artery; Ao, aorta; A-P, aortic-pulmonary; PA, pulmonary artery; v, vein. See Color Plate

Illustration continued on opposite page



Diagrams from Textbook of Respiratory Medicine; Murray and Nadel; 4th Edition 2005 ISBN 0-7216-0327-0

TNM staging

Stage Grouping for 8th Edition of the TNM Classification for Lung Cancer

Stage	T	N	M
Occult carcinoma	Tx	N0	M0
0	Tis	N0	M0
IA1	T1a (mi)	N0	M0
	T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0

	T4	N1	M0
IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
IIIC	T3	N3	M0
	T4	N3	M0
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

T – Primary Tumour

Tx		Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy.
T0		No evidence of primary tumour
Tis		Carcinoma in situ
T1		Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e. not in the main bronchus)[1]
	T1a(mi)	Minimally invasive adenocarcinoma[2]
	T1a	Tumour 1 cm or less in greatest dimension[1]
	T1b	Tumour more than 1 cm but not more than 2 cm in greatest dimension[1]
	T1c	Tumour more than 2 cm but not more than 3 cm in greatest dimension[1].
T2		Tumour more than 3cm but not more than 5 cm; or tumour with any of the following features[3] ▪ Involves main bronchus regardless of distance from the carina, but without involvement of the carina. ▪ Invades visceral pleura. ▪ Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or the entire lung.
	T2a	Tumour more than 3 cm but not more than 4 cm in greatest dimension
	T2b	Tumour more than 4 cm but not more than 5 cm in greatest dimension
T3		Tumour more than 5 cm but not more than 7 cm in greatest dimension, or directly invades any of the following structures: chest wall (including parietal pleura and superior sulcus tumours), phrenic nerve, parietal pericardium; or associated with separate tumour nodule(s) in the same lobe as the primary.
T4		Tumour more than 7 cm in greatest dimension, or invades any of the following structures: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; or associated with separate tumour nodule(s) in a different ipsilateral lobe to that of the primary.

N – Regional Lymph Nodes

NX		Regional lymph nodes cannot be assessed.
N0		No regional lymph node metastasis.
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s).
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).

M – Distant Metastases

M0		No distant metastasis

M1		Distant metastasis present.
	M1a	Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion[4]
	M1b	Single extrathoracic metastasis[5]
	M1c	Multiple extrathoracic metastases in one or several organs

[1] The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

[2] Solitary adenocarcinoma, (</=3cm) with a predominately lepidic pattern and </= 5mm invasion in any one focus.

[3] T2 tumors with these features are classified as T2a if ≤4 cm in greatest dimension or if size cannot be determined, and T2b if >4 cm but ≤5 cm in greatest dimension.

[4] Most pleural (pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor and the fluid is nonbloody and not an exudate. When these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor

[5] This includes involvement of a single distant (nonregional) lymph node.

Courtesy of IASLC

MRC Dyspnoea score

Grade 1 - Only get breathless on strenuous exercise.
Grade 2 - Get breathless when hurrying on the level or up a hill.
Grade 3 - Walk slower than people of the same age on the level, or up a slight hill.
Grade 4 - Stop for breath after walking 100 yards, or after a few minutes on the level.
Grade 5 - Too breathless to leave the house.

Eligibility criteria for radical radiotherapy

- Histologically or cytologically proven non-small cell lung cancer and radiological diagnosis agreed in the MDT where histological confirmation is either not feasible or failed.
- MDT staged I-IIIB disease. Stage IV disease can be considered if there is a radical option (SABR or surgery) to treat site of metastasis
- Performance status 0 - 2. PS 3 only if deemed fit for RT after assessment by consultant.
- If for concurrent chemo/RT there should be no contraindications for platinum-based chemotherapy e.g. poor renal function, poor bone marrow reserve.
- Considered an acceptable tumour volume for radical radiotherapy (V_{20} for normal lung – expected to be < 30%).
- FEV1 > 1 Litre/50% predicted– or at the discretion of Consultant Clinical Oncologist.
- Transfer factor DLCO ≥ 40%.
- Superior sulcus or Pancoast tumours if treated with concurrent chemoradiotherapy, need to be assessed for suitability for surgery prior to starting treatment.
- Post-operative radiotherapy to be considered if R1 resection

Not eligible

- Poor performance status, generally > 2, but can be considered if PS 3 at discretion of consultant. (i.e. poor general condition with significant co-morbidities e.g. heart failure, uncontrolled diabetes mellitus/hypertension, immunosuppressive treatment, ischaemic heart disease etc.).

