

Peer Review File

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Reviewer A

Well written and clinically relevant study. Although the sample size for training and validation is small, it is understandable as it involves a select group of patients who papillary thyroid microcarcinoma treated with total thyroidectomy and central lymph node dissection.

1. **Title:** Happy.
2. **Running title:** Happy.
3. **Abstract:** Happy.
4. **Keywords**
 - a) Perhaps need to enter central compartment lymph nodes and metastasis separately.
 - b) Otherwise: Happy.
5. **Key findings:** Happy.
6. **Introduction:** Happy.
7. **Methods**
 - a) Patient source: Happy.
 - b) Clinical data: Happy.
 - c) US image acquisition: Happy.
 - d) Assessment of lymph node status in the central cervical zone
 - i. Make it central compartment, for consistency.
 - ii. Otherwise: Happy.
 - e) Region of interest division and feature extraction: Happy.
 - f) Feature filtering: Happy.
 - g) Establishment and verification of the model: Happy.
 - h) Visual analysis of the model: Happy.
 - i) Statistical analysis: Happy.
8. **Results**
 - a) Clinical features: Happy.
 - b) Radiomics features: Happy.
 - c) GBDT model establishment and verification: Happy.
 - d) SHAP
 - i. Please use the full name for the subtitle instead of the abbreviation.
 - ii. Otherwise: Happy.

- e) Illustrations
 - i. Figure 1 does not seem to be necessary. Its contents can be captured fully and comprehensively in the text.
 - ii. Figure 2: The contents are minute and difficult to read. Perhaps only the steps or process flow should be displayed. The caption needs to be improved and made self-explanatory.
 - iii. Figure 3: Happy.
 - iv. Figure 4: Size need to be increased.
 - v. Figure 5: Happy.
 - vi. Figure 6: Happy.
 - vii. Figure 7: Size need to be increased.
 - viii. Table 1: Happy.
 - ix. Table 2: Happy.

9. Discussion

- a) Central compartment instead of central region for consistency.
- b) “was revealed up to 50.6% of patients” . Need to add ‘in’, which is missing.
- c) Check and revise: “while CLNM increased the detection rate by only 8.9%”.
- d) Write 2 in word in “there is no clear correlation between the 2”.
- e) Limitations
 - i. Correct typo: “Second, Even ...”.
 - ii. BRAF mutation is not relevant as it was not part of the study and has not been mentioned anywhere before.

10. References: Happy.

11. Conclusion

- a) Need to start with conclusion derived directly from findings from the study in line with the title of the study and its aim.
- b) Otherwise: the only statement currently in the conclusion is fine as a follow-up.

12. TRIPOD checklist: Happy.

Reply: Dear Reviewer. Thank you for your careful review, your suggestions will make the article more rigorous and complete. Based on your suggestions, we have corrected the content of the Keywords, Methods, Results, Discussions, Conclusions, etc. The images in the text have been replaced to add clarity. It should be noted that the purpose of Figures 1 and 2 is to provide a summary of our inclusion and exclusion criteria and workflow, and the purpose of the pictorial is to provide the reader with a clear understanding of this part. In addition, the clarity of Figure 4 cannot be further improved because the software is unable to generate a clearer picture, but this does not affect the convergence trend of the prediction performance metrics of the model. We make a uniform correction to the "central compartment lymph node metastasis" in the

article.

Reviewer B

This is an interesting paper that deals with the preoperative radiomics prediction model for central compartment lymph node metastases (CLNM) in PTMC patients using gradient-boosting decision tree (GBDT model).

L 184: "structurally clear lymph nodes" were defined as CLNM negative on US. Abnormal ultrasound features suggestive of CLNM are defined as fine punctate calcification, cystic degeneration, and peripheral vascular signs". THE AUTHORS SHOULD ADD also "thyroid -like" features of typical metastatic lymph nodes and add the following reference: Leenhardt L, Erdogan MF, Hegedus L, Mandel SJ, Paschke R, Rago T, Russ G. 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. Eur Thyroid J. 2013 Sep;2(3):147-59. doi: 10.1159/000354537. Epub 2013 Sep 5. PMID: 24847448; PMCID: PMC4017749.

