Overview

Stereotactic Ablative Body Radiotherapy for Lung Cancer

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Abstract

Lung stereotactic ablative radiotherapy (SABR) is a method of delivering high ‘ablative’ doses of radiotherapy to tumours in the lung. It was developed at the Karolinska Institute in the early 1990s using the methods established in cranial radiosurgery with multiple beams prescribed to an isodose and using a custom designed stereotactic body frame for immobilisation. Since then, aligned with the advances in radiotherapy technology and techniques (e.g. four-dimensional computed tomography simulation and image-guided radiotherapy), there has been a rapid increase in the use of lung SABR for both early stage lung cancer and lung metastases. For peripheral primary lung cancers less than 5 cm in diameter, high rates of local control and low levels of acute and late toxicity are consistently reported in the published literature. Compared with historical control rates of stage I lung cancers treated with conventionally fractionated radiotherapy, SABR seems to offer higher rates of local control, lower levels of acute toxicity and a better quality of life after treatment. However, the full results of randomised controlled trials of SABR versus conventionally fractionated are awaited and will provide higher-level evidence. For central lung tumours, very high SABR doses can be associated with significant toxicity. Dose-adapted fractionation schedules seem to have much lower rates of toxicity and prospective trials, including the completed RTOG 0813 study and the on-going EORTC LUNGTEC study, should provide further evidence of safety and establish organ at risk tolerances. SABR can also be used for tumours metastatic to the lung with high rates of local control and is a reasonable alternative to surgery in selected patients. Going forward, prospective trials are underway to establish the safety and efficacy of SABR in oligometastatic disease. Population-based outcomes will be crucial in supporting/establishing SABR as the treatment of choice in medically inoperable patients with peripheral stage I lung cancers. Randomised phase III trials will hopefully extend the evidence base and show the safety and the utility of SABR in early central tumours and oligometastatic disease.

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Key words: Ablative; lung cancer; oligometastases; radiotherapy; stereotactic

Statement of Search Strategies Used and Sources of Information

This paper reflects expert opinion and current literature accessed by the authors; no formal search strategy has been defined.

Introduction

The American Society of Radiation Oncology and the American Society of Radiology have defined stereotactic body radiotherapy as an ‘external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extra-cranial target within the body, using either a single dose or a small number of fractions’ [1].

The concept of stereotactic guidance was originally developed in the 1940s by Lars Leksell for neurosurgical and neurological research. He designed a stereotactic apparatus for locating points within the brain using an external, three-dimensional frame of reference based on the Cartesian coordinate system [2]. This facilitated the development of radiosurgery which was delivered using multiple pencil beams to radio-ablate discrete areas of the brain.

The term ablative refers to the destruction of a functioning tissue or tumour by delivering a large radiation dose to induce necrosis within the planning target volume (PTV) both directly through cell kill and indirectly via other mechanisms, particularly on the vasculature. This is in contrast to conventionally fractionated radiotherapy, where the aim is to sterilise the cancer cells within the PTV but yet...
maintain the integrity of the normal tissue structure within the PTV. The precision and accuracy required for stereotactic radiotherapy enables ablative doses to be delivered to the PTV, due to a rapid fall off of dose outside the PTV, surrounding normal tissues are relatively spared. This work established the twin principles of modern stereotactic body radiotherapy, although in most countries the nomenclature has changed from stereotactic body radiotherapy to stereotactic ablative radiotherapy (SABR) to emphasise the ablative nature of the treatment. Although these terms are interchangeable and both are widely used in the literature, we use the term SABR throughout this article.

Unlike intracranial radiosurgery, where the PTV is immobile within the skull and therefore relatively easy to fix in relation to the radiation source, at extra-cranial sites there are the problems of internal organ motion and external patient movement. To overcome these issues, Lax et al. [3] developed a custom-designed stereotactic body frame to immobilise the chest and abdomen. Constructed of wood and plastic to minimise artefacts in computed tomography scanning, the stereotactic body frame was designed to fit in the bore of computed tomography, magnetic resonance imaging and positron emission tomography (PET) scanners. A vacuum bag supported and fixed the patient in the frame. The ‘stereotactic’ system consisted of radio-opaque markers implanted in the inside of the frame and was used in conjunction with repeated computed tomography scanning before treatment [3].

