60734-Answering Reviewers

Round-1:

Reviewer #1

1. Q: I believe studies on needle tract seeding compile both techniques (aspiration vs capillary) as one and do not differentiate when looking at the incidence of seeding.

   A: Some articles have reported that FNCB reduced trauma to cells and tissues [1], and suction release before needle withdrawal during FNAB has been proposed to minimize the risk of NTS [2, 3]. So there is a difference between “aspiration” and “capillary”, and should be discussed separately when looking at the incidence of seeding.

   [1] Rizvi SA, Husain M, Khan S et al (2005) A comparative study of fine needle aspiration cytology versus non-aspiration technique in thyroid lesions. Surgeon 3:273–276.

   [2] Pitman MB, Abele J, Ali SZ et al (2008) Techniques for thyroid FNA: a synopsis of the National Cancer Institute Thyroid Fine- Needle Aspiration State of the Science Conference. Diagn Cytopathol 36:407–424.

   [3] Wu M, Burstein DE (2004) Fine needle aspiration. Cancer Invest 22:620–628.

2. Q: How do the authors know this was a FNCB not a FNAB? Was it documented in the patient's notes?

   A: Because ultrasound-guided FNCB was performed by one of the authors (Dr. Zhou Liang), it has documented on the Line 90-91. In order to avoid readers from appearing the same doubt, the operator's name has been added in the corresponding paragraph.

3. Q: The article needs significant improvement of the language and grammar. There are also multiple spelling errors.

   A: The manuscript has been edited by a professional English language editing company, and the English Language Certificate has been provided.

4. Q: All abbreviations require the full name the first time it is used eg TSH, Tg-Ab.

   A: I have checked and revised the full text.

5. Q: If the FNCB was 4 years ago, how did the authors know it the seeding was at the same location as the puncture needle path? (line 115 - 116). Could this have been seeding along a previous drain site from the initial surgery?

   A: Since the puncture operation was done by Dr. Zhou Liang (one of the authors), there was a record of where the needle was inserted and which path was taken, and the path was consistent with the seeding transfer path. Regarding the possibility of the seeding along a previous drain site from the initial surgery, from the point of analysis, we did not separate the skin and subcutaneous tissue layer throughout the surgery, and most of the implants were located in the subcutaneous tissue layer. Secondly, the surgical incision was on the middle of neck, and the mass was located on the right side of the neck, so the possibility of seeding transfer caused by the initial surgery was very low.

6. Q: Figure 1 are presumably the ultrasound images from the initial diagnosis of thyroid cancer. They are not congruent with the main topic of the article which is the local recurrence at the needle tract site. Also, the images are from 6 / 7 years ago, not 4 years as described by the paper.

   A: Maybe the ultrasound images are not congruent with the main topic. However, the first treatment resulted in subsequent complication of NTS, so I guess that readers are also interested in these medical records. The other question: 2014-ultrasonography, FNCB and initial surgery; 2015-found subcutaneous nodule; 2018-nodule removed. The patient came to our hospital due to anterior neck nodules in 2018, 4 years before 2018, that was, in 2014,

an ultrasound examination was performed, so the case records were calculated based on the patient's current hospitalization for subcutaneous mass as the time point. In order to express clearly, I use “what year it is” instead of “X years ago” in certain paragraphs.

7. Q: Trend of TgAb could be related to pregnancy as it is known to decrease during pregnancy with a rise at post-partum.

   A: This patient’s fetus two months, while she went to the hospital was found to be pregnant, the TgAb was 36.19 (2016/12/26), so at the pregnant point in time, TgAb was not tested, because she didn’t know she was pregnant at that time. And two months postpartum, the TgAb was 153.8 (2017/9/1), because in China, many new moms practice the tradition of postpartum confinement after the birth of a child, so she came to our hospital and tested TgAb two months postpartum. During pregnancy, trend of TgAb was know to rise not decrease. This trend supported previous studies that pregnancy might increase the risk of disease progression [4-7]. Once the subcutaneous nodule was removal, the level of Tg-Ab declined rapidly and presented a downtrend in the following days.

[4] Shindo H, Amino N, Ito Y, Kihara M, Kobayashi K, Miya A, Hirokawa M, Miyauchi A 2014 Papillary thyroid microcarcinoma might progress during pregnancy. Thyroid 24(5):840–844.

[5] Kimura M, Amino N, Tamaki H, Mitsuda N, Miyai K, Tanizawa O 1990 Physiologic thyroid activation in normal early pregnancy is induced by circulating hCG. Obstet Gynecol 75:775–778.