Line 324: Please MODIFY AS: "Detecting CLNM might be affected by several reasons like sternumocclusion and endotracheal gas" AND ALSO BY THE TINY SIZE OF SUSPECTED LYMPH NODES, AND PARA RETRO TRACHEAL LOCATION.

LINE 329 "...neck-positive lymph nodes (21.3%), while CLNM OR CONTRAST ENHANCED CT ????" increased the detection rate by only..."

Please check and modify accordingly.

Figure 1 caption:....."non- thyroid papilloma" ?? is it a typo ? please explain or modify. Please put the stress on the characteristics of the final model in your conclusion.

HAVING ruled out chronic lymphocytic thyroiditis reduces the value of the nomogram.

Reply: Dear Reviewer Thank you for your advice. We corrected the ultrasound features of lymphatic metastases and cited the recommended literature. As suggested, lines 324 and 329 have been rewritten. The "non-thyroid papilloma" in the exclusion criteria in Figure 1 means that in the thyroid tissue on the same side, the pathology indicates that in addition to PTMC, there are other pathological types in the thyroid tissue, such as thyroid follicular tumor. This may affect subsequent extraction of radiomics features. The conclusions have been rewritten to reflect the strengths of this research model. Patients with thyroiditis were excluded in this study, considering that there are diffuse

changes in ultrasound images in patients with thyroid inflammation, which may affect radiomics analysis, and we will conduct further radiomics studies in patients with thyroid malignancy and thyroiditis.

Reviewer C

The topic is very interesting and this is certainly the future of diagnostics. In general, it is big dilemma whether should to perform prophylactic central neck dissection in papillary thyroid microcarcinomas, and even in larger papillary carcinoma. In most patients there is no need to perform prophylactic central neck dissection and put them at risk of permanent hypoparathyroidism. However, in some patients, unrecognized central lymph node metastases may be reason for local recurrence. With prophylactic central neck dissection, patients with central lymph node metastases are transferred to a higher stage of the disease and than they receive radioactive iodine therapy.

This is a promising diagnostic method considering that neck ultrasound have low sensitivity in detection central lymph nodes, but it requires an experienced radiologists and technical support.

Line 206-208 - "Among the clinical features of the training and validation cohort, the Student's t-test and chi-square test were used to identify clinical risk factors associated with CLNM.", I think this sentence should be moved to "statistical analysis"

Line 259 - The percentages are wrong, they differ from those in the table 2 (50.7 and 49,1 are correct)

Line 262 - "pathologic CLNM". You should delete "pathologic", because Central Lymph Node Metastasis are certainly pathological

Line 324 - Sternum can not affect detecting lymph node in central (VI) neck region because that region is above the sternum. It can affect detection only mediastinal lymph node, and also VII lymph node - lymph node in upper anterior mediastinum.

Line 341 - Since you referred to the studies, you should cite them.

Line 346 - Insert references of the studies you refer to

Line 353 - Which studies, cite them.

Line 392 - Which studies?

Line 395 - Probably you mean studies 28 and 34, so you should put them on the end on the sentence

Line 398 - You discuss about your results, so you should remove references (28,34) and put them at the end of the previous sentence

Reply: Dear Reviewer, Thank you for your advice. As suggested, we have deleted lines

206 to 208 and reflected them in the statistical analysis section. The percentages mentioned in line 259 are the proportion of patients with lymph node metastasis in the training and validation cohorts, which are 50.7% and 49.1%, respectively, and this set of data is not a reflection of the data in Table 1 and does not contradict the data in Table 1. In response to the recommendations, we have made corrections to lines 262 and 324. We cited the studies mentioned in the article, corrected irregularities in the citations, and re-examined whether the citations were standardized.

Reviewer D

1. References

a. The citation of reference (30) is missing. Please check and revise. References should be cited consecutively and consistently according to the order in which they first appear in the text.

Reply a: Dear editor, thank you for reviewing the article. We have added reference (30).

b. The authors mentioned “**studies...**”, while only one reference was cited. Change “Studies” to “A study” or add more citations. Please revise. Please number references consecutively in the order in which they are first mentioned in the text.