Since Blomgren et al. [4] reported the first clinical outcomes from patients treated with SABR in 1995 and coupled with large advances in radiotherapy technology in the past 20 years, there has been a rapid uptake of SABR for both primary and metastatic lung cancers across the world.

Basic Principles of Lung Stereotactic Ablative Radiotherapy

To deliver an ablative dose to a lung cancer it is mandatory to:

- Accurately identify and delineate the target and organs at risk (OARs);
- Employ a strategy to deal with respiratory motion if significant;
- Ensure precise and accurate daily delivery of radiation to the intended target.

Accurately Identify and Delineate the Target

Computed Tomography Simulation

The value of computed tomography in radiotherapy planning was established in the late 1970s [5–7] and Babcock [8] reported that computed tomography planning was found to be valuable in the planning the majority (84%) of thoracic radiation patients. However, due to respiratory motion, standard free-breathing computed tomography both distorts and generally underestimates the tumour volume (Figure 1) [9,10]. Therefore, contouring the gross

![Fig 1. Motion artifact on free breathing helical CT (1a) compared to cone beam CT (1b) Tumour size underestimation in a tumour with significant motion free breathing helical CT (2a) compared to a 4DCT (2b).]
tumour volume (GTV) on a single free-breathing computed tomography scan is both an inaccurate representation of the tumour dimensions and of the mean tumour position relative to other organs. In defining the tumour and OARs it is important to both contour on mediastinal and lung windows and use the information from other imaging modalities, such as PET and magnetic resonance imaging.

Strategies to Deal with Respiratory Motion

Four-dimensional Computed Tomography Simulation

Kilovoltage fluoroscopy cannot quantify tumour motion accurately as small tumours are often not seen clearly, particularly in the lateral view, and the resolution of the tumour margin is limited.

Therefore, a number of methods have been used to define the internal target volume (ITV): multiple helical computed tomography scans, slow computed tomography and the preferred method in most institutions, four-dimensional computed tomography (4DCT), where multiple computed tomography images are acquired over a period of time to capture all phases of breathing. Simultaneously, an external monitor, linked to the computed tomography scanner, measures the patients' breathing patterns so that acquired image slices can be allocated or 'binned' to different phases of respiration, producing 3DCT images set at multiple phases of respiration (thus adding the fourth dimension of time). From the 4DCT an ITV can be created using a variety of methods, which include:

1. Contouring on the maximum exhale, inhale and mid-ventilation and fusing these volumes to form the ITV;
2. Creating the ITV from the maximum intensity projections;
3. Creating the ITV from the minimum intensity projections.

All three techniques are valid for ITV generation and the method used in each institution should be tailored to local equipment and systems but have a robust quality assurance procedure to ensure that the 4DCT is an accurate representation of breathing motion [11]. By contrast, the Netherlands Cancer Institute use GTV contoured on a time-weighted average computed tomography dataset and a margin recipe to generate the PTV based on the tumour motion [12,13].

If significant respiratory motion is seen at 4DCT then a number of techniques can be used to deal with this:

1. Allowing for motion in the planning process;
2. Restricting motion with abdominal compression or breath-hold technique;
3. Respiratory gating with external surrogates or implanted fiducials.

The most straightforward approach is to allow for motion in the planning process, as in most cases the internal motion of the tumour can easily be encompassed without exceeding normal tissue constraints. In addition, some patients who are candidates for lung SABR cannot tolerate abdominal compression, are unable to comply with breath-hold or have irregular breathing patterns, such that respiratory gating is impossible.

Deliver the Highest Required Dose to the Tumour without Increasing the Dose to Critical Normal Organs

Lung SABR typically delivers doses in excess of a biological equivalent dose (BED) of 100 Gy (estimated for acute effects assuming an α/β ratio of 10) to lung tumours and therefore it is essential that the dose outside the PTV is minimised to ensure tolerance doses to OARs are not exceeded. To achieve this either multiple beams (typically ≥7 beams including one or more non-coplanar beams) or arc-based therapy are used.

Prescribing to an isodose covering the PTV and not the isocentre enables the delivery of a high dose to the tumour by allowing dose heterogeneity across the PTV, for example with the centre of the tumour receiving up to 150% of the prescription dose and allowing a rapid dose fall off outside the PTV (Figure 2). Conformity indices such as the R100, R50, V95 and V90 can be used to ensure PTV dose coverage and minimise dose spillage (see Table 1 for definitions) [14]. The critical OAR doses are discussed in the clinical section below.

