



## Correspondence to the editorials on “Comparison of stereotactic body radiotherapy versus metastasectomy outcomes in patients with pulmonary metastases”

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*Response to:* Petrella F, Spaggiari L. Comparison of pulmonary metastasectomy and stereotactic body radiation therapy for the treatment of lung metastases. *J Thorac Dis* 2019;11:S280-2.

Matsuo Y. Stereotactic body radiotherapy as an alternative to metastasectomy for pulmonary oligometastasis. *J Thorac Dis* 2019;11:S1420-2.

Qiu H, Katz AW, Milano MT. Stereotactic body radiation therapy versus metastasectomy for oligometastases. *J Thorac Dis* 2019;11:1082-4.

Malik NH, Keilty DM, Louie AV. Stereotactic ablative radiotherapy versus metastasectomy for pulmonary metastases: guiding treatment in the oligometastatic era. *J Thorac Dis* 2019;11:S1333-5.

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It is our great honor to receive valuable opinions from the world-wide experts on our published article entitled “*Comparison of stereotactic body radiotherapy versus metastasectomy outcomes in patients with pulmonary metastases*” (1). This published paper was the retrospective study for outcomes in 51 patients underwent local ablative treatments for them up to three pulmonary oligometastases. Twenty-one patients received stereotactic body radiation therapy (SBRT) and other 30 patients underwent metastasectomy. Univariate and multivariate analyses were applied to evaluate the efficacy of each treatment modality and to assess the correlation of individual variables with treatment outcome. The conclusions from the analyses were two folds: (I) both the SBRT and metastasectomy are the suitable and comparable to ablate pulmonary metastasis but (II) both are not likely to offer a clear benefit when synchronous metastases are present beyond the treated lesion. The study had many limitations in aspects of its retrospective nature, small cohort, short follow-up, and strong heterogeneities in baseline characteristics within and between the groups.

Despite the limitations, many physicians showed great interests on our work and left the valuable comments in their editorials entitled “*Stereotactic body radiotherapy as an alternative to metastasectomy for pulmonary oligometastasis*” by Matsuo (2), “*Comparison of pulmonary metastasectomy and stereotactic body radiation therapy for the treatment of lung metastases*” by Petrella and Spaggiari (3), “*Stereotactic ablative radiotherapy versus metastasectomy for pulmonary metastases: guiding treatment in the oligometastatic era*” by Malik *et al.* (4), and “*Stereotactic body radiation therapy versus metastasectomy for oligometastases*” by Qiu *et al.* (5).

We read that the first two editorials did not raise any special criticism to our paper. However, we were very impressed because they made well-organized overviews on oligometastasis in their editorials. Matsuo gave the systematic overview on the historical background of oligometastasis treatment with the easy-to-understanding explanation on currently muddled concept of oligometastasis (6). The editorial by Petrella and Spaggiari provided in-depth information regarding the concerns for

implementing pulmonary metastasectomy, including the treatment efficacy, role of preoperative assessment, and several debates on the nodal involvement status and number of developed metastases on surgery outcome.

The other two editorials by Malik *et al.* and Qiu *et al.* also mostly agreed with our work, but they raised two important concerns for implementing local-directed therapy for oligometastasis treatment. The first was the caution regarding the limitations of our work. Qiu *et al.* stated that our finding must be interpreted cautiously because of small number of patients included and Malik *et al.* underlined the need of perspective randomized trials. We entirely agree on this concern. Unfortunately, there have been no randomized evidences, but only limited evidences on this issue. Therefore, it is necessary to accumulate much amount of individual data on this issue and carefully cross-validate them relative to each other. We believe that we added a rationale data on this bunch of limited data and contribute to make their evidence levels little more robust. Ultimately, however, the prospectively randomized evidence is urgently needed. Both the editorials thankfully introduced a number of randomized trials that are currently under analysis and design, such as SABR for the comprehensive treatment of oligometastatic tumors (SABR-COMET) phase II (7) and stereotactic ablative radiotherapy for oligometastatic non-small cell lung cancer (SARON) phase III trials (NCT02417662). We also will keep an eye on the trials with the hope that the trials will be able to provide robust quality evidence in near future.

In addition, both the editorials underlined the important role of patient selection to offer surgery or SBRT. We fully agree with the absolute necessity for the right patient selection procedure and regret that we did not address the point in our original paper. Because of the fundamental difference between surgery and SBRT, these two modalities are not the same in any situations but one is relatively superior over the other. In some situations, this relative superiority may be apparent. For example, SBRT may be superior when treating multiple metastases across the different lobes, whereas surgery is favorable if multiple metastases are scattered within the same lobe. On the other hand, in some other situations, to which we may face more frequently, one's advantage over the other is rather ambiguous. We don't like to argue that the two modalities are interchangeable even in the situations, but need an effort to find potential synergy with one of two modalities. The right decision making is very difficult in the situations mainly because of absence of robust evidence.

Therefore, overall review procedure for a comprehensive evaluation for baseline characteristics of each patient must be accompanied. We believe that the multidisciplinary discussion is the best way we can take, as stipulated by Malik *et al.* Although not explicitly mentioned in the original paper, our patients were indeed offered surgery or SBRT basically through multidisciplinary discussion.

Lastly, Qiu *et al.* pointed to some missing data of (I) the exact number of treatment lesions for patients treated for multiple lesions and (II) the number of metastases diagnosed and that actually treated. We would like to respond to this. Seven patients in SBRT group were treated for two lesions, one in SBRT group for three lesions, and all other patients in both groups for one lesion. Multiple lung metastases were diagnosed in 14 patients, 7 of whom (all in SBRT group) were treated for multiple lesions. Four of these 7 were treated for all metastases diagnosed, but three of them were not. We note, however, that no meaningful result was drawn from the supplementary data because of too small sample size.

We appreciate to all the physicians giving us the comments, which expanded our understanding on this issue and made the clinical meaning of our findings clearer.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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