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Review Comments-Reviewer A

Comment 1: First, the title needs to clearly indicate the diagnostic accuracy of T2WI for the differential diagnosis between Ade and Sq.

Reply 1: Thank you for your suggestion. Our study explored the value of the radiomic in distinguishing Ade from Squ with solid components >8 mm. We have clearly indicate the diagnostic accuracy and modified our title.

Changes in the text: We have modified our title as advised. (see Page 1,line4)

Comment 2: Second, the abstract needs revisions. The background did not indicate the knowledge gap on the diagnostic accuracy of MR-Rad for NSCLC and the clinical needs for this research focus. The methods need to describe the inclusion of subjects, the generation of training and validation samples, and how the diagnoses of Ade and Sq were ascertained. The results need to briefly summarize the clinical characteristics of the study sample and the sensitivity and specificity as diagnostic accuracy parameters. The conclusion needs detailed comments for the clinical implications of the findings.

Reply 2:

1. We sincerely appreciate the valuable comments. In the background, we have described the accuracy and limitations of radiomics-related studies, and the clinical needs for this research focus.
2. In the methods, we have described the inclusion of subjects, the generation of training and validation samples, the gold diagnosis of Ade and Sq.
3. In the results, we have added description of the clinical characteristics of the study sample and the sensitivity and specificity of the diagnostic model based on radiomics.
4. In the conclusion, we have added comments for the clinical implications of the findings.

Changes in the text: We have modified our test as advised. (see Page 1,line30~31), (see Page 2,line1,line5~9,line17~20,line27~29).

Comment 3: Third, in the introduction of the main text, the authors need to review all available diagnostic model for the subtype of NSCLC including clinical and biomarkers used and their diagnostic accuracy and have comments on their limitations to suggest the needs for new diagnostic models including T2WI-based radiomic features. Please

also explain why the T2WI-based model can accurately predict the subtype of NSCLC.

Reply 3:

1. We sincerely appreciate the valuable comments. We have reviewed available diagnostic model for the subtype of NSCLC including clinical and biomarkers used and their diagnostic accuracy and have comments on their limitations.
2. According to the analysis of some previous research results, the T2WI-based model can accurately predict the subtype of NSCLC and it has a certain feasibility.

Changes in the text: We have modified our test as advised. (see Page 4,line13~20,line32~33)(see Page 5,line1~2,line7~8)

Comment 4: Fourth, the methodology of the main text needs to describe the clinical research design, sample size estimation, ethics approval, and assessment of clinical factors. In statistics, please ensure $P < 0.05$ is two-sided. Because of the small sample size, the 95% CIs of all diagnostic accuracy parameters should be reported. Please describe the details of how the clinical features and radiomic scores were combined for the diagnosis of subtype of NSCLC.

Reply 4:

1. We think this is an excellent suggestion. We've added a description of the clinical research design, sample size estimation, ethics approval, and assessment of clinical factors to the article.
2. Our study has ensured $P < 0.05$ is two-sided in statistics. The 95% CIs of all diagnostic accuracy parameters were reported in Table 5.
3. We have described the details of Nomogram Construction to expound how the clinical features and radiomic scores were combined for the diagnosis of subtype of NSCLC.

Changes in the text:

1. We have modified our test as advised. (see Page 8, line 22~30)
2. We have modified our test as advised. (see Page 9, Line 14). (table 5)
3. We have modified our test as advised. (see Page 8, line 22~30), (see Page 10, line 13~16), (see Page 11, line 1~4)

Review Comments-Reviewer B

Comment 1. Please define the abbreviation in Abstract.

on identifying pathological subtypes of lung cancer. Here we explored the value of the the contrast-enhanced MRI-T2WI-based radiomic analysis in distinguishing Ade from

Reply: We have modified Abstract as advised. (see Page2,line2-3)

Comment 2. Please structure your Main Text as: **Introduction, Methods, Results, Discussion, Conclusion**. Please add “Conclusion” section for your manuscript.

Reply: We have added “Conclusion” section for our manuscript. (see Page15, line5-11)

Comment 3. Please unify the approval number.

29 Committee of the First Affiliated Hospital of Soochow University (No. (2022
30 Lunyan Batch No.) 507) with the informed consent of all individual participants.↵
22 Ethics Committee of the First Affiliated Hospital of Soochow University (approval No.
23 LYP2022-507) Informed consent was obtained from all the participants.↵

Reply: We have unified the approval number as No.LYP2022-507.(see Page9,line1-2)

Comment 4. We helped add Helsinki statement to Methods section, and also made minor revisions to the consent statement. Please confirm.

Reply: We have confirmed these revisions.

Comment 5. References

a. There are two references included in your paper, please keep the final version and remove the other one.

b. The format does not meet our requirement. You should manage your references in accordance with the following order: Name of the authors (last name + first name (initial)). Reference title. Journal name (space) Year; Volume number: Page number.

5 2. Yang X, He J, Wang J, et al. CT-based radiomics signature for differentiating solitary
6 granulomatous nodules from solid lung adenocarcinoma. *Lung Cancer* 2018;125:109-14. [↕](#)
7 3. C Z, L Y, L W, et al. - Identification of immunohistochemical markers for distinguishing lung. -
8 *J Thorac Dis* 2015 Aug;7(8):1398-405 doi: 103978/jissn2072-143920150725:- 1398-405. [↕](#)
9 4. Y L, J K, Y B, et al. - Radiomic Features Are Associated With EGFR Mutation Status in Lung. -
10 *Clin Lung Cancer* 2016 Sep;17(5):441-448e6 doi: 101016/jcllc201602001:- 441-8.e6. [↕](#)
11 5. M S, A L, A DA, et al. - Liquid biopsy for lung cancer early detection. - *J Thorac Dis* 2018
12 Apr;10(Suppl 7):S882-S897 doi: 1021037/jtd20180381:- S882-S97. [↕](#)
13 6. Liang W, Zhao Y, Huang W, et al. Liquid biopsy for early stage lung cancer. *J Thorac Dis*
14 2018;10:S876-s81. [↕](#)
15 7. M J C, E S Y. - Liquid biopsy is a valuable tool in the diagnosis and management of lung cancer.
16 - *J Thorac Dis* 2020 Nov;12(11):7048-7056 doi: 1021037/jtd20200420:- 7048-56. [↕](#)

And “.” is not required here, please remove them.

