

Following SABR for early-stage NSCLC, two discrete patterns account for the majority of patients with recurrence (Chapter 2). Almost 50% of patients develop isolated distant recurrence, while one third develop potentially salvageable loco-regional recurrences without any distant disease. For the later, the median time to recurrence is 13 months, at which time CT surveillance should be performed most frequently.

Confounding the early diagnosis of local recurrence are post-SABR fibrotic changes. The systematic assessment of high-risk CT features (enlarging opacity at primary site; sequential enlarging opacity; enlarging opacity after 12-months; bulging margin; loss of linear margin and loss of air bronchogram) accurately differentiates local recurrence from fibrosis (Chapter 3). When three or more high-risk CT features are present, both the sensitivity and specificity for detecting recurrence are greater than 90%. In addition, delivery technique should be accounted for when assessing post-treatment fibrosis, as mass-like fibrosis is more likely with fixed-beam non-coplanar SABR delivery than when SABR is delivered using rotational arcs (Chapter 4).

Patients cured of their initial early stage NSCLC are at a significantly higher risk of having a second lung cancer than the National Lung Screening Trial population. Therefore, the use of CT surveillance post-SABR has the potential to improve survival, not only through detecting recurrences but also by detecting second primary NSCLC at an early stage (Chapter 5). However, re-irradiation in the thorax carries a significant risk of toxicity and accurately accounting for previously delivered treatment is complex due to post-SABR lung fibrosis. Deformable image registration is more accurate than rigid registration in accounting for previous radiation and using

this approach may reduce toxicity (Chapter 6). Additionally, such treatment should be delivered in the context of strict quality assurance for outcomes to be optimised (Chapter 7).

The use of SABR for central tumors is associated with a 9% risk of grade 3 and 4 toxicity, which is higher than that seen when treating peripheral tumors. However, with the use of an appropriate dose fractionation scheme, local control following SABR for central tumors is similar to that seen for peripheral tumors and the risk of treatment related mortality is less than 1% (Chapter 8). In addition to dose fractionation, multiple other factors need to be considered to ensure the risk of morbidity and mortality is minimized when SABR is used for central tumors. Attention should be paid to the high dose distribution within treatment targets and the accuracy of daily image guidance (Chapter 9). With these in mind, population based outcomes may be improved further if SABR is appropriately used for central tumors, particularly with strategies to reduce toxicity. Tumor tracking is one such strategy, enabling smaller treatment volumes even when the uncertainties of target delineation and tumor deformation are accounted for (Chapter 10).

The treatment of second primary NSCLC arising post-pneumonectomy is safe and can result in prolonged survival (Chapter 11 and 12). However when treating such patients, plans should be optimized to reduce the volume of normal lung exposed to radiation. Additionally, when large central tumors present post-pneumonectomy, hypofractionated radiotherapy may be safer than SABR.

To put SABR outcomes into context, they should be compared to surgery, the widely accepted standard of care. Propensity-matched analyses, using the same definitions of recurrence, suggest SABR outcomes are no different to those following surgery (Chapter 13). The choice between treatments should therefore be individualised, taking into account the risks of toxicity and how individual patients consider these. Following surgery for early stage NSCLC, 30-day and 90-day mortality may be as high as 5% and 10%, respectively (Chapter 14). Implementing SABR as the initial treatment of early stage NSCLC, and reserving surgery for the subgroup of patients with a salvageable recurrence, may represent a strategy that could reduce treatment-related risks for the majority of patients (Chapter 15).