Peer Review File

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Reviewer A:

- Comment: The only thing I miss in this excellent overview is how to interpret the post-RT fibrosis. The authors address this topic twice but only rather short (line 123-124/514-519). In clinical practice, it can be very challenging for the clinician and often causes unrest with the patients. A number of interesting papers were published regarding this subject, e.g. PMID 27325481, 29102278.

  Answer: Differentiation of local recurrence/persistence and radiogenic fibrosis is not always easily made, and the lack thereof can be unsettling for clinicians and patients alike. However, distinguishing between post-radigenic fibrosis and local recurrence or persistence is of great importance when it comes to initiating a salvage treatment. Therefore, PET-imaging is suggested in the clinical part of the article and also in international guidelines as one way to determine the dignity of the lesion, however this can be limited by disturbance due to inflammatory reactions. A promising approach in this matter is radiomics and is briefly discussed in the technical part. Literature on high risk CT features is indeed interesting and of importance to the readership of this article, however the topic of post-SBRT follow up allows for a standalone review article. Limited in respect to the given word count we have added a sentence acknowledging high risk CT features.

- Comment: Please enter space between the words stages and T1

  Answer: We removed the space between the words.

- Comment: Also, what can we do in case a local recurrence is confirmed: re-irradiation, surgery? I would strongly suggest to add a paragraph on this matter.

  Answer: We added a paragraph on the specific topic of salvage SBRT after initial SBRT (lines 286).

- Comment: Specify the overall survival do you mean long-term e.g. 5-year?

  Answer: We specified overall survival as OS at 5 years.

- Comment: Could you address the use of a cut-off value, above which treatment is justified?

  Answer: In patients without biopsy confirmation, the treatment decision should be made after multidisciplinary discussion according to international guidelines (2–4). While biopsy confirmation is desirably, obtaining histological confirmation is

not always feasible. In the article cited, the formula for calculation the probability of malignancy is multiparametric and complex (1), and serves as an instrument of assistance in morphologic tumor evaluation. However exact the tool, the need for interdisciplinary treatment decisions according to institutional standards is still called for. To the best of our knowledge there is no literature providing high grade evidence in terms of associating a cut-off percentage to indicating treatment start, or an association with outcome.

- Comment: Please enter space between the bracket and “and”

  Answer: The space was added.

Reviewer B:

- Comment: Page 6 line 119. Expand on what is considered "high risk features" that would result in the recommendation for chemotherapy after SBRT and what data that is based on.

  Answer: We have added some high-risk features according to the NCCN guidelines, where the evaluation of adjuvant chemotherapy is recommended. The guideline provides literature that the recommendation is based upon. We feel that citing the studies would be beyond the scope and word limit of this article, as they are very specific to stage IB and higher.

- Comment: Page 6 line 131 be specific about what outcomes were better in the surgery group than the SBRT group the meta-analysis

  Answer: We specified that improved outcome in both (matched and unmatched) groups after surgery (compared to SBRT) was reported surgery in terms of overall survival and cancer-free survival.

- Comment: Typo on page 8 line 179

  Answer: We removed the duplicate/typo from line 179.

- Comment: Discuss in more detail the options for fractionation schemes (8, 10, 12 fractions) for ultracentral tumors.

  Answer: SBRT to ultracentral tumor location can also be subject for a standalone article. As the wordcount for this article is unfortunately limited, we have added the setup of the SUNSET trial as an example of a trial currently seeking to evaluate a safe and efficient fractionation schedule.

References

1. Herder GJ, van Tinteren H, Golding RP, Kostense PJ, Comans EF, Smit EF, u. a. Clinical prediction model to characterize pulmonary nodules: validation and added value of 18F-fluorodeoxyglucose positron emission tomography. Chest. Oktober 2005;128(4):2490–6.

2. Wood DE. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for Lung Cancer Screening. Thorac Surg Clin. 1. Mai 2015;25(2):185–97.

3. Videtic GMM, Donington J, Giuliani M, Heinzerling J, Karas TZ, Kelsey CR, u. a. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. Pract Radiat Oncol. 1. September 2017;7(5):295–301.

4. Guckenberger M, Andratschke N, Dieckmann K, Hoogeman MS, Hoyer M, Hurkmans C, u. a. ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer. Radiother Oncol. Juli 2017;124(1):11–7.