

London Cancer
**Radiotherapy Guidelines
for Treatment of Lung
Cancer**

June 2014

Contents

- 1. Non-Small Cell Lung cancer 3
 - 1.1. Indications 3
 - 1.2. Post-operative treatment (adjuvant) 7
 - 1.3. Early Stage Disease : T1/T2 and N0 (or proximal N1) External beam 3D conformal radiotherapy or IMRT 7
 - 1.4. Stereotactic Ablative Radiotherapy or Stereotactic Body Radiotherapy..... 10
 - 1.5. Cyberknife available at St Bartholomew’s Hospital and Mount Vernon Hospital.... 13
 - 1.6. Radical Chemo-Radiation or Radical Radiotherapy alone for locally advanced NSCLC. 13
 - 1.7. Palliative Settings 14
- 2. Small Cell Lung Cancer 17
 - 2.1. Palliative Radiotherapy 17
 - 2.2. Radical Radiotherapy 17
 - 2.3. CONVERT Study Planning target volume (PTV)..... 18
- 3. References 20

1. Non-Small Cell Lung cancer

1.1. Indications

1	Radical	Post-operative (adjuvant) for residual disease post resection
2	Radical	Early Stage Disease T1/T2 , N0/N1 inoperable for medical reasons or patient choice
3	Radical	Stereotactic Ablative Body Radiotherapy (SABR): T1/T2 < 5cm peripheral tumours
4	Radical	Cyberknife T1/T2 < 3 cm tumours
5	Radical	Stage IIB /IIIA (some stage IIIB) chemo-radiation or radiation only dependent on PS, size of PTV
6	Palliative	Advanced disease poor PS stage III or Stage IV (symptomatic)
7	Palliative	Symptomatic metastases i.e. bone, brain, nodes, skin

Adapted from Malthus Project Decision Tree: NSCLC, March 2013

NSCLC	Stage I	Surgery	Complete resection	No radiotherapy
			Positive margins	Radical radiotherapy
		No surgery - medically inoperable		Radical radiotherapy
	Stage II	Surgery	Complete resection	No radiotherapy
			Positive margins	Radical radiotherapy
		No surgery - medically inoperable		Radical radiotherapy
	Stage IIIA	Surgery [non bulky nodal disease]	N0-1	No radiotherapy
			Positive margin, ≥N2	Radical radiotherapy
		No surgery	Definitive radical radiotherapy	
	Concurrent chemo-radiotherapy			
	Stage IIIB	Good performance status	Radiotherapy or sequential chemo-radiation	
			High dose palliative radiotherapy	
Poor Performance Status		Palliative chemotherapy		
Stage IV	Focal symptoms	Palliative chemotherapy /biological treatment		
		Palliative radiotherapy		
	No focal symptoms	No radiotherapy		

Non Small Cell Lung Cancer	Stage 1 16% (ECRIC, LUCADA)	Surgery 80% Malthus consensus	Complete resection	No radiotherapy ²⁷ ECRIC 93%
			Positive margins	Radiotherapy ECRIC 7% 60 Gy* 30# 55 Gy/20# 66Gy 33#
		No surgery - medically inoperable 20%	Radiotherapy 60-66 Gy /30-33# ,55 Gy/20# CHART* ^{14,15,21} 54 Gy/36#/12d, T1-2 ≤5 cms SBRT ^{1,11} [Stereotactic Body Radio-Therapy] 54Gy/3# over 2 weeks > 40 hours apart, < 8 days apart ECRIC RT 57%/ ECRIC 43% no treatment	
	Stage 2 7% LUCADA, 8% ECRIC	Surgery 80%	Complete resection	No radiotherapy ²⁷ ECRIC 79%
			Positive margins ²	Radiotherapy 60* Gy/30-33# ECRIC 21% 55 Gy/20#
		No surgery - medically inoperable 20%	Radiotherapy 60-66* Gy /30-33# ,55 Gy/20# CHART ^{14,15,21} 54 Gy/36#/12d, ECRIC 55% RT, 45% no Tx T1-2 ≤5 cms SBRT ^{1,11} [Stereotactic Body Radio-Therapy] 54Gy/3# over 2 weeks > 40 hours apart, < 8 days apart If stage 2 concurrent CT/RT ^{13,26}	
	Stage 3a 10% LUCADA Normalised	Surgery 10% [non bulky nodal disease]	NO-1	No Radiotherapy ECRIC 71%
			Positive margin, ≥N2 ^{2,27}	Radiotherapy ECRIC 29% 55/20#, 60* Gy/30# if +ve margin 50/20 ≥ N2 disease Lung ART 54/30#
		No surgery 90%	Definitive RT 40% Concurrent chemo-radiotherapy ^{13,26} 60-66* Gy in 30-33#, 55 Gy/20# If unable to have chemotherapy consider CHART ^{14,15,21} 54 Gy/36#/12 otherwise 66/33# or 55/20# Superior sulcus tumour consider preop crt 45 Gy/25# then surgery.	
			Palliative radiotherapy 60% high dose palliative 36 Gy /12#, 30 Gy/10# ²⁴ Poor performance status focal symptoms – palliative 20 Gy/5#, 16Gy/2, 10Gy/1 #Thoracic radiotherapy	

