Author's response to reviews

**Title:** Sentinel lymph node biopsy is unsuitable for routine practice in young female patients with unilateral low-risk papillary thyroid carcinoma

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**Author's response to reviews:** see over
To reviewer Pieter Raijmakers:

1 The inclusion/randomization of patients needs some clarification:
   -- is this a population of consecutive female patients?

   To: Thank you! In the second paragraphs of “SLN Biopsy” section of “PATIENTS AND METHODS”, we have mentioned “patients were randomly assigned to Group 1 or Group2”. The randomization procedure was done by the statistician of my institution, the same as all other randomize trials. The details were getting those randomized number from computer, assign to patients, patients who got odd number to receive the treatment 1, others were treatment 2.

2 Author state they included patients with unilateral papillary thyroid carcinoma. However, papillary thyroid carcinoma can be multifocal. Multifocal papillary carcinoma might cause false negative results of the SN.

   To: Thank you! In the first paragraphs of “PATIENTS AND METHODS” section, we mentioned that “Patients with multifocality were excluded after ultrasound test before randomization”.

3 Clarification of the lymphoscintigraphy is needed:
   -- the SLN biopsy procedure includes a lymphoscintigraphy procedure, this applies only for the patients randomized to the combined traced group.
   -- what was the dose of the applied 99m Tc-colloid tracer?
   -- How was the colloid injected?

   To: Thank you for your very good suggestions. I added that information of lymphoscintigraphy as your suggestion in “SLN Biopsy” section marked in red color. The dose was described in “SLN Biopsy” section: “One dose of 99mTc sulfur colloid (about 0.5ml) was injected in the primary tumor for lymphoscintigraphy and intraoperative lymph node detection”. We injected the colloid by no-echoguided procedure.

   --- The imaging procedure of the SN needs clarification: typically, dynamic planar images are made after injection of SN, a dynamic SPECT procedure, as described in this manuscript, is somewhat atypical. (SPECT images take at least 20-30 minutes to make.)
   --- specific question: more than 1 SPECT scan was made? How many SPECT scans were made?
   -- which gamma-camera was used?

   To: Thank you! We used dynamic planar module of the SPECT. We took at least two SPECT scan, normally first for 10-15 minutes after injection, second time is next day before surgery. As following photos we have not added in article (because the publish fee for photo is very high):

We used PHILIPS Vertex V60, and added that information in the “SLN Biopsy” section in red color.
4 SN biopsy:--how many surgeons participated in this study?........Is?
To: A clinical trial needs good cooperation within the departments in our country. All doctors in our department have done great contribution for the trial. Our chief director who was the corresponding author managed almost surgeons. He has over 25-year experience of thyroid surgery, with over 10-year SN biopsy experience in breast cancer and thyroid.

5 Data-analysis
Is the general accepted calculation of FNR of SN used?
To: Thank you for your opinion! The purpose of our paper was to share the experience of our clinical trial. We wish our experience may help clinical doctor practice. FNR may be not a general accepted calculation for SN, however, we think it suitable for our research.

6 Authors should clarify the histological analysis of the SN
To: Thank you very much! I have added “Lymph nodes including each SLN were sectioned along the long axis into two sections and then were submitted for routine hematoxylin-eosin (H-E) staining. Each tissue block was sectioned serially (successive 5 um sections)” in “SLN Biopsy” section in red color.

7 The authors should clarify the specific research question.
To: Thank you very much! We have discussed partly in the discus section. However, the import reason for why our research is different from others is the subpopulation of my study. Thus we thought it was not necessary to discuss or compare to other researches.

8 The title of the article does not include the study design.
To: It is a good suggestion! If we added the “randomized study…” in the title, it may look too long for readers.

9 The significantly higher SN identification rate for the combined technique vs the single agent is not mentioned in the conclusion (abstract)
To: Thank you! We have mentioned in other words as the same meaning as you, “the combined technique of SLN biopsy could help more accurate lymph node staging and better identification of SLN located out of the central compartment” in the conclusion section(abstract).

10 The discussion is to long and the first part is describing the SN biopsy in.....with two different SN detection methods.
TO: Thank you very much. We have deleted the first part according to your suggestion!

To reviewer Barbara Jarzab:
1 The alternative to SLN is the intraoperative......whether if could help to disclose the metastatic lymph nodes without formal SLNB
To: Thank you very much. This is a good question. We have mentioned “all patients with a preoperative diagnosis of PTC by fine-needle aspiration, clinically node-negative detected by
clinical exam and ultrasound were asked to participate in this study “in the “Patient” section. Patients with enlarged lymph nodes were excluded by ultrasound. That was the reason we did not describe the intraoperative macroscopic evaluation of lymph nodes status of the patients.

2 Authors correctly state ...However,...I would rather consider their negative results as more general ones.
To: We found most of your comments and ideas were very similar with ours. However, the objective of the research is Chinese population, not including no-Chinese people. We could make the conclusion only according to my trial. Larger and multiple international randomize trials are needed in future. However, we wish this negative result may help other clinical doctor ‘practice.

3 At the description of ...,the most unclear point is the question whether central lymphadenectomy was performed routinely.
To: Thank you very much. We did central lymphadenectomy routinely. We made more clearly describe in “material and methods” part in red color.

4 The introduction ...however, due to high FNR, SNLB does not improve the selection of patients who need modified lymphadenectomy.
To: Thank you very much. We are general surgeons focusing on three types of cancer, breast cancer, thyroid cancer, and colon cancer. We have seen lots of surgeons transferred different procedures from breast cancer or other solid cancer to thyroid in China. We disagreed with those practice. In fact, we did not prefer the use of SLN in thyroid, although it is very successful in breast cancer.