East of England Radiotherapy Network:

Lung & Lung Oligometastases Stereotactic Ablative Radiotherapy (SABR) Protocol

Contents

1.0 Indications and patient population

This protocol covers treatment in the following situations:

1. Patients with medically inoperable early-stage peripheral Non-Small Cell Lung Cancer (NSCLC) and centrally located NSCLC.
2. Patients with lung oligometastases

1.1 Treatment eligibility

1.1a Peripheral, central, and ultra-central lung tumours

For the purposes of the protocol the following definitions are used:

Peripheral tumours are defined as:

- GTV_4D or GTV_3D+IM that are outside of the IASLC central zone (see Figure 1 below).

Central tumours are defined as:

- GTV_4D or GTV_3D+IM within IASLC central zone but not classed as ultra-central

Ultra-central tumours are defined as:

- GTV_4D within 1cm of proximal bronchial tree or overlapping central OARs (great vessels, heart, oesophagus and trachea) or brachial plexus

1.1b Inclusion and exclusion criteria

Primary NSCLC:

PS 0-2 (and selected PS 3 patients)

Histologically confirmed early stage (T1-2N0M0, and selected patients with T3N0M0) NSCLC.

In cases where biopsy not possible/ non-diagnostic then patients with an MDT lung cancer diagnosis based on PET positive lesions enlarging on serial CTs may also be considered. It is recommended to use predictive models such as Herder/ Brock to predict risk of malignancy if not histologically proven.

Patients should either be medically inoperable or have had the option of surgery also discussed.

Lung Oligometastases:

Patients should meet the following criteria as per NHS England commissioning document:

Inclusion criteria

- Confirmed histological diagnosis of cancer (haematological malignancies excluded)
- Metachronous disease, with a disease-free interval between primary treatment and manifestation of metastases of at least 6 months
- 1-3 sites of extracranial disease only at the time of disease presentation, confined to one or two of the following organs: bone, spine, lymph nodes, liver, lungs, adrenals
- Maximum of 2 vertebral metastases
- Maximum size of 5 cm for any single metastasis
- Life expectancy of more than 6 months
- WHO Performance Status 0-2

Exclusion criteria

- Haematological malignancies
- Evidence of intracranial disease
- For spine metastases, evidence of spinal cord compression or spinal instability
- For lung metastases, evidence of severe interstitial lung disease
- For liver metastases, poor liver function/Child-Pugh score B
- More than 3 sites of metastatic disease, **or** development of new metastases post treatment of a maximum of 3 lesions
- Patients who require irradiation of a whole nodal field
- Previous SABR to the same site of metastatic disease

1.1c Complex and high-risk scenarios for SABR

All the following scenarios should be discussed with a minimum of one other SABR consultant before offering SABR:

- Tumours diameter >5 cm (metastatic lesions > 5cm size fall outside the NHSE commissioning criteria).
- Patients with central tumours where is no 4D dataset, and only a GTV_3D
- Patients with central tumours where the treating consultant is planning to use the 5-fraction regimen.
- Synchronous or metachronous multiple primary tumours
- Local relapse after SABR. Consider salvage surgery first if clinically appropriate.
- Previous radiotherapy within the planned treatment volume.
- Clinically significant pulmonary fibrosis. Discussion with ILD team is also recommended here.

- Currently undergoing systemic therapy (chemotherapy, immunotherapy or biological therapy). Hormonal therapy permitted
- History of active auto-immune diseases, including systemic lupus erythematosus, rheumatoid arthritis, C.R.E.S.T., systemic sclerosis, scleroderma.

Ultra-central tumours, as defined above, should not be treated with SABR outside of a clinical trial.

1.1d Essential Pre-Radiotherapy investigations for patients

Patients should have whole body imaging within 6 weeks of MDT discussion, confirming eligibility for SABR.