Stage 3b 19% LUCADA Normalised	Good performance status 50%	20% Radiotherapy – Concurrent CT/RT ^{13,26} 66G*y in 30#, 55Gy/20# over 4/52 ECRIC no treatment or surgery 37% 10% If unable to have chemotherapy consider CHART ^{14, 15, 21} 54Gy/36#/12d or 55/20# or 66/33#. 20 % - May consider chemo first and then sequential radical radiotherapy if reduced bulk. If excellent performance status and very large tumour [curative dose not possible as not encompassable] – 50% of patients are palliative High dose palliative 39/13#, 36 Gy/12#*, 30 Gy/10# ²⁴ Palliative RT to chest if symptoms – 20 Gy/5#, 17*16 Gy/2#16*16 Gy/2#, 10Gy/1#
	Poor performance status 50%	25% Palliative chemo 75% Palliative RT 20Gy 5#, 16-17Gy 2#, 10Gy single#
Stage 4 48% Lucada, 40% ECRIC	Focal symptoms 50%	Give chemotherapy /biological treatment. Palliative Radiotherapy to chest ECRIC RT 50 % 39/13#*, 36 Gy/12# ¹⁶ [very good performance status] 30 Gy/10# ²⁴ ,20Gy/5#, 16-27Gy/2 ¹⁶ , 10Gy/1# Bone metastases 20 Gy/5#, 8Gy/1*# QUARTZ trial 20 Gy/5# vs no RT Brain 20 Gy/5# - If metastasis resected consider 30 Gy/10#
	No focal symptoms 50%	No radiotherapy ECRIC RT 50 %

Figures in red are clinical estimates : Malthus Project NSCLC Radiotherapy decision tree
March 2013

LUCADA : National Lung Cancer Audit Programme

ECRIC : Eastern Cancer Registration and Information Centre

1.2. Post-operative treatment (adjuvant)

Radiotherapy is not recommended in completely resected N0-1 disease.

Where there has been incomplete resection or unexpected N2 disease radiotherapy may be offered as it has been shown to reduce local recurrence.

Performance status and residual lung function needs to be taken into account. FEV1 > 0.8 L/min. Case should be reviewed at MDT with surgical input and target volume should be identifiable by clips and encompassed by a simple volume.

Dose is dependent on whether the residual disease is macroscopic or microscopic.

- Macroscopic: 55Gy in 20 fractions over 4 weeks using 6 MV photons in a single phase.
- Microscopic: 50Gy in 20 fractions over 4 weeks using 6 MV photons in a single phase.

NB in certain situations e.g. tumour close to the spinal cord or in Pancoast tumours it may be preferable to use lower dose-per-fractions regimens e.g. 66Gy/33F for macroscopic tumour and 60Gy/30F for microscopic tumour.

1.3. Early Stage Disease : T1/T2 and N0 (or proximal N1) External beam 3D conformal radiotherapy or IMRT

Information required

- Referral form indicating RA/IMRT or 4D CT as applicable
- Healthcare records including copy of MDT decision
- Cytology/histology report including EBUS if available.
- Bronchoscopy report and pulmonary function tests
- Staging CXR/CT chest/abdomen, PET if performed- imaging and reports
- Chemotherapy investigations if appropriate including FBC, U+E, LFTs, EDTA
- Consent

Dose : Either is acceptable

55 Gy in 20 F using 6MV photons over 4 weeks in a single phase

Or 64-66 Gy in 32-33 F using 6MV photons over 6 ½ weeks in a single phase

Planning and treatment technique

Radical radiotherapy technique: Linear Accelerator: 6 – 10 MV photons

Patient treatment position	Supine, with arms above head. Immobilisation using chest board and fixed arm position. The patient should be breathing normally.
Patient data acquisition	<p>A planning CT scan should be performed in the treatment position, whilst the patient undertakes a normal respiration, using 2 - 3 mm slices through the entire target volume and 5 cm margins in the superior/inferior direction. The whole lung (apex to diaphragm) should be covered using at least 2 cm slices to allow dose-volume histograms to be calculated. For all cases suitable for radical radiotherapy, every effort should be made to obtain PET/CT scan to enable the clinician to delineate between tumour and collapsed lung/consolidation and positive lymph nodes. Further information may be available from EBUS.</p> <p>Intravenous contrast should be used, when patient renal function permits and where central disease should be distinguished from vasculature.</p> <p>Where possible 4D CT scanning should take place to identify the complete tumour movement during respiration.</p> <p>Where uncertainty exists in delineating gross tumour volume (GTV) attempts should be made to discuss all images with diagnostic radiologist and experienced lung clinical oncologist to define extent of active tumour and possible involved lymph nodes either at lung MDT or at specific meeting with radiologist and clinical oncologist.</p>
<p>GTV – CTV – PTV</p> <p>Margins</p> <p>Planning target volume (PTV)</p>	<p>Peripheral tumours: Use Lung Window settings and outline tumour to include spicules as CTV. Enlarge to PTV by 1.5 cm superior / inferiorly and by 1.0 cm laterally.</p> <p>For central and mediastinal tumours / nodes : use mediastinal window settings for GTV. Add 0.5 cm in all directions for CTV then enlarge accordingly 1.5 cm superior / inferiorly and 1.0 cm laterally.</p> <p>This is a guide and for larger tumour volumes, discussion should take place with experienced consultant for alternative settings.</p> <p>Majority of lung tumours in the lower lobes in proximity to the diaphragm may show greater excursion during respiration than tumours located in the upper lobes.</p> <p>4D CT scanning will eventually help demonstrate the full excursion of tumour during normal respiration and will help reduce margins.</p>

