Letter to the editor concerning Senan et al., [Radiother Oncol 2004;71:139–146]

To the Editor

We read with interest the article of Senan and coauthors ‘Literature-based recommendations for treatment planning and execution in high-dose radiotherapy for lung cancer’ [7]. In this synopsis, clinically relevant information is presented for modern three-dimensional treatment planning of lung cancer patients, based on a large number of articles addressing primarily technical issues. In many aspects, this analysis should obviously be of great value for every radiation oncologist. It seems questionable, however, whether the recommendations on appropriate photon energies, i.e. ≤10 MV, should be generally accepted in clinical routine, given that a large study comparing different energies for a significant number of patients has yet to be performed. In particular, the following questions arise:

1. The recommendation to prefer low to high photon energies when irradiating lung tumours is based primarily on a decreased electron disequilibrium with lower photon energies compared to higher energies. The increased lateral electron transfer with higher photon energies results in a broadening of the penumbra and a decrease of dose at the target in the lung. This problem has repeatedly been reported in the physical literature.

   The largest differences between low- and high-energy photons were found in experiments with single photon fields. For the use of opposed fields, the differences between low and high-energy photons were found to be pronounced less compared to single photon fields regarding both penumbra width (difference between 6 and 18 MV ca. 2.5 mm for medium-sized opposed fields) and reduction of central axis dose (difference <5% for opposed fields). Considering the wide spread use of conformal techniques, it should be discussed whether these recommendations also apply for multiple fields or even intensity modulated radiotherapy [1–3,5,11].

2. Much of the hesitation in using high-energy photon beams for lung treatments results from the inaccuracies of traditional dose calculation algorithms, which do not account for the increased electron range in the lower density lung material. For these correction-based algorithms there is ample evidence of their inability to predict the dose accurately in low-density media. Thus it is reasonable to suggest that in the absence of a dose calculation algorithm that fully accounts for the lateral electron range in low-density media, lower energy photon beams should be preferred over higher energies to ensure target coverage.

   However, conformal dose distributions using traditional dose calculation algorithms often show lower entry doses, lower lung doses and higher dose homogeneities in the target with high compared to low photon energies. These effects are more pronounced in patients with large transversal and lateral diameters. Being aware of the reported benefits of low photon energies regarding beam width and target dose on the one side, however, being unable to quantify them on the other side, renders decision making for the radiation oncologist a difficult job.

   Fortunately, more and more current treatment planning systems have, or are in the process of developing, superposition/convolution-based algorithms. These algorithms can correct for electronic disequilibrium conditions to first order, though small discrepancies with these algorithms remain at the boundaries of different density media. Given that we now have sufficiently accurate algorithms, the question of energy comes down to balancing the increased lateral spread of dose with higher energy beams, with the improved depth-dose penetration characteristic of higher energy beams along the beam axis [3,6].

3. In clinical routine, most lung carcinomas treated with radiotherapy are not located in the periphery of the lung (patients with these tumours preferably undergo surgery). The majority of tumours are situated centrally, adjacent to or infiltrating the mediastinum. Moreover, practically all lymph nodes, whether irradiated electively or not, are found in the mediastinum or the peribronchial regions. Most treatment plans therefore prefer beam arrangements where the major portion of the dose is delivered by fields transversing the mediastinum. Electron scattering in the mediastinum is much lower than in the lung. Lateral or oblique fields passing through the lung are usually low-weighted for maximum lung sparing. The question is whether the recommendation to use low-energy photons also apply to centrally located tumours. It also appears necessary to consider tumour sites and radiotherapeutic techniques when selecting photon energy.

   A whole variety of open questions is related to the radiation treatment of lung tumours involving dose, extent of the clinical target volume, tumour movement due to respiration, interobserver variability in target volume definition, estimation of toxicities and others. The amount of errors from all these unresolved fundamental issues by far exceeds variations arising from different photon energies [4,8–11].

   In summary, the selection of photon energies in the treatment of lung cancer patients remains a complex task. From the clinical point of view, the selection of photon energy should be a differentiated process, considering in particular also patient-, tumour- and treatment-specific parameters.

References

Correlation between dose subfractions: in regard to Tomé et al. [Radiother Oncol 2004;72:113–114]

To the Editor

With great interest, we read the debate about the theoretical predication on the effect of prolonged fraction delivery time published in this journal [3,4,6]. The influence of prolonged fraction delivery time is an important issue for clinical practice and has been addressed by many other investigators [1,5,7]. All studies pointed to the significant impact of prolonged fraction delivery and cautioned the clinical practice to take prolonged dose delivery time into consideration. The question remains, whether the model prediction is consistent with experimental observations. Tomé et al. [6] argue that this effect is well predicted by current biological repair models in the range of conventional dose fraction. However, we found that there was a misinterpretation of the linear–quadratic formulas in Tomé et al.’s model calculation [6], and this error was not well identified in Mu et al.’s response letter [4].

The problem arose because of the misapplication of Eq. (4) in Tomé et al.’s article [6], instead of Eq. (3) as mentioned by Mu et al. [4]. Eq. (3) is appropriate to use for the calculation of the surviving fraction for a single subfraction of dose $\Delta$. However Eq. (4) is incorrect for the calculation for $m$ subfractions when the separation time between subfractions $\delta T$ is smaller than or close to the repair half-time $T_{1/2}$ of cell sublethal damage. The underlying assumption in Eq. (4) is that there is no correlation among fractions; the sublethal damages produced by the current fraction are completely repaired before the next fraction starts. This premise is generally satisfied in the commonly-used daily fractionation (the separation time is about 24 h while the repair half-time is at the order of one hour), therefore Eq. (1) in Tomé et al.’s paper [6] is valid. However, the premise does not exist in the subfractionation experiments of Mu et al. [4]. In their experiment, $\delta T$ is about 3 min while the derived $T_{1/2}$ is 24 min. In this case, the general form of $G$ should be used [2,7]. Nevertheless, the calculation with the detailed subfraction scheme will produce almost the same results as calculated with Eq. (4) of Mu et al.’s paper [3]. As a matter of fact, Wang et al. [7] have demonstrated that the dose protraction effect is largely determined by the overall delivery time, regardless of the dose rate pattern within the delivery time.

It is certainly encouraging to see Tomé et al. [6] made an effort to address the inconsistency of theoretical predications with Mu et al.’s in vitro measurements [3]. However, they did not provide a valid argument in their Letter to the Editor [6]. Whether or not the biological modeling can correctly predict and quantitate the effect of prolonged fraction delivery time remains open to debate and must ultimately be validated in clinical studies.

References