2.0 Localisation

Localisation	Notes	
Position	Supine	
Arm/ leg/ head/ thorax position	Arms above head Arms by side	Must be a comfortable and reproducible position For patients who are unable to tolerate arms up
Immobilisation and supports	Winged chest board with optional vac bag	Elbows positioned to avoid collision with gantry or imaging during CBCT and treatment
Organ pre-requisites		
Contrast	Contrast may not be required for all cases but will be useful for central tumours and delineation for some OARs such as brachial plexus and great vessels. Ensure renal function acceptable.	
CT acquisition	Slice thickness:	2- 3mm
	Scanning limits: whole lung	Upper cervical spine to lower edge of liver, taking care to include all lung parenchyma on the scan
	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
a. Small peripheral tumours	54/3	3	
b. Peripheral tumour close to chest wall/ larger peripheral tumours, and selected central tumours	55/5	3	For selected central tumours, this should follow discussion with second SABR consultant/local SABR team
c. All other central (but not ultra-central) tumours	60/8	3	

- Treatment is given on alternate dates with a minimum inter-fraction interval of 24 hours and a maximum inter-fraction interval of 4 days.
- For patients with 2 or more metastases being treated, the clinician will consider if targets should be treated on the same day or not. This may depend on tumour size and location.

4.0 Target volumes

The volumes will be outlined according to local protocols and with reference to the Global Harmonisation Group descriptions.

4.1 3D scanned GTV/CTV/ PTV

- **GTV_3D =** all visible disease as defined on CT, and any additional imaging.
- **CTV _3D**= GTV_3D with no margin in most cases. If there is uncertainty regarding the extent of the tumour on available imaging, or if there is extra-capsular tumour extension, then a CTV margin of up to 5mm can be added to the GTV.
- **PTV** = CTV_3D + 0.5cm.

4.2 4D Scanned (thoracic/ upper abdominal nodal metastases) GTV/ CTV/ PTV

- A 4D GTV is created using the 4DCT dataset.
- **GTV_4D** = all visible disease, covered in all phases of the breathing cycle.
- **CTV_4D** = GTV_4D with no margin in most cases (see 4.1 above)
- **PTV** = CTV_4D + 0.5cm

Note: These are the minimum allowable PTV margins. Larger margins may be used at the clinical oncologist's/local department's discretion where there is more uncertainty in set-up, tumour motion etc.

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 and the report of the AAPM TG 263

- All organs at risk will be contoured on the 3D planning CT.

5.1 Constraints

		54Gy/ 3#		55Gy/ 5#		50 – 60Gy/ 8#	
		Objective	**Constraint**	**Objective**	**Constraint**	**Objective**	**Constraint**
PTV	V100%	≥95%	-	≥95%	-	≥95%	-
	V90%	≥99%	-	≥99%	-	≥99%	-
	D95%	100%		100%		100%	-
	D0.1cc	130 – 140% (70.2 – 75.6Gy)	110-140% (59.4 – 75.6Gy)	130-140% (71.5 – 77Gy)	110-140% (60.5 – 77Gy)	130 – 140% (78 – 84Gy for 60Gy) Only if not central	*110 – 120% (66 – 72Gy for 60Gy) for central tumours 110 - 140% (66 - 84Gy for 60Gy) Only if not central
Conformity Index (V100% / PTV V100%)	PTV ≤ 20cc	≤ 1.25 (ideal 1.2)	≤ 1.40	≤ 1.25 (ideal 1.2)	≤ 1.40	≤ 1.25 (ideal 1.2)	≤ 1.40
	PTV 20-40cc	≤ 1.20 (ideal 1.1)	≤ 1.30	≤ 1.20 (ideal 1.1)	≤ 1.30	≤ 1.20 (ideal 1.1)	≤ 1.30