	<p>Where it is difficult to achieve coverage with the 95% isodose on the end slices, a slightly lower minimum dose will be accepted in preference to a clinically inappropriate increase in field length.</p> <p>Prophylactic nodal irradiation should not be employed.</p>
Normal Tissues and Organs at Risk (OAR)	<p>The spinal cord, both lungs, heart and oesophagus should be outlined.</p> <p>No more than 10 cm oesophagus should be included in PTV. The spinal cord position must be identified throughout the PTV. Maximum radiation dose to 10 cm spinal cord should not exceed 44 Gy in 2 Gy per fraction or 36Gy in 2.75 Gy fraction size.</p> <p>Every effort should be made to exclude normal lung tissue. Less than 35% of 'normal' lung (i.e. whole lung excluding Gross Tumour Volume) should receive a radiation dose of ≥ 20 Gy i.e. V20 < 35% but <30% preferable.</p> <p>The heart can receive the total dose (TD) to < 30% of its volume. For > 50% of cardiac volume, dose < 50% of TD is recommended.</p>
Treatment planning	<p>One or two phases may be used, depending on usual considerations regarding radiation tolerance of spinal cord, normal lung tissue and heart.</p> <p>Use of 3D conformal radiotherapy is required unless 4D planning is employed. Beams eye views may be useful in the design of individual shielding.</p> <p>4D planning may be used for suitable tumours if the participating centre is able to do. Isodose distribution must be provided at the central plane. Dose volume histograms (DVH) for the PTV and normal lung will be calculated in order to obtain full knowledge of the 3D dose distribution.</p>
Simulation	<p>A simulation check is required for all treatment fields and the position of blocks used should be indicated on the simulator films.</p>
Dose specification and fractionation	<p>The PTV should receive 55 Gy in 20 daily fractions of 2.75 Gy over a period of 28 days.</p> <p>Alternative schedules are 64-66 Gy in 32-33 daily fractions over 6 ½ weeks. This may also allow for 2 phases for larger PTV coming off some mediastinal lymph nodes, when some uncertainty might exist on positivity of some PET warm lymph nodes.</p>

	<p>The dose will be specified at the ICRU reference point and fully corrected for heterogeneity. The dose distribution within the PTV should ideally be within $\pm 5\%$ of the prescribed dose, and no more than $\pm 7\%$ of the prescribed dose.</p> <p>In some situations it may not be possible to meet the above inhomogeneity requirements. If this is the case, a dose range of 107% - 90% will be accepted if the participating clinician confirms that this is the best achievable dose distribution and the area receiving less than 95% is not regarded as critical.</p>
Treatment delays	<p>Every effort should be made to deliver the prescribed dose of radiotherapy in the prescribed time.</p> <p>If unavoidable delays occur, that could increase the overall treatment time, e.g. due to machine breakdown, compensation should if possible be made by one of the following mechanisms: giving two fractions on a subsequent day, with a minimum interval of six hours between fractions, or treating on a weekend day, or adjusting fraction size to deliver the total prescribed dose within the allotted time.</p> <p>If the radiation schedule is interrupted for more than 1 week due to intercurrent illness consideration should be given to discontinuing treatment. Further treatment will depend upon the clinical situation and is at the discretion of the responsible clinician. Interruptions for < 1 week due to intercurrent illness or radiation toxicity will be recorded and treatment should be completed as planned.</p>

1.4. Stereotactic Ablative Radiotherapy or Stereotactic Body Radiotherapy

Stereotactic Ablative Radiotherapy (SABR) or Stereotactic Body Radiotherapy (SBRT) should only be performed in specialist centres with dedicated MDT and team with experience of > 25 cases /year. Dose schedule to be determined as per national SBRT group. [See SABR UK Consortium Version 4.0 January 2013]

Inclusion Criteria	<ul style="list-style-type: none"> • MDT diagnosis of NSCLC based on findings of positive histology, positive PET scan or growth on serial CT scan • Clinical stages of T1 N0 M0 or T2 ($\leq 5\text{cm}$) N0 M0 or T3 ($\leq 5\text{cm}$) N0 M0 • [radiologically N2 (CT or PET), patients only eligible if possible nodal disease is subsequently confirmed as histologically negative with mediastinoscopy or endoscopic bronchial or oesophageal ultra-sound biopsy]
--------------------	---

	<ul style="list-style-type: none"> • Not suitable for surgery because of medical co-morbidity, lesion is technically inoperable or patient declines surgery after surgical assessment (or option of assessment) • WHO performance status 0-2 • Peripheral lesions outside a 2cm radius of main airways and proximal bronchial tree. This is defined as 2cm from the bifurcation of the second order bronchus e.g. where the right upper lobe bronchus splits (See bronchial tree diagram) • Age \geq 18 years
Exclusion Criteria	<ul style="list-style-type: none"> • NSCLC patients with T2 or T3 primary tumours > 5cm • T3 primary NSCLC tumours involving the mediastinal structures or central T3 primary tumours. • Metastatic lung tumours • Any tumour that is not clinically definable on the treatment planning CT scan e.g. surrounded by consolidation or atelectasis. • If tumour has respiratory motion \geq 1cm despite using techniques to reduce tumour motion, only proceed with treatment if target delineation is reliable and suggested normal tissue and tumour planning constraints can be achieved. • Tumours within 2cm radius of main airways and proximal bronchial tree (figure II.1). • Primary NSCLC tumours with clinical evidence of regional or distant metastasis after appropriate staging studies. • Previous radiotherapy within the planned treatment volume Presence of pulmonary fibrosis (unless the increased risk of SABR has been fully considered and the patient has been appropriately consented) • Chemotherapy administered within 6 weeks prior to study entry or planned for < 6 weeks following SABR. <p>See diagram bronchial tree and exclusion zones:</p>
Tumour Delineation	<p>Gross Tumour Volume (GTV) = The GTV is defined as the radiologically visible tumour in the lung, contoured using lung settings. Mediastinal windows may be suitable for defining tumours proximal to the chest wall. Where available, information from PET/CT will be incorporated into delineating the GTV.</p> <p>Clinical Target Volume (CTV) = The CTV is the GTV with no margin for microscopic disease extension. This is the accepted standard in the majority of SABR trials.</p> <p>Internal Target Volume (ITV) = tumour volume obtained using a 4DCT scan. This is defined as tumour contoured using either the (i)</p>

