



# **Radiotherapy for lung cancer**

## **RCR consensus statements**

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## RCR lung cancer consensus statements

### 1. Optimising patients for radical radiotherapy for lung cancer

- 1.1. Perform a positron emission tomography-computed tomography (PET-CT) scan within the six weeks before commencing treatment (and ideally within four weeks) for all patients having curative-intent radiotherapy. If the time interval is greater than six weeks, consider repeating the PET-CT scan to confirm the treatment strategy and target volume.
  - 1.2. Offer immediate testing for programmed death-ligand (PD-L1) to patients with unresectable stage III non-small cell lung cancer (NSCLC).
  - 1.3. Undertake systematic pathological nodal staging (for example staging endobronchial ultrasound and biopsy) in any patient with enlarged intrathoracic lymph nodes on CT imaging (>10 millimetres [mm] short axis) or fluorodeoxyglucose (FDG)-avid intrathoracic lymph nodes on PET. Do not rely on radiological nodal staging alone.
  - 1.4. Perform individualised assessment and optimisation before curative radiotherapy. This should include:
    - a. Spirometry and diffusion capacity testing within six weeks of radiotherapy
    - b. Advice about physical activity including referral to dedicated activity programmes where possible
    - c. Screening for malnutrition and dietetic advice as appropriate
    - d. Advice for smokers for example '*Very brief advice*', the offer of medication to treat tobacco addiction and referral to a specialist team for more intensive support.
  - 1.5. Do not exclude patients from curative radiotherapy on the basis of pulmonary function tests alone. Pulmonary function test cut-off values should only serve as a guide. The final decision regarding fitness for radical radiotherapy should include the patient's functional capacity and acceptance of risk from the treatment after a full discussion of potential risks/benefits and alternative treatment strategies.
  - 1.6. Be aware that patients who have had radical radiotherapy are at risk of fragility fractures of the vertebrae which may be visible on routine post-treatment imaging. Consider referral to a fractures liaison service or rheumatologist.
  - 1.7. Assess patients for relevant co-morbidities (for example lung fibrosis, auto-immune conditions, use of radio-sensitising medication) and liaise with the relevant specialist team to assess the impact on the feasibility of treatment and the potential for increased toxicities.
  - 1.8. Consider all patients receiving radical radiotherapy for prophylactic treatment of pneumocystis jiroveci pneumonia (PJP) during or after their treatment if they are thought to be at risk, for example: lymphocyte count <0.6 x10<sup>9</sup>/L, patients on steroids for more than four weeks or patients having combined-modality treatment. Treatment should continue until lymphocyte count >0.6x10<sup>9</sup>/L and/or for a minimum of six weeks post radiotherapy.
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## 2. Technical aspects of radical radiotherapy for lung cancer

- 2.1. Employ advanced techniques such as intensity-modulated radiation therapy (IMRT)/volumetric modified arc therapy (VMAT) to facilitate radical dose delivery, improve conformality and reduce dose to organs at risk (OAR).
- 2.2. Use intravenous contrast for radiotherapy planning for stage II/III unless contraindicated. Consider for stage I to assist with OAR delineation.
- 2.3. Obtain and reconstruct relevant prior radiotherapy (for example previous breast cancer radiotherapy) to permit composite planning and safe delivery of lung cancer radiotherapy.
- 2.4. Assess physical disability that may affect treatment position and employ strategies to enable the delivery of radiotherapy (for example physiotherapy, alternative treatment positions such as arms down, analgesia).
- 2.5. Use four-dimensional computed tomography (4DCT) or alternative motion assessment at CT simulation for all patients having curative-intent radiotherapy unless the patient is unable to manage the technique.
- 2.6. Do not use elective nodal irradiation.
- 2.7. Perform daily online volumetric cone-beam CT imaging for radical lung radiotherapy.
- 2.8. Each centre should have a peer-review programme for lung cancer radiotherapy. Peer review should involve assessment of contours and may involve review of plans.

## 3. Stereotactic ablative radiotherapy (SABR) for early stage NSCLC

- 3.1. Stereotactic radiotherapy is the standard of care for peripherally located, medically inoperable lung cancers. To facilitate treatment locally for patients, all radiotherapy centres should have SABR technical capabilities and should be commissioned to offer lung SABR after completion of a lung SABR quality-assurance programme.
- 3.2. Offer patients an appointment with both a thoracic surgeon and a clinical oncologist to discuss the risks and benefits of each treatment if they have a lung cancer suitable for SABR and are thought to be at higher risk of complications from appropriate surgical resection.
- 3.3. Consider patients with centrally, but not ultra-centrally, located tumours for SABR as per the recommendations in the UK SABR consortium guidelines. Consider treating these patients with eight fractions.
- 3.4. Do not treat patients who have an ultra-centrally located lung tumour with SABR outside a clinical trial.

## 4. Combined-modality treatment of locally advanced NSCLC

- 4.1. Discuss all operable stage III NSCLC patients in a multidisciplinary team meeting that includes both a surgeon and a clinical oncologist. Patients being considered for preoperative treatment should see a surgeon and an oncologist before starting treatment to confirm suitability for each therapy.
- 4.2. Perform a diagnostic CT in the penultimate week of concurrent chemoradiotherapy (CRT) in operable patients having preoperative treatment to exclude out-of-field progression.

