Peer Review File

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Reviewer A

We read with great interest the manuscript titled "Prone Positioning in Cone Beam CT-Guided Robotic Bronchoscopy: A Strategy to Minimize Atelectasis and Improve Access to Posteromedial Lower Lobe Nodules" submitted to Journal of Thoracic Disease. This timely manuscript describes the authors experience with proning for image-guided robotic-assisted bronchoscopy for challenging, posterior and infero-medially located small lung nodules (<20 mm in diameter). While intriguing, there is some concern regarding this manuscript's structure, language, and scientific merit, that raises doubts regarding it's adequacy for publication, as described below.

Major Comments

- The manuscript addresses an important and timely scientific question, and the topic is of clear relevance to the field. The study has potential to make a meaningful contribution; however, the presentation suffers from significant structural and language issues. The current organization lacks clarity, is cumbersome, with ideas not flowing logically, and several sections do not provide sufficient distinction between background, methods, results, and discussion/conclusions. In its present form, these issues prevent the work from meeting the standards required for a scientific publication. Substantial reorganization and professional language editing would be necessary before the scientific contribution could be fully appreciated by the readership

A: We sincerely thank the reviewer for these thoughtful and constructive comments. We carefully considered the concerns regarding clarity, organization, and language. In response, we have undertaken a substantial revision of the manuscript, including a complete restructuring to ensure clear distinction between the background, methods, results, and discussion/conclusion sections. In addition, the text has been thoroughly rewritten and professionally edited to improve language, flow, and readability.

- The abstract requires a major revision of language. There is much background, which can be significantly condensed to allow more language to describe the methods, results and conclusions. Also, the abstract will benefit from grammatical language editing.

A: We thank the reviewer for this comment. The abstract has been revised to reduce background, emphasize methods, results, and conclusions, and improve grammar and clarity.

- The Introduction is too long, too detailed, and lacks focus to direct the reader to the purpose of this paper. The introduction serves to provide the relevant background, define the data deficiency, and briefly describe the purpose of the current study in addressing the data gap. Much of the current language provides extensive detail about background. Please consolidate into 3 paragraphs as described above. May move some of the language to the Discussion if needed.

A: Thank you for this important observation. We have carefully revised the Introduction to address these concerns. The section has been fully rewritten and reorganized into concise paragraphs, focusing on the relevant background, defining the data gap, and clearly outlining the purpose of the study. We believe this restructuring is aligned with the reviewer's recommendations.

- The authors place much emphasis on smaller size nodules. Various size thresholds are cited through the manuscript (i.e., 20 mm, 15 mm etc); however, no supportive data are provided to establish these size thresholds as crucial. Please choose the relevant size threshold and align across the manuscript. Please provide the rationale for a specific size threshold, supported by relevant citations.

A: Thank you. The manuscript has been fully revised, and a consistent size threshold has been applied throughout with supporting rationale and citations.

- The Methods would benefit from extensive language revision. I suggest the authors review previously published similar retrospective studies to assist with structuring the Methods. Sub-sections, such as Study Population, Proning Protocol, Bronchoscopy, Statistical Analysis, would be helpful in providing more structure.

A: Thank you. The Methods section has been thoroughly revised to improve clarity and flow, with a step-by-step description of the protocol we created for performing RAB in the prone position. These changes were made to improve structure, ensure reproducibility, and align with the standards of similar retrospective studies.

- The Methods section should be reinforced with the type of robotic-assisted bronchoscopy system and the type of CBCT/AF systems used in this study, to provide more context and allow direct translation to other institutions.

A: We thank the reviewer for this helpful suggestion. The Methods section has been revised to specify the robotic-assisted bronchoscopy system (Ion, Intuitive Surgical) and , the CBCT platform (SmartCT, Azurion image-guided therapy system). These details were added to provide context and facilitate reproducibility at other institutions.

Changes in the text: Lines 42-46

- The authors should provide more detail regarding patient selection, specifically, what defined lesions as "posterior lower lung" – which anatomic landmarks were used?

A: Thank you. The Methods section has been revised to clarify patient selection criteria. Lesions were defined as posterior and medial lung nodules if located posterior to the vertebral body on the axial CT plane. This definition has been added to provide a clear anatomic landmark for reproducibility.

Changes in the text: Lines 30-31

- The inclusion and exclusion criteria need to be better defined. Currently, there is only one exclusion criterion. Is that the only criterion implemented during this study?

A: Thank you. The Methods now clearly state that inclusion criteria were age ≥18, procedure within the study period, and CT-confirmed posterior lower lung nodule, with the only exclusion criterion being high-risk CAD.

Changes in the text: Lines 32-39

- The criteria implemented for the definition of diagnostic sampling and procedure accuracy are not adequately described in the study Methods.

A: Thank you. The answer section has been revised to define diagnostic sampling as obtaining malignant or benign pathology and non-diagnostic sampling. Procedure accuracy was defined by tool-in-lesion confirmation on CBCT/AF and corresponding diagnostic pathology.

- I am concerned about the brevity of the results section. No no details are provided on the study population, lesion characteristics, and procedure performance and outcomes.

