Author’s response to reviews

Title: Diagnosis of thyroid nodules for ultrasonographic characteristics indicative of malignancy using random forest

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Author’s response to reviews:

Reviewer #1: I have no questions.
Response: Thanks a lot.

Reviewer #2:

1. The authors have used the term FNA towards the end of the manuscript, could it means FAN biopsy, which was also referred to at a point in manuscript? Ambiguous terms should be explicitly defined.
Response: Thanks a lot. FNA is the abbreviation of “Fine Needle Aspiration”. We have given its definition. Please see line 2 of the second paragraph on Page 9 in the revised manuscript.

2. In the first manuscript, there were cases where the author used FAN biopsy instead of FNA biopsy. Fine Needle Aspiration (FNA) biopsy should be defined before it is used as abbreviation. According to the response to the comment by the authors, "We have not used the term FNA but FAN biopsy", it should be FNA biopsy not FAN biopsy.
Response: Thanks a lot. We have defined it before it is used as abbreviation. Moreover, it is FNA biopsy. We have corrected the typing error. Please see line 2 of the second paragraph on Page 9 in the revised manuscript.
Reviewer #3:

1. Is it necessary to add a subsection of materials and another of methods? In section 2 you have followed 2. 2.1 and 2.1.1 without any content between them. Please organize the section and subsections of materials and methods.
Response: Thank you for your good suggestion. We have adopted your suggestion and organized the section and subsections of materials and methods. For simplicity, we only presented subsection and removed subsubsection (e.g., 2.1.1) in the revised manuscript. Please see Page 3 in the revised manuscript.

2. Please improve the format of figure 1. Why did you add the cube shapes? I suggest removing effects from the frames and selecting a solid color. Also, the fonts are distorted. The validation metrics AUC, FI etc should not be in another section? e.g. In validation?. Improve this figure please.
Response: Thank you for your good suggestion. We have changed format of Figure 1 including removing effects from the frames and selected a solid color. Please see Figure 1 on Page 15 in the revised manuscript.

3. Add reference of the packages you used for the hyperparameters.
Response: Thanks a lot. The references for the used R package have been added. Please see line 1, Section 2.5 on Page 5 in the revised manuscript.
For the reference of the packages for tuning hyperparameters, we have added the corresponding website. Please see line 1, the fourth paragraph on Page 5 in the revised manuscript.

4. Section 3 is similar to section 2. You have 3, 3.1 and 3.1.1 without content !! please re organize this.
Response: Thanks a lot. We have adopted your good suggestion and organized the section and subsections of materials and methods. For simplicity, we only presented subsection and removed subsubsection (e.g., 3.1.1) in the revised manuscript. Please see Section 3 on Pages 5--8 in the revised manuscript.

5. I see several formatting errors throughout the document. Spaces, different fonts, font sizes, quality of figures. This is not acceptable for a publication.
Response: Thank you for pointing out these errors. We have reedited this paper with LaTex in the revised manuscript.

6. The results obtained do not exceed what was reported in Bin, Zhang, Jie, et al. Machine Learning-Assisted System for Thyroid Nodule Diagnosis. Thyroid: official journal of the American Thyroid Association, Jun 2019; 858-867. I do not see in the discussion a comparison with other authors. Therefore, the results is reducing to feature selection using LASSO. The level of risk is only the posterior probability of the classifier.
Response: From our results, we have recommended the usage of RF method, which is consistent with that given in Zhang et al. (2019), but it does not show that our results obtained do not exceed what was given in Zhang et al. (2019), because RF is a popular machine learning method rather than Zhang et al.’s method, and has widely applied to various studies. More importantly, our hybrid method incorporating LLR and RF can not only select important US features via LASSO but also
obtain risk score via the LR model with the selected predictors, which is our basis for classification. But Zhang et al. (2019) only compared the performance of RF and conventional classifiers, but they did not provide a quantitative approach to assess the risk of the malignant nodule and consider to calculate the risk score of thyroid nodules, which leads to unknown information on the level of risk for the classifier. Please see the first paragraph on Page 9 in the revised manuscript.

According to your suggestion, we have given a comparison with other authors in Discussion. Please see the first paragraph of Discussion Section on Page 8, the first paragraph on Page 9, and the third paragraph on Page 10 in the revised manuscript.

The level of risk is not the posterior probability of the classifier. It is defined as a class probability that is the percentage of the malignant nodules correctly identified. We have given its definition. Please see line 2, the third paragraph on Page 5 in the revised manuscript.

7. They did not add the US sample images.
Response: Thanks a lot. We have added the US sample images to the revised paper. Please see Figure 1 in the revised manuscript.