7 3. C Z, L Y, L W, et al. - Identification of immunohistochemical markers for distinguishing lung. -
8 *J Thorac Dis* 2015 Aug;7(8):1398-405 doi: 103978/jissn2072-143920150725:- 1398-405. [↕](#)
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10 *Clin Lung Cancer* 2016 Sep;17(5):441-448e6 doi: 101016/jcllc201602001:- 441-8.e6. [↕](#)
11 5. M S, A L, A DA, et al. - liquid biopsy for lung cancer early detection. - *J Thorac Dis* 2018
12 Apr;10(Suppl 7):S882-S897 doi: 1021037/jtd20180381:- S882-S97. [↕](#)
13 6. Liang W, Zhao Y, Huang W, et al. Liquid biopsy for early stage lung cancer. *J Thorac Dis*
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15 7. M J C, E S Y. - liquid biopsy is a valuable tool in the diagnosis and management of lung cancer.
16 - *J Thorac Dis* 2020 Nov;12(11):7048-7056 doi: 1021037/jtd20200420:- 7048-56. [↕](#)

*Example of the correct format: Lin X, Li W, Lai J, et al. Five-year update on the mouse model of orthotopic lung transplantation: Scientific uses, tricks of the trade, and tips for success. *J Thorac Dis* 2012;4:247-58.

c. And please also check if the authors' names are matched to their references cited.

12 tomography (CT) images. Ji et al. showed that by constructing an radiomic model
13 predicting the classification of lung adenocarcinoma and squamous cell carcinoma
14 based on Stage-Specific PET Radiomic, the AUC of it in the validation cohort was
15 0.886. The radiomic-clinical nomogram integrating radiomic features with independent
16 clinical predictors exhibited more favorable discriminative performance, with AUC of
17 0.978 in the validation cohort (18). The radiomic model, based on CT constructed by
18 Zhu et al. had an AUC of 0.893 (95%CI: 0.789 to 0.996) in the validation cohort, with
19 a sensitivity of 0.828 and a specificity of 0.906 (19). However, CT and positron emission
20 tomography (PET)/CT are radiotoxic, and CT offers less precise visualization of soft
21 tissue detail than magnetic resonance imaging (MRI). In addition, the tumor tissue
22 function information provided by MRI has certain predictive value for the pathological
23 classification of lung cancer. Clinically, pure ground-glass opacity neoplastic lung
24 nodules are more likely to be Ade, whereas nodules with solid components are difficult
25 to identify. Research has shown that MRI has a sensitivity of 60-75% for solid lung
26 nodules measuring 4-6 mm, 80-99% for solid lung nodules measuring 6-8 mm, and
27 100% for solid nodules with a diameter of >8 mm (20-24). According to the Lung-
28 RADS (23), solid nodules measuring ≥6 mm belong to grade 3 and above nodules that
29 require short-term follow-up or further clinical management. MRI has shown good
30 sensitivity and specificity for solid nodules sized ≥6 mm (i.e., Lung-RADS grade 3 and
31 above nodules) (20). The study conducted by Lac et al. identifies the tumor histological
32 type from MR T2-weighted images, with classification performance similar to those
33 reported in PET/CT and in multiphase CT in lung cancers (25). More studies have

Reply: a. We have kept the final version and remove the other one. (see References)

b. We have revised the format to meet the requirement. Please confirm.(see

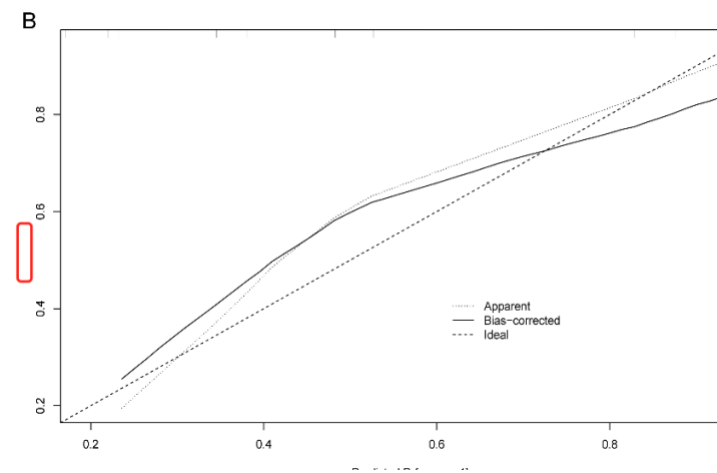
References)

c. We have revised the manuscript to ensure the authors' names are matched to their references cited.(see Page4,line15-22),(see Page5,line1-4)

Comment 6. Please also define AUC in Figure 5 legends.

Reply: Although we didn't use AUC in Figure 5 legends, we add the definition of AUC in accordance with your suggestion. Please confirm the need to add this definition.(see Figure 5 legends)

Comment 7. Figure 7: Please also provide description for Y-axis in figure 7B, do not share.



Reply: We have changed the Figure 7 and renamed it as “Figure7-revised.We will send the revised figure as separate file TIFF format to you.(see Figure7)