	<p>maximum intensity projection scan, (ii) maximum inspiratory and expiratory scans or (iii) as contoured on all 10 phases of a 4DCT scan.</p>
Organs at Risks (OAR)	<p>Spinal cord The spinal cord should be contoured on all slices based on the bony limits of the spinal canal.</p> <p>Oesophagus The oesophagus will be contoured using mediastinal windowing on CT to correspond to the mucosal, submucosa, and all muscular layers out to the fatty adventitia.</p> <p>Brachial Plexus The defined ipsilateral brachial plexus originates from the spinal nerves exiting the neural foramina on the involved side from around C5 to T2. However, for the purposes of this protocol only the major trunks of the brachial plexus will 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 the bifurcation of the brachiocephalic trunk into the jugular/subclavian veins (or carotid/subclavian arteries), and following along the route of the subclavian vein to the axillary vein ending after the neurovascular structures cross the 2nd rib.</p> <p>Heart The heart will be contoured along with the pericardial sac. The superior aspect (or base) for purposes of contouring is defined as the superior aspect of pulmonary artery (as seen in a coronal reconstruction of the CT scan) and extended inferiorly to the apex of the heart.</p> <p>Trachea and proximal bronchial tree The trachea and bronchial tree will be contoured as two separate structures using lung windows. For this purpose, the trachea will be divided into two sections: the proximal trachea and the distal 2 cm of trachea. The proximal trachea will be contoured as one structure, and the distal 2 cm of trachea will be included in the structure identified as proximal bronchial tree. Differentiating these structures in this fashion will facilitate the eligibility</p>
Planning Dose Constraints	See table II2 SABR UK Consortium Version 4.0
Tumour Dose Schedules	<p>18 Gy x 3 fractions</p> <p>12 Gy x 5 fraction</p> <p>11 Gy x 5 fraction</p>

	ideally 2-4 days between fractions
Diagram of exclusion zone	

1.5. Cyberknife available at St Bartholomew's Hospital and Mount Vernon Hospital

Accuray Cyberknife, as a specialist form of Stereotactic Ablative Body Radiotherapy (SABR), has been recommended by the National Cancer Action Team : National Radiotherapy

Implementation Group Report 2011, as the "Standard of Care" for Stage I NSCLC : Suitable for peripheral lung cancers less than 3 cm size. T1 N0 M0

All other stages : Recommended as a Clinical Trial

Referral to Barts Stereotactic MDT or Mount Vernon MDT

1.6. Radical Chemo-Radiation or Radical Radiotherapy alone for locally advanced NSCLC.

Good PS locally advanced stage IIB, IIIA, some IIIB, small volume PTV.

Care should be taken to identify those patients who have stage III disease, with N2 or some N3 disease, who are of good performance status and have a small PTV that allows for radical external beam radiotherapy and for lung V20 to remain less than 35% (preferably less than 30%).

Dose: 55 Gy in 20 F over 4 weeks or 64-66 Gy in 32-33 F over 6 ½ weeks.

For those of excellent performance status, also consider chemo-radiotherapy.

Either sequential or Concurrent, for details see later.

Concurrent Chemo-Radiation: Suggested schedule for 4 week RT with concurrent chemotherapy Cisplatin/Vinorelbine

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1	RT #1	RT #2	RT #3	RT #4	RT #5		
	Vin						
	Cis						

Week 2	RT #6	RT #7	RT #8	RT #9	RT #10		
	Vin						

Week 3	RT #11	RT #12	RT #13	RT #14	RT #15		
					Vin		

Week 4	RT #16	RT #17	RT #18	RT #19	RT #20		
					Vin		
	Cis	Cis	Cis	Cis			

RT # = Fraction of radiotherapy

Vin = Vinorelbine iv 15mg/m², NB alternative :oral Vinorelbine 60mg/m²

Cis = Cisplatin iv 20 mg/m²

Radiotherapy to be delivered within 6 hours of chemotherapy.

Radical Radiotherapy technique as above.

Those patients who have lower performance status : consider sequential chemo-radiation or radical radiation alone.

IDEAL –CRT : Clinical Trial

Isotoxic Dose Escalation and Acceleration in Lung Cancer ChemoRadiotherapy: A phase I/II trial of concurrent chemoradiation with dose-escalated radiotherapy in patients with cisplatin and vinorelbine on Days 1 and 8 (vin only), and days 29 and 36 (vin only). 63 Gy in 30 Fractions minimum before dose escalation depending on toxicity.

- Histologically confirmed NSCLC
- Stages II, IIIA and IIIB
- FEV1 ≥ 40% of predicted or ≥ 1 L
- DLCO ≥ 40% of predicted

1.7. Palliative Settings

Indications

The main purpose is to palliate symptoms, although in some patients of good performance status, higher doses of radiotherapy have been shown to result in a modest improvement in survival.