- 4.3. Surgery should take place within three to five weeks of completing CRT when trimodality therapy is used
  - 4.4. Offer concurrent CRT with radiotherapy as the standard of care for fit (World Health Organization [WHO] performance status [PS] 0–1) inoperable stage III NSCLC patients.
  - 4.5. Offer adjuvant durvalumab to all patients within 42 days of completing definitive CRT unless the tumour is PD-L1 negative (<1%), there is a contraindication to anti PD-L1 therapy, WHO PS has declined ( $\geq 2$ ), side-effects of CRT have not resolved or there is evidence of disease progression on a CT scan.
  - 4.6. Consider sequential chemotherapy followed by radical radiotherapy when the patient is fit for both chemotherapy and radical radiotherapy and:
    - Is not fit enough to receive concurrent CRT or
    - A radiotherapy plan and dosimetric assessment using advanced planning techniques show that OAR doses are unacceptably high for a concurrent CRT technique.
5. **Radiotherapy for advanced lung cancer**
- 5.1. Offer rapid access to treatment when using palliative radiotherapy primarily for symptom control.
  - 5.2. Consider low-dose palliative radiotherapy for symptomatic patients with poor PS (WHO 3–4) or who are unsuitable for systemic therapy.
  - 5.3. Consider higher dose palliative radiotherapy for patients with good PS (WHO 0–2). Use 30–39 Gray (Gy) in 10–13 fractions.
  - 5.4. Use CT-based planning for courses of ten or more fractions to improve OAR dose distributions. Record lung and cord doses as a minimum.
  - 5.5. Ensure patients are discussed with a thoracic oncologist if they are being considered for stereotactic radiotherapy or surgery for cerebral metastases so that prognosis and other treatment options are considered.
  - 5.6. Consider stereotactic radiosurgery (SRS) or surgery in all suitable lung cancer patients with brain metastases according to national guidelines.
  - 5.7. Consider whole-brain radiotherapy for selected patients (for example those with a good prognosis and who have a good PS [WHO 0–1]) with multiple cerebral metastases who are ineligible for SRS or surgery.
6. **Treatment of small cell lung cancer (SCLC)**
- 6.1. Offer concurrent CRT to patients with stage I–III SCLC. Commence radiation concurrently with cycle one or cycle two of chemotherapy.
  - 6.2. Offer patients having concurrent CRT 45 Gy in 30 fractions twice daily over three weeks. If they decline twice-daily treatment, use 66 Gy in 33 fractions once daily.
  - 6.3. Consider performing a radiotherapy planning CT scan after two cycles of chemotherapy to allow maximum tumour shrinkage in patients with large volume stage III SCLC where OAR dose constraints cannot be met before treatment. Start thoracic radiotherapy with the third cycle of chemotherapy.
  - 6.4. Offer once-daily radiotherapy to patients with stage I–III SCLC who respond to chemotherapy but are not suitable for concurrent CRT.

- 6.5. Offer prophylactic cranial irradiation (PCI) using 25 Gy in ten fractions to patients whose disease responds to primary treatment. 20 Gy in five fractions may also be considered in stage IV (extensive stage) SCLC.
- 6.6. Offer PCI with caution to patients for whom the risk may outweigh the potential benefit (for example stage I disease, age >75 years, and in patients with neuro-cognitive co-morbidity).
- 6.7. Do not give PCI concurrently with systemic therapy outside a clinical trial.
- 6.8. Consider consolidation thoracic radiotherapy using 30 Gy in ten fractions for patients with stage IV disease whose disease responds to chemotherapy if they have evidence of residual thoracic disease and if they are eligible for PCI.
- 6.9. The gross tumour volume (GTV) after a partial response to chemotherapy should include the post-chemotherapy primary tumour volume and the pre-chemotherapy-involved lymph nodes.
- 6.10. The clinical target volume (CTV) in patients with SCLC who have had a complete response to chemotherapy should include the pre-chemotherapy involved lymph nodes and, in some cases, the site of primary disease based on the pre-chemotherapy imaging.

## Introduction

Despite recent advances in systemic therapy for lung cancer, radiotherapy remains a key treatment modality for many patients, offering the potential to cure patients with localised disease and to provide effective palliation of symptoms for those with advanced disease. Optimal sequencing of systemic and radiation therapies is increasingly complex and requires multidisciplinary input to ensure patients have the opportunity to receive the best possible treatment.

Survival outcomes from lung cancer in the United Kingdom are poor and among the worst in Europe. Recently published data has identified that in England in 2016 only 40% of patients with stage IIIA disease received treatment with curative intent, with less than 20% receiving multimodality treatment. Similarly, almost a quarter of patients diagnosed with stage I disease in 2015/16 received no documented treatment. The reasons for this are multifactorial but include variation in access to appropriate treatments and delayed implementation of evidence-based advances in care.

The RCR consensus process was initially developed in 2016 to help reduce variation in UK radiotherapy practice in postoperative radiotherapy for breast cancer. The resulting statements were very well received by radiotherapy teams and the process of involving experts from each UK centre encouraged their widespread adoption. The lung cancer statements are the next in a planned series of annual RCR projects in different tumour types. They should serve as a practical stimulus for lung cancer teams to review their current radiotherapy service to ensure that they are able to deliver optimal treatment for their patients. They should be adopted in parallel with those in the National Institute for Health and Care Excellence (NICE) lung cancer guideline.

If all the recommendations are adopted in each centre then outcomes for UK lung cancer patients will undoubtedly improve.

