

Peer Review File

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Reviewer A

The authors present an overview of the existing robotic bronchoscopy platform. It is informative, but would be strengthened by some comments/edits as listed below.

Comment 1: Introduction

"In diagnostic innovation, robotic bronchoscopy has emerged as a game-changing technology for early lung cancer detection ..." - I don't think there is enough evidence to support some of the terms used - game changing, superior, modality of choice, significant leap, unparalleled precision, pivotal - at this time as non-robotic modalities, ie digital tomosynthesis or ENB with CBCT guidance or comparable in terms of diagnostic yield. I would soften the tone/language here significantly.

Reply 1: Thank you for your remark. While we consider robotic bronchoscopy as an impressive advancement for diagnosing pulmonary nodules, we agree with the heightened tone and have edited the manuscript accordingly to soften the language throughout.

Comment 2: Ion

"Modalities such as fluoroscopy, radial endobronchial ultrasound (rEBUS), and cone-beam CT can confirm navigation success" - I don't think this is how navigation success has ever been reported. The mentioned tools/modalities are for secondary confirmation, not primary confirmation, which is how navigation success is defined, ie the platform being able to reach the virtual target. Please correct/clarify

Reply 2: Thank you for emphasizing on this. We have edited the description to clarify that target reach information is provided by the Ion Endoluminal system, and other technologies such as fluoroscopy, radial endobronchial ultrasound, and cone-beam CT are used as supportive tools to ascertain virtual target reach on page 6, lines 69-71, of the revised manuscript.

Comment 3: It would be appropriate to include more of the studies looking at Ion and integrate them into this section. In particular, the first real world study (PMID 33547938) and the largest study (PMID: 36369295) should be referenced here and expanded upon as well as included in Table 2.

Reply 3: Thank you for your recommendation. We have added both referenced studies in the Ion Endoluminal section, pages 6-7, as well as Table 2, to include their findings and outcomes.

Comment 4: Discussion

Similar to the above regarding the introduction, I would tone the language down to be less laudatory and more circumspect.

Reply 4: Thank you for your remark. We have edited the manuscript accordingly to soften the language throughout.

Comment 5: I would also not include the authors' personal cases in the discussion section. While these are interesting, they would be better placed in the review of each platform. As they are only regarding ssRAB or Ion, I would also suggest removing them as not to seem biased towards one system vs another.

Reply 5: Thank you for your remark. We have moved one of our recently published experiences with Ion Endoluminal for biopsying multiple nodules within the same procedure from the "Discussion" section to the "Ion Endoluminal Evidence" section on page 7, lines of the revised manuscript. All other personal experiences cited in the "Discussion" section are mentions of single-case scenarios and comparisons to other diagnostic techniques such as CT-guided transthoracic biopsy.

Comment 6: Nodule marking

"RAB may play a crucial role in marking nodules during the perioperative phase for minimally invasive thoracic surgery(42)." I would also include the following reference

DOI: <https://doi.org/10.1016/j.atssr.2023.02.010>

Reply 6: Thank you for your suggestion. We have included the above-mentioned reference to expand on nodule marking with robotic bronchoscopy, in preparation for thoracic surgery.

Comment 7: PNx and bleeding

I would frame these findings in the context of why the authors think RAB may have lower outcomes, at least reported in the referenced studies, compared to ENB or non-ENB guided procedure. Providing this information would serve to foster more discussion as intended rather than just stating the numerical values again.

Reply 7: Thank you for your input. We have expanded our insights into the plausible explanations for RAB's lower complication rates compared to other non-RAB bronchoscopic techniques as well as CT-guided biopsies, on page 13, lines 229-240 of the revised manuscript. Briefly, we compare the inherent nature of bronchoscopic versus percutaneous approaches, where RAB does not involve puncturing through the chest wall and aerated lung parenchyma, which naturally increases the risk of pneumothorax and bleeding. Compared to other bronchoscopic techniques, RAB has the advantages of pre-procedural planning based on contiguous thin-cut CT to create a three-dimensional reconstruction of the airway, navigational plan towards the virtual target, live feedback on distance to target and pleura, and a stable robotic arm with thinner working channel that allows for farther reach and interchangeable biopsy tools. These factors together enhance the safety profile of RAB over other diagnostic approaches.