In the case of patients with advanced disease, but who are not symptomatic, the use of radiotherapy is controversial. Several studies have shown no apparent benefit in survival in the use of immediate radiotherapy versus delayed radiotherapy and no difference in

symptom control or quality of life. Therefore, in this group, there should be a discussion with the Clinical Oncologist regarding the options of using palliative radiotherapy upfront or withholding radiotherapy until symptoms arise.

Palliation of chest symptoms: Historically, there have been many different types of radiotherapy schedules for palliation. The aim is to relieve the symptoms of cough, haemoptysis, chest pain, breathlessness or venous compression.

Information required

- Referral Form indicating diagnosis, stage and intent.
- Healthcare records including copy of MDT decision
- Cytology/ histology report including EBUS if available.
- If histology not conclusive, MDT decision required stating clinical and/or radiological diagnosis of bronchogenic carcinoma
- Bronchoscopy report
- Staging CXR/CT chest/abdomen, PET if performed- imaging and reports
- Consent

Immobilisation

Head Rest, Knee fix, Vacbag

Orientation

The patient must be able to lie flat for a period of at least 20 minutes for accurate radiotherapy planning to take place. An initial assessment should be carried out by the Clinical Oncologist regarding the WHO clinical performance status (CPS) of the patient and their ability to comply and lie flat.

Supine, arms above head fixed or by side if not possible

Localisation

3D conformal planning using CT data with IV contrast if requested

Planning CT scan with 2.5mm helical slices

Scan from thoracic inlet to 2.0cm below diaphragm (ensuring coverage of both lungs)

Target Definition

GTV: Primary tumour and involved LNs

CTV: GTV and margin to cover sub clinical disease

PTV: CTV plus margin Normally in the range of:

0.8cm-1.0cm Right /Left and Anterior/Posterior

1.0cm-1.5cm margin Superior/Inferior

Technique

A parallel opposed field technique, using Megavoltage photons from linear accelerator. The field should include the primary tumour and ipsilateral nodal disease at the mediastinum and immediate drainage lymph nodes where practically possible with a margin for movement and set-up error. For those patients with better clinical performance status and locally advanced disease within the thorax (but no metastases outside the thorax), a higher

palliative radiotherapy dose has been shown to result in a modest improvement in survival. In poorer performance patients and those with distant metastases (stage IV), a single fraction or two fractions are sufficient for symptom control [MRC lung cancer working group studies 1992, 1996]. The rate of symptom control is approximately 55%-65% using external beam radiotherapy.

The following table may be used as a guideline to palliative radiotherapy dose schedules:

Stage	WHO Clinical Performance Status (CPS)	Radiotherapy Dose Prescription
Locally advanced disease, not suitable for radical radiotherapy	0-1	36Gy in 12 #, maintaining cord tolerance 30 Gy in 10 # over 2 wks 20Gy in 5 # over 1 wk 17Gy in 2 # over 8 days
	2	10Gy single #
	3	10Gy single #
Metastatic disease outside thorax	0-3	8 or 10Gy single #
Any stage	4	8 or 10Gy single # or consider no radiotherapy but use symptomatic and supportive care

Side effects of treatment

Immediate: 6-12 hours: nausea, vomiting and chest discomfort occasionally seen, particularly after larger radiotherapy fractions. This may be alleviated with Paracetamol, Domperidone/Metoclopramide and Dexamethasone tablets 4mg bd x 1 day.

Intermediate: 2–4 weeks: radiation induced oesophagitis: may be managed with medication such as Gaviscon, Sucralfate or simple analgesia such as soluble paracetamol. Occasionally, candidiasis may be responsible and treated using Fluconazole tabs 50mg x 7 days or equivalent.

Delayed: 6–12 weeks or longer: radiation pneumonitis may be noted. This may be treated with a course of steroids for 4-6 weeks: Prednisolone 20mg od x 2 weeks, then slowly reduce to zero.

2. Small Cell Lung Cancer

2.1. Palliative Radiotherapy

Schedules are similar in technique and fractionation to those used in non-small cell lung cancer .

Consolidation thoracic radiation has been shown to improve absolute three year survival (from 8.9% to 15.3%) and improves local control in those with limited disease who have had a complete response to chemotherapy (Warde 1995).

2.2. Radical Radiotherapy

Standard three field radical radiotherapy techniques should be used if possible. There is evidence now that when radical radiotherapy is used with chemotherapy, for limited stage SCLC, the timing of the radiotherapy should be no later than after cycle 2 of chemotherapy

- Patient lies supine with arms above head
- CT Planning scan carried out for localisation of Gross Tumour Volume (GTV) and any relevant lymph nodes
- CTV and PTV must be delineated by Clinical Oncologist at Consultant level or experienced SpR (part I FRCR or year 3+) then checked by a Consultant Clinical Oncologist.
- Conformal Radiotherapy technique to be used where available.
- Computerised isocentric plan made by Physicist and approved by Clinical Oncologist
- Three or four field technique is often used to maximise high homogeneous dose to Clinical Target Volume whilst keeping radiation dose to normal tissue to a minimum.
- Gross Tumour Volume : GTV is delineated using mediastinal window settings on CT planning Scan.
- Clinical Target Volume CTV comprises the GTV with 0.5 cm margin in all directions.
- If lung window setting used, visible disease and spiculations is CTV.
- Planning Target Volume PTV: is the CTV with 1.5 cm margin in all directions

Planning CT scan should therefore be undertaken after cycle 1 of chemotherapy, so that radiation may start after cycle 2 of chemotherapy. Chemotherapy is suspended until radiation is completed.