A: Thank you. The Results have been expanded to provide detailed information on patient demographics, ASA classification, BMI, lesion size and distribution, as well as procedure times and performance. Pathology outcomes are now fully described, including the distribution of malignant, benign, and non-diagnostic cases, to give a comprehensive picture of diagnostic yield and study outcomes.

Changes in the text: 169-199

- The discussion section could benefit from a significant revision. Instead of organizing the discussion by concept, would recommend using standard sections:
o Restate research question/hypothesis
o Summarize key findings
o Interpret your findings
o Compare to existing literature
o Provide limitations
o Provide implications
o Provide future directions

A: Thank you for all suggestions. The discussion completely revised to meet all above points

- We restate the research objective, namely evaluating the feasibility and diagnostic yield of prone position RAB with CBCT-AF for posteromedial nodules.
- A concise summary of the study results is provided, including patient demographics, lesion distribution, procedure times, and the overall diagnostic yield of 89.3%.
- The findings are interpreted in the context of the physiologic benefits of prone positioning, specifically the reduction in anesthesia-related atelectasis and CT-to-body divergence.
- Comparisons are made to prior studies on PTNB, RAB in the supine position, and anesthesia-related strategies for atelectasis management.
- Study limitations are clearly stated, including the retrospective single-center design, lack of a direct supine comparator group, and potential issues with generalizability.
- Clinical implications are discussed, including the potential role of prone RAB with CBCT-AF in improving diagnostic accuracy for anatomically challenging nodules.
- Future directions are outlined, including multicenter prospective trials, refinement of patient selection criteria, cost-effectiveness evaluation, and incorporation of prone positioning techniques and CPR simulation into future teaching.

Reviewer B

Nice and interesting study, needs more patients, in order to build up the advantages of prone position.

Reviewer C

Dear Authors,
Thank you for work.
Management of CT body divergence and anesthesia induced and procedural related atelectasis is relevant to current practice of CBCT RAB radial prone guided lung biopsy and lung nodule ablation.
My comments

(1) Please include referenced name of navigational system and augmented fluoroscopy system used in Methods section.

A: Thank you. The Methods section has been revised to specify the robotic-assisted bronchoscopy system (Ion, Intuitive Surgical, Sunnyvale, CA) and the cone-beam CT with augmented fluoroscopy platform (SmartCT, Azurion image-guided therapy system, Philips, Best, The Netherlands). These details can be found in the Methods section

Changes in the text: Lines 42-46

(2) Method of placing patients in prone position should be described or referenced.

A: Thank you. We have provided a detailed description of the method for placing patients in the prone position. A step-by-step protocol was created and included in the Methods section (Proning Protocol subsection) to ensure clarity, reproducibility, and standardization across cases.

Changes in the text: Lines 55-166

(3) Ideal to have a larger sample size than 19 cases.
A: Thank you. Since the initial submission, the study cohort has been expanded from 19 to 28 patients, and the manuscript has been updated accordingly in the Methods, Results, and Discussion sections.

(4) Result section should mention table 1 and write baseline characteristics of patient cohort into Result section.

A: Thank you. The Results section has been revised to explicitly reference Table 1 and to incorporate baseline characteristics of the patient cohort, including age, sex, ASA classification, BMI, and lesion distribution.

Changes in the text: Lines 168-181

(5) Important to include false negative rate in cases with no cancer found on biopsy or have cases follow up for stipulated period of time post negative biopsy.

A: Thank you. As noted in the revised Results, three cases (10.7%) were non-diagnostic and not malignant. All of these patients are undergoing scheduled CT chest surveillance at 3 months to assess for false negatives; at the time of reporting, none of these follow-up scans were yet due. This clarification has been added to the Results and Discussion sections.

Changes in the text: 187-199

(6) Gattinoni pioneered work on prone positioning for ARDS and had demonstrated improvement and increase in ventilation and aeration of posterior aveoli units on CT scan. Please consider my suggested reference.
a. Gattinoni et al. American Journal of Respiratory and Critical Care Medicine Volume. 164, Issue 9 (2001)
b. Gattinoni et al. Anesthesiology and Perioperative Science. Volume 1, article number 3, (2023)

A: We thank the reviewer for this excellent suggestion. Both references by Gattinoni et al. have been reviewed and incorporated into the Discussion to highlight the physiologic rationale of prone positioning in improving posterior alveolar ventilation and aeration. These citations strengthen the scientific context of our study.

Changes in the text: Lines 205-207

(7) CPR in prone position is of great interest especially in emergency collapse. Please do a literature search and include relevant references.
a. Qian Liu et al. Resusc Plus. 2024 Oct 4;20:100787

A: Thank you for this helpful suggestion. We performed a focused literature update on CPR in the prone position and incorporated the recommended citation (Qian Liu et al., Resusc Plus, 2024;20:100787). We added these references to the Discussion (safety considerations paragraph) and briefly summarized key techniques and implications for intraoperative emergencies during prone bronchoscopy.

Changes in the text: Lines 272-284

(8) Figure 7. Image provides important information on equipment set up and space management. Please consider providing a sharper high-resolution image with clear labelling of equipment involved.

A: We thank the reviewer for this valuable suggestion. We have reviewed the images again and selected those that provide the highest resolution possible.