Comment 8: Comparison?

The above ties into the overall concern with the discussion, which is the lack of a clear comparison between the available RAB modalities or between RAB and non-RAB modalities. While that may be beyond the scope of the paper as a whole, at least a passing comment or two would be appropriate or woven throughout the discussion.

Reply 8: Thank you for emphasizing on this. We agree that as robotic bronchoscopy continues to expand, there is a need to directly compare between robotic platforms as well as other diagnostic approaches. We have commented on this and added the few studies, including meta-analysis assessing several techniques such as RAB, rEBUs, ENB, VB, that address this concern in the "Discussion" section, pages 12-14 of the revised manuscript.

Comment 9: Conclusions

As for the intro and discussion, I would soften the language here as well.

Reply 9: Thank you for your remark. We agree and have edited the manuscript accordingly to soften the language throughout, including the "Conclusion".

Comment 10: Abstract

Same comment regarding softening the language applies throughout.

Reply 10: Thank you for your remark. We agree and have edited the manuscript accordingly to soften the language throughout, including the "Abstract".

Comment 11: Figure 1

I do not see the tool in lesion in the presented cross-sectional imaging. The catheter is seen, and the nodule is seen, but there is no clear tool being shown or that it is in the lesion. Please correct the legend or the figure.

Reply 11: Thank you for your review. We have replaced the image with another case in which the tool-in-lesion is more evident.

Comment 12: Figure 2

I don't see the value of adding this figure in as it does not add to the paper. I would delete.

Reply 12: Thank you for your suggestion. We agree and have removed Figure 2 from the manuscript.

Comment 13: Figure 5 and 6

Again, I do not think that adding figures of these cases are of significant value. I would delete both.

Reply 13: Thank you for your suggestion. We agree and have removed Figures 5 and 6 from the manuscript.

Reviewer B

This is a concise, well-written review of the major navigation systems currently

available. A few minor points:

Comment 1: Line 16 - Would rephrase "high diagnostic" as "high diagnostic yield"

Reply 1: Thank you for your remark. We have edited accordingly to "high diagnostic yield".

Comment 2: Line 69 - Would also mention that the CT cuts need to be contiguous, i.e. the spacing needs to be at least as thin as the cuts used.

Reply 2: Thank you for recommendation. We have modified accordingly to state the CT cuts are contiguous in the "Ion Endoluminal" section, page 5, line 58 of the revised manuscript.

Reviewer C

Comment 1: Reference 6 (Yarmus) is a deeply flawed paper. Their EMN system was an older version without software updates and the room wasn't mapped (as required by the manufacturer) for the EMN equipment. Also, the operators in this study had never been trained on the superDimension platform. I would strongly advise against using a study performed like this with all its flaws to put forth the argument for Robotics. I agree robots are great: this study does not make a good argument and honestly never should have been published.

Reply 1: Thank you for your feedback. We agree the study may be flawed and may not provide an accurate assessment of both systems fairly. We have decided to remove it, and on that note, have removed all cadaveric studies to include animal and/or human studies only.

Comment 2: Reference 8 (Dekel) thank you for explaining the yield for lesions 2cm and smaller was MARKEDLY reduced from what was reported over-all (which was influence by the 3 and 4 cm lesions). Nice work.

Reply 2: Thank you for your remark. As robotic bronchoscopy and other supportive tools continue to advance, the ability to sample smaller and harder-to-reach nodules will become more necessary to improve diagnostic yield and earlier lung cancer diagnosis.

Comment 3: Reference 10: please clarify if they used cone beam (this group typically does) as this has a major influence on the reported yield, especially with GGOs.