- Patients with a pleural effusion. If a pleural effusion appeared after an invasive procedure and is not considered to be related to the cancer can still be considered for radical treatment.
- Caution should be given in considering radical radiotherapy for patients with persistent or massive haemoptysis.
- Untreated SVCO
- Evidence of pulmonary fibrosis on CXR or CT scan, even with normal PFT.

Treatment plan

- The intention of this treatment is curative, **this should be discussed with the patient and clearly documented on the consent form.**
- If potentially radical then patients should be listed for discussion in the radical lung planning meeting
- To minimise overall treatment time Radical Radiotherapy (including concurrent chemoRT) should commence on a Monday except under exceptional circumstances and should be discussed with consultant prior to treatment if unavoidable.
- Patients with early stage I and II can be treated with radical RT alone.

  Consider SABR if T1-3 and <5cm, N0 peripheral and non operable (refer to Lung/SABR MDT Velindre) or conventionally fractionated radiotherapy (45 - 66Gy in 15-30F) if not.
- Patients with more advanced disease i.e. stage II and III which is amenable to a radical volume should be considered for concurrent chemoRT unless poor PS in which case consider sequential treatment or radiotherapy alone
- Concurrent chemo should start with day 1 adiotherapy provided this can be achieved in a timely manner or consider starting cycle one chemotherapy whilst preparing for concurrent chemoRT (to be delivered with cycle 2).
- All patients with bulky or large volume disease (not encompassable in a radical volume) should start on combination chemotherapy with Cisplatin/Carboplatin and Vinorelbine, and receive preferably 2 cycles before starting on combined chemoradiotherapy. The 3rd and 4th cycles will coincide with radiotherapy as a concurrent treatment.
- The request for a re-staging CT scan and a planning CT scan (CT-Sim) after 2 cycles (before commencing on concurrent chemoradiotherapy) should be made at the start of the 2nd cycle of chemotherapy. The timing of the diagnostic CT scan (preferably D_{15} of the 2nd cycle) should be mentioned in the request form.
- NB-It is not always possible to time the restaging CT scan, planning CT scan and scheduling chemotherapy concurrently due to reasons other than on clinical grounds and a maximum of 2 weeks flexibility is acceptable at the discretion of the oncologist.
- Patients who are not fit for concurrent chemoradiotherapy (PS2) should be considered for sequential Radical Radiotherapy after 2 - 4 cycles of chemotherapy.
- GCSF should be added to the chemotherapy regimen in patients who experience ≥ grade 3 neutropenia or febrile neutropenia to avoid dose reductions and treatment delays

- Patients unfit for or with contra-indications to combination platinum doublet chemotherapy should be considered for radical radiotherapy alone.

Radiotherapy immobilisation

To maintain the accuracy of patient positioning, radical patients are treated supine with arms immobilised using a commercially available thorax support. Lower abdomen and extremities are immobilised using a commercially available patient positioning device.

Radiotherapy localisation

3D CT with contrast is the standard modality (see RTQW2018: Planning-CT scans), but 4D can be used at the discretion of the treating Clinician (see RTQW2019: 4DCT scans) to account for individual tumour motion.

Gross Tumour Volume (GTV) is delineated to include all the known primary and nodal disease as identified on the diagnostic CT/PET-CT/EBUS, and no prophylactic lymph node irradiation is included. The primary tumour volume will be contoured on the planning scan using lung window settings and the lymph nodes on the mediastinal window settings. If the patient has received induction chemotherapy, the GTV will include the post-chemotherapy tumour volume and the pre-chemotherapy lymph node volume.

