Author's response to reviews

Title: The maximum standardized uptake value of 18F-FDG PET scan to determine prognosis of hormone-receptor positive metastatic breast cancer

Authors:

Jian Zhang (syner2000@163.com)
Zhen Jia (tzjiazhen@126.com)
Joseph Ragaz (joseph.ragaz@ubc.ca)
Ying-Jian Zhang (yjzhang111@yahoo.com)
Min Zhou (zhoumin2000@yahoo.com)
Yong-Ping Zhang (zhangyp_nuclear@163.com)
Gang Li (lgf1112@yahoo.com.cn)
Bi-Yun Wang (drwangbiyun2002@hotmail.com)
Zhong-Hua Wang (wangzh@126.com)
Xi-Chun Hu (huxicun@gmail.com)

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Correspondence: huxicun@gmail.com

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Dear Editor,

Thank you very much for your suggestions to us for the revision and improvement of our manuscript.

Based on the advice received, we submitted this list of responses to the comments. The major changes in the revised version have been marked in red.

The reviewer’s advice has been greatly appreciated. Thank you again for the reviewer’s time and effort. Please feel free to contact me if you have any other suggestions. Many thanks and best wishes for your work.

Sincerely yours,

Xi-Chun Hu

Reviewer 1:

1. Methods. Many complicated factors seem to influence on FDG uptake at metastatic lesions in the patients studied here. Treatment (first-line therapy) before FDG PET scan may significantly show influence on FDG uptake at metastatic lesions. The assessment of metastatic lesions on pretreatment (without first-line therapy) FDG PET scan may be desirable for the proposed analysis. I can not see the locations of metastasis in the text or Tables. Are these lymph node or bone. Bone metastasis of breast cancer is often osteoblastic, and osteoblastic bone metastatic foci usually show low FDG uptake, regardless of biologic behavior of tumor cells. Therefore, I think that the location of metastasis is important factor influencing on FDG uptake. Please
describe the locations of metastasis in patients with non-visceral metastasis, which were evaluated in the present study.

**Answer:** Thanks for the reviewer’s kind suggestion, however, only relapsed patients without previous systemic or locoregional therapy in the metastatic setting were included in our study and all Baseline PET scans were performed before the first line treatment. That is to say, first line treatment could not influence the Baseline SUVmax, while the Baseline SUVmax might be influenced by previous adjuvant/neoadjuvant therapy. We have collected the information and analyzed this influenced in Table 1, however no significant difference of SUVmax was found among 5 arms (with different adjuvant/neoadjuvant therapies).

The locations of metastasis and corresponding analyses have been added in the table 1 and manuscript. Please check them. Visceral metastases were present in 70 patients (52.2%) and non-visceral metastases included only lymph node involved (13.4%), only bone involved (14.9%), only skin and soft tissue involved (3.7%), and mixed (20.1%). In patients with visceral metastases, almost all the SUVmax were obtained from visceral lesions. As the reviewer kindly mentioned, bone metastasis of breast cancer is often osteoblastic and usually show low FDG uptake, we found that in patients without visceral metastases, the median SUVmax of patients with bone involved only was relatively lower than the others, but this is not statistically significant (P = 0.063) (Table 1).

2. **Discussion.** Osteoblastic bone metastatic foci in patients with breast cancer usually
show low FDG uptake, regardless of biologic behavior or proliferative potential of
tumor cells. Is the assessment of FDG uptake in all the metastatic lesion regardless of
the location (bone, lymph node, or soft tissue) adequate for this kind study or not?
Please discuss this issue.

**Answer:** Just as the reviewer’s comment, the location of metastatic lesion could
also influence the SUVmax regardless of biologic behavior of tumor cells. In patients
with visceral metastases (± non-visceral metastases) of this study, almost all the
SUVmax were obtained from visceral lesions, which resulted in little need to analyze
the influence of location in such setting. Only in patients without visceral metastases,
the assessment of influence on SUVmax by metastatic locations such as bone, lymph
node, skin or soft tissue might be important. However, we did not find any significant
differences among these locations (P = 0.235), even between patients with bone
involved only and the others (P = 0.063) in terms of median SUVmax. We have
discussed this issue in the Discussion part, please check them. Of course, it might be
necessary for us to conduct another study including larger-sample-sized patients with
non-visceral metastases to illucidate this issue. Thanks.

**Reviewer 2:**

1. I think that the work is good enough; only one suggestion about figure: sometimes
they are difficult to read.

**Answer:** Thanks for the reviewer’s suggestion, we have added some words to help
understand the figure.