Author's response to reviews

Title: The Use of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in the Diagnosis of Thyroid Lesions

Authors:

Mimi Phan (mphan@bcm.edu)
Keerthana Keshava (keerthanakeshava@gmail.com)
Jose M Garcia (jgarcia1@bcm.edu)
Daniel G Rosen (dgrosen@bcm.edu)
Horiana Grosu (bogdana_14@yahoo.com)
Donald R Lazarus (Donald.Lazarus@bcm.edu)
Juan Iribarren (iribarre@bcm.edu)
Roberto F Casal (casal@bcm.edu)

Version: 4
Date: 6 November 2014

Author's response to reviews: see over
Dear Editor,

We would like to thank you for giving us the opportunity to respond to the reviewer’s concerns. In this revised manuscript, we have tried to fully address the reviewer’s constructive criticisms.

**Reviewer 1:**

**Major Compulsory Revisions**

*Comment:* The authors presented in their paper clinical cases of patients with mediastinal lymph nodes or masses that were qualify for the EBUS-TBNA. Malignancy was identified in 3 (25%) patients: metastatic adenocarcinoma of the breast, large B-cell lymphoma, and metastatic adenocarcinoma of lung origin. Thyroid tissue in the background of these biopsies, by the authors, confirms presence of metastases to the thyroid. Please clarify whether the authors have other evidence to prove this thesis (e.g. histopathological examination). Moreover, most thyroid lymphomas (B-cell lymphomas – more then 50% cases are diffuse large B-cell lymphoma and 10-23% cases are extranodal marginal zone B-cell lymphomas) – there are primary thyroid malignances.

*Response:* We agree with the reviewer’s concern. In each case, we introduced a new needle into the thyroid gland under endobronchial ultrasound guidance and real time visualization of the needle/thyroid, without the needle traversing any other structure. We are certain that the breast and lung cancer lesions within the thyroid were metastatic, and these were confirmed by immunohistochemistry. In the case of the large B-cell lymphoma, though we agree that it could be a primary lymphoma of the thyroid, the patient had multiple other sites, including an adrenal gland that was biopsied and also confirmed to be the same type of lymphoma.

**Minor Essential Revisions**

*Comment:* The remaining 9 samples were deemed to be benign lesions (follicular nodules =7, multinodular goiter =1, Hürthle cell adenomas in background of multinodular goiter =1). These results there are not according to the Bethesda System for Reporting Thyroid Cytopathology, by which should now be formulated cytological diagnosis.

*Response:* We have changed the reports on the benign lesions to conform to the Bethesda System.
Reviewer 2:

Overall this is a well written small retrospective study, however it is the largest cohort published thus far.

Major Revisions-

Comment 1. Was the same needle sued to biopsy sites in thorax and thyroid nodules for those patients having EBUS-TBNA?

Response 1. No. A dedicated needle was always utilized to sample the thyroid gland in every case to prevent cross-contamination. In addition, the thyroid gland was the first target in all cases.

Comment 2. What was the normal follow up of patients post EBUS could some of these patients have attended a family physician with complications? Did everyone follow up at the study centre after the procedure? Could complications have been missed?

Response 2. All our patients had several follow-up visits with multiple physicians in the subsequent months after our biopsies. Thanks to our electronic medical records, it was easy for us to review all these encounters, and we did a 12-month clinical follow-up. None of the patients suffered any complication from our biopsies within the 12-month follow-up period.

Comment 3. Discussion re safety of this procedure- in my opinion the potential for complication of placing a contaminated needle in a thyroid nodule full of protein just below the pharynx through the airway is higher than placing it in a lymph node full of lymphoid tissue- i hypothesise that this may be associated with higher risk- thus until a prospective randomized trial is published, i think the authors comment that complications of placing a needle into a lymph node is the same as a thyroid nodule are probably the same might need to be tempered for now.

Response 3. We agree with the reviewer about the concern on potential local infection, since the needles we utilize are not sterile after they are passed through the bronchoscope. However, we do not know that thyroid glands are more prone to infection than lymph nodes. The only available report on an infectious complication of an EBUS-TBNA of a thyroid nodule corresponds to a “cystic” nodule, described by the author as a “hypoechoic fluid-containing lesion in the right lobe of the thyroid”. This may
have predisposed that patient to develop the thyroid abscess. Nevertheless, in agreement with the reviewer, we have emphasized this concern of potential infectious complication.

Comment 4:
minor revisions-
1. discussion is a little long and meanders a little with statements based on a limited number of patients (12)- please read over and possibly shorten

Response 4:
We have tried our best to shorten the discussion.