Clinical Target Volume (CTV) is grown by adding a symmetrical 0.5cm margin to the GTV. The CTV expansion includes microscopic spread and may be edited to account for anatomical barriers i.e. vertebrae but only if it is not thought to invade the structure.

Planning Target Volume (PTV) is formed by adding a 0.5-1.0cm margin transaxially, and a 1.0-1.5cm margin in the sup/inf directions to CTV. Margin size selection will take into account tumour location and individual patient factors as determined by the clinician who has clinically reviewed the patient.

In summary, with 3DCT, the target volume margins are as follows:

CTV	GTV + 0.5cm
PTV	CTV + 0.5-1.0cm (1.0-1.5cm sup/inf)

With 4DCT planning, a motion adapted 4D-GTV is contoured using one of the 2 following techniques. First the GTV is delineated on the contrast-enhanced CT as described above and the structure copied and re-named. The GTV is then adjusted on each phase of the 4D dataset and the contour expanded to account for motion. NB the structure should NOT be made smaller unless to correct for an error. Alternatively, a combined GTV Exhale (defined on the maximum exhale 4D-CT dataset) and GTV Inhale (defined on the maximum inhale 4D-CT dataset) is created. Whichever technique is used the target volume should be visually confirmed on all respiratory phases on axial, coronal and sagittal views, by playing a cine-movie of the datasets representing different phases of the respiratory cycle to ensure all areas of disease are encompassed.

The motion adapted 4D-GTV should be expanded by 0.5cm to create the CTV. The CTV should then be expanded by 0.7cm axially and 0.9cm sup/inf to create the PTV.

In summary, with 4DCT, the target volume margins are as follows:

CTV	4D-GTV + 0.5cm
PTV	CTV + 0.7cm (0.9cm sup/inf)

When planned, the ideal dose distribution of PTV should be –5%, +7% of prescribed dose, and is prescribed as per ICRU 83 (**target median dose = prescription ± 2% for lung**) as inverse planned, as per 'Prescribing Radiotherapy' (RTQW3007).

PTV coverage by the 95% isodose may not be possible where the target volume is surrounded by air in which circumstance coverage by the 90% isodose is clinically acceptable. 6MV photons will be utilised.

Planning technique (VMAT arc/s) is described within 'Lung Treatment Planning WI' (QWORK3.144).

Chemotherapy regimens

Induction or upfront chemotherapy

The appropriate chemotherapy regimens should be selected in chemocare (full dose platinum/vinorelbine or platinum/vinorelbine/rad) and up to 4 cycles are given in total (maximum 2 cycles concurrent with radiotherapy as below).

Concurrent chemoradiotherapy regimen

	Week 1	Week 2	Week 3	Week 4	Week 5 (30F)	Week 6 (30F)
Cisplatin 80 mg/m^2 OR Carboplatin AUC 5	↑Cis or Carbo platin			↑Cis or Carbo platin		
Oral Vinorelbine 40 mg/m^2	↑Vin	↑ Vin		↑Vin	↑ Vin	
Radiotherapy 20 or 30#	↑↑/////↑↑↑	↑////↑↑↑↑	↑↑/////↑↑↑	↑ ////↑↑↑↑	↑ ////↑↑↑↑	↑↑↑////↑↑
Day	1	8	15	21	28	35

Please see the pages 13 and 14 for dose modification. The Cisplatin dose is calculated based on an estimated GFR. If the estimated GFR is < 60 ml/min based on Cockcroft-Gault formula, the EDTA clearance should be performed before starting Cisplatin.

Radical radiotherapy Dose and fractionation

RT ONLY Either single agent, sequential or post-op	5500 cGy Tumour dose in 20#, 5 # a week over 4 weeks. Daily dose per fraction = 275 cGy 6000/6600 cGy Tumour dose in 30#, 5# per week over 6 weeks. Daily dose per fraction = 200/220 cGy 4500/5010 cGy Tumour dose in 15#, 5# a week over 3 weeks. Daily dose per fraction = 300/334 cGy can be considered 5000/5500 cGy Tumour dose in 20#, 5# a week over 4 weeks, if post-operative.