**Dr Ceri Powell, Chair of the Working Group**

**Dr Tom Roques, RCR Clinical Oncology, Medical Director, Professional Practice**

## What are consensus statements?

Consensus statements are developed by a group of experts on a topic for which 'consensus is sought using an explicit methodology to identify area of agreement and disagreement' (Rosenfield *et al*, 2015). The consensus statements reflect the group's collective analysis and evaluation of the best available evidence as well as their expert opinion on a topic.

Clinical consensus statements are not to be confused with clinical practice guidelines. While clinical consensus statements and clinical practice guidelines both provide recommendations on clinical practice, there are subtle but important differences between them. Clinical guidelines are usually based on a formal systematic review of high-level evidence, whereas consensus statements are most appropriate on topics where evidence is limited or lacking making a consensus approach the best way to address variability in clinical practice and improve patient outcomes.

## RCR consensus methodology

A working group of lung cancer experts (see acknowledgements for details) was brought together to develop a series of statements around optimal lung cancer radiotherapy practice. The group was asked to focus on topics where there was current variation in the UK and was asked to avoid duplicating other guidelines unless there were good reasons for reiterating them. Six broad topic areas were selected. Following an appraisal of the available research literature, statements were drafted and refined over a six-month period.

Lung radiotherapy leads from each of the 62 UK cancer centres were invited to share a first draft with their multidisciplinary lung teams and to provide feedback. Feedback received was incorporated into a subsequent draft.

On 11 November 2019, lung radiotherapy leads from each centre were invited to attend a consensus meeting at the RCR to discuss and vote on the draft statements. 42 centres were represented; two patient representatives were also in attendance and contributed to the discussions (see acknowledgements for details).

Evidence was presented to support each of the statements and discussion was facilitated by the working group. Many statements were refined based on the meeting discussion. Representatives were then asked to vote on each statement on behalf of their centre, with one vote per centre.

The following voting categories were agreed to indicate strength of voting. Consensus in the responses was defined as an agreement of at least 70% from participants.

Unanimous support	100%
Very strongly supported	90–99%
Strongly supported	70–89%
Majority support	60–69%
Equipoise	50–59%
Rejected	<50%

Members of the working group took notes of the discussion.

Following the consensus meeting the resulting statements were sent to relevant stakeholder groups (see acknowledgements for details). Following additional feedback received from stakeholders and from those working group members who could not attend the meeting, the final statements were agreed and approved for publication by the RCR's Clinical Oncology Professional Support and Standards Board.

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## References

1. Bloomfield D; Core group facilitated by The Royal College of Radiologists. Development of postoperative radiotherapy for breast cancer: UK consensus statements – a model of patient, clinical and commissioner engagement? *Clin Oncol (R Coll Radiol)* 2017; **29**(10): 639–641.
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4. Rosenfield RM, Nnacheta LC, Corrigan MD. Clinical consensus statement development manual. *Otolaryngol Head Neck Surg* 2015; **153**(Suppl 2): S1–S14.
5. The Royal College of Radiologists. *Postoperative radiotherapy for breast cancer: UK consensus statements*. London: The Royal College of Radiologists, 2016.

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## Key references

### General

1. ASTRO guideline on definitive and adjuvant radiation therapy in non-small cell lung cancer (NSCLC) June 2015, reaffirmed 2017. [www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements/ASTRO-39;s-guideline-on-definitive-and-adjuvant-RT](http://www.astro.org/Patient-Care-and-Research/Clinical-Practice-Statements/ASTRO-39;s-guideline-on-definitive-and-adjuvant-RT) (last accessed 28/4/20).
  2. McAleese J, Baluch S, Drinkwater K. The quality of curative-intent radiotherapy for non-small cell lung cancer in the UK. *Clin Oncol (R Coll Radiol)* 2015; **27**(9): 498–504.
  3. Møller H, Coupland VH, Tataru D *et al*. Geographical variations in the use of cancer treatments are associated with survival of lung cancer patients. *Thorax* 2018; **73**(6): 530–537.
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1.  
Optimising patients for  
radical radiotherapy  
for lung cancer

(For localised small cell or non-small cell lung cancer including patients with oligometastases receiving a curative dose.)

Statement	Voting outcome
1.1. Perform a PET-CT within the six weeks before commencing treatment (and ideally within four weeks) in all patients having curative-intent radiotherapy. If the time interval is greater than six weeks, consider repeating the PET-CT scan to confirm treatment strategy and target volume.	Strongly supported
1.2. Offer immediate testing for PD-L1 to patients with unresectable stage III non-small cell lung cancer.	Very strongly supported
1.3. Undertake systematic pathological nodal staging (eg, staging endobronchial ultrasound and biopsy) in any patient with enlarged intrathoracic lymph nodes on CT imaging (>10 mm short axis) or FDG-avid intrathoracic lymph nodes on PET. Do not rely on radiological nodal staging alone.	Very strongly supported
1.4. Perform individualised assessment and optimisation before curative radiotherapy. This should include: <ul style="list-style-type: none"> <li>a. Spirometry and diffusion capacity testing within six weeks of radiotherapy</li> <li>b. Advice about physical activity including referral to dedicated activity programmes where possible</li> <li>c. Screening for malnutrition and dietetic advice as appropriate</li> <li>d. Advice For smokers, eg, 'Very brief advice', the offer of medication to treat tobacco addiction and referral to a specialist team for more intensive support.</li> </ul>	Unanimous support
1.5. Do not exclude patients from curative radiotherapy on the basis of pulmonary function tests alone. Pulmonary function test cut-off values should only serve as a guide. The final decision regarding fitness for radical radiotherapy should include the patient's functional capacity and acceptance of risk from treatment after a full discussion of potential risks/benefits and alternative treatment strategies.	Unanimous support