Ensure Precise and Accurate Daily Delivery of Radiation to the Intended Target

Given the radio-ablative doses used in lung SABR it is essential that the dose is delivered to the target and there are three key components that need to be addressed to ensure accuracy:

1. Immobilisation;
2. On-treatment image guidance;
3. On-treatment respiratory motion management.

Immobilisation

The main aims are to make the patient comfortable and stable. This can be achieved by a number of methods either with specific SABR immobilisation devices or customisation of existing methods, e.g. addition of customised vacuum bags to more standard immobilisation systems (wing, thoracic or breast boards) [15].

On-treatment Image Guidance

The use of megavoltage imaging for matching to the tumour and/or a bony surrogate is not acceptable and can result in significant geographical misses [16]. As detailed in the National Radiotherapy Implementation Group report (Figure 3), daily online imaging matching to the tumour with three-dimensional volumetric imaging (cone-beam computed tomography) or implanted fiducials is mandatory for lung SABR and repeat imaging during a treatment fraction should be considered, particularly if the treatment exceeds 30 min [15,16]. For larger tumours (>3.5 cm) real-
time tracking is feasible using kilovoltage fluoroscopy and can be considered to monitor intrafraction motion [17].

On-treatment Respiratory Motion Management
If available, monitoring for intrafraction changes with fluoroscopy, implanted fiducials or surface anatomy tracking can be used, although this requires specialist equipment. However, gating based on external surrogates alone should be carefully assessed, as tumour motion may not correlate with external body surface motion [18].

Clinical Considerations
Many different dose-fractionation schedules have been used for SABR. However, most centres use a risk-adapted scheme based on the tolerance of adjacent OARs. The OAR tolerances used in lung SABR have largely been based on the studies by Timmerman et al. [19,20] and other retrospective series. The doses endorsed by the UK SABR consortium are shown in Table 2 and are based on the ROSEL study [21]. However, these doses are empirically based on existing literature and are constantly being re-evaluated. When treating peripheral tumours, the grade 3 or higher toxicity rates are <5% [22]. Typical late toxicities include radiation fibrosis, rib fracture, intercostal neuralgia and pleural effusion. Irradiating tumours in the lower lobe and upper lobe may very rarely lead to liver dysfunction and brachial plexopathy, respectively. There are published reports of OAR tolerances for the brachial plexus [23,24], oesophagus [25] and pericardium [20], but the most robust data are on airways, lung and chest wall and are discussed below.

Airways
The phase II dose-escalation studies carried out by Timmerman et al. [20] clearly show that doses higher than 20 Gy in three fractions are associated with increased toxicity, as are tumours close to the main airways, the so-called no fly zone (Figure 4). Patients treated for tumours

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Table 1

<table>
<thead>
<tr>
<th>Conformity index</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>R100</td>
<td>Ratio of the 100% prescription isodose volume to the PTV</td>
</tr>
<tr>
<td>R50</td>
<td>Ratio of the 50% prescription isodose volume to the PTV</td>
</tr>
<tr>
<td>V95</td>
<td>Volume of the PTV receiving 95% (or higher) of the prescription dose</td>
</tr>
<tr>
<td>V90</td>
<td>Volume of the PTV receiving 90% (or higher) of the prescription dose</td>
</tr>
</tbody>
</table>

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Fig 2. Example of SABR plan for a right upper lobe tumour receiving 55 Gy in 5 fractions with isodoses as shown on the right in Gy. The ITV is in turquoise and the PTV is in blue (created by a 5 mm universal expansion margin).

in the peripheral lung had 2 year freedom from severe toxicity of 83% compared with only 54% for patients with central tumours [20]. However, more recent evidence has shown that using risk-adapted SABR schedules for centrally located lung tumours is associated with low rates of acute toxicity [24,26,27]. We await the results of the RTOG 0813 central SABR study and toxicity and efficacy will be further assessed in a multi-institutional EORTC LUNGTEC phase II study of using SABR to treat central tumours, which will start recruitment in 2015.