	Daily dose per fraction = 250/275 cGy
Concurrent Chemo-Radiotherapy (cCRT)	Either 6000/6600 cGy Tumour dose in 30#, 5 # a week over 6 weeks Daily dose per fraction = 200/220 cGy Or 5500cGy Tumour dose in 20#, 5# per week over 4 weeks Daily dose per fraction = 275 cGy

All lung patients receiving radical dose radiotherapy are considered category 1 patients (eligible for treatment on bank holiday weekends) and gaps in treatment should be avoided. See RTQW4001.

Palliative Radiotherapy

Patients with chest symptoms, not suitable for OR who decline to have chemotherapy OR have recurrent disease after chemotherapy.

Patients with chest pain, haemoptysis, obstructive symptoms.

High dose palliative radiotherapy should be considered in fit patients (PS 0,1,2) who are otherwise not candidates for radical radiotherapy.

6 MV photons – justifications for using 10MV photons should be recorded in the radiotherapy or treatment sheet.

Aim to keep the PTV to a minimum to cover the tumour, and reduce side effects.

Acceptable Dose and fractionation

1000 cGy Tumour Dose in a single fraction.
1700 cGy Tumour Dose in 2 #s, 1 # a week.
2000 cGy Tumour Dose in 5 #s, 5 # a week
2500 cGy Tumour Dose in 5#, 5 # a week
3600 cGy Tumour Dose in 12 #s, 5 # a week
3900 cGy Tumour Dose in 13 #s 5 # a week.

Any treatment over 10 fractions should be planned conformally to avoid exceeding cord tolerance.

Organs at risk

Radiotherapy Physics Technologists will routinely outline anatomical structures as indicated in the 'Lung Treatment Planning WI' (QWORK3.144). Where Dose Volume Histogram (DVH) information for other anatomical structures is required, the anatomical structure(s) will be outlined by the Consultant Clinical Oncologists or nominated Specialist/Speciality Registrars. It is the Consultant Clinical Oncologist's responsibility to review outlined OARs (amending if deemed necessary) when delineating.

- ***Spinal cord*** - The spinal canal (bony limits) should be contoured, before growing a 0.3cm PRV, to be used for dose reporting.
- ***Heart+A_Pulm*** - The whole heart should be contoured to include the pericardium, with the major blood vessels (superior to the organ) and the inferior vena cava (towards the inferior extent) excluded. The superior extent is the cranial aspect of the pulmonary artery, as visualised on coronal images (as per ADSCaN trial guidance).
- ***Normal lung*** - The PTV and field arrangement should be chosen to produce the lowest possible lung dose. Both lungs should be contoured as one structure using the pulmonary window. The GTV,

liver, trachea/ipsilateral bronchus should be excluded from this structure. This is locally named 'R_Lungs'.

- ***Oesophagus*** - The entire oesophagus (mucosa, submucosa and all muscular layers out to the fatty adventitia) should be contoured as a solid organ from the lower border of the cricoid cartilage to the gastro-oesophageal junction.
- ***Brachial plexus*** - For upper lobe tumours, the major trunks of the brachial plexus should 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 2nd rib. PRV is generated for Brachial Plexus with a 0.3cm isotropic ma gin.

If doses exceed the specified limits, a justification must always be recorded on the MOSAIQ notes – see tables of dose limitations below

Dose Constraints

Please see 'Dose Constraints: LUNG (NSCL)' (QFORM3.165)

Treatment verification

Either Cone Beam CT (CBCT) or Electronic Portal Imaging (EPI) methods of verification may be carried out.

CBCT is the preferred method of IGRT for Physic led pathway patients. ProSoma-led Palliative cases and clinically marked patients generally receive 2D EPI Verification.

Details of the 2D EPI verification protocol are outlined in RTQW4009. CBCT Verification details are outlined in RTQW4130, RTQW4139.

Patients in radiotherapy trials will be imaged according to trial protocol; it is the responsibility of the Clinical Oncologist acting as Principal Investigator to check that any trial imaging requirements meet with the departmental imaging strategy. Any additional imaging dose required for the trial is to be justified (in the IR(ME)R sense.