Statement	Voting outcome
1.6. Be aware that patients who have had radical radiotherapy are at risk of fragility fractures of the vertebrae which may be visible on routine post-treatment imaging. Consider referral to a fractures liaison service or rheumatologist.	Strongly supported
1.7. Assess patients for relevant co-morbidities (eg, lung fibrosis, auto-immune conditions, use of radio-sensitising medication) and liaise with the relevant specialist team to assess the impact on the feasibility of treatment and the potential for increased toxicities.	Unanimous support
1.8. Consider all patients receiving radical radiotherapy for prophylactic treatment of pneumocystis jiroveci pneumonia (PJP) during or after their treatment if they are thought to be at risk eg, lymphocyte count <0.6 x10 <sup>9</sup> /L, patients on steroids for more than four weeks, patients having combined-modality treatment. Treatment should continue until lymphocyte count >0.6x10 <sup>9</sup> /L and/or for a minimum of six weeks post radiotherapy.	Strongly supported

### Notes on optimising patients for radical lung cancer radiotherapy

- Selecting the right patients to receive curative lung cancer radiotherapy is important and often difficult. The right staging tests can help avoid the over-treatment of patients who have more advanced disease and the under-treatment of those with imaging abnormalities not due to cancer. Patients with lung cancer often have significant co-morbidities and impaired lung function but these factors alone should not preclude radiotherapy treatment without careful thought and discussion with the patient. Optimising function before curative radiotherapy can help more patients successfully complete treatment.
- The Lung Cancer Clinical Expert Group (CEG) in association with NHS England has recently published standards of care for lung cancer which set out 'Lung cancer diagnostic standard of care bundles' for patients presenting with varying stages of lung cancer. Together with a service specification for endobronchial ultrasound (EBUS). These can be accessed online at [www.roycastle.org/for-healthcare-professionals/clinical-expert-group/](http://www.roycastle.org/for-healthcare-professionals/clinical-expert-group/)
- Ideally PD-L1 testing should be immediate (that is, reflex) for all stage III patients. This is particularly pertinent for the borderline resectable patients where a positive PD-L1 might influence decision-making between surgery and concomitant chemo-radiotherapy.

- The International Atomic Energy Agency (IAEA) consensus report 2014 states that, 'Long delays in time to treatment could result in a geographic miss if RT fields no longer encompass the entire tumour or all involved nodal stations. To avoid this issue it is suggested that radiotherapy should commence no later than four weeks after acquisition of the PET-CT'. Recognising the scarcity of PET resource in the UK, six weeks was accepted as a pragmatic compromise though it is recognised that this falls short of the international guidance cited above. If full mediastinal staging with EBUS +/- mediastinoscopy has been performed within four weeks of the start of radiotherapy, it may not be necessary to repeat a PET-CT scan.
- Screening for malnutrition should be performed using a validated tool and those who are malnourished should be referred to a specialist dietitian for dietary advice relating to nutritional status and symptom management.
- Vertebral collapse can occur when the radiation treatment has delivered a significant dose to vertebral bodies. Fractures noted on imaging may be reported with ambiguous or confusing terminology. It is recommended that clinicians receiving these reports are alert to descriptions of changes in vertebral height and facilitate early referral to local rheumatology services. Consideration may be given to including information on the risk of vertebral fracture following radical dose radiotherapy in the end-of-treatment letter to the patient and their general practitioner (GP).
- There is unpublished evidence that PJP infections occur more frequently in patients having lung cancer radiotherapy. These can be life-threatening. PJP prophylaxis is routinely used when treating some other cancers and is recommended in lung cancer patients judged to be at risk (as defined above). The duration of PJP prophylaxis in prolonged lymphopenia may be a concern and it is recommended that local guidelines are developed in conjunction with the microbiology service.
- It is acknowledged that there is limited evidence in the field of pre-habilitation and that this is an active area of ongoing research. The appropriate metrics (for example patient reported outcome measures [PROMS]) are yet to be defined. Clinical trials in this area are strongly encouraged, particularly to identify what level of benefit is required to justify an intervention.

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## References for optimising patients for radical lung cancer radiotherapy

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  2. Brunelli A, Charloux A, Bolliger CT *et al*. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). *Eur Respir J* 2009; **34**(1): 17–41.
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9. Royal Osteoporosis Society. Clinical guidance for the effective identification of vertebral fractures 2017. [www.guidelines.co.uk/musculoskeletal-and-joints-/ros-guideline-identification-of-vertebral-fractures/454148.article](http://www.guidelines.co.uk/musculoskeletal-and-joints-/ros-guideline-identification-of-vertebral-fractures/454148.article) (last accessed 29/4/20)
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## 2. Technical aspects of radical radiotherapy for lung cancer

