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Reviewer A

The authors studied “The characteristics of emphysema and pulmonary perfusion derived from spectral CT in smokers”
Introduction: OK
Methods
Comment 1: Study population: Please add a consort diagram to outline how patients were selected and excluded.
Reply 1: We think this is an excellent suggestion. We have added the consort diagram of the study (Figure 1) at Method part (see Page 3, line 55; Page 16, line 397-399).

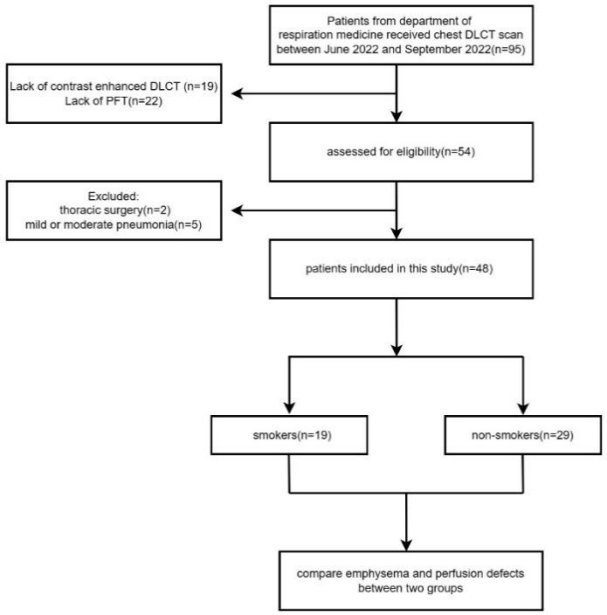

Figure 1 Flow diagram of the study
And the serial number of other figures were also changed in the revised manuscript. All the revised text were marked in red in the revised paper.

Comment 2: Please add a reference as to why 1 month of smoking is sufficient to be called a smoker.
Reply 2: We sincerely appreciate the valuable comment. We defined smokers according to the reference of "Yu N, Yuan H, Duan HF, Ma JC, Ma GM, Guo YM, Wu F. Determination of vascular alteration in smokers by quantitative computed tomography measurements. Medicine (Baltimore). 2019;98(7):e14438. doi: 10.1097/MD.0000000000014438. PMID: 30762753; PMCID: PMC6408080." In this article, “non-smokers” were defined as subjects who had never smoked, or their total years of smoking were<1 month; “current smokers” were defined as subjects who actively smoked at baseline; “former smokers” were defined as subjects who had quit smoking more than “1 to 2 years” at baseline, and did not start smoking again during the whole observation time. In our study, we divided the patients into two groups, smokers and non-smokers. While, smokers were not further divided into current smokers and former smokers due to the small sample size. Therefore, we have added this limitation to the discussion (see Page 11, line 278-280). At the same time, we have added this reference on the definition of smokers and non-smokers into the Methods and Reference part respectively in the revised manuscript(see Page 3, line 64; Page 13, line 344-346). And the serial number of some other references were also changed in the revised manuscript.
All the revised text were marked in red in the revised paper.

Comment 3: Also please mention if other potential causes of perfusion abnormalities such as pulmonary vaso-occlusive disease, obliterative bronchiolitis and hypersensitivity pneumonitis, were excluded.
Reply 3: We feel great thanks for your professional review work on our article. As you are concerned, we have definitely excluded other potential causes of perfusion abnormalities such as pulmonary vaso-occlusive disease, obliterative bronchiolitis and hypersensitivity pneumonitis when patients were recruited. However, we are very sorry for our undetailed writing about Methods part. We have revised the text "Patients with chest surgery, bilateral pleural effusion, history of obviously anomalous lung lesions on a CT scan or radiographic features of lung infiltration, and cardiac or renal diseases were eliminated" to "Patients with chest surgery, bilateral pleural effusion, history of diseases that might cause perfusion abnormalities such as pulmonary vaso-occlusive disease, obliterative bronchiolitis and hypersensitivity pneumonitis, obviously anomalous lung lesions on a CT scan or with radiographic features of lung infiltration, and cardiac or renal diseases were excluded" for addressing your concerns and hoping that it is now clearer(see Page 3, line 49-53). All the revised text were marked in red in the revised paper.

Comment 4: Spectral DLCT scanning protocol: How much IV contrast was used in terms of iodine in grams.
Reply 4: Thanks for your comments. The administered iodinated contrast agent volume (Accupaque, 350 mg/mL; GE Healthcare GmbH, Solingen, Germany) was based on patient body weight(kg) as 1.0ml/kg. The range of weights was 54-76kg(mean weight 68.92±5.80kg). Therefore the 18–26 g of iodine used in our study. We have added this text into the Methods part in the revised manuscript(see Page 4, line 82-85). All the revised text were marked in red in the revised paper.

