Peer Review File

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Reviewer A

The authors report that the identification of specific computed tomography (CT) features, particularly the percentage of solid components (PSC), and morphological characteristics,
provides a valuable approach for predicting spread through air spaces (STAS). Since the detailed information of STAS is not available before surgery, their methods may be useful to identify patients with STAS, who the predictive prognosis is worse than that of without STAS. However, several points should be addressed.

Major points

1) The TNM classification should clearly state what edition was used. Version 9 is now used. It would be necessary to add a note to Methods to indicate which Version was used for TNM for this study.

Reply 1: we used Version 9 of TNM classification
Changes in the text: we have added related content. (see Page 5, line155-156)

2) line 180-##Pathological features. Table 2
Related to #1, TNM and Stage should be described with more detailed classification. a, b, and other subcategories also have prognostic significance and should be considered down to the subclassification.

Reply 2: we have added related content. (see Page 17, line519)

3) Did the authors search for driver mutation status and PD-L1 expression? Especially in Stage III cases, where neoadjuvant or adjuvant therapy could affect the prognosis. Driver gene mutation status and PD-L1 expression should be included in the consideration. If it cannot be considered, it should be listed as a major limitation.

Reply 3: No, we didn't search for driver mutation status and PD-L1 expression;
Changes in the text: we have added related content and it was listed as a major limitation. (see Page11, line376-378)

Minor points

1) Table2
The word 'Phase' is incorrect and needs to be corrected. It should simply be stated as 'I"II", or 'Phase' should be deleted.

Reply 1: we have modified our text as advised (see Page 17, line 519)

2) Although the authors mention that it is a retrospective study in limitation part, this should also be clearly stated in the Methods section.

Reply 2: we have added related content as advised (see Page4, line 127)

Reviewer B

Strengths:

Clinical Relevance: The study addresses an important clinical issue—STAS in lung cancer—which has significant implications for surgical decision-making and patient outcomes. The findings are directly applicable to clinical practice, especially in refining treatment strategies.

Comprehensive Analysis: The manuscript provides a thorough analysis of clinical, pathological, and CT features, offering a multifaceted approach to understanding STAS. This comprehensive approach adds depth to the study and provides valuable insights for clinicians.

Novel Contributions: The study contributes novel findings, particularly the identification of CT features such as the percentage of solid components (PSC) as an independent factor for predicting STAS. This is a valuable addition to the existing literature.

Robust Statistical Analysis: The use of multivariate logistic regression to identify independent factors and the ROC curve analysis to determine cut-off values are well-executed and enhance the credibility of the findings.

Areas for Improvement:

Discussion on Limitations: While the limitations are mentioned, the discussion could be expanded to include potential sources of bias, particularly in the selection of the control group (STAS-negative patients). A more detailed discussion on how these limitations might affect the study's conclusions would be helpful.

Reply 1: We have added 61 samples to the negative group

Changes in the text: we have modified our text as advised. (Page11, line 363-365)

CT Feature Analysis: The manuscript emphasizes the importance of CT features, but the rationale for selecting specific features, such as lobulation and ground-glass opacity, could be more clearly articulated. Additionally, explaining why some features, like satellite foci, were only present in a small percentage of cases would strengthen the analysis.

Reply 2: Lobulation and spiculation are the key features in diagnosing lung tumors. Pathologically, the lobulation sign can indicate the tumor's expansive growth and suggest variations in the growth rates of cells surrounding the tumor. It was widely recognized. Owing to the constraints of this article's length, we have omitted further explanation.
Changes in the text: Regarding satellite foci we have added related content as advised. (Page 11, line 353-357)

STAS in Non-LUAD Cases: The study notes that STAS is not limited to lung adenocarcinoma but does not thoroughly explore the implications of STAS in other types of lung cancer (e.g., squamous cell carcinoma, neuroendocrine carcinoma). A deeper analysis of these cases would add value and broaden the study's impact.
Reply 3: Other lung cancer types constitute merely 15 /121 cases in the STAS-positive group, and due to the limited sample size, further investigation is not feasible.
Changes in the text: we have modified our text as advised. (Page11, line 365-369)