Statement	Voting outcome
2.1. Employ advanced techniques such as IMRT/VMAT to facilitate radical dose delivery, improve conformality and reduce dose to OAR.	Unanimous support
2.2. Use intravenous contrast for radiotherapy planning for stage II/III unless contraindicated. Consider for stage I to assist with OAR delineation.	Very strongly supported
2.3. Obtain and reconstruct relevant prior radiotherapy (eg, previous breast cancer radiotherapy) to permit composite planning and safe delivery of lung cancer radiotherapy.	Very strongly supported
2.4. Assess physical disability that may affect treatment position and employ strategies to enable the delivery of radiotherapy (eg, physiotherapy, alternative treatment positions such as arms down, analgesia).	Unanimous support
2.5. Use 4DCT or alternative motion assessment at CT simulation for all patients having curative-intent radiotherapy unless the patient is unable to manage the technique.	Very strongly supported
2.6. Do not use elective nodal irradiation.	Very strongly supported
2.7. Perform daily online volumetric cone-beam CT imaging for radical lung radiotherapy.	Very strongly supported
2.8. Each centre should have a peer-review programme for lung cancer radiotherapy. Peer review should involve assessment of contours and may involve review of plans.	Very strongly supported

### Notes on technical aspects of radical radiotherapy for lung cancer

- The delivery of accurate radiotherapy to tumours arising in the lung poses a series of complex challenges to clinical departments.
- Administration of intravenous contrast for radiotherapy planning for stage II/III disease is recommended unless contraindicated. It is also beneficial for stage I disease to assist with OAR delineation such as the heart and brachial plexus. Departments may consider

administering contrast during 4DCT acquisition if technical capabilities allow rather than undertaking a separate 3D scan with contrast.

- Image-guided radiotherapy (IGRT) in lung cancer is accepted as standard. Studies have demonstrated that the use of IGRT improves patient positioning and provides improved geometric and dosimetric conformance with the intended treatment plan. IGRT is also beneficial when the intention is to minimise dose to OAR, which may influence morbidity and mortality.
- At each fraction of radiotherapy IGRT can verify the position of the tumour or OAR so that action can be taken to improve treatment accuracy if needed. There are, however, some specific challenges inherent in IGRT for tumours contained within the lung.
  - Tumours within the lung can be difficult to see with megavoltage portal imaging.
  - Tumours within the lung can move significantly with respiration and mediastinal organ motion.
  - During treatment, changes in the external anatomy (for example weight loss) and internal anatomy (for example tumour increase/decrease, collapse or re-inflation of the lung) can occur.
- The most important issue to be addressed with IGRT is lung motion. Tumours contained in the lung can move independently of bone anatomy. Therefore, to deliver the radiotherapy accurately, the tumour must be imaged directly using volumetric imaging or a surrogate such as implanted fiducial markers or transponders. There is growing evidence to support the daily acquisition of volumetric imaging (such as cone-beam CT scans) for patients receiving radical radiotherapy for lung cancer though it is recognised that many departments will face significant challenges with implementation of this recommendation.
- Internal organ motion during the respiration and cardiac cycle presents a particular challenge to ensuring accurate thoracic radiotherapy. Studies have reported that the largest magnitude of movement is seen in tumours of the lower lobe that are not attached to adjacent structures. Motion of the tumours due to the cardiac cycle has been reported at around 3 mm.
- For patients with significant tumour movement (typically >5 mm), motion management strategies should be used. A number of methods exist to minimise the influence of tumour and/or OAR movement during radiotherapy treatment. Deciding on the optimal strategy to employ is multifactorial and department specific. Potential strategies may include breath-hold techniques, gating based on external and internal surrogates, accounting for motion when defining radiotherapy target margins and abdominal compression.
- The method of IGRT required for each patient may depend on the treatment intent, the size of the planning target volume (PTV) margins planned/needed and the fractionation schedule.
- Peer review of radiotherapy contours can help to ensure a consistent approach to treatment and reduce both random and systematic errors. In addition to the assessment of contours, peer review may involve review of plans and of patient selection and treatment modality (for example SABR versus conventionally fractionated radiotherapy and concurrent versus sequential CRT).

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## Technical aspects of radical radiotherapy for lung cancer references

1. Higgins J, Bezjak A, Hope A *et al.* Effect of image-guidance frequency on geometric accuracy and setup margins in radiotherapy for locally advanced lung cancer. *Int J Radiat Oncol Biol Phys* 2011; **80**(5): 1,330–1,337.
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### 3. Stereotactic ablative radiotherapy (SABR) for early-stage non-small cell lung cancer (NSCLC)

Statement	Voting outcome
3.1. Stereotactic radiotherapy is the standard of care for peripherally located, medically inoperable lung cancers. To facilitate treatment locally for patients, all radiotherapy centres should have SABR technical capabilities and should be commissioned to offer lung SABR after completion of a lung SABR quality-assurance programme.	Very strongly supported
3.2. Offer patients an appointment with both a thoracic surgeon and a clinical oncologist to discuss the risks and benefits of each treatment if they have a lung cancer suitable for SABR and are thought to be at higher risk of complications from appropriate surgical resection.	Unanimous support
3.3. Consider patients with centrally, but not ultra-centrally, located tumours for SABR as per the recommendations in the UK SABR consortium guidelines. Consider treating these patients with eight fractions.	Unanimous support
3.4. Do not treat patients who have an ultra-centrally located lung tumour with SABR outside a clinical trial.	Unanimous support

#### Notes on stereotactic ablative radiotherapy (SABR) for early-stage NSCLC

- International randomised trials and national registry data have demonstrated superiority of SABR over conventionally fractionated radiotherapy for early-stage, peripherally located, medically inoperable lung cancers. Population data have shown improved outcomes with an increase in use of SABR compared to no treatment. SABR for peripherally located, early-stage tumours is well tolerated.
- Prospective trial data have reported severe toxicity such as bronchial stenosis, fatal haemoptysis and central fistula after SABR to central and ultra-central tumours when ablative doses were delivered to critical structures.
- All eligible patients require access to SABR and, given the high incidence of co-morbidities/advanced age in this population, treatment should be delivered as close to their homes as possible. To facilitate this, networks will need to be developed to link centres setting up SABR services with established SABR centres so that they can provide support for the review of complex cases and peer review, and to share best practice.
- More than 40% of potential SABR-eligible patients currently receiving fractionated RT or no treatment in England would have to travel >45 minutes to access SABR.

