Reviewer’s report

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

**Version:** 2  **Date:** 7 March 2011

**Reviewer:** Pieter Raijmakers

**Reviewer’s report:**

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 Group 2”. 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.
   Reviewer:
   The randomization process is clear, the question regarding consecutive patients is not answered.

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”.
   Reviewer: pre-operative ultrasound screening has a limited sensitivity, the issue is: how many patients had a multifocal papillary thyroid carcinoma after surgery (in the pathology screening of the whole thyroid specimen) Multifocal (micro-)carcinoma is not unusual, authors should describe the frequency of multifocal papillary thyroid carcinoma in the final pathology results.

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.

Reviewer: The injection procedure remains unclear to me, injection of a tracer in small thyroid tumours is difficult without echo-guidance. The authors should clearly state they did not use echo-guidance for the injection procedure.

A volume of 0.5 ml is not the dose, what is the dose of the 99mTc colloid in Mbq (Megabecquerel)?

---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.

Reviewer: thanks for the images, publication of planar SN images is not necessary.

The word SPECT is misleading and is an incorrect description of the imaging procedure: planar images were used for SN scintigraphy. This should be
changed in the manuscript. Furthermore, it is normal in a manuscript to mention the type of gamma-camera used for this study.

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.

Reviewer: The question remains whether all participating surgeons had specific experience with thyroid SN procedures, the authors should clarify this issue in the manuscript.

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.

Reviewer: The manuscript describes a high FNR. This is the main topic of the manuscript and it might be an important conclusion. However, the FNR calculation needs clarification and should be performed according to general guidelines. Authors have not answered this question.

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.

Reviewer: Immunohistological analysis may reveal more lymph node metastasis compared to HE staining. This might explain the relative higher FNR of this study, therefore authors may add this to a limitations section of the discussion section of the manuscript.

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.

Reviewer: It is not uncommon to compare the results of a specific study with results of earlier results, the manuscript may improve with a comparison of earlier results of SN studies of thyroid cancer patients.

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.
Reviewer: it is a guideline of BMC CANCER, not a rule.

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).
Reviewer: rephrasing this sentence might be better

10 The discussion is too 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!
Reviewer: ok