		54Gy/ 3#		55Gy/ 5#		50 – 60Gy/ 8#	
		Objective	Constraint	Objective	Constraint	Objective	Constraint
	PTV ≥ 40 cc	≤ 1.15 (ideal 1.1)	≤ 1.20	≤ 1.15 (ideal 1.1)	≤ 1.20	≤ 1.15 (ideal 1.1)	≤ 1.20
Modified Gradient Index (V50% /PTV V100%)	PTV ≤ 20cc	≤ 9 (ideal 7)	≤ 11	≤ 9 (ideal 7)	≤ 11	≤ 9 (ideal 7)	≤ 11
	PTV 20-40cc	≤ 6.5 (ideal 5.5)	≤ 7.5	≤ 6.5 (ideal 5.5)	≤ 7.5	≤ 6.5 (ideal 5.5)	≤ 7.5
	PTV 40 – 60cc	≤ 6 (ideal 5)	≤ 7	≤ 6 (ideal 5)	≤ 7	≤ 6 (ideal 5)	≤ 7
	PTV 60 – 90cc	≤ 5 (ideal 4)	≤ 7	≤ 5 (ideal 4)	≤ 7	≤ 5 (ideal 4)	≤ 7
	PTV ≥ 90cc	≤ 4.5 (ideal 4)	≤ 6.5	≤ 4.5 (ideal 4)	≤ 6.5	≤ 4.5 (ideal 4)	≤ 6.5
BrachialPlex_L BrachialPlex_R	D0.1cc	-	≤24Gy	≤30.5Gy	≤32Gy	≤35Gy	≤39Gy
Heart+A_Pulm	D0.1cc	≤26Gy	≤30Gy	≤29Gy	≤38Gy	≤40Gy	≤46Gy **
Trachea	D0.1cc	-	≤30Gy	≤35Gy	≤38Gy	-	≤40Gy
Bronchus_Prox	D0.1cc	-	≤30Gy	≤35Gy	≤38Gy	-	≤40Gy
Lungs-GTV	V20Gy	≤10%	≤15%	≤10%	≤15%	≤10%	≤15%
	V5Gy	-	-	-	-	-	-
	Dmean	≤8Gy	-	≤8Gy	-	≤8Gy	-
Chestwall_L, Chestwall_R	D0.1cc	≤36.9Gy	≤110%$	≤43Gy	≤110%$	-	≤110%$
	D30cc	≤30Gy	-	-	-	-	-

		54Gy/ 3#		55Gy/ 5#		50 – 60Gy/ 8#	
		Objective	Constraint	Objective	Constraint	Objective	Constraint
GreatVes (Great Vessels)	D0.1cc	-	≤45Gy	-	≤53Gy	≤60Gy	≤65Gy
SpinalCanal (inc. medulla)	D0.035cc	-	≤20.3Gy	-	≤25.3Gy	-	≤32Gy
Oesophagus	D0.1cc	-	≤25.2Gy	-	≤35Gy	-	≤40Gy
	V48Gy	-	-	-	-	-	-
	V45Gy	-	-	-	-	-	-
Stomach	D0.1cc	-	≤22.2Gy	≤33Gy	≤35Gy	-	-
	D0.5cc	-	-	-	-	-	-
	D10cc	-	≤16.5Gy	≤25Gy	-	-	-
	D50cc	-	-	≤12Gy	-	-	-
Liver	Dmean	≤13Gy	≤15Gy	≤13Gy	≤15.2Gy	-	-
	V10Gy	-	-	≤70%	-	-	-
	D(VTOT -700cc)$^{+}$	≤15Gy	≤17Gy	≤15Gy	-	-	-
Spleen	Dmean	<10Gy	-	<10Gy	-	<10Gy	-
SkinRind (the 5mm rind within Skin contour)	D0.1cc	≤33Gy	-	≤39.5Gy	-	≤48Gy	-
	D10cc	≤30Gy	-	≤36.5Gy	-	≤44Gy	-
>2cm from PTV (PTV ≤ 20cc)	D0.1cc	-	≤ 35.1Gy	-	≤ 35.8Gy	-	≤ 35.8Gy
>2cm from PTV (PTV > 20cc)	D0.1cc	-	< 37.8Gy	-	≤ 38.5Gy	-	≤ 38.5Gy

*This is a suggested objective to reduce the risk of delivery of a hot spot to a central region. However, the objectives for the conformity indices and modified gradient indices are higher priority than this 110-120 Dmax objective for central tumours.

**If this cannot be met, drop dose to 50Gy

$ This is a suggested constraint to reduce risk of rib fracture. The constraint does not apply if the overlap of the PTV and chest wall is such that the hotspot cannot be pushed out of the chest wall without compromising PTV coverage.

$^{+}$ Cold constraint (V_{TOT} – xcc) is the total volume of organ minus a specified volume

PTV dose constraints as per UK SABR CONSORTIUM, 2019.