- To promote shared decision-making, joint surgical/oncological clinics to discuss the pros and cons of resection and SABR simultaneously may be considered for patients suitable for both treatments.

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### Stereotactic ablative radiotherapy (SABR) for early stage NSCLC references

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#### 4. Combined-modality treatment of locally advanced NSCLC

Statement	Voting outcome
4.1. Discuss all operable stage III NSCLC patients in a multidisciplinary team meeting that includes both a surgeon and a clinical oncologist. Patients being considered for preoperative treatment should see a surgeon and an oncologist before starting treatment to confirm suitability for each therapy.	Very strongly supported
4.2. Perform a diagnostic CT in the penultimate week of concurrent chemoradiotherapy (CRT) in operable patients having preoperative treatment to exclude out-of-field progression.	Strongly supported
4.3. Surgery should take place within three to five weeks of completing CRT when trimodality therapy is used.	Unanimous support
4.4. Offer concurrent CRT as the standard of care for fit (WHO PS 0–1) inoperable stage III NSCLC patients.	Very strongly supported
4.5. Offer adjuvant durvalumab to all patients within 42 days of completing definitive CRT unless the tumour is PD-L1 negative (<1%), there is a contraindication to anti PD-L1 therapy, WHO PS has declined ( $\geq 2$ ), side-effects of CRT have not resolved or there is evidence of disease progression on a CT scan.	Unanimous support
4.6. Consider sequential chemotherapy followed by radical radiotherapy when the patient is fit for both chemotherapy and radical radiotherapy and: <ul style="list-style-type: none"> <li>a. Is not fit enough to receive concurrent CRT</li> <li>b. A radiotherapy plan and dosimetric assessment using advanced planning techniques show that OAR doses are unacceptably high for a concurrent CRT technique.</li> </ul>	Very strongly supported

### Notes on combined-modality treatment of locally advanced NSCLC

- According to the 2018 National Lung Cancer Audit (NLCA) report, approximately 20% of patients in England, Wales, Guernsey and Jersey have stage III disease at diagnosis.
- The 2017 NLCA Annual Report showed the one-year overall survival for UK stage III NSCLC patients was 42.5% and only 32% of stage III NSCLC patients received treatment with curative intent.
- There is considerable variation in how stage III NSCLC is treated. Over half of 6,276 patients diagnosed with stage III NSCLC in England in 2016 received palliative intent treatment (34%) or no active anti-cancer treatment (36%). Only 17% of patients in the group were treated with radical radiotherapy (with 676 [11%] also receiving chemotherapy). In this cohort, one-year overall survival was 32.9%.
- Although preoperative treatment may improve outcome in selected patients, this should not be considered down-staging treatment. Patients being considered for CRT followed by surgery must be operable at baseline. The definition of operable is highly variable between MDTs but it is not the purpose or role of this guidance to clarify the definition of tumour operability.
- A large meta-analysis comparing concurrent chemoradiotherapy (cCRT) and sequential chemoradiotherapy (sCRT) for unresected stage III NSCLC reported an absolute survival benefit of 5.7% at three years, and 4.5% at five years, in favour of the concurrent approach (Aupérin *et al*, 2010).
- The PACIFIC trial (2018) is the first study to demonstrate a significant overall survival advantage for unresectable stage III NSCLC patients receiving cCRT followed by adjuvant durvalumab and is considered the current international standard of care. No published data are available regarding dose to OARs or irradiated volume therefore no recommendation is made to commence adjuvant durvalumab at an early time point within the 42-day window. Although patients within the subgroup analysis demonstrated improved outcomes when durvalumab was started within 14 days of completion of CRT, it was felt that these patients were likely to reflect a better prognosis group with a quicker recovery from their CRT and hence were not representative of the PACIFIC population as a whole.
- While concurrent CRT is considered the standard of care for fit inoperable stage III NSCLC patients, sequential chemotherapy and radical radiotherapy is an effective and appropriate option for certain patients.

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### Combined-modality treatment of locally advanced NSCLC references

1. Adizie JB, Khakwani A, Beckett P *et al*. Stage III non-small cell lung cancer management in England. *Clin Oncol (R Coll Radiol)* 2019; **31**(10): 688–696.
2. Albain KS, Swann RS, Rusch VW *et al*. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. *Lancet* 2009; **374**(9687): 379–386.
3. Aupérin A, Le Péchoux C, Rolland E *et al*. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *J Clin Oncol* 2010; **28**(13): 2,181–2,190.
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- cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. *Lancet Oncol* 2015; **16**(2): 187–199.
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## 5. Radiotherapy for advanced lung cancer

