Peer Review File

Reviewer A

I would like to suggest that it is important for the authors to describe the image acquisition parameters (for instance, kernel resolution and other scanner parameters, as well as parameters related to acquisition protocols) and image physical dimension parameters (pixel spacing, slice thickness) of the CT scans, as they have been acquired at two centers. They should further describe how they would address the impact of this image parameter heterogeneity on the radiomic features, to ensure that the results obtained are reproducible across multi-institutional data studies.

Reply: Thank you for your valuable suggestion. First, we added the image acquisition parameters and image physical dimension parameters of the CT scans accordingly (see Table S1) to present complete information. Then, to our knowledge, the tube voltage and slice thickness might have a potential influence on the radiomics features, and thus we chose the same tube voltage, slice thickness and reconstruction method even though the images were acquired by different scanners. It would reduce the impact of image parameter heterogeneity on the radiomic features.

Reviewer B

1) First, the title is not accurate since the diagnostic model was based on both demographic information and radiological features. The authors need to indicate the clinical research design of this study, i.e., a diagnostic test or a diagnostic accuracy study.
   Reply: Thank you for your valuable suggestion. We have revised the title to "A CT-based radiomics integrated model for discriminating pulmonary cryptococcosis granuloma from lung adenocarcinoma—a diagnostic test" further to indicate the clinical research design of the study. Besides, we used "integrated model" in the title to describe the formation of our model, which was based on demographic information, radiological features and radiomics features.

2) Second, the abstract needs some revisions. The background did not explain why the diagnostic model based on both demographic information and radiological features can accurately make differential diagnosis between pulmonary cryptococcosis granuloma from lung adenocarcinoma and what the knowledge gap is on the

methods to address this clinical difficulty. The methods need to describe the sociodemographic variables and radiological features used in the model and the calculation of sensitivity and specificity. The results need to summarize the clinical characteristics of the clinical samples and report the sensitivity and specificity of the diagnostic model. The conclusion needs comments for improving the diagnostic accuracy of the model.

Reply: Thank you for your valuable suggestion. The abstract has been revised accordingly following your advice (see Page 2-3, Line 45-80).

3) Third, the introduction of the main text did not review the available methods for making the differential diagnosis between the two conditions and why a diagnostic model based on demographic information and radiological features can accurately facilitate the differential diagnosis. The other concern is the limitations of diagnosis made by experienced and unexperienced radiologists.

Reply: Thank you for your valuable suggestion. In our study, we mainly focused on the value of CT-based radiomics features in the differentiation between the two conditions, and include individuals with normal immunity which may not exhibit significant symptoms or laboratory findings. Thus, we mainly reviewed the applications and limitations of diagnostic imaging for the two diseases. Furthermore, we added the point you mentioned in our introduction part to emphasize the importance of accurate diagnosis from CT images (see Page 4, line 113-114).

4) Fourth, in the methodology of the main text, please describe the clinical research design, sample size estimation, data collection of sociodemographic variables and clinical characteristics. In statistics, AUC cannot be the only indicator of diagnostic accuracy. Please describe the calculation of sensitivity and specificity, as well as provide their threshold values for a good diagnostic model.

Reply: Thank you for your valuable suggestion. The clinical research design and data collection of sociodemographic variables and clinical characteristics have been described in the methods part (see Line 206-210). And the statistical part has also been revised (see Page 7, Line 226).