**Table 2**

Dose fractionation selection as detailed in the UK SABR consortium guidelines [53]

<table>
<thead>
<tr>
<th>Description</th>
<th>Dose</th>
<th>Schemata</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard fractionation</td>
<td>54 Gy in 3 fractions</td>
<td>![Diagram]</td>
</tr>
<tr>
<td>A tumour whose planning target volume (PTV) does not abut the chest wall or mediastinal structures</td>
<td></td>
<td>![Diagram]</td>
</tr>
<tr>
<td>Conservative fractionation</td>
<td>55–60 Gy in 5 fractions</td>
<td>![Diagram]</td>
</tr>
<tr>
<td>For tumours whose planning target volume touches or extends into the ribs/pleura.</td>
<td></td>
<td>![Diagram]</td>
</tr>
<tr>
<td>Very conservative fractionation</td>
<td>60 Gy in 8 fractions</td>
<td>![Diagram]</td>
</tr>
<tr>
<td>For tumours where the dose constraints for an organ at risk cannot be met at the 3 or 5 fraction constraints.</td>
<td></td>
<td>![Diagram]</td>
</tr>
</tbody>
</table>

**Chest Wall**

For the chest wall it is well documented that patients with tumours close to the ribs treated with SABR are at higher risk of pain and late rib fractures. Many dosimetric and patient-specific parameters have been found to be significant in individual series, although whether the chest wall dose should be reduced, particularly if it compromises PTV coverage, remains controversial [28–30]. In line with the established practice at the VU University Medical
Centre, Amsterdam, the Netherlands, in the UK we use a risk-adapted approach with a dose reduction from 54 Gy in three fractions to 55 Gy in five fractions if the PTV is in contact with the chest wall and the UK SABR consortium guidelines suggest chest wall dosimetric tolerances (Table 3).

Normal Lung Doses

Given that most patients who receive lung SABR have poor respiratory function, it is important to reduce the normal lung doses as much as possible to reduce the risk of radiation pneumonitis and fibrosis. Typically, the percentage volume of lung tissue receiving ≥20 Gy (V20) doses seen in lung SABR are much less than in conventional three-dimensional conformal radiotherapy and as a result the report rates of clinically significant pneumonitis (≥common toxicity criteria grade 3) are low. Small series have suggested dose constraints for symptomatic pneumonitis, with Bongers et al. [31] showing that a contralateral lung mean lung dose of >3.6 Gy was predictive of pneumonitis with volumetric modulated arc therapy and Guckenberger et al. [32] showing that the ipsilateral mean lung dose was 12.5 Gy (±4.3 Gy) compared with 9.9 Gy (±5.8 Gy) for patients who developed radiation pneumonitis. However, the number of patients who developed pneumonitis in these series was small and therefore it is difficult to make firm conclusions on absolute levels for lung constraints based on the existing data.

Clinical Evidence

Stereotactic Ablative Radiotherapy: Evidence in Early Lung Cancer

Lung cancer remains the leading cause of cancer mortality worldwide. Stage I non-small cell lung cancer (NSCLC) is curable and surgery is considered the standard of care for fit, good performance status patients, with 5 year overall survival of around 60% [33–35]. However, a significant proportion of patients with stage I NSCLC are elderly and/or have medical co-morbidities and therefore are not candidates for surgery. The National Lung Cancer Audit, the database of lung cancer treatment in England and Wales, reported that the overall resection rate for patients with histologically confirmed NSCLC was 20.8% and 21.4% in patients <65 years and aged 65–74 years, respectively, compared with 13.9% for patients aged >75 years in 2008–2012 [35]. The historical alternative curative treatment to surgery was conventional radical radiotherapy with historically low rates of 5 year local control (52–58%) and overall survival of 10–34% [36–39].

Suitable patients should be discussed in a multidisciplinary team meeting to ensure appropriate case selection. For those patients where pathological confirmation is not possible or has been unsuccessful, SABR can still be considered if there are clinical and radiological features suggestive of lung cancer (e.g. significant smoking history,