Statement	Voting outcome
5.1. Offer rapid access to treatment when using palliative radiotherapy primarily for symptom control.	Very strongly supported
5.2. Consider low-dose palliative radiotherapy for symptomatic patients with poor PS (WHO 3–4) or who are unsuitable for systemic therapy.	Very strongly supported
5.3. Consider higher dose palliative radiotherapy for patients with good PS (WHO 0–2). Use 30–39 Gy in 10–13 fractions.	Very strongly supported
5.4. Use CT-based planning for courses of ten or more fractions to improve OAR dose distributions. Record lung and cord doses as a minimum.	Very strongly supported
5.5. Ensure patients are discussed with a thoracic oncologist if they are being considered for stereotactic radiotherapy or surgery for cerebral metastases so that prognosis and other treatment options are considered.	Very strongly supported
5.6. Consider stereotactic radiosurgery (SRS) or surgery in all suitable lung cancer patients with brain metastases according to national guidelines.	Unanimous support
5.7. Consider whole-brain radiotherapy for selected patients (eg, those with a good prognosis and who have a good PS [WHO 0–1]) with multiple cerebral metastases who are ineligible for SRS or surgery.	Very strongly supported

### Notes on radiotherapy for advanced lung cancer

- The randomised control trial evidence for palliative radiotherapy treatment NSCLC comes from studies that compared dose/fractionation that were conducted before firstline systemic treatment was standard of care.
- The dose/fractionations tested in the Medical Research Council (MRC) studies in the 1990s were widely adopted across the UK and remain the basis of current practice. The statements seek a consensus around patient selection and planning for palliative thoracic radiotherapy practice.

- For patients with a better performance status and/or those potentially suitable for multiple lines of systemic therapy, higher dose fractionation regimens are recommended. CT-based planning for courses of ten or more fractions is recommended to improve OAR dose distributions though it may be necessary to commence treatment using a simple field-based approach if rapid symptom control is required. Treatment may subsequently be switched to an optimised plan once available.
- As systemic therapy and outcomes for patients with stage IV NSCLC improve there is an increasing role for focal treatment of brain metastases. All suitable lung cancer patients with brain metastases should be considered for SRS or surgery according to national guidelines. This discussion should involve a thoracic oncologist so that alternative/sequencing of systemic treatments can be considered for the individual patient.
- Following the publication of the QUARTZ trial the use of palliative radiotherapy for the treatment of cerebral metastases declined significantly. However, with the application of modern radiotherapy techniques and an increased understanding of the biology of the disease there is recognition (but no randomised trial evidence) that palliative radiotherapy could be indicated for the treatment for cerebral metastases in subsets of lung cancer patients.

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### Radiotherapy for advanced lung cancer references

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4. Stevens R, Macbeth F, Toy E, Coles B, Lester JF. Palliative radiotherapy regimens for patients with thoracic symptoms from non-small cell lung cancer. *Cochrane Database Syst Rev* 2015; **14**(1): CD002143.

## 6. Treatment of small cell lung cancer (SCLC)

Statement	Voting outcome
6.1. Offer patients with stage I–III SCLC concurrent CRT. Commence radiation concurrently with cycle one or cycle two of chemotherapy.	Very strongly supported
6.2. Offer patients having concurrent CRT 45 Gy in 30 fractions twice daily over three weeks. If they decline twice-daily treatment, use 66 Gy in 33 fractions once daily.	Strongly supported
6.3. Consider performing a radiotherapy planning CT scan after two cycles of chemotherapy to allow maximum tumour shrinkage in patients with large volume stage III SCLC where OAR dose constraints cannot be met before treatment. Start thoracic radiotherapy with the third cycle of chemotherapy.	Very strongly supported
6.4. Offer once-daily radiotherapy to patients with stage I–III SCLC who respond to chemotherapy but are not suitable for concurrent CRT.	Very strongly supported
6.5. Offer prophylactic cranial irradiation (PCI) using 25 Gy in ten fractions to patients whose disease responds to primary treatment. 20 Gy in five fractions may also be considered in stage IV (extensive stage) SCLC.	Unanimous support
6.6. Offer PCI with caution in patients for whom the risk may outweigh the potential benefit (eg, stage I disease, age >75 years, and in patients with neuro-cognitive co-morbidity).	Unanimous support
6.7. Do not give PCI concurrently with systemic therapy outside a clinical trial.	Unanimous support
6.8. Consider consolidation thoracic radiotherapy using 30 Gy in ten fractions for patients with stage IV disease whose disease responds to chemotherapy if they have evidence of residual thoracic disease and if they are eligible for PCI.	Very strongly supported

Statement	Voting outcome
6.9. The GTV after a partial response to chemotherapy should include the post-chemotherapy PTV and the pre-chemotherapy involved lymph nodes.	Unanimous support
6.10. The CTV in patients with SCLC who have had a complete response to chemotherapy should include the pre-chemotherapy-involved lymph nodes and, in some cases, the site of primary disease based on the pre-chemotherapy imaging (see notes below).	Unanimous support