Integration with Radiomics: The manuscript mentions the potential for future integration with radiomics but does not elaborate on how this might be achieved. Providing a more detailed perspective on how radiomics could enhance the study's findings would be a forward-looking addition.
Reply 4: we have added related content as advised. (Page 11, line 369-376)

Cut-off Values and Clinical Application: While the ROC curve analysis is a strength, the manuscript could provide more context on how the identified cut-off values (e.g., for PSC) would be applied in clinical practice, particularly in guiding surgical decisions.
Reply 5: We have mentioned how to use PSC and diameter in the discussion. (Page 9, line306-309)

Conclusion:
The manuscript is strong in its clinical relevance, comprehensive analysis, and statistical rigor. However, addressing the limitations, expanding on certain analytical points, and providing a clearer pathway for clinical application would make the manuscript even more impactful. Consider revising these areas to strengthen the manuscript's overall quality and make the peer review more favorable.

Reviewer C

This study aimed to elucidate the characteristics associated with the presence or absence of STAS (spread through air spaces). The authors identified several factors related to STAS, which are expected to be useful for readers. However, several aspects need to be addressed:

1) The authors included 157 lung cancer patients in their study, of which 60 were without STAS. Given that previous reports have indicated that the frequency of STAS in lung adenocarcinoma is approximately 15%, it would be reasonable to expect a higher number of patients without STAS. The authors should explain why they selected only 60 non-STAS patients for comparison out of a potentially much larger pool.
Reply 1: STAS represents a rare pathological occurrence. When comparing data, the negative group possesses a significantly larger dataset than the positive group. To bolster the statistical efficiency of our study, we determined that the control group should comprise a minimum of 121 cases, adhering to a 1:1 ratio. However, our initial control group contained only 60 cases. To enhance the reliability of our findings, we selected an additional 61 samples randomly from the STATS-negative cases, augmenting the original control group. This approach ensured that both the experimental and control groups consisted of 121 cases. Then we reanalyze the data. Throughout this process, we ensured that our sample size was derived from standard random sampling techniques, and the expanded sample size remained compliant with ethical standards.
Changes in the text: we added some data as advised (Page 4, line 131) and have modified our text as advised. (Page16, line 513-Page19, line531)

2) The authors describe the characteristics of each group, such as gender ratio and age, by stating them separately for the STAS-positive and STAS-negative groups. However, to make the information clearer, it would be more effective to present the data in a comparative format. For example, it would be clearer to write, "The gender ratio was X in the STAS-positive group and Y in the STAS-negative group. The ages were XX years (mean/median) in the STAS-positive group and YY years in the STAS-negative group." This format allows readers to directly compare the characteristics of each group more easily.
Reply 2: we have modified our text as advised. (Page 6, line 193-195)

3) The authors identified cut-off points for tumor diameter and the percentage of solid components. A tumor diameter of 1.5 cm is showed as a cut off-point but is a common size. Tumors with a diameter of less than 1.5 cm are relatively rare. These values may not hold significant meaning. When they validate their cut-off points in other patient groups, that data becomes useful. Here, the ROC curve does not need to be included.

Reply 3: The presence of STAS was associated with a risk for recurrence in patients with small adenocarcinoma who had undergone limited resection. Increasing evidence indicates that limited resection is adequate for part-solid nodules smaller than 2cm. However, in cases of early-stage lung cancer with STAS, the recurrence rate following limited resection is notably higher compared to lobar resection. Currently, guidelines have not reached a consensus on the necessity of adjuvant chemotherapy or targeted therapy for stage IA lung cancer post-surgery. Therefore, we posit that the presence of STAS holds significant importance in determining the prognosis of small lung cancer and in clinical treatment decision-making. Furthermore, based on the author's statistics, nodules with a diameter of less than 1.5cm comprised 39 out of 121 in the STAS-positive group and 35 out of 121 in the STAS-negative group. Consequently, the author incorporated this data into the ROC curve analysis.