Condensed lung cancer review

Stereotactic ablative radiotherapy (SABR) has become much more commonly used for the treatment of early-stage (Stage I-IIA), inoperable, peripheral lung cancers since 2013. This follows mainly from the CHISEL trial, which showed that SABR schedules of 54Gy/3# or 48Gy/4# (for tumours close to the chest wall) were associated with greater freedom from treatment failure in this patient group, compared to conventional or moderately hypofractionated regimens of 60-66Gy/30-33# and 55Gy/20# (Ball et al. 2019).

However, early-stage central tumours (located within 2cm of the proximal bronchial tree (PBT) or brachial plexus) are still treated more cautiously. Three-fraction SABR treatments have been shown to carry a high treatment-related mortality risk in this group (Timmerman et al. 2006). Since then multiple prospective and retrospective case series, using different dose-fractionation regimens, have yielded mixed results (UK SABR Consortium 2019). The NORDIC HILUS trial found that SABR toxicity was significantly worse in patients whose tumours were close to the main or lobar bronchi, suggesting that 'central' tumours should be further segregated according to anatomical location (Lindberg et al. 2017). The SABR Consortium guidelines recommend a cautious fractionation schedule of 60Gy/8# for patients whose tumours lie 1-2cm from the PBT, based on some promising retrospective data . In reality, there is wide variation in the treatment of this patient group. 'Ultracentral' tumours (<1cm from the PBT) continue to be treated by moderately hypofractionated, conventional, or accelerated regimens (UK SABR Consortium 2019).

During the COVID pandemic, hypofractionated schedules have been used where possible (Faivre-Finn et al. 2020). Newly established schedules include a 30-34Gy/1# SABR dose for patients with small, peripheral tumours and good performance status, and a 50-60Gy/15# schedule for (ultra)central tumours unsuitable for SABR. New indications for short SABR schedules include 48-54Gy/3# schedules for patients whose tumours lie close to the chest wall, and increasing use of 50Gy/5# for central tumours that would have previously been considered for 8# SABR. The focus on (ultra)hypofractionated regimens may well continue beyond the pandemic. (Banfill et al. 2020)

Trials comparing SABR to surgery in operable patients have struggled with poor accrual (Chang et al. 2015). Based on clinical consensus, the NICE guidelines recommend that lobectomy be performed in preference to SABR, but to consider SABR as an alternative to surgery when only a more conservative procedure can be tolerated (National Institute of Health and Care Excellence 2019). Again, the COVID-19 pandemic has increasingly led to SABR being used in operable patients due to reduced surgical capacity.

For resectable Stage IIIA-N2 NSCLC, NICE guidelines recommend consideration of neoadjuvant chemoradiotherapy followed by surgery as a first-line option, based on some evidence that it improves progression-free survival (National Institute of Health and Care Excellence 2019). However, only two small trials compare this to chemoradiotherapy alone, and there is less evidence of an overall survival benefit (Albain et al. 2009; Eberhardt et al. 2015). Furthermore, Stage III NSCLC patients rarely have a good enough performance status to undergo this treatment, and so despite including trimodality therapy in the decision tree, we do not expect that it can be used frequently (Adizie et al. 2019).
Postoperative radiotherapy (PORT) in Stage III-N2 patients is also contentious. Systematic reviews have suggested that PORT does not provide benefit in these patients, however the included studies used radiotherapy techniques that would now be considered outdated, and

some more contemporary retrospective studies have suggested that PORT may be beneficial (Burdett et al. 2016; Robinson et al. 2015). More recently, the LungART trial has shown that PORT (54Gy/27-30#) is associated with increased cardiopulmonary toxicity, with no survival advantage, in Stage III-N2 disease (Le Pechoux et al.) Nevertheless, PORT may yet be useful in a subset of these patients, such as those with R1 resections or extracapsular N2 disease.

Targeted therapies such as tyrosine kinase inhibitors (TKIs) can now be given to patients with locally advanced NSCLC with the relevant sensitising mutation. Theoretically this could reduce radiotherapy demand for Stage III NSCLC; however, in current practice targeted therapies are used mainly in the Stage IV patient cohort. This, combined with the fact that only a minority of patients carry the relevant driver mutations (National Lung Cancer Audit 2020), means that targeted therapies do not currently impact radiotherapy fraction use.

Palliative radiotherapy for NSCLC metastases to the brain decreased after the QUARTZ trial, which showed that there was no significant difference in overall survival or QALYs between groups treated with whole brain radiotherapy (WBRT) or supportive care only (Mulvenna et al. 2016). However, WBRT is increasingly used nowadays in patients with multiple brain metastases, as many of these patients have a better performance status than those recruited in QUARTZ. We have adopted the RCR recommendations for treatment of brain metastases, which include consideration of adding WBRT to stereotactic radiosurgery (SRS) in patients who are relatively well and with a lower burden of cerebral disease alone (Royal College of Radiologists 2019).
Patients with fewer brain metastases can undergo surgery or stereotactic radiosurgery (SRS) alone. Since the brain is often the first site of metastasis for NSCLC, some of these patients will have radically treatable thoracic disease in addition to their brain metastases. Both of these sites can therefore be treated radically with radiotherapy following systemic therapy, with good results (Schroeder et al. 2019). There is growing interest in using SABR to treat low-burden synchronous metastases elsewhere, and this is currently being reviewed in the SARON trial (Conibear et al. 2018).

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