Other medication

- The chemotherapy regimen is used with the standard pre-medication, hydration and post medication as per protocol
- Consider prophylactic septrin for patients undergoing concurrent chemo/RT and monitor lymphocyte count. Septrin can be discontinued once lymphocyte count has recovered.
- GCSF is recommended if clinically indicated – e.g. neutropenic sepsis or prolonged neutropenia.
- Use of steroids should be carefully monitored, and prescription of Proton Pump Inhibitor is recommended.
- Treatment of oesophagitis depends on the severity. Mild Oesophagitis is treated with pain control using soluble paracetamol, codeine, gaviscon, antacid/oxetacaine, raspberry mucilage +/- fluconazole. Mild to moderate Oesophagitis requires Oromorph, with dietary advice, and patients should be seen by the

dietician. Severe Oesophagitis, some grade 3 and some grade 4, may require hospital admission with IV hydration and parenteral nutrition.

- Radiation pneumonitis is treated with steroids, and a troublesome cough may require strong cough suppressants such as opiods.

Thoracic Reirradiation

Reirradiation of lung cancer for either recurrence or new primary is feasible either for purely palliation of symptoms (e.g.- haemoptysis, SVCO, pain, impending collapse or spinal cord compression etc.) or to achieve a long term local control or even a potential cure and in this situation a consideration should be given the suitability of the patient for SABR.

Depending on the clinical situation each patient should be carefully considered for reirradiation and any potential risk of excessive toxicity to normal tissue be discussed with the patient and should be justified clinically. It is advised to review these patients in planning meeting for discussion and peer review.

There is no standard dose/fraction for reirradiation and this is at the discretion of the Consultant based on fallowing factors which can be safely delivered (Please see references).

Following factors need to be considered when determining the suitability of a patient for reirradiation.

1- Intention-Purely palliative or long term local control/potential cure
2- Fitness of the patient and comorbidities
3- Approximate life expectancy
4- Previous dose/fraction, response and time since previous radiation and any residual toxicity
5- Overlapping of RT fields and acceptable doses to OAR (there is no standard OAR dose available for reirradiation).

On-treatment review

- All radical patients (including In Patients) should have weekly clinical assessment by either oncologist or review radiographer with FBC, LFT and U & E and weight. Palliative patients receiving 5 or more fractions should be reviewed at least once during treatment.
- Patient symptoms such as pa n, dyspnoea or any other toxicity of treatment should be recorded in the radiotherapy notes.
- During each review, the clinician should make a best clinical judgement with regard to continuing or stopping the treatment if the patient experiences severe side effects, after consultation with patient.

Follow up arrangements

- Once treatment is completed the radiotherapy team should inform Consultant secretary who will arrange appropriate FU
- Post treatment baseline CT scan is generally recommended at 3 months post treatment.
- If suitable for adjuvant immunotherapy then scan to assess response at 4 weeks.
- Patients will be seen 3-monthly for the 1st year following completion of treatment, 4-6 monthly during the 2nd and 3rd year and annually thereafter. Imaging will be performed at each follow up visit as detailed in the table below or sooner if clinically indicated.

- Additional CXR and CT scans during follow up are performed at the discretion of the clinicians or MDT.

Time since completion of treatment	Recommended imaging
3 months	Contrast enhanced CT chest/abdo
6 months	CXR
9 months	Contrast enhanced CT chest/abdo
12 months	CXR
15 months	Contrast enhanced CT chest/abdo
18 months	CXR
2 years	Contrast enhanced CT chest/abdo
2.5 years	CXR
3 years	Contrast enhanced CT chest/abdo
4 years	Contrast enhanced CT chest/abdo
5 years	Contrast enhanced CT chest/abdo

Dose modifications

Dose modification based on blood counts/adequate bone marrow reserve.