[6] Hirsch D, Levy S, Tsvetov G, Weinstein R, Lifshitz A, Singer J, Shraga-Slutzky I, Grozinski-Glasberg S, Shimon I, Benbassat C 2010 Impact of pregnancy on outcome and prognosis of survivors of papillary thyroid cancer. Thyroid 20:1179–1185.

[7] Leboeuf R, Emerick LE, Martorella AJ, Tuttle RM 2007 Impact of pregnancy on serum thyroglobulin and

detection of recurrent disease shortly after delivery in thyroid cancer survivors. Thyroid 17:543–547

Reviewer #2

1. Q: In your discussion please elaborate on the differences between FNAB and FNCB. What was the needle size that was used? Do you use FNCB routinely as opposed to FNAB that is more commonly used?

   A: The only difference between FNAB and FNCB is whether there is suction during puncture, which has been added to the “Discussion” (Line 157-159). And I have added the needle size on Line 89. In our hospital, we use FNCB routinely instead of FNAB.

2. Q: Text – you use Tg-Ab levels as follow up. What were the Tg levels?

   A: Due to the presence of abnormally increased TgAb, the Tg is very low and stabe below 0.03 ng/ml. The description of this part has been added on Line 110.

3. Q: This is a poorly written manuscript with numerous English errors. English style needs major revisions throughout.

   A: The manuscript has been edited by a professional English language editing company, and the English Language Certificate has been provided.

Reviewer #3

1. Q: This manuscript does not indicate the exact gauge needles the patient used. What gauge was used for this patient?

   A: I have added the needle size on Line 89.

2. Q: Do you have an external photo or ultrasonogram of the subcutaneous mass?

   A: In fact, the medical records are incomplete in this case. Initially, the subcutaneous nodule was thought to be a sebaceous cyst, so when the patient was willing to treat it, we did the operation directly for her without ultrasound examination and photos. Furthermore, this nodule was relatively small and could not be seen by inspection, but could be felt only by palpation.

3. Q: Have you ever thought about the possibility of drop metastasis during surgery other than NTS? It would be nice if there was an explanation for this.

   A: We did not separate the skin and subcutaneous tissue layer throughout the surgery, and most of the implants were located in the subcutaneous tissue layer. And the surgical incision was on the middle of neck, and the mass was located on the right side of the neck, so the possibility of seeding transfer caused by the initial surgery was very low. We highly agree with your suggestion, and I believe that readers will have such doubts, so we have added this part of the explanation in the original text (Line 144-148).

4. Q: "Earlier diagnosis of NTS based on serum biomarkers or genetic characteristic might improve the survival in PTC patients with NTS." This phrase of conclusion seems to need correction.

   A: I agree with your suggestion and made the following changes: Serum biomarkers and

genetic characteristics could help in the treatment and follow-up of PTC patients with NTS.

Science editor:

In fact, the medical records are incomplete in this case. Initially, the subcutaneous nodule was thought to be a sebaceous cyst, so when the patient was willing to treat it, we did the operation directly for her without ultrasound examination and photos. Furthermore, this nodule was relatively small and could not be seen by inspection, but could be felt only by palpation. In the operation, we did not separate the skin and subcutaneous tissue layer, and most of the implants were located in the subcutaneous tissue layer. And the surgical incision was on the middle of neck, and the mass was located on the right side of the neck, so the possibility of seeding transfer caused by the initial surgery was very low. We highly agree with your suggestion, and I believe that readers will have such doubts, so we have added this part of the explanation in the original text (Line 144-148). Although the initial diagnosis of thyroid cancer in 2014 and nodule removed in 2018, we chose to publish this case at such a long interval because we would like to take a longer follow-up time to determine the treatment effect and recurrence. In fact, the patient has no signs of re-examination so far, which has been mentioned in this article.

Company editor-in-chief:

I have browsed this website based on the recommendation and read the corresponding introduction. Considering that this manuscript needs to be resubmitted within 14 days and time is tight, so the manuscript has been edited by other professional English language editing company, and the English Language Certificate has been provided.

Round-2:

Dear sir,

I have revised my manuscript according to the second-round review report.

Reviewer1:

1. Q: Pg 5 Line 12 extra-thyroidal 2. Pg 5 Line 12 lymph nodes 3. Pg 5 Line 21 transverse surgical scar... was

A: Point 1-3 have revised in the manuscript;

4. Q: Pg 6 Line 2 months

A: Point 4: it is "months" in my manuscript, but I download the "manuscript" file from the site, it is "mo". Anyway, in the "upload file" it is "months".

5. Q: Pg 8 Line 21 Did you mean "offers a favorable prognosis" instead of comparable?

A: Point 5: "offers a favorable prognosis" instead of "presents a comparable prognosis". I agree with the proposal, and have revised in the manuscript.