<table>
<thead>
<tr>
<th>OAR</th>
<th>Volume (cm³)</th>
<th>3 Fractions</th>
<th>5 Fractions</th>
<th>8 Fractions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Tolerance</td>
<td>Minor deviation</td>
<td>Tolerance</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>0.01</td>
<td>18 Gy</td>
<td>18–22 Gy</td>
<td>25 Gy</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0.1</td>
<td>24 Gy</td>
<td>24–27 Gy</td>
<td>27 Gy</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>0.1</td>
<td>24 Gy</td>
<td>24–26 Gy</td>
<td>27 Gy</td>
</tr>
<tr>
<td>Heart</td>
<td>0.1</td>
<td>24 Gy</td>
<td>24–26 Gy</td>
<td>27 Gy</td>
</tr>
<tr>
<td>Trachea/Bronchus</td>
<td>0.1</td>
<td>39 Gy</td>
<td>20–32 Gy</td>
<td>32 Gy</td>
</tr>
<tr>
<td>Lungs_GTV</td>
<td></td>
<td>V20 &lt; 10%</td>
<td>N/A</td>
<td>V20 &lt; 10%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V12.5 &lt; 15%</td>
<td></td>
<td>V12.5 &lt; 15%</td>
</tr>
<tr>
<td>Compliance with the following constraints may also be considered</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver (valid if &gt;1000 cc of liver imaged)</td>
<td>V15 &lt; 700 cc</td>
<td>N/A</td>
<td>V15 &lt; 700 cc</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>V21 &lt; 33%</td>
<td>N/A</td>
<td>V30 &lt; 60%</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>V15 &lt; 505</td>
<td>N/A</td>
<td>Mean &lt;20 Gy</td>
<td>32 Gy</td>
</tr>
<tr>
<td>Chest wall</td>
<td>30.0</td>
<td>30 Gy</td>
<td>N/A</td>
<td>39 Gy</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>37 Gy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
growing lesion and PET positivity) and the consensus of the lung multidisciplinary team that the diagnosis is lung cancer [40,41].

Despite there being a lack of phase III evidence for SABR, there is sufficient evidence supporting its role in managing early NSCLC, especially in medically inoperable patients with peripheral tumours. A pooled analysis of single centre and phase II studies reported 42% 3 year overall survival with SABR compared with 20% for conventional radiotherapy [42]. A more recent meta-analysis has shown 3 year local control of 88% combining the results from 30 studies [43]. These results are clearly superior to historical conventional radiotherapy series and similar to those achieved with surgery.

Indeed when allowance is made for patient selection, the survival outcome for SABR is similar to surgery. Thus, SABR is now regarded as a standard of care for medically inoperable peripheral early stage lung cancer and for patients that decline surgery [44,45].

A variety of SABR dose-fractionation regimens have been historically used to treat early lung cancer. However, systematic reviews report that dose-fractionation regimens that deliver a BED ≥ 100 Gy (estimated for acute effects assuming an α/β ratio of 10) are associated with better local control [46–48].

Senthil et al. [49] showed that local, regional and distant recurrence occurred relatively early after SABR treatment at 14.9 months (95% confidence interval 11.4–18.4), 13.1 months (7.9–18.3) and 9.6 months (6.8–12.4), respectively. In this large series, a small proportion of patients (6%) also developed new pulmonary lesions characterised as second primary tumours at a median of 18.0 months (95% confidence interval 12.5–23.5) after treatment [49]. In line with the UK SABR consortium guidelines we routinely carry out post-SABR computed tomography imaging at 6, 12 and 24 months after treatment to detect local, nodal and distant recurrences [50]. However, local control after SABR can be difficult to define on post-SABR radiological imaging due to the complex lung tissue changes that evolve after treatment [51–53]. PET/computed tomography after SABR can be used to aid the detection of local recurrence [54,55] as can careful assessment of serial computed tomography scans after treatment looking for the presence of high-risk features [56]. In this analysis by Huang et al. [56], significant high-risk features included an enlarging opacity at the treatment site, a sequential enlarging opacity, an enlarging opacity after 12 months, a bulging margin, loss of linear margin and air bronchogram loss. Of these six high-risk features the best individual predictor was the presence of an enlarging opacity occurring 12 months after treatment [56].

Radical differences between SABR and conventionally fractionated radiotherapy both in terms of practicality as well as the radiation dose delivered make it difficult to successfully complete phase III trials. There is non-randomised evidence showing improved quality of life with SABR compared with conventionally fractionated radiotherapy [57] and that quality of life is maintained after SABR [58]. However, we await the full results of the completed SPACE trial comparing 70 Gy/35 fractions with 22 Gy/three fractions [59] and the ongoing CHISEL trial comparing 54 Gy/three fractions/2 weeks versus 60–66 Gy/33 fractions/6.5 weeks.