Organs at Risk OAR

Both lungs are delineated

Spinal Cord is delineated, within thoracic cavity

Oesophagus is delineated

Dose limiting tissues include spinal cord : A 10 cm length of spinal cord should not receive more than 45 Gy in 2 Gy # or equivalent. In special circumstances the dose to the spinal cord may receive 45 Gy if 1.8 Gy fractions used and length of spinal cord irradiated is less than 10 cm.

Radical Radiotherapy should start within 4 weeks of consultation with Clinical Oncologist (Royal College of Radiologist recommendation for category I type tumour)

Dose:

45 Gy in 30 Fractions twice daily (given concurrently with cisplatin/etoposide) over 3 weeks³¹ : considered standard in some USA / European centres. But further results awaited from CONVERT Study

55 Gy in 20 Fractions over 4 weeks: (Smaller Target Volume)

40.05 Gy in 15 Fractions over 3 weeks: (Larger Target Volume)

In situations where there is residual small cell lung cancer disease in the mediastinum, which cannot easily be encompassed with three field technique, is to use an anterior and posterior opposed fields and treat to 40 Gy in 15 fractions. Lead shielding is used for the posterior field so that maximum dose to spinal cord is 35Gy (shield posterior field for last 4 fractions).

Consideration should be given to enter patient into CONVERT Trial : A 2-arm randomised trial comparing:

- a) 45Gy in 30 fractions BD radiotherapy schedule (given concurrently with cisplatin/etoposide)
- b) 66Gy in 33 fractions OD radiotherapy schedule (given concurrently with cisplatin/etoposide)

2.3. CONVERT Study Planning target volume (PTV)

The CT data will be transferred to the planning system.

- The GTV (gross tumour volume) will be contoured by a qualified radiation oncologist specialised in thoracic malignancies. The contouring should be carried out using the mediastinal and the lung windows. The GTV is defined as identifiable tumour and involved lymph nodes (nodal involvement on CT scan is defined as nodes ≥ 1 cm in short axis). If PET scan is available for staging, the GTV should include PET positive lymph nodes.
- The CTV (clinical target volume) comprises the GTV with a 0.5 cm margin of radiologically normal tissue in all directions. It will take into account microscopic spread. Manual adjustment of CTV is permitted to reduce dose to the spinal cord for example, when disease is adjacent to a structure such as a vertebra but is not thought to invade the structure
- The PTV comprises the CTV with a 1 cm margin superiorly and inferiorly, and 0.8 cm margin laterally, at the 95% isodose. The CTV to PTV expansion should not be reduced as it is allowing for set up errors and organ motion.

Prophylactic nodal irradiation should not be employed.

Prophylactic cranial irradiation (PCI)

PCI may improve three year survival from 8.9% to 15.3% in patients with limited disease a complete response to chemotherapy (Auperin 1999) and should be considered after discussion with patient. A parallel pair technique is used with 6 MV photons and treatment dose is 25 Gy in 10 fractions to the mid plane. This should be no later than 6 weeks after the final dose of chemotherapy.

PCI is also recommended for patients with Extensive Stage Small Cell, whose disease has responded well to first line chemotherapy.

3. References

1. Nagata Y, Wulf J, Lax I, Timmerman R, Zimmermann F, Stojkovski I, Jeremic B. Stereotactic radiotherapy of primary lung cancer and other targets: results of consultant meeting of the International Atomic Energy Agency. *Int J Radiat Oncol Biol Phys*. 2011 Mar 1;79(3):660-9.
2. Smith SL, Palma D, Parhar T, Alexander CS, Wai ES. Inoperable early stage non-small cell lung cancer: Comorbidity, patterns of care and survival. *Lung Cancer*. 2011 Apr;72(1):39-44.
3. Gopal RS, Dubey S, Rosenzweig KE, Chang JY, Decker R, Gewanter RM, Kong FM, Lally BE, Langer CJ, Lee HK, Movsas B. ACR Appropriateness Criteria® on Induction and Adjuvant Therapy for Stage N2 Non-Small-Cell Lung Cancer: expert panel on radiation oncology-lung. *Int J Radiat Oncol Biol Phys*. 2010 Nov 15;78(4):969-74. Epub 2010 Aug 31.
4. Perez CA, Pajak TF, Rubin P, Simpson JR, Mohiuddin M, Brady LW, Perez-Tamayo R, Rotman M. Long-term observations of the patterns of failure in patients with unresectable non-oat cell carcinoma of the lung treated with definitive radiotherapy. Report by the Radiation Therapy Oncology Group. *Cancer*. 1987 Jun 1;59(11):1874-81.
5. Schaake-Koning C, van den Bogaert W, Dalesio O, Festen J, Hoogenhout J, van Houtte P, Kirkpatrick A, Koolen M, Maat B, Nijs A, et al. Effects of concomitant cisplatin and radiotherapy on inoperable non-small-cell lung cancer. *N Engl J Med*. 1992 Feb 20;326(8):524-30.
6. O'Rourke N, Macbeth F. Is concurrent chemoradiation the standard of care for locally advanced non-small cell lung cancer? A review of guidelines and evidence. *Clin Oncol (R Coll Radiol)*. 2010 Jun;22(5):347-55. Epub 2010 Apr 27.
7. Kunitoh H, Kato H, Tsuboi M, Shibata T, Asamura H, Ichonose Y, Katakami N, Nagai K, Mitsudomi T, Matsumura A, Nakagawa K, Tada H, Saijo N; Japan Clinical Oncology Group. Phase II trial of preoperative chemoradiotherapy followed by surgical resection in patients with superior sulcus non- small-cell lung cancers: report of Japan Clinical Oncology Group trial 9806. *J Clin Oncol*. 2008 Feb 1;26(4):644-9.
8. Kwong KF, Edelman MJ, Suntharalingam M, Cooper LB, Gamliel Z, Burrows W, Hausner P, Doyle LA, Krasna MJ. High-dose radiotherapy in trimodality treatment of Pancoast tumors results in high pathologic complete response rates and excellent long-term survival. *J Thorac Cardiovasc Surg*. 2005 Jun;129(6):1250-7.
9. Fairchild A, Harris K, Barnes E, Wong R, Lutz S, Bezjak A, Cheung P, Chow E. Palliative thoracic radiotherapy for lung cancer: a systematic review. *J Clin Oncol*. 2008 Aug 20;26(24):4001-11.
10. Albain KS, Swann RS, Rusch VW, Turrisi AT 3rd, Shepherd FA, Smith C, Chen Y, Livingston RB, Feins RH, Gandara DR, Fry WA, Darling G, Johnson DH, Green MR, Miller RC, Ley J, Sause WT, Cox JD. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small- cell lung cancer: a phase III randomised controlled trial. *Lancet*. 2009 Aug 1;374(9687):379-86. Epub 2009 Jul 24.

