Author’s response to reviews

Title: Clinical Diagnostic Value of Simultaneous Amplification and Testing for the Diagnosis of Sputum-scarce Pulmonary Tuberculosis

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Author’s response to reviews:

Lucilaine Ferrazoli, Ph.D. (Reviewer 1): The authors followed all recommendations. However, there are still few corrections.

L 94 - Replace pulmonary tuberculosis by PTB
We have replaced in INTRODUCTION, L 94

L 134 - Replace MTB by MTBC
We have replaced in PATIENTS AND METHODS, L 134

L 135 - Correct: "on analysis of AFB in resected lung tissues". Remove (find the acid fast bacilli).
We have corrected in PATIENTS AND METHODS, L 135.

L 164 - Replace Mycobacterium tuberculosis by M. tuberculosis
We have replaced in PATIENTS AND METHODS, L 163.
L 237 - Replace Mycobacterium tuberculosis by Mycobacterium tuberculosis complex
We have replaced in RESULTS, L 233.

L 278 - Replace MTB by MTBC
We have replaced in RESULTS, L 271.

BALF is used from the beginning of the manuscript in full and only in the discussion is abbreviated.
We have replaced from the beginning of the manuscript to the end.

Max Salfinger (Reviewer 2): This manuscript describes the comparison between a NAAT and AFB smear and culture from BAL collected from 764 patients suspected with pulmonary TB.

L85-'nontuberculous' mycobacteria (NTM)
We have corrected.

L90-Is SAT-TB really a point-of-care molecular test?
Yes, it is.

111-sputum-scarce PTB individuals; did the authors try sputum induction in patients not able to expectorate a sputum?
Yes, we did.

L157-What was the final concentration of NaOH used for decontamination of the BAL? How long were the samples exposed to NaOH-15, 20, 25 or 30? Did the authors used NALC as well?
The final concentration of NaOH is 4%. The samples exposed to NaOH for 15-20 minutes. We did use NALC.

L166-Please explain in more detail how the samples were processed for conventional smear and culture and for SAT-TB. Was SAT-TB performed on a processed sediment obtained by the conventional work-up? Please provide more details about SAT-TB. Is there an amplification control for detecting amplification inhibitors built in? What was the concentration used and exposure time for the SAT-TB work-up?

We have added in the text.

190-764 patients were analyzed and 70% were diagnosed with TB; however, only 116 out of 536 (22%) patients with TB were confirmed by microbiology. This is a low figure. Can you explain further in the DISCUSSION section?

We choose the sputum scare patients, not all TB patients.

L197-120 PTB patients (96 were only culture positive and 20 smear positive) - what happened to the missing 4?

4 were only smear positive.

L235-A GeneXpert cartridge costs $100 - Is China not eligible for a discounted price of $10?

In China, the cost of a GeneXpert is $100 and not covered by public medical insurance.

L239-Was SAT-TB assay performed 7 days a week?

Yes.

L245-How does the SAT-TB control for amplification inhibitors?

We have added in the text.

L259-Only 2 patients were diagnosed with NTM - any explanations? Smears can be AFB positive in NTM disease; therefore, one should not call them false-positive.

Yes.
References- This author suggests deleting reference 8 and 9. They are not relevant for this study. The Roche TB assay is no longer on the market.

We have deleted reference 8 and 9.

Table 1

Were 764 SAT-TB assays performed? How do you explain in the Non-TB patients 12 positive SAT-TB (false positives?), 4 positive culture (false positives?), and 4 positive smear (false positives or NTM?)

false positives

Table 2

Please provide the actual figures and not just the % value.

We add the actual figures in the text.