Author’s response to reviews

Title: A Retrospective Analysis on Metastatic Rate of the Internal Mammary Lymph Node and Its Clinical Significance in Adjuvant Radiotherapy of Breast Cancer Patients

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Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “A Retrospective Analysis on Metastatic Rate of the Internal Mammary Lymph Node and Its Clinical Significance in Adjuvant Radiotherapy of Breast Cancer Patients” (ID: BCAN-D-19-02456R2). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

ZhaoZhi Yang (Reviewer 1):
Q: Line 31/33 "metastatic lymph nodes could also be observed above the upper edge of the first rib (Fig.2 EF), with a metastatic rate of 7%". In this sentence, we don't know whether the metastatic lymph nodes is belong to internal mammary node or supraclavicular node. If they were supraclavicular node, these could be from axillary lymph node chain. And, based on this point, we couldn't conclude "It is suggested that the upper bound of the internal mammary lymphatic chain should be up to the subclavian vein with a 5-mm margin, thus connecting to the caudal border of supraclavicular clinical target volume in breast cancer patients at high risk of recurrence". From the authors's logistic, maybe anterior mediastinal lymph node should be included in the radiation field. So, this study just showed us that the recurrence rate of IMNs could be underestimated.

Figure 2 E-F is not suitable in the title "Distribution of the metastatic internal mammary/anterior mediastinal lymph nodes"

A: Firstly, the output tube of the IMNs is also connected to the supraclavicular lymph nodes, so in our
opinion, the IMNs are consistent with the medial supraclavicular lymph nodes, and the radiation injury is acceptable, so we suggested that the upper bound of the internal mammary lymphatic chain can be moved up appropriately which connecting to the caudal border of supraclavicular clinical target volume in breast cancer patients at high risk of recurrence.

Secondly, the prophylactic irradiation of regional lymph node, along with chest wall or breast irradiation, has long been the standard for breast cancer patients with considerable risk of relapse. But it is not recommended the irradiation of the anterior mediastinal region, on one hand, the region of prophylactic irradiation is the next station of metastatic lymph node region, so if there is no metastatic lymph node in the internal mammary lymphatic chain, the irradiation of the anterior mediastinal region is not necessary; on the other hand, the irradiation of the anterior mediastinal region can increase cardiac and pulmonary toxicity markedly.

Thirdly, the Figure 2 E-F can be included in Figure 3 with the Legend “metastatic lymph node above the upper edge of the first rib”.

San Gang Wu (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.
A: We don’t upload the comments as an attachment this time, thanks for your suggestions.

Toshiaki Iwase, M.D., Ph.D. (Reviewer 3): I will accept the paper for publication without further revision.
A: Thanks for your good comments and hard work.

We would like to express our great appreciation to you and reviewers for comments on our paper. Looking forward to hearing from you.
Thank you and best regards.
Yours sincerely
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