Haemoglobin ≥ 10 g/dl

White blood cells 4 × 10^9/litre

Platelets ≥ 75 × 10^9/dl

Neutrophils > 1.5 × 10^9/litre

ANC × 10^9/litre	Platelets × 10^9/litre	Cisplatin + Vinorelbine
> 1.5	> 75	Full dose
< 1.5	< 75	Delay treatment, repeat blood counts after 3 days
Febrile neutropenia **or** grade 4 neutropenia **or** neutropenia > 7 days	Grade 4 thrombocytopenia **or** grade 2 thrombocytopenia with bleeding	- Consider dose reduction by 20%, using GCSF. - Radiotherapy should be continued if medically fit.

Dose modification based on liver function

AST/ALT	Bilirubin	Cisplatin + Vinorelbine
< 3 × ULN	< 5 × ULN	Full dose
> 3 × ULN	> 5 × ULN	- Delay chemotherapy by 1 week and reassess. - Radiotherapy should be continued if medically fit.

Dose modification based on renal function.

If the calculated GFR is < 60 ml/ minute, EDTA clearance should be performed before starting on Cisplatin.

GFR	Cisplatin	Vinorelbine

> 60 ml/minute	Full dose	Full dose
50 – 60 ml/minute	Full dose	Full dose
40 – 50 ml/minute	50% dose	75% dose
< 40 ml/minute	Discontinue	Discontinue

Other toxicities

Pulmonary toxicity (pneumonitis)		Cisplatin and Vinorelbine are not known to cause pulmonary side effects.
Radiation pneumonitis	Grade I and II	continue treatment, may require a cough suppressant and steroids.
	Grade III and IV	discontinue radiotherapy and re-assess after symptomatic treatment.
Ototoxicity	Action dependent on the severity & clinical assessment	- Consider reducing the dose of Cisplatin or substituting with Carboplatin. - If the symptoms (tinnitus, high frequency hearing loss) worsen, discontinue all platinum chemotherapy. - Continue with Vinorelbine at full dose.
Peripheral neuropathy	≥ Grade 2	- Substitute with Carboplatin, then 50% Cisplatin after recovery to ≤ Grade 1 - Discontinue Vinorelbine. - Continue with radiotherapy
Diarrhoea	Grade 3 or 4	- Reduce dose of Cisplatin and Vinorelbine by 25%. - Continue radiotherapy if medically stable.
Mucositis	Grade 3 or 4	- Reduce Vinorelbine by 25%, and discontinue Cisplatin. After recovery, resume at the original prescribed dose. - If mucositis is within the radiotherapy field, discontinue radiotherapy.
Oesophagitis	Grade 3 or 4	- Discontinue radiotherapy and chemotherapy, and treat actively. - Reassess on a daily basis to determine restart of radiotherapy.

References

Kirkpatrick JP[1], van der Kogel AJ, Schultheiss TE. **Radiation dose-volume effects in the spinal cord.** Int J Radiat Oncol Biol Phys. 2010 Mar 1;76(3 Suppl):S42-9. doi: 10.1016/j.ijrobp.2009.04.095

Auperin A et al. Meta-**Analysis of Concomitant Versus Sequential Radiochemotherapy in Locally Advanced Non–Small-Cell Lung Cancer**. JCO 2010; 28(13) 2181-90.

Bestall J C. et al. **Usefulness of the medical research council (MRC) dyspnoea scale as a measure of disability in patients with CPOD**. Thorax July 1999; 54:581-586.

Everett e. et al. **Concurrent chemoradiotherapy for unresectable stage III NSCLC**. Clinical cancer research. Vol II, 50455-50505. July 1, 2005.

Hak Choy. Et al: **Concurrent chemoradiotherapy for inoperable stage III NSCLC**. Current oncology reports 2003, 5:113-317.

James R. et al: **Guidelines on treatment of stage IIIB NSCLC**. Chest 2003; 123:2215-2255.

Ohe Y. **Chemoradiotherapy for lung cancer: current status and perspectives – review article**. International journal of clinical oncology 2004. Volume 9, No. 6, pages 435-443.

Kayoko T. et al. **Predictive value of DVH parameters after concurrent chemoradiation for lung cancer**. International journal of Radiation Oncology; Biology; Physics. Volume 55, No. 1, pages 110-115, 2003.