11. Timmerman R, Galvin J, Michalski J, Straube W, Ibbott G, Martin E, Abdulrahman R, Swann S, Fowler J, Choy H. Accreditation and quality assurance for Radiation Therapy Oncology Group: Multicenter clinical trials using Stereotactic Body Radiation Therapy in lung cancer. *Acta Oncol.* 2006;45(7):779-86. Review.
12. Pisters KM, Evans WK, Azzoli CG, Kris MG, Smith CA, Desch CE, Somerfield MR, Brouwers MC, Darling G, Ellis PM, Gaspar LE, Pass HI, Spigel DR, Strawn JR, Ung YC, Shepherd FA; Cancer Care Ontario; American Society of Clinical Oncology. Cancer Care Ontario and American Society of Clinical Oncology adjuvant chemotherapy and adjuvant radiation therapy for stages I-IIIa resectable non-small-cell lung cancer guideline. *J Clin Oncol.* 2007 Dec 1;25(34):5506-18. Epub 2007 Oct 22.
13. Aupérin A, Le Péchoux C, Rolland E, Curran WJ, Furuse K, Fournel P, Belderbos J, Clamon G, Ulutin HC, Paulus R, Yamanaka T, Bozonnat MC, Uitterhoeve A, Wang X, Stewart L, Arriagada R, Burdett S, Pignon JP. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *J Clin Oncol.* 2010 May 1;28(13):2181-90. Epub 2010 Mar 29.
14. Saunders M, Dische S, Barrett A, Harvey A, Griffiths G, Palmar M. Continuous, hyperfractionated, accelerated radiotherapy (CHART) versus conventional radiotherapy in non-small cell lung cancer:
15. mature data from the randomised multicentre trial. CHART Steering committee. *Radiother Oncol.* 1999 Aug;52(2):137-48.
16. Hatton MQ, Martin JE. Continuous hyperfractionated accelerated radiotherapy (CHART) and non-conventionally fractionated radiotherapy in the treatment of non-small cell lung cancer: a review and consideration of future directions. *Clin Oncol (R Coll Radiol).* 2010 Jun;22(5):356-64. Epub 2010 Apr 18.
17. Lester JF, Macbeth FR, Toy E, Coles B. Palliative radiotherapy regimens for non-small cell lung cancer. *Cochrane Database Syst Rev.* 2006 Oct 18;(4):CD002143. Citation: Lester JF, MacBeth F, Toy E, Coles B. Palliative radiotherapy regimens for non-small cell lung cancer. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD002143. DOI: 10.1002/14651858.CD002143.pub2.
18. Rowell NP, Williams CJ. Radical radiotherapy for stage I/II non-small cell lung cancer in patients not sufficiently fit for or declining surgery (medically inoperable). *Cochrane Database Syst Rev.* 2001;(1):CD002935. Citation: Rowell NP, Williams C. Radical radiotherapy for stage I/II non-small cell lung cancer in patients not sufficiently fit for or declining surgery (medically inoperable). *Cochrane Database of Systematic Reviews* 2001, Issue 1. Art. No.: CD002935. DOI: 10.1002/14651858.CD002935.
19. Rowell NP, Williams CJ. Radical radiotherapy for stage I/II non-small cell lung cancer in patients not sufficiently fit for or declining surgery (medically inoperable): a systematic review. *Thorax.* 2001 Aug;56(8):628-38.
20. Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus. *Cochrane Database Syst Rev.* 2001;(4):CD001316. Citation: Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in

