

Peer Review File

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Responses to reviewer A

Comment 1: In the discussion line 247 u mentioned about use of PET for better staging, but did not seemed to be analysed in your data. was there a difference in failure pattern (LF, RR, DM) based on the use of PET staging given about a third of your patients did not seem to have done it?

Reply 1: Please accept our sincere gratitude for your valuable questions.

First of all, we have re-checked this discussion in line 247 concerning PET-CT, it is kind of unsuitable to discuss this here, thus we decide to delete and revise this discussion.

Second, before the treatment of SBRT for the patients with early-stage non-small cell lung cancer, we indeed recommended PET-CT scanning for patients to improve staging, but not all the patients were willing to pay for the relative high fees for the PET-CT. However, it is certain better to perform radiotherapy for these patients rather than not.

Third, if the included patients did not perform PET-CT, the positive imaging features of malignancies by CT or consensus of the multidisciplinary team of surgeons, oncologists and radiologists were necessary. we have revised the inclusion criteria as follow in lines 113-120: Patients who were unable or refused to undergo a surgical operation after multidisciplinary discussion received SBRT. Patients who had American Joint Committee on Cancer (AJCC) clinical stage I or II T1–3N0M0 NSCLC, based on either radiographic evaluation or biopsy confirmed by pathology, were included. Patients who did not have biopsy confirmation should be in accord with the following criteria: (1) positive imaging features of malignancies, such as progressive enlargement of lesions, the increase in the density or proportion of ground-glass opacity (GGO), or the appearance of vascular perforation and spiculation signs at the edge in contrast-enhanced CT or 1-3 mm thin-section CT; (2) positive lesions in positron emission tomography/computed tomography (PET/CT); (3) consensus of the multidisciplinary team of surgeons, oncologists and radiologists.

Finally, we revised the Table 1 and the expression in the discussion lines 248-254 as follows: In line with Timmerman *et al.* [10] and others [18, 19], DM and RR was the predominant type of recurrence. Sun *et al.* [16] reported that about one-third of the patients who developed DM or regional nodal recurrence within 6 months that was thought to potentially have arisen from an occult tumor. The adjuvant treatment of chemotherapy, or especially immunotherapy, might effectively manage occult metastases and therefore improve patients' prognoses.

Changes in the text: I have modified our text as advised (see lines 113-120; lines 249-255), and all the changes have been marked in red.

Comment 2: Quite a few of the patients did 8 or more fractions, despite mostly being peripheral and the mean size is 2.2cm. could you comment why this is so?

Reply 2: Thank you for your valuable questions. The expression of "The OAR constraints u mentioned were followed i.e. RTOG and AAPM" was a clerical error. Indeed, all the OAR dose constrains were performed and optimized to limit high doses and protect organs at risk, and

dose limits were adhered to institutional practices.

Changes in the text: I have modified our text as advised (see lines 134-137), and all the changes have been marked in red.

Comment 3: The OAR constraints u mentioned were followed i.e. RTOG and AAPM do not have 8 or fraction regimens, could i suggest you rephrase this adhered to institutional practices or create a table for the OAR constraints used.

Reply 3: Thank you for your suggestion. The expression of “The OAR constraints u mentioned were followed i.e. RTOG and AAPM” was a clerical error. Indeed, all the OAR dose constrains were performed and optimized to limit high doses and protect organs at risk, and dose limits were adhered to institutional practices.

Changes in the text: I have modified our text as advised (see lines 134-137), and all the changes have been marked in red.

Comment 4: In the highlights box, point 3. Distant mets driven by modality. What does this mean? can i suggest rephrase it to distant mets is the most common failure pattern. You might as want to emphasis the low <5% G3 toxicity outcomes at 5 years.

Reply 4: Thank you for your valuable suggestion. First of all, this sentence is indeed difficult to understand, so we decide to delete this sentence and expression. Second, we totally agree your advices, and we have changed the highlights box as “SBRT achieved high rates of tumor control and low toxicity for patients with early-stage NSCLC; This study offered robust long-term outcome data of SBRT in Chinese population, which was few reported in China before” in lines 49. Thirdly, we added some discussion about the highlights of our study in lines 265-269.

Changes in the text: I have modified our text as advised (see line 49 and lines 265-269), and all the changes have been marked in red.

Comment 5: Where there a difference in failure pattern based on histology? e.g. non squamous vs squamous.

Reply 5: Thank you for your valuable question. We only collected 28 patients with early-stage squamous cell lung cancer who received SBRT, thus this sample size is not representative and sufficient enough to analyze the differences in failure pattern based on histology. In addition, we discussed this question in the limitation as follow: Third, due to the relatively small sample size, we did not analyze the differences of failure patterns based on subtype histology, and we will collect a larger cohort of patients than this study to finish this analysis in the future.

Changes in the text: I have modified our text as advised (see lines 276-279), and all the changes have been marked in red.

Comment 6: This article does add to the general knowledge to SBRT lung outcomes and in this light is helpful. However, there is little to new knowledge it provides.

Reply 6: Thank you for your valuable comments. First, although several foreign studies reported the clinical outcomes of SBRT in early-stage lung cancer, the popularization and utilization of SBRT is later in China than in foreign countries, as let alone the reports of long-term outcome data of SBRT in Chinese population. Second, we have revised the highlights and

emphasize the rarity of similar reports in China, and we have changed the highlights box as “SBRT achieved high rates of tumor control and low toxicity for patients with early-stage NSCLC; This study offered robust long-term outcome data of SBRT in Chinese population, which was few reported in China before” in lines 49. Thirdly, we added some discussion about the highlights of our study in lines 265-269.

Changes in the text: I have modified our text as advised (see line 49 and lines 265-269), and all the changes have been marked in red.

Responses to reviewer B

Comment: The authors conducted a retrospective study to examine the effectiveness and adverse effects of SBRT for 145 patients with medically inoperable NSCLC. They concluded that SBRT achieved excellent local control and minimal toxicity in patients with early-stage NSCLC. The most common sites of recurrence were distant metastases which was driven by tumor biology rather than the radiotherapy modality being SBRT itself.

I think this paper summarizes the data of their hospitals well. However, there are many papers on the treatment results of SBRT for NSCLC. I think this paper lacks novelty. In addition, I think it would be better to add the data of FEV1 (L) to Table 1.

Reply: Thank you for your valuable comments.

First, although several foreign studies reported the clinical outcomes of SBRT in early-stage lung cancer, the popularization and utilization of SBRT is later in China than in foreign countries, as let alone the reports of long-term outcome data of SBRT in Chinese population. Second, we have revised the highlights and emphasize the rarity of similar reports in China, and we have changed the highlights box as “SBRT achieved high rates of tumor control and low toxicity for patients with early-stage NSCLC; This study offered robust long-term outcome data of SBRT in Chinese population, which was few reported in China before” in lines 49. Thirdly, we added some discussion about the highlights of our study in lines 265-269. Finally, we have added the data of FEV1 (L) to Table 1.

Changes in the text: I have modified our text as advised (see line 49, lines 265-269 and Table 1), and all the changes have been marked in red.