*and **many studies** believe that there is no clear correlation between the two (36), ...*

***some studies** have shown that obesity promotes the occurrence and development of thyroid malignant tumors (37), ...*

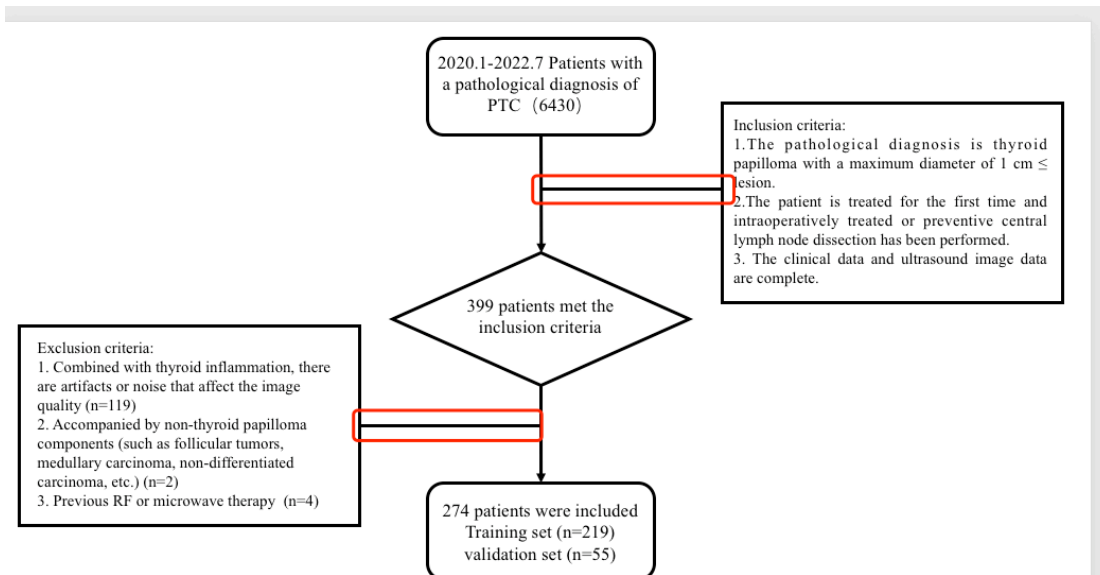
*In the process of image group feature selection, we used WEKA software, which can be widely used in the processing of high-throughput information in various **studies** (39).*

***Some studies** have explored the relationship between ultrasound texture analysis and lymph node metastasis of PTMC, but the results show that texture analysis can not predict lymph node metastasis in patients with PTMC (40).*

Reply b: Dear editor, thank you for your suggestions. We have modified some of the wording in the article that refers to relevant research.

2. Figure 1

Please add arrows in the flowchart in every step.



Reply: Dear editor, thank you for your suggestions. We improved the flow chart.

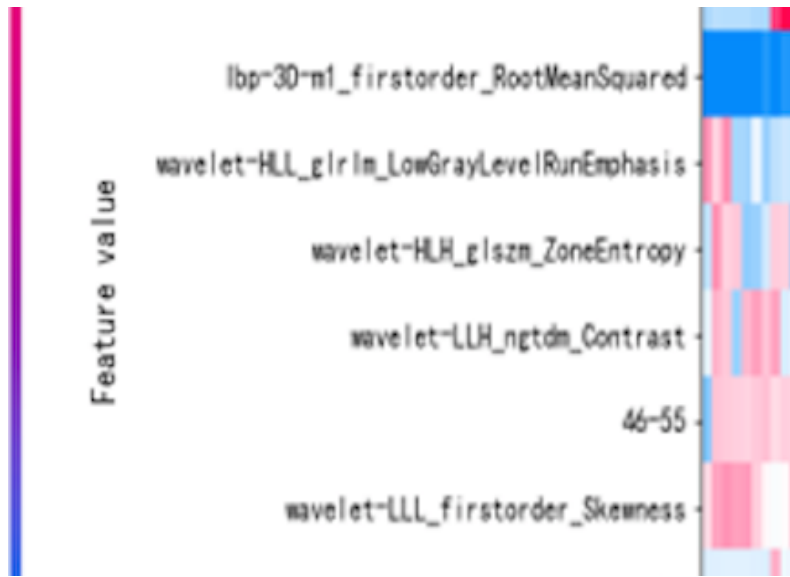
3. Please remove the legend from **figure 2**. Some panels are not clear enough. Please revise and resubmit it to us as a separate file in jpg or tiff format with **high resolution**.