OAR dose constraints as per UK 2022 Consensus[20] publication.

Splenic constraint is based on recent RCR recommendation.

6.0 Planning process/ technique

- All patients will be treated using Volumetric Modulated Arc Radiotherapy (VMAT).
- An additional 4D CT planning scan will in most cases be needed to allow creation of a 4D GTV.

7.0 Peer Review/ Contour QA

- Prospective peer review of target and OARs by a second Oncologist with SABR experience is strongly recommended. A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.
- The peer review process and outcomes should be audited.

8.0 Target verification

Modality	Frequency	Match point	Additional information
CBCT	Daily	Tumour match	Adjust to OARs if required

9.0 Side effects

9.1 Possible early or short-term side effects	
Expected (50- 100%)	**Initial management (if appropriate)**
Tiredness	
Common (10- 50%)	**Initial management (if appropriate)**

9.1 Possible early or short-term side effects	
Mild temporary shortness of breath and cough	Does not usually require intervention (see below)
Chest wall and/or rib pain	Simple analgesia likely to be sufficient
Mild nausea	Metoclopramide or Domperidone Ondansetron
Inflammation of the lung, causing CXR changes	No intervention if asymptomatic
Less common (Less than 10%)	**Initial management (if appropriate)**
Moderate to severe 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.
Skin soreness, itching and colour changes in treatment area	Aqueous Cream/E45 Antihistamines
Rare (Less than 1%)	**Initial management (if appropriate)**
Coughing up small amounts of blood	Supportive management
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)**
Less common (Less than 10%)	**Initial management (if appropriate)**
Long-term shortness of breath or cough	Respiratory team input Home oxygen if needed
Mild to moderate chest wall/rib pain	Analgesia
More prone to rib fractures in treatment area	
Risk of damage to the nerves to the arms/hands	
Risk of damage to the heart	
Rare (Less than 1%)	**Initial management (if appropriate)**
Airway narrowing or risk of bleeding from airways	
A different cancer in the treatment area	

9.2 Possible late or long-term side effects	
Risk to life (very rare)	

10.0 References

Timmerman, R., et al., Stereotactic body radiation therapy for inoperable early stage lung cancer. Jama, 2010. 303(11): p. 1070-6.

Nagata, Y., et al., Clinical outcomes of a phase I/II study of 48 Gy of stereotactic body radiotherapy in 4 fractions for primary lung cancer using a stereotactic body frame. Int J Radiat Oncol Biol Phys, 2005. 63(5): p. 1427-31.

Lagerwaard, F.J., et al., Outcomes of risk-adapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. Int J Radiat Oncol Biol Phys, 2008. 70(3): p. 685-92.

Onishi, H., et al., Stereotactic hypofractionated high-dose irradiation for stage I nonsmall cell lung carcinoma: clinical outcomes in 245 subjects in a Japanese multi-institutional study. Cancer, 2004. 101(7): p. 1623-31.

McGarry, R.C., et al., Stereotactic body radiation therapy of early-stage non-small-cell lung carcinoma: Phase I study. Int J Radiat Oncol Biol Phys, 2005. 63(4): p. 1010-5.

Timmerman, R., et al., Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. J Clin Oncol, 2006. 24(30): p. 4833-9.

Timmerman, R., et al., Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer. Chest, 2003. 124(5): p. 1946-55.

Hoppe, B.S., et al., Acute skin toxicity following stereotactic body radiation therapy for stage I. Int J Radiat Oncol Biol Phys., 2008. 72(5): p. 1283-6.

Milano, M.T., L.S. Constine, and P. Okunieff, Normal tissue toxicity after small field hypofractionated stereotactic body. Radiat Oncol, 2008. 3: p. 36.

Yamashita, H., et al., Exceptionally high incidence of symptomatic grade 2-5 radiation pneumonitis after stereotactic radiation therapy for lung tumors. Radiat Oncol, 2007. 2: p. 21.

Underberg, R.W., et al., Benefit of respiration-gated stereotactic radiotherapy for stage I lung cancer: an analysis of 4DCT datasets. Int J Radiat Oncol Biol Phys, 2005. 62(2): p. 554-60.

