Peer Review File

Article information: http://dx.doi.org/10.21037/tlcr-20-805

Reviewer A:

We thank the reviewer for these constructive comments and have tried to follow them in the revised manuscript.

Comments:

1. This paper is not only for radiation oncologists only and there are a lot of abbreviations which need to be defined for non-radiation oncologists.
Reply: Indeed, the reviewer raises a relevant point. We have explained now all abbreviations throughout the manuscript at the point of first appearance.

2. Line 84 Should you not put therapeutic radiation oncology with a capital like for European Society?
Reply: changed as requested

3. Line 171 IOA should be defined
Reply: done

4. Line 183 OAR same comment
Reply: done

5. Line 191 TPS should be written treatment planning system
Reply: done

6. Line 203 L=_600 _ should be omitted
Reply: done

7. Line 206 apply: A simple should probably be apply: a
Reply: done

8. Line 217 I am wondering if you should not add a s to guideline
Reply: not done, as it is only one guidenline

9. Line 306 RTQA should be defined
Reply: done

10. Line 313 RT planning (39) should probably be planning (39)

Reply: it is radiotherapy planning, should now be clear with abbreviations explained

Reviewer B:

We thank also this reviewer for the valuable comments and have tried to follow them.

Comments:

1. Although the manuscript is overall well written, some sentences may benefit from editorial review by a native English speaker.

Reply: indeed, none of the authors is a native English speaker. Therefore, we would be happy, if during final editing, an editorial language review would be provided.

2. Line 67: Please add a citation supporting the statement of superior diagnostic accuracy of FDG-PET/CT.

Reply: done

3. Line 69 & Abstract: FDG-PET/CT is described as an "indispensable standard tool for diagnostic workup, staging and response assessment". Although increasingly used in clinical practice, I would argue that the role of PET-CT for response assessment is not as clearly defined (i.e.: recommended in guidelines) as presented here. If the authors agree, they may consider rephrasing (e.g. "indispensable standard tool for diagnostic workup and staging, and a useful modality for response assessment", or similar).

Reply: done as proposed

4. Line 85: To my knowledge, ESTRO stands for "European Society for Radiotherapy and Oncology" (see e.g. estro.org). Please also ensure that all other abbreviations are defined at first mention (e.g. IAEA is not defined; NSCLC is defined on line 88, but previously mentioned on line 41).

Reply: indeed, the reviewer is right, we have corrected this and we have also explained all abbreviations at their first appearance.

5. Lines 123-125: Please add a citation supporting the statements on the predictive value of PET-CT.

Reply: done as requested

6. Line 155: The statement "…residual post-chemotherapy FDG-accumulations should not be used for the delineation of the gross tumor volume" is slightly confusing, as the reader may conclude that these areas should be excluded from the

GTV (which is obviously not correct, as described in other parts of the manuscript). Suggest rephrasing for clarity.
Reply: rephrased to: “As even one cycle of chemotherapy (30) can lead to a decrease in FDG-uptake, residual post-chemotherapy FDG-accumulations should not be used as the only source of information for the delineation of the gross tumour volume. When sequential chemotherapy is followed by definitive RT, it is highly recommended to perform a first FDG-PET-CT scan before induction chemotherapy and a repeat chest CT with IV iodine contrast prior to the start of RT. If this is not done, the pre-chemotherapy-CT scan might inform GTV-delineation better than post-chemotherapy-PET.”

7. Lines 206 – 216: The authors describe the approach taken for FDG-based target volume definition, including a standardized semi-automated contouring algorithm used for the majority of cases in the PET-plan trial. Coming from a center that does not have access to this method, I wonder if a recommendation (or statement) could be included that gives a more specific, practical recommendation on common thresholds (e.g. for percentage of SUVmax) used for contouring in clinical practice. I understand that citation 31 is used as a general reference for the integration of PET-CT into radiotherapy workflows, but some readers (incl. myself) may not have access to the full text. If specific recommendations cannot be made due to lack of data, perhaps a statement can clarify this.
Reply: we have now added some more information on the use of automatic contouring: “Even when PET is co-registered with CT, any approach other than that should be used with caution in experienced centers. When there automatic contouring algorithms are used (even “simple” SUV- or percent-thresholding), those should be calibrated and their results should always be validated in clinical routine, e.g. versus well visible findings in CT.”

8. Line 301: I believe “Mountain-Dresler” (not Dressler) is correct.
Reply: indeed. Corrected.

9. Table, line 369: “Do only use a PET/CT scan for contouring in a planning system, if it was acquired in RT treatment position” – Please rephrase this statement, as not all centers are able to acquire a PET/CT scan in treatment position. The statement currently reads as if use of a PET/CT scan not acquired in treatment position was forbidden, which is contrary to ESTRO ACROP guidelines (“PET-CT scan is recommended and should be done preferably in planning position”).
Reply: Indeed, it is a crucial issue how to use PET-scans, which have not been acquired in treatment position. We have now added some more explanation: “Do only

coregister a PET/CT scan for contouring in a planning system, if it was acquired in RT treatment position. If not, view images separately side by side."

10. Table, line 379: I believe "ITV" should be "CTV" here?
Reply: indeed, corrected.