In the absence of phase III data there is compelling data from population-based studies reported from Holland showing a clear improvement in overall survival from early lung cancer over a given period of time with the only change being the introduction of SABR. SABR did not negatively affect surgical excision rates or the resulting survival [60]. Given such a large body of evidence, most countries, including the UK, have now endorsed the use of SABR in medically inoperable early NSCLC patients.

**Stereotactic Ablative Radiotherapy for Lung Metastases**

No controlled trial of ablative treatment of lung metastases has ever been published. However, a commonly cited prospective international registry of patients having resection of lung metastases has shown a 5 year survival of 36% and a 15 year survival of 22% [61]. Even if one excludes cases of germ cell tumours from this series, the long-term survival is remarkably good, suggesting that some patients with lung metastases can be cured of their disease by surgery. It follows, given that SABR produces a high level of local control in primary lung cancer, this modality could be considered for patients with lung metastases who are medically unfit for surgery. A systematic review published in 2010 combining the results of six studies, analysed the outcome of 334 patients with lung metastases treated with SABR and reported a local control rate at 2 years of 78% and 2 year survival of 54% [62]. Further reports have shown a broadly similar outcome [63–65]. However, there is no consensus as to the criteria of patients who might benefit from SABR, although most centres do not treat more than two metastases at a time. The local control rate reported for metastases may be lower, at around 80%, than that generally obtained for treating primary lung cancer, where the results of a recent meta-analysis showed local control at 1 year of 96% and 88% at 3 years [43]. This could be due to metastases being intrinsically more radioresistant than lung primaries, different methods of assessing local control in patients who are clearly at greater risk of developing further lung metastases or perhaps re-seeding. A study comparing patients treated by surgery (in 76% of cases), which was the first choice with SABR reserved for patients thought to be medically inoperable, showed broadly similar outcomes, with 4 year rates of local control being 85 and 83% for SABR versus surgery, respectively, and remarkably good 5 year survival figures of 49% and 41% (not statistically significant) [65]. Thus, in conclusion, on the basis of limited evidence, SABR offers a reasonable alternative to surgical resection for patients with lung metastases with no evidence of extrathoracic disease and in whom SABR can be safely delivered. Prospective trials in oligometastases, such as the already commenced COMET trial, the SARON and CORE UK
SABR trials (which should open in 2015), should further clarify the role of SABR in oligometastatic disease.

**Research and Future Directions**

Reports from institution-based case studies are providing preliminary evidence for SABR as an effective treatment in operable patients as well as central tumours [24,26]. Hence, future trials in lung SABR are aimed at (i) comparing SABR with surgery in borderline operable patients, (ii) safety of SABR in treating central tumours, (iii) the role of SABR in treating oligometastatic disease.

**Discussion**

The introduction of SABR has been led by the major improvements in radiotherapy planning and delivery, as well as imaging technology over the past few years. PET scanning has improved the diagnostic accuracy of early stage lung cancer, in the absence of histology. Using the criteria of serial growth on imaging and PET positivity gives a predictive value in excess of 90% for the diagnosis of lung cancer [66]. 4DCT scanning enables the GTV and ITV to be precisely attenuating free filters and on board computed tomography can deliver treatment accurately in less than 15 min. This has all been introduced in the absence of phase III studies. However, given the superior dose distribution in terms of the dose to tumour and normal tissues it seems extremely unlikely that SABR will be inferior to conventional radiotherapy. The preliminary results of the SPACE trial have shown equivalence in terms of survival. However, the authors of this study recommended SABR because of its greater convenience for patients, with an overall treatment time of about a quarter of conventional radiotherapy, lower rates of toxicity and being more cost effective [59]. Therefore, SABR will continue to be the standard option of care for inoperable NSCLC in most oncology institutions.

**Conclusion**

Advances in planning, treatment delivery and on board imaging mean that ablative radiotherapy can be safely delivered in early peripheral lung tumours. Population-based outcomes will be crucial in supporting/establishing SABR as the treatment of choice in medically inoperable patients with such tumours. Randomised phase III trials will hopefully extend the evidence base and show safety and the utility of SABR in early central tumours and oligometastatic disease.

**Conflict of Interest**

There are no conflicts of interest.

**References**