Price A. **State of the art radiotherapy for lung cancer**. Review article, Thorax 2003. 58; pages 447-452.

Rowell N P, O'Rourke N P. **Concurrent chemoradiotherapy in NSCLC**. Cochrane systematic review (online)18th October 2004, Issue 4.

Southwest oncology group. **Induction chemoradiation and surgical resection for superior sulcus NSCLC. Long term results of southwest oncology group trial 9416** (Intergroup trial 0160). Journal of clinical oncology 2007 Volume 25, No. 3; pages 313-318.

Thomas E. et al: **Combined modality therapy for stage III NSCLC**. July 2006. The Oncologist Volume 11, No.7, 809-823.

Zatloukal P. et al. **Concurrent vs sequential chemoradiotherapy with Cisplatin and Vinoralbine in locally advanced NSCLC – a randomised study**. Lung cancer(2004) 46, 87-98.

Utracka-Hutka B. et al. **Novelbine (NVB) oral (o) with Cisplatin (CDDP) as induction and concomitant radiotherapy. Final results of an international phase II trial in stage III NSCLC**. ASCO 2007 annual meeting, category – lung, Abstract no. 7691. Journal of Clinical Oncology. Volume 25, No. 185 (June 20 supp) 2007.

Fournel P. et al. **Randomised Phase III trial of sequential chemoradiotherapy compared with concurrent chemoradiotherapy in locally advanced NSCLC**. Journal of Clinical Oncology. Volume 23, No 25, September 1, 2005.

Beckmann G. et al. **Oral Vinoralbine and Cisplatin with concomitant radiotherapy in stage III NSCLC – a feasibility study**. International Journal for Cancer Research and Treatment. Volume 29, No. 4, 2006.

Review Article-Annals of Palliative Medicine, Vol 3,No 2 (April 2014). Thoracic reirradiation for lung cancer: a literature review and practical guide ,Review Article- Annals of palliative medicine,C Suzanne Drodge[1], Sunita Ghosh[2], Alysa Fairchild[1,1]Department of Radiation Oncology, [2]Department of Experimental Oncology, Cross Cancer Institute, Edmonton, Alberta, Canada.

Tim J. Kruser, MD,[*] Bradley P. McCabe, MS,[†] Minesh P. Mehta, MD,[‡] Deepak Khuntia, MD,[§] Toby C. Campbell, MD,[||] Heather M. Geye, MS,[*] and George M. Cannon, MD[*] **Reirradiation for Locally Recurrent Lung Cancer Outcomes in Small Cell and Non-small Cell Lung Cancer.** Am J Clin Oncology. 2014 Feb:37(1): 70-76.

Aktan M, Kanyilmaz G, Koc MAras S. **Thoracic Re-irradiation for Locally Recurrent Lung Cancer.** Asian Pac J Cancer Prev. 2016 Nov 1;17(11):5041-5045.

Prof Dirk De Ruysscher, MD, Corinne Faivre-Finn, MD, Cecile Le Pechoux,MD, Stephanie Peeters, MD, Jose Belderbos, MD. **High dose re-irradiation following radical r diotherapy for non-small cell lung cancer.** The Lancet Oncology, Vol 15,No 13, e620-e624 December 2014.

Maguire J, Khan I, McMenemin R et al SOCCAR**: A randomised phase II trial comparing sequential versus concurrent chemotherapy and radical hypofractionated radiotherapy in patients with inoperable stage III non-small cell lung cancer and good performance status.** Eur J cancer 2014 50(17) 2939-2949

Antonia SJ, Villegas A, Daniel D et al. **Overall survival with Durvalumab after Chemoradiotherapy in stage III non-small-cell lung cancer**. NEJM 379 (2018) 2342-2350

The Royal College of Radiologists. **Radiotherapy for lung Cancer. RCR consensus statements**. LONDON RCR 2020

NICE guideline NG122. **Lung Cancer: Diagnosis and Management** March 2019. www.nice.org.uk