**Author's response to reviews**

**Title:** Stereotactic body radiation therapy for post-pulmonary lobectomy isolated lung metastasis of thoracic tumor: survival and side effects

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**Version:** 3

**Date:** 2 September 2014

**Author's response to reviews:** see over
Dear reviewers and editor,

Thanks for your comments. According to your opinions, we already modified our manuscript and we would like to answer them in details here.

Reviewer 1

Major

#1. Inclusion criteria

I feel the number of patients who received SBRT after lobectomy was small (<10%) in this study. That might be related to the inclusion criteria for this study. Please clarify the criteria for ILM, especially in distinction with a second primary lung cancer.

The authors reviewed patients treated during Oct 2008 and Dec 2013. The last period of the follow-up was also Dec 2013. So, the follow-up period was too short (median 14.0mo, range 6.0-47.0mo) to evaluate OS or local control. Why did the authors include patients with such a short follow-up?

We know it is very difficult to distinguish the metastatic tumor and the secondary lung cancer. In our study, only 4 patients received tissue biopsy and it had been confirmed as a metastatic tumor. ILM in this study was defined as a circular shape 18F-fluorodeoxyglucose positron-emission tomography (FDG-PET) or computed tomography (CT) imaging, without
any lobulated signs of original tumor within 3 years after pneumonectomy.

Among the patients with thoracic tumor, lung metastasis usually was multiple. And in such situation, chemotherapy or target therapies are the suitable options. A few patients were diagnosed with single isolated lung metastasis during follow-up. So, we identified only 23 patients and treated them with SBRT. In one paper you mentioned in the comments, the authors only identified 13 patients out of 406 patients treated with SBRT after pneumonectomy (Thompson R, et al. J Thorac Oncol 2014).

We are sorry for this mistake. The time we retrospectively analyzed was from Oct 2009 to Dec 2013 and most of patients were diagnosed with ILM in the recent years, consequently leading to a somewhat short follow-up period. In our clinical practice, the median OS among the patients with metastatic thoracic tumor was 10-14 months. We also noticed that if one metastatic tumor emerged, more metastatic tumors would emerge soon. In this study, 78.3% of patients received chemotherapy or EGFR-TKIs, but the survival time was still lower than the second primary tumor which reported by Senth S et al (J Thorac Dis 2013).

According to your opinions, we had already added the definition of ILM in the “Materials and methods” section in the revised MS. In addition, we addressed the limitation of the number and follow-up period
#2. DVH parameters for RP

The authors chose $V_{5-30}$ and MLD of ipsi-, contra- and bi-lateral lungs, and PTV volume for the DVH analysis. From Table 4, $V_5$ for the ipsilateral lung was higher than expected, even in the RP 0-1 group. This may be related to lung volume reduction by the prior lobectomy. I suspect that a small lung volume after lobectomy was related to the high $V_5$ value, that leads to such a high incidence of RP.

Please provide the data on tumor location (ipsi- or contra-lateral to lobectomy) and lung volumes separated into ipsi- and contra-lateral.

The data on tumor location was summarized in Table 1. Totally, 52.2% (12/23) and 47.8% (11/23) of ILM were located on the contra-lateral lobe and the ipsi-lateral lobe respectively.

The lung volumes separated into ipsi- and contra-lateral lobe were added in the Table 2. In summary, the median volume of the contralateral lung was 1373.4 cm$^3$, with a range of 1255.8-1712.3 cm$^3$. The median volume of the ipsilateral lung was 942.2 cm$^3$, with a range of 786.8-1233.4 cm$^3$.

#3. Comparison with reports on SBRT after pneumonectomy

As the authors pointed, little data are known specific to the
post-lobectomy situation. However, a few papers are available on SBRT after pneumonectomy. Please add a discussion on comparison with the papers.

*Sorry for our negligence. The corresponding discussion and cited papers had been added in the revised MS.*

**Minor**

#1. L81-83: I cannot find the description on the recommendation of SBRT for ILM. The authors cited an old version of NCCN guideline. Please cite a newer version, and clarify which section describes the recommendation.

*We already cited a newer version of NCCN guideline in the revised MS. The section describes the recommendation is:*
#2. L125: There are many PET tracers including FDG, FLT, Met, and so on. Please specify the tracer for PET.

*The PET tracer used in this study was $^{18}$FDG-PET. We already had specified it in the revised MS.*

#3. L141-143: Why did the start date of evaluation differ between OS and PFS? OS was defined periods between the start date of treatment and the last follow-up, while PFS was periods since the last date of SBRT.

*Sorry for our mistakes. OS was also defined from the last date of SBRT in this study. We already made the changes in the revised MS.*

#4. L167-168: Can the “initial stage after surgery” be rephrased as pathological stage confirmed with surgery?

*Thanks for your recommendation. We already rephrased these words in the revised MS.*

#5. L180: Please clarify the type of “image guidance during treatment.” Is it stereo fluoroscopy like ExacTrac, cone-beam CT or others?

*Thanks for your recommendation. We already specified the image guiding technique as the cone-beam CT in the revised MS and table 2.*

**Discretionary Revisions:**
#1. L242: The authors cited a paper by Rusthoven in 2009 as “recently.” It is now a year of 2014. So, “recently” is not suitable. The authors frequently used the words “recent” or “recently”.

*Sorry for this negligence. We already deleted the word “recently” in the revised MS. And according to the editor’s comments, we already got the English editing help from Edanz.*

**Reviewer 2**

In page 9 line 154 “senitivity" must be corrected as “sensitivity”

*Sorry for our mistake. We already corrected the word in the revised MS.*

**Editor**

*According to your comments, we already got the help from Edanz, and improved our English language in the revised MS.*

And we also highlight all changes we made. If there is any problem, please let us know.

Sincerely yours,

Authors