Reply 3: Thank you for your comment. Mobile cone-beam CT was used as a secondary tool to confirm successful navigation in this study for subsolid nodules. We have clarified this on page 7, line 102 on the revised manuscript, as well as all other referenced studies.

Comment 4: Large multi-centered Ion study was published by Folch. yield low 80s. needs to be added.

Reply 4: Thank you for your remark. We have added author Folch's available studies.

Comment 5: For your introduction to Noah, make sure you add this is a disposable scope. this has become relevant with TPT code starting Jan 1, 2024.

Reply 5: Thank you for emphasizing on this. We have highlighted the single-use, disposable nature of the scope in the "Galaxy System" section, pages 10-11, line 196 and lines 179-181.

Comment 6: Frontier study (presented at AABIP) is being published soon. In final revision. This is the first in human study from Australia.

Reply 6: Thank you for your input. We have added the preliminary results presented at AABIP 2023 in the "Galaxy System" section, page 11, lines 193-195 of the revised manuscript.

Comment 7: In the conclusions you write: In our experience, we have achieved significant milestones with ssRAB, conducting successful mediastinal pleura and peripheral pleural-based nodule biopsies (Figure 5A-B), bilateral peripheral nodule and multiple nodule (Figure 6) biopsies within the same procedure: please clarify if this was done with conebeam/mobile cone beam or was done without imaging.

Reply 7: Thank you for your comment. For the above-mentioned experiences, ssRAB was used in combination with rEBUS and mobile cone-beam CT. However, we have since edited the manuscript and these references have been either removed or cited accordingly.

Comment 8: One key thing missing: please outline how all 3 platforms suffer equally from CTBD (you just mention there is some present in general) and how each one attempts to fix it (Ion with Cios 3D system, Monarch with GE 3D c-arm and Noah with standard 2D c-arm with tomosynthesis). Without some form of advanced imaging, the robotic platforms all suffer from CTBD and that hampers the yield in small lesions. Would also make note that integration with the mobile cone beam you mention does NOT give you augmented fluoroscopy and required purchase of additional equipment. If you're going to use your case examples, please make it clear what was required to make that happen.

Reply 8: Thank you for emphasizing on this. For each of the robotic platforms, we have expanded on the use of secondary intraprocedural imaging to confirm tool-in-lesion and overcome the challenges of CT-to-body divergence, in the "Discussion" section, page 14, lines 248-281, of the revised manuscript.

Comment 9: Another thought would be to consider operational costs to each platform (since the base robot costs the same). Bhadra has published on the limits of reprocessed scopes and the costs involved. These decisions on not just made on yield, but on operational costs as well.

Reply 9: Thank you for your suggestion. We have added a comment on approximate costs for robotic platforms and supportive equipment, which heavily impact any institution's operational budget and supply-demand analysis, in the Discussion section, pages 16-17, lines 297-309.

Comment 10: figure 1b is not your figure. it's from an intuitive promotional material and should be changed. you just need 1a,c,d

Reply 10: Thank you for your recommendation. We have edited Figure 1 accordingly.

Comment 11: Figure 3: if you're going to show Ion work screens, show them for monarch

Reply 11: Thank you for your remark. In our institution, the Ion Endoluminal System is used, therefore we are able to provide greater content, including a closer look into the working screen. For Monarch, the images come from publicly available content courtesy of Johnson & Johnson, which still include the robot station and working screen.

Comment 12: Figure 4: if you're going to show Ion work screens, show them for Galaxy.

Reply 12: Thank you for your remark. In our institution, the Ion Endoluminal System is used, therefore we are able to provide greater content, including a closer look into the working screen. For the Galaxy System, our images come from publicly available content courtesy of Noah Medical, which still include the robot station and working screen.

Comment 13: Be cognizant of your understandable bias (you have/use the Ion, so it's understandable). Overall a nice narrative, just needs some things added and cleaned up.

Reply 13: Thank you for your remark. We agree with the heightened tone and have edited the manuscript accordingly to soften the language throughout.