### Notes on treatment of small cell lung cancer

- Small cell lung cancer (SCLC) is the second most common thoracic malignancy, representing approximately 13% of newly diagnosed lung cancers.
- Historically, standard treatment for SCLC has been with a combination of chemotherapy and thoracic radiotherapy with PCI for limited-stage disease, and chemotherapy alone followed by PCI for extensive-stage disease.
- In recent years, several practice-changing radiotherapy phase III clinical trials have been reported for both limited-stage and extensive-stage SCLC, including:
  - The CREST trial (2015) which reported a two-year survival benefit with thoracic consolidative radiotherapy for extensive stage SCLC
  - The CONVERT trial (2017) which did not report significant survival and toxicity differences between once- and twice-daily thoracic radiation therapy with modern radiation doses, fields and techniques in limited-stage SCLC.
  - The Japanese PCI trial (2017) which challenged the role of PCI when brain magnetic resonance imaging (MRI) surveillance is performed in extensive-stage SCLC. This has not been recommended for adoption into routine practice (with consequent implications for MRI capacity) within this document as the trial population was not congruent with that recruited into the EORTC trials. The outcomes of planned randomised trials of MRI surveillance versus PCI in both limited- and extensive-stage SCLC are awaited.
- The results of these clinical trials and impact on routine practice have been heavily debated in recent years. In addition, the expected introduction of immunotherapy into the treatment of SCLC may challenge the role of PCI and consolidation thoracic RT in metastatic SCLC. Data on the integration of PCI and consolidation thoracic RT with immunotherapy is currently lacking.
- SCLC generally responds rapidly to chemotherapy. This can pose a challenge when defining the post-chemotherapy radiotherapy treatment volume. In situations where complete response to chemotherapy has been achieved, the pre-chemotherapy diagnostic imaging should be used to define a CTV. The CTV should include:
  - The pre-chemotherapy involved lymph nodes

- The pre-chemotherapy primary tumour volume. For central tumours extending into lung parenchyma, manual editing of the CTV is recommended to limit the volume of normal lung parenchyma irradiated. For peripheral tumours within the lung parenchyma only, the pre-chemotherapy primary tumour volume should NOT be included in the CTV.

It is strongly recommended that treatment volumes in these challenging cases are subject to peer review.

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### Treatment of small cell lung cancer references

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2. Faivre-Finn C, Snee M, Ashcroft L *et al.* Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *Lancet Oncol* 2017; **18**(8): 1,116–1,125.
3. Fried DB, Morris DE, Poole C *et al.* Systematic review evaluating the timing of thoracic radiation therapy in combined modality therapy for limited-stage small-cell lung cancer. *J Clin Oncol* 2004; **22**(23): 4,837–4,845.
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5. Slotman B, Faivre-Finn C, Kramer G *et al.* Prophylactic cranial irradiation in extensive small-cell lung cancer. *N Engl J Med* 2007; **357**(7): 664–672.
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7. Takahashi T, Yanamaka T, Seto T *et al.* Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol* 2017; **18**(5): 663–671.

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## Acknowledgements

### Members of the Working Group

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  - Dr Shobhit Bajjal, Consultant Medical Oncologist, University Hospitals Birmingham NHS Foundation Trust
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  - Dr Matthew Evison, Consultant Chest Physician, Manchester University NHS Foundation Trust
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-

## Consensus participants

The following centres were represented at the RCR lung cancer consensus meeting held on 11 November 2019:

Aberdeen Royal Infirmary	Peterborough City Hospital
Addenbrooke's Hospital	Plymouth Oncology Centre
Beatson West of Scotland Cancer Centre	Queen's Hospital, Romford
Belfast City Hospital	Royal Derby Hospital
Berkshire Cancer Centre	Royal Devon and Exeter Hospital (Wonford)
Sussex Cancer Centre	Royal Marsden NHS Foundation Trust
Bristol Oncology Centre	Royal Preston Hospital
Castle Hill Hospital	Royal Stoke University Hospital
Cheltenham General Hospital	Royal Surrey County Hospital
Colchester General Hospital	Royal United Hospital Bath
Edinburgh Cancer Centre	South Devon Hospital
Imperial College Cancer Centre	South West Wales Cancer Centre
Ipswich Hospital	The Christie Hospital
Leeds Cancer Centre	The Oxford University Hospitals NHS Trust
Leicester Royal Infirmary	University College Hospital
Musgrove Park Hospital	University Hospital Birmingham
Northern Centre for Cancer Care, Freeman Hospital	University Hospital Coventry
Norfolk and Norwich University Hospital	University Hospital Southampton
North Middlesex University Hospital	Velindre Cancer Centre
North West Cancer Centre, Altnagelvin	Weston Park Hospital
Nottingham University Hospital	

We are also very grateful to patient representatives, Paul Cosford and Tom Haswell, who attended and contributed to the day.

The first draft of the consensus statements were circulated to each of the 62 UK cancer centres to discuss with the multidisciplinary lung teams and to provide feedback. Feedback received was incorporated into the draft voted on at the consensus meeting on 11 November 2019.

Almost all the centres that provided feedback to the first draft attended the consensus meeting and are therefore included in the list of centres above. The following centres provided feedback to the initial draft but were not able to attend the November meeting:

- Dorset Cancer Centre, Poole Hospital
- Guy's and St Thomas' Hospital NHS Trust
- Worcester Oncology Centre

### Stakeholder consultation

The statements agreed at the consensus meeting were circulated to relevant stakeholder groups for comment. We are grateful for all the comments that were received and have reflected on this feedback to improve the document.

The following stakeholders have confirmed their support of this document:

- Association of Chartered Physiotherapists in Oncology and Palliative Care (ACPOPC)
- The British Dietetic Association Oncology Specialist Group
- British Thoracic Oncology Group (BTOG)
- Institute of Physics and Engineering in Medicine (IPEM)
- NHS England Lung Cancer Clinical Expert Group
- Society and College of Radiographers (SCoR)
- Roy Castle Lung Cancer Foundation



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