Editor's note:
In the era of personalized medicine, a critical appraisal new developments and controversies are essential in order to derived tailored approaches. In addition to its educative aspect, we expect these discussions to help younger researchers to refine their own research strategies.

Controversies on Lung Cancer: Pros and Cons

Rebuttal from Ms Woodford and Dr Senthi

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Professor Nestle and Dr. Belderbos' argument against the use of stereotactic body radiotherapy (SBRT) for central non-small cell lung cancer (NSCLC) centers on the fact there is little prospective high quality evidence to declare it safe. This is indeed true and highlights the importance of their multi-national phase II study (LungTech) and RTOG 0813 in guiding optimal patient care (1). However, there are aspects of their argument that should be discussed further, in particular data referenced from Cannon and Langendijk which may not be applicable to T2N0 central NSCLC.

The dose escalation study from Cannon *et al*. assessed patients with locally advanced NSCLC, the vast majority of whom had stage III disease (2). SBRT for such disease represents a significantly higher risk scenario and cannot be used to infer the risks of treating central T2N0 disease. Using a schedule of 50 Gy in ten fractions (BED_3 =133 Gy), Milano *et al*. observed a 40% (4/10) crude risk of treatment related death for node-positive stage II-III NSCLC following SBRT (3). Despite almost doubling the biologic equivalent dose, Chaudhuri *et al*. found an SBRT scheme of 50 Gy in five fractions (BED_3 =217 Gy) for node negative tumors directly abutting the major airways (including the trachea), resulted in no grade 2 or higher toxicity at 2 years (4). Even with small patient numbers it is clear there is a distinction between these clinical scenarios.

The endobronchial brachytherapy study from Langendijk *et al*. indeed found that almost half the patients receiving a single 15 Gy fraction died of massive hemoptysis (5). However, as stated in the paper, using a brachytherapy prescription of 15 Gy at 1 cm, results in catheter and potentially bronchial surface doses of 90-105 Gy. Here the principle organ at risk receives a significantly higher dose than the tumor itself and such toxicity is not surprising. Exactly the opposite is true with SBRT, whereby modern delivery techniques result in planned doses to the adjacent bronchus being significantly less than the center of the tumor.

Professors Nestle and Belderbos also postulate that conventional radiotherapy for large and/or central tumors has the potential to improve lung reperfusion, while SBRT will almost certainly reduce it and consequently decrease pulmonary function. Although we have witnessed extreme examples of this (6), generally following SBRT patients do not appear to suffer any quality of life detriment (7). In a prospective study of patient reported quality of life, central location did not influence global health status and respiratory symptoms, respectively measured by standardized EORTC questionnaires QLQ C30 and QLQ LC13 (8).

Clearly SBRT for central tumors has complexities beyond those for peripheral tumors and should not represent the starting point for a new SBRT program. The need for more high quality data has rightly compelled some within the radiation oncology community to place considerable effort into seeking it. Until then, the available data appears to be sufficient for clinicians to offer willing

patients the opportunity for cure when SBRT is their only or preferred treatment option.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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