FIGURE 2
Flow chart of the study.

Reply: Dear editor, thank you for your suggestions. The clarity of Figure 2 cannot be further improved. The content of Figure 2 is a flow chart of the research. All the content in the figure is reflected in the article. After consideration, we decided to delete Figure 2. And renumber all the pictures in the article.

4. **Figure 7** is **not clear enough** for publication. It would be much appreciated if you could provide it with a higher resolution as possible as you could. The preferred format is JPG or TIFF.



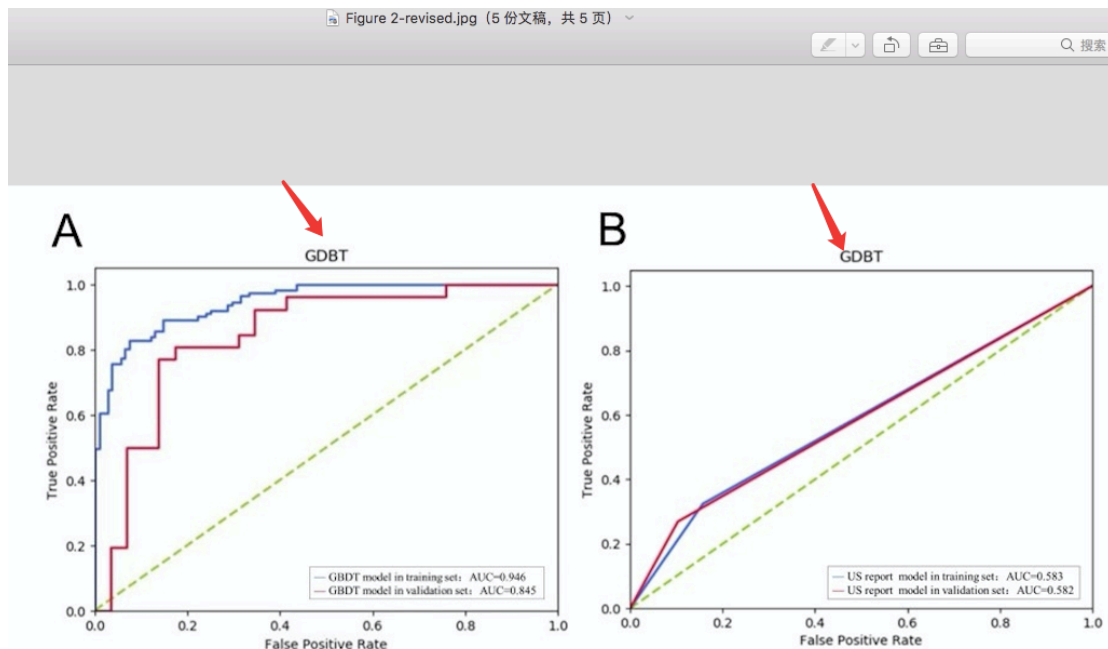
Reply: Dear editor, thank you for your suggestions. We've replaced the image with a higher resolution one.

5. Ref. 36 and Ref. 38 are the same. Please check and revise.

Reply: Dear editor, thank you for your suggestion. We have deleted Ref. 38 and modified the citation number.

6. Figure 2

Should GDBT be GBDT? Please check and revise.



Reply : Dear editor, thank you for your suggestion. We modified Figure 2.

7. Table 1 and Table 2

Please indicate how the data are presented in Tables in a footnote below the corresponding table/figure.

For example, Data are presented as N (%). Data are presented as mean \pm standard deviation, median (interquartile range), or number (frequency).

Reply : Dear editor, thank you for your suggestion. We have made corresponding changes.