Comment 5: Emphysema quantification. The text is unclear, please re-write for clarity.
Reply 5: Thanks for your suggestion. We have re-written this part of Emphysema Quantification according to the Reviewer's suggestion. We reviewed assessment methods of emphysema and PD, and made minor modification to the qualitative analysis methods, and conducted data analysis again. We tried our best to improve the manuscript and these changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in the revised paper. We appreciate for Reviewers' warm work earnestly and hope that the correction will meet with approval(see Page 5, line 105-118; Page 6, line127-130).

Discussion:
Comment 6: Please add section on image quality and radiation dose. Prior studies described artifacts in iodine maps with single source DECT (Singh R et al. Comparison of image quality and radiation doses between rapid kV-switching and dual-source DECT techniques in the chest. Eur J Radiol. 2019 Oct;119:108639. doi: 10.1016/j.ejrad.2019.08.008. Epub 2019 Aug 13. PMID: 31442929).
Reply 6: We think this is an excellent suggestion. According to your comments, we perused the Singh R et al.'s literature of "Comparison of image quality and radiation doses between rapid kV-switching and dual-source DECT techniques in the chest" carefully. And we have added the evaluation of image quality and radiation dose based on the Singh R et al.'s method into the Methods(Page 4-5, line92-103) and Results(Page 7, line168-178) part.
The details are as follows: "Two thoracic radiologists (with 8 and 10 years of experience, respectively) independently assessed iodine density images for each DLCT examination on the Philips workstation (Extended Brilliance Workspace TM, Cleveland, OH, USA) based on the method of Singh, R et al.[17]. They performed qualitative assessment of overall diagnostic quality based on the existence and severity of artifacts. And image quality was graded on 3-point scale (1= No artifacts; 2= minimal artifacts with no effect on diagnostic interpretation; 3= artifacts with substantial effect on diagnostic confidence, diagnosis not possible). The artifact types including cardiac motion artifacts, contrast streaking, beam hardening, metallic implant related artifacts were evaluated as well. CT dose index volume (CTDIvol), size-specific dose estimates (SSDE),and dose length product (DLP) were recorded for each patient." were added in the Method

part. "Both radiologists reported minimal artifacts in 19/29(65.5%) exams of non-smokers and 13/19(68.4%) exams of smokers($\chi2$=0.044, P=0.835). No artifacts were reported in the remaining 10/29(34.5%) exams and 6/19(31.6%) exams in non-smokers group and smoker group, respectively($\chi2$=0.044, P=0.835). None of the severe artifacts resulted in diagnosis not possible. Artifacts included contrast streaking from subclavian veins, cardiac pulsation artifacts, and beam hardening at the level of the shoulders. And all the artifacts were categorized as minimal. Image quality was deemed good to meet the diagnosis for all examinations. The CTDIvol, SSDE and DLP were 10.61±5.24mGy, 15.54±4.84 mGy,402.24±87.27 mGy*cm, respectively." were added in the Results part. All the revised text were marked in red in the revised paper.

We would like to express our sincere appreciations of your valuable feedback that we have used to improve the quality of our manuscript.

Comment 7: If regular amount IV contrast is used these can cause contrast streak artifacts at lung apices and around SVC and therefore lower IV contrast volume is recommended for DECT (Digumarthy SR. Low contrast volume dual-energy CT of the chest: Quantitative and qualitative assessment. Clin Imaging. 2021 Jan;69:305-310. doi: 10.1016/j.clinimag.2020.10.006. Epub 2020 Oct 6. PMID: 33045474).

Reply 7: Thanks for your comments. In our study, the administered iodinated contrast agent volume (Accupaque, 350 mg/mL; GE Healthcare GmbH, Solingen, Germany) was based on patient body weight(kg) as 1.0ml/kg. The range of weights was 54-76kg(mean weight 68.92±5.80kg). As a result, the 18–26 g of iodine used in our study. While 9-13g of iodine used in Digumarthy SR et al.'s study of "Low contrast volume dual-energy CT of the chest: Quantitative and qualitative assessment". Therefore, the regular amount iodine was used in our study. However, we added the evaluation of image quality according to the comments. Although, the existence of artifacts included contrast streaking from subclavian veins, cardiac pulsation artifacts, and beam hardening at the level of the shoulders, all the artifacts were categorized as minimal artifacts with no effect on diagnostic interpretation. Image quality was deemed good to meet the diagnosis for all examinations. In future studies, we hope to further investigate lung perfusion changes of iodine maps with low iodinated contrast agent volume in smokers. Therefore, we have added this limitation to the discussion (see Page 11, line 283-286).

