Author's response to reviews

Title: Innovative method using circulating tumor cells for prediction of the effects of induction therapy on locally advanced non-small cell lung cancer

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Author's response to reviews:

Jul 11, 2013
Mr Vipin Zamvar
Prof. David Taggart
Editor-in-Chief
Journal of Cardiothoracic Surgery

Dear Editors-in-Chief, and reviewers:

Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comment.

1. The first statement of the abstract needs to be re-written or reverse it with the second statement. It sounds better.

The background of abstract has been changed as the reviewer indicates, and now appears as follows:

The existence of circulating tumor cells (CTCs) in patients with lung cancer has been reported. The purpose of this study was to assess whether CTCs are predictive of the pathological effects of induction chemoradiotherapy for patients with non-small cell lung cancer.

2. In the methods, I would put the type of system used, not just it was automated.

We have put the type of system used in the methods section of the abstract as the reviewer indicates:

Peripheral and pulmonary venous blood samples from the involved lobe were
collected intraoperatively, and the number of CTCs was counted using the CellSearchTM system, epithelial cell adhesion molecule-based immunomagnetic technique.

3. Your sample size is small, your conclusion is that the presence of CTCs reflects pathological non-CR. Should this be may reflect? The major limitation of the study which you note is the size. A larger study to validate the results would be the next step.

We agree with the reviewer’s indications about our conclusion. CTCs count was negative in cases of CR, while positive in other cases in this study. We noted that it would need to be studied before definitive conclusions could be made in the discussion section. Greater patient numbers are desirable for further study. However, accumulating the patients of induction therapy in single-institution will take time too much. We believe that a larger study can be performed in multi-institutions by submitting this result.

4. You need to explain what is a minor response and a major response. What is the difference. That seemed unclear to me

We have revised the explanation of the definition of pathological response to be more explicit in the methods section (page 6). The sentence appears as follows:

Multiple hematoxylin- and eosin-stained sections of each tumor were reviewed by a pathologist and then re-reviewed by another pathologist. After resectioning the entire tumor and scrutinizing multiple cross-sections, this pathologist carefully calculated the percentage of nonviable tumor cells. The percentage of nonviable tumor cells was defined as the combined percentage of scar and necrosis. Pathological CR denotes that viable tumor cells do not exist in the resected specimen; a major response denotes that viable tumor cells remained in one-third of resected specimens; a minor response denotes that viable tumor cells remained in more than one-third of resected specimens; and no response denotes that no pathological changes were observed in the tumor cells of the resected specimen.

5. Of the patients who underwent pneumonectomy, did you find more CTCs?

No, we did not. Two were CR and one was major response in patients who underwent pneumonectomy. The number of CTCs was 5 in that major response patient. In the other major response patients who underwent lobectomy, the numbers of CTCs were 4, 12, and 60, respectively.

1. Page 6 line 10; How pathological diagnosis was defined should be cleared. For example, authors defined from the comment of clinical records, a pathologist made new examination for diagnosis of response and so on. If pathologists contributed to make diagnosis, appreciation is needed as acknowledgement.

We have revised in our manuscript the pathological diagnosis of the methods section as the reviewer indicates (page 6):

“Multiple hematoxylin- and eosin-stained sections of each tumor were reviewed by a pathologist and then re-reviewed by another pathologist. After resectioning
the entire tumor and scrutinizing multiple cross-sections, this pathologist carefully calculated the percentage of nonviable tumor cells. The percentage of nonviable tumor cells was defined as the combined percentage of scar and necrosis.” and “The pathologists were blinded to all clinical, radiological, and surgical findings. Pathological diagnosis was defined according to the pathologists’ comments on the clinical records.”

We have added acknowledgement for pathologists as the reviewer indicates.

1. Page 4 lines 3-4: Registry data is preferable such as report from Japanese Joint Committee of Lung Cancer Registry.

2. Page 8 lines 15-16; pvCTC count was negative in all CR cases, thus “pvCTC count … major/minor response.” had better be changed to “CTC count was negative in cases of CR, while positive in other cases.”
   We have revised our manuscript as the reviewer indicates (page 8): In patients who underwent induction chemoradiotherapy, pvCTC count was negative in the case of CR, whereas it was positive in the other cases.

3. Page 10 line14: The information of “clustered cells hardly extracted from the blood by CellSurch system” is needed.
   We have added this sentence to the discussion:
   In CTC detection, clustered cells were hardly extracted from the blood using the CellSearchTM system.

4. Page 11 lines 10-11: The last sentence is not necessary because there are no data regarding this concept.
   We have deleted the sentence concerned from the conclusions section.

We appreciate the reviewers’ constructive comments.

Sincerely,

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