- carcinoma of the bronchus. Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD001316. DOI: 10.1002/14651858.CD001316.
21. Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. *Clin Oncol (R Coll Radiol)*. 2002 Oct;14(5):338-51.
 22. Saunders M, Dische S, Barrett A, Harvey A, Gibson D, Parmar M. Continuous hyperfractionated accelerated radiotherapy (CHART) versus conventional radiotherapy in non-small-cell lung cancer: a randomised multicentre trial. CHART Steering Committee. *Lancet*. 1997 Jul 19;350(9072):161-5.
 23. Bradley J, Graham MV, Winter K, Purdy JA, Komaki R, Roa WH, Ryu JK, Bosch W, Emami B. Toxicity and outcome results of RTOG 9311: a phase I-II dose-escalation study using three-dimensional conformal radiotherapy in patients with inoperable non-small-cell lung carcinoma. *Int J Radiat Oncol Biol Phys*. 2005 Feb 1;61(2):318-28.
 24. Firat S, Byhardt RW, Gore E. The effects of comorbidity and age on RTOG study enrollment in Stage III non-small cell lung cancer patients who are eligible for RTOG studies. *Int J Radiat Oncol Biol Phys*. 2010 Dec 1;78(5):1394-9. Epub 2010 Jun 18.
 25. Gijssbert W.P.M. Kramer, Stofferinus L. Wanders, Ed M. Noordijk, Ernest J.A. Vonk, Hans C. van Houwelingen, Wilbert B. van den Hout, Ronald B. Geskus, Mirjam Scholten, Jan-Willem H. Leer Results of the Dutch National Study of the Palliative Effect of Irradiation Using Two Different Treatment Schemes for Non-Small Cell Lung Cancer. *J Clin Oncol* 23:2962-2970.
 26. Dillman RO, Herndon J, Seagren SL, Eaton WL Jr, Green MR. Improved survival in stage III non-small-cell lung cancer: seven-year follow-up of cancer and leukemia group B (CALGB) 8433 trial. *J Natl Cancer Inst*. 1996 Sep 4;88(17):1210-5.
 27. O'Rourke N, Roqué I Figuls M, Farré Bernadó N, Macbeth F. Concurrent chemoradiotherapy in non-small cell lung cancer. *Cochrane Database Syst Rev*. 2010 Jun 16;(6):CD002140. Citation: O'Rourke N, Roqué i Figuls M, Farré Bernadó N, Macbeth F. Concurrent chemoradiotherapy in non-small cell lung cancer. *Cochrane Database of Systematic Reviews* 2010, Issue 6. Art. No.: CD002140. DOI: 10.1002/14651858.CD002140.pub3.
 28. Non Small Cell Lung Cancer Radiotherapy Clinical Decision Tree Malthus : Updated March 2013
 29. Postoperative radiotherapy for non-small cell lung cancer. Citation: PORT Meta-analysis Trialists Group. Postoperative radiotherapy for non-small cell lung cancer. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD002142. DOI: 10.1002/14651858.CD002142.pub2
 30. QUARTZ. Quality of life after treatment for brain metastases. A phase III multi-centre randomised controlled trial to assess whether optimal supportive care alone (including Dexamethasone) is as effective as optimal supportive care (including Dexamethasone) plus whole brain radiotherapy in the treatment of patients with inoperable brain metastases from non-small cell lung cancer. A National Cancer Research Institute (NCRI) approved trial, funded through Cancer Research UK, sponsored by the Medical Research Council (MRC) and conducted by the MRC Clinical Trials Unit.

31. Turrisi AT III, Kim K, Blum R, et al.: Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *New England Journal of Medicine* 340(4): 265-271, 1999.

Guidelines

Pisters KM, Evans WK, Azzoli CG, Kris MG, Smith CA, Desch CE, Somerfield MR, Brouwers MC, Darling G, Ellis PM, Gaspar LE, Pass HI, Spigel DR, Strawn JR, Ung YC, Shepherd FA; Cancer Care Ontario; American Society of Clinical Oncology. Cancer Care Ontario and American Society of Clinical Oncology adjuvant chemotherapy and adjuvant radiation therapy for stages I-IIIa resectable non small-cell lung cancer guideline. *J Clin Oncol*. 2007 Dec 1;25(34):5506-18. Epub 2007 Oct 22.

D'Addario G, Felip E; ESMO Guidelines Working Group. Non-small-cell lung cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol*. 2009 May;20 Suppl 4:68-70.

Crinò L, Weder W, van Meerbeeck J, Felip E; ESMO Guidelines Working Group. Early stage and locally advanced (non-metastatic) non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2010 May;21 Suppl 5:v103-15.

The Diagnosis and Treatment of Lung Cancer. Methods, Evidence and Guidance. February 2005. Commissioned by the National Institute for Clinical Excellence. (NICE draft 2010 - to be published 2011)

The Royal College of Radiologists. Radiotherapy dose-fractionation. The Royal College of Radiologists, London, 2006. <http://www.rcr.ac.uk/publications>

National Cancer Action Team. National Radiotherapy Implementation Group Report. Stereotactic Body Radiotherapy. Guidelines for Commissioners, Providers and Clinicians in England 2011.

ACR Appropriateness criteria on induction and adjuvant therapy for Stage N2 non small cell lung cancer: Expert panel on Radiation Oncology – Lung. Ramesh Gopal et. Al. *Int J Radiation Oncology Biol Phys*; Vol 1.78, No 4: 969-974, 2010.

Management of unresected stage III non-small cell lung cancer: A Clinical Practice Guideline. Okaware G, Mackay JA, Evans WK, Ung YC and the Lung Cancer Disease Site Group. Evidence-based series #7-3 (Version 2.2005).

Guidelines on the radical management of patients with lung cancer. *Thorax* 2010 65:iii I-iii27.

Resources

Stereotactic Ablative Body Radiation Therapy (SABR) : A Resource SABR UK Consortium
Version 4.0 January 2013.

<http://ncat.nhs.uk/radiotherapy/treatments> : National Radiotherapy Implementation Group
Report. Stereotactic Body Radiotherapy. Guidelines for Commissioners, Providers and
Clinicians in England 2011.