Comment 8: Is there a difference in image quality and artifacts between arterial and venous phases.

Reply 8: Thanks for your comments. We evaluated the image quality of iodine maps from arterial phase and venous phases respectively. The results showed that the presence of minimal artifacts in 32/48(66.7%) exams of all patients for iodine maps from arterial phase, while the presence of minimal artifacts in 30/48(62.5%) exams of all patients for iodine maps from venous phase. There was no significant difference for image quality of iodine maps between arterial phases and venous phase($\chi2$=0.182, P=0.670). Contrast streaking artifacts from subclavian veins on iodine maps from venous phase were less than that from arterial phases. We indeed to investigate the value of iodine maps from arterial phases in assessing lung perfusion changes in smokers in our study. Therefore, we did not compare the difference of image quality and artifacts between arterial and venous phases in the revised text.

Reviewer B

1. The leading structure of the Abstract should be Background instead of Objectives. Please provide the background information of this study and limit the word count under 350 for the entire Abstract.

Reply: We have added the background of the abstract in the manuscript file. (see Page 2, line 31-33). The word count of abstract was under 350.

We would suggest to add more background information to fit the subtitle.

Reply: "Assessment of the lung perfusion characteristics is very significant to timely treatment and prevent disease progression in smokers" have been added to the background of the abstract.(see Page 2,line 33-34)

Reply: We have added the background of the abstract

2. A subtitle - Conclusions is required for the Main Text.

Reply: We have added the subtitle of conclusions for the main text in the manuscript file.(see Page 13, line 349)

3. DLCT/PD/FEV1/FVC should be defined upon first use in the Main Text.
Reply: we have checked across the whole main text and DLCT/PD/FEV1/FVC have been defined upon first use in the Main Text.
The full term of DLCT in the Highlight box should be checked.
Reply: We have revised the full term of DLCT. "spectral dual-layer detector spectral(DLCT)"have been revised as "spectral dual-layer detector computed tomography(DLCT)".(Page 3, line 63). Meanwhile, We check the main text and change the "DLCT" into the "spectral DLCT"(Page2,line 38; Page 3, line60; Page3,line 63;Page 4,line93,98;Page 5,line100,108;Page 12,line305).

4. Table 1
*F/M should be defined in the explanatory legend.
*The total numbers of patients by Sex(F/M) are not equal to 19 and 29 reported in the column headers. Please confirm.
Reply: We sincerely thank the Editors for careful reading. F/M have been defined in the explanatory legend. (see Page 17,line447-448). The numbers of patients by Sex have been corrected.(see Page17, line 446). We are very sorry for our undetailed writing.

5. Table 2
A header is required in the first column.
Reply: Variables of header have been added in the first column for the table 2.(Page 18, line456)

6. Table 3
*A header is required in the first column.
*FEV1/FVC/PFT should be defined in the explanatory legend.
Reply: Variables of header have been added in the first column for the table 3.(Page 18, line461); FEV1/FVC/PFT have been defined in the explanatory legend.(Page 18, line 462-464)

7. Figure 1
*The number of patients assessed for eligibility deducting the exclusion criteria does not equal 48 and needs to be checked.
Reply: We have provided an editable version in a separate word file. Meanwhile, we have corrected the number of patients assessed for eligibility deducting the exclusion criteria.(Page19,line466). We are very sorry for our undetailed writing.

8. Figure 2A
The colors should be explained in the legend.
Reply: We have explained the colors in the legend.(Page20,line 486-487).

9. Figure 3A
The colors and F at the bottom of the figure should be explained in the legend.
Reply: We have explained the colors of the figures(Page 21,line 497). F at the bottom of the figure mean direction, for example, foot position(F). F could be deleted in the pictures.

10. All the abbreviations in the figures should be defined in the explanatory legend.
Reply: We have checked all the abbreviations in the explanatory legend of figures. All the abbreviations have been defined.
Figure 1: the definition of DLCT/PFT needs to be provided.

Reply: We have provided the definition of DLCT and PFT in the explanatory legend of figure 1(Page 17, line 452-453).Meanwhile, we change the “DLCT” to “spectral DLCT” in the Figure 1.

11. CT/FEV_1/HU/FVC/ANOVA/IQR should be defined upon first use in the Abstract. The full term is suggested to replace the abbreviation when the word is only used once in the Abstract.
Reply: CT/FEV1/HU/FVC/ANOVA have been defined upon first use in the Abstract. In order to limit the word count under 350 for the entire Abstract, Data expressed as median (Inter-Quartile Range) have been deleted, p value were still displayed in the result of abstract.