Purdie, T.G., et al., Respiration correlated cone-beam computed tomography and 4DCT for evaluating target motion in Stereotactic Lung Radiation Therapy. Acta Oncol, 2006. 45(7): p.915-22.

Purdie, T.G., et al., Cone-beam computed tomography for on-line image guidance of lung stereotactic radiotherapy: Localization, verification, and intrafraction tumor position. Int J Radiat Oncol Biol Phys, 2007. 68(1): p. 243-52.

Franks, K.N., et al., Incorporating heterogeneity correction and 4DCT in lung stereotactic body radiation therapy (SBRT): The effect on target coverage, organ-at-risk doses, and dose conformity. Med Dosim, 2010. 35(2): p. 101-7.

Hurkmans, C.W., et al., Recommendations for implementing stereotactic radiotherapy in peripheral stage IA non-small cell lung cancer: report from the Quality Assurance Working Party of the randomised phase III ROSEL study. Radiat Oncol, 2009. 4: p. 1.

UK_SBRT_CONSORTIUM, Stereotactic Body Radiation Therapy (SBRT) for Patients with Early Stage Non-small Cell Lung Cancer: A Resource. v6.1, Jan 2019.

Thomas, S.J., Evans, B.J., Harihar, L., Chantler, H.J., Martin, A.G. and Harden, S.V., 2019. An evaluation of the mid-ventilation method for the planning of stereotactic lung plans. Radiotherapy and Oncology, 137, pp.110-116.

Chang JY, Bezjak A, Mornex F. Stereotactic Ablative Radiotherapy for Centrally Located Early Stage Non–Small-Cell Lung Cancer: What We Have Learned. Journal of Thoracic Oncology. 2015;10(4):577-85.19.

Tekatli H, van 't Hof S, Nossent EJ, Dahele M, Verbakel W, Slotman BJ, et al. Use of Stereotactic Ablative Radiotherapy (SABR) in Non-Small Cell Lung Cancer Measuring More Than 5 cm. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2017;12(6):974-82

Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines - Radiotherapy and Oncology (thegreenjournal.com) Appendix A Supplementary Data 1

UK 2022 Consensus on Normal Tissue Dose-Volume Constraints for Oligometastatic, Primary Lung and Hepatocellular Carcinoma Stereotactic Ablative Radiotherapy; Diez, P. et al.; Clinical Oncology, Volume 34, Issue 5, 288 – 300

Zeng, K.L. et al. Accelerated Hypofractionated Radiotherapy for Centrally Located Lung Tumours Not Suitable for Stereotactic Body Radiotherapy or Chemoradiotherapy; Clinical Oncology 35 (2023) e173-e181

Clinical Commissioning Policy Stereotactic ablative radiotherapy (SABR) for patients with metachronous extracranial oligometastatic cancer (all ages) (URN: 1908) [200205P]; March 2020. 1908-cc-policy-sbar-for-metachronous-extracranial-oligometastatic-cancer.pdf (england.nhs.uk)

Stereotactic Ablative Body Radiotherapy (SABR): A resource; UK SABR Consortium; January 2019. SABRconsortium guidelines 2019 v6.1.0

Standardizing nomenclatures in Radiation Oncology: The report of the AAPM Task Group; January 2018. TG-263: Standardizing Nomenclatures in Radiation Oncology (aapm.org)

Mir R et al (June 2020). Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines. *Radiotherapy and Oncology* **150** (2020), 30-39. Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines - Radiotherapy and Oncology (thegreenjournal.com)

Center for Innovation in Radiation Oncology; Contouring atlases, templates and tools. NRG > About Us > Center for Innovation in Radiation Oncology (nrgoncology.org)

Diez P et al (May 2022). UK 2022 Concensus on normal tissue dose-volume constraints for oligometastatic, primary lung, and hepatocellular carcinoma Stereotactic Ablative Radiotherapy. *Clinical Oncology* **34** (2022), 288-300. UK 2022 Consensus on Normal Tissue Dose-Volume Constraints for Oligometastatic, Primary Lung and Hepatocellular Carcinoma Stereotactic Ablative Radiotherapy - Clinical Oncology (clinicaloncologyonline.net)

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12.0 Amendment History

A record of changes in this document

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