Peer Review File

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Reviewer A

Comment 1. This article would serve well as a response to the article published by Chen and colleagues.
Reply 1: Thank you for your kind comment.
Changes in the text: nil

Comment 2. Are the authors able to provide a table or flow chart (based on their experience) to help guide the reader as to which imaging platform may be more beneficial based on type of case?
Reply 2: Thank you for your suggestion. We believe that more experience with the Cios Spin will be required before we can make evidence-based recommendations regarding the exact nodule characteristics that is possible for this technique. However, we have made brief recommendations in our article that small ground glass nodules of Suzuki Type I-II should be avoided, especially in regions where atelectasis is prone, for example the lower lobes. (Lines 127-129) For ablation and biopsy cases where accurate positioning of tools into the nodule is of utmost importance, Cios spin should be avoided if the lesion is very peripheral or lack bronchus sign.
The two cases (Case 4 and Case 9) where mobile C-arm failed (Paragraph starting at Line 104) were of Suzuki Type II and III (this information now available in the Table).
Changes in the text: A new table (Table 1) has been added to the manuscript with details of the 10 cases.

Reviewer B

Comment 1: The authors present a series of 10 cases selected for ENB biopsy, dye marking or microwave ablation comparing the mobile 3D C-arm machine (Cios Spin®) with a floor-mounted cone beam CT in a hybrid operating theatre. I recognise this manuscript category (Letter to the Editor) does not allow much space, but more detailed characteristics of the cases are missing. Specifically, in terms of the radiologic features of the nodules - Suzuki type, Hounsfield units, location, bronchus sign etc. – since image resolution and fine adjustment appears to be the main limitations related to mobile 3D C-arm machine (Cios Spin®). These informations would maybe also be of some guidance for other centres planning to introduce this new technology and, in their efforts, to perform the undefined important case selection.
Reply 1: Thank you for your helpful suggestions. A table has been added with nodule and procedural details as suggested.
Changes in the text: “Table 1” has been added.

Comment 2: Any thoughts on how the inferior image resolution of the mobile 3D C-arm

machine (Cios Spin®) may impact determination of ablation margins?
Reply 2: Thank you for your insightful comment. The inferior image resolution of Cios Spin would severely impact determination of ablation margins when the lesion itself is subsolid in nature, for example Suzuki Type I – IV, because the ablated region would appear as ground-glass nature as well. We noticed that Cios Spin may be inferior to floor-mounted DynaCT in terms of tissue differentiation between different degrees of sub-solidity. Therefore, our recommendation is to perform Cios Spin ENB ablation only for solid nodules.
Changes in the text: nil (Brief recommendations based on our 10-case experience on nodule selection criteria have been detailed in Lines 127-138.)

Comment 3: I think there is great potential in the use of the mobile 3D C-arm for ENB-guided procedures and it is definitely feasible. Nevertheless, the conclusion made by the authors based on this small comparative series in expert hands may be slightly over-enthusiastic and subjectively imprinted. I would advise the authors to also emphasise on the many unknowns before this technology can be safely expanded to all ENB applications, in particular ablation.
Reply 3: We definitely agree that our small series cannot fully justify the use of mobile C-arm machines for complicated procedures like ENB ablation of lung nodules, but our series aim to prove its feasibility and versatility in multiple applications.
Changes in the text: Conclusion has been changed as per suggested, please see Lines 143-148.

Reviewer C

Comment 1: -for a clear view, the authors should make a table resuming the cases with at least these elements: type of nodule, size, location, type of procedure (Diagnostic, dye marking, ablation) and accuracy of the technics between C-arm and CBCT
Reply 1: Thank you for your insightful suggestion. A table detailing nodule and procedural characteristics have been added as suggested.
Changes to the text: "Table 1" has been added.

Comment 2-for endoscopic ablation case's, since it is an emerging procedure not validated in first intention in lung cancer, the authors should precise if the patients are enrolled into prospective register like Chen et all made. Please precise.
Reply 2: All ENB ablation cases in this series have been enrolled in our registry, which is an on-going data collection practice. The results of the initial cases of ENB ablation performed with DynaCT has been published in TLCR earlier this year (Chan JWY, Lau RWH, Ngai JCL, et al. Transbronchial microwave ablation of lung nodules with electromagnetic navigation bronchoscopy guidance-a novel technique and initial experience with 30 cases. *Transl Lung Cancer Res*. 2021;10(4):1608-1622). All patients are fully informed of its experimental nature and have had alternatives explained to them (eg. SBRT, or percutaneous ablation, etc). Informed consent has been obtained from all patients.
Changes to the text: please see Lines 93-95.

Comment 3- All the authors performing such technics should be more cautious about safety

margin. To be compared, all the authors should detail the workflow of their treatment zone, the limitations with heat dissipation in contact with blood vessel for example.

Reply 3: We recognize that safety is of utmost importance with any new technique. Nodules that are not suitable for ENB ablation include those that are <5mm from important mediastinal structures, inclusion of branchial plexus/phrenic nerve in predicted ablation zone, those that are within 5mm from a large blood vessel with diameter of >5mm, etc. These have been detailed in our previous publication (Chan JWY, Lau RWH, Ngai JCL, et al. Transbronchial microwave ablation of lung nodules with electromagnetic navigation bronchoscopy guidance-a novel technique and initial experience with 30 cases. *Transl Lung Cancer Res*. 2021;10(4):1608-1622). Due to word limit in this "Letter to the Editor", we are unable to include such details in the present article.

Changes to the text: nil

Comment 4:-I understand the difficulty of the access of hybrid operating room. Nevertheless, when talking about ablation, you really need to be precise. No doubt should remain.

Reply 4: We certainly echo that precision and accuracy is the cornerstone for ablation procedures. From our limited series of 10 cases, we find that accurate access to nodule and/or accurate margin determination may be difficult for ground glass nodules utilizing the mobile C-arm technique. Therefore, as mentioned in the article, we withheld the use of Cios Spin during the procedure for cases 4 and 9 and subsequently completed the procedure with floor-mounted DynaCT similar to our usual practice. Future studies should investigate the nodule characteristics which would predict procedure success with mobile C-arm.

Changes to the text: nil

Comment 5- All the authors performing such technics should raise limitations compared to SABR treatment which is a real competitor. In the future, if the technic still emerges, what we could hope, direct comparison between SABR and thermal ablation in term of local recurrence and overall survival will need to be evaluated.

Reply 5: Thank you for your insights. We agree that the major competitor of ENB ablation is SABR which has been well-established for local treatment of lung cancers in surgically unfit patients. Potential advantages of transbronchial ablation include the ability to perform same session biopsy before ablation, lack of radiation toxicity, and is a one-off procedure compared to the labour-intensive SABR regime which usually requires repeated doses over several weeks. We completely agree that a controlled trial between SABR and ENB ablation should be conducted, but this may be beyond the scope of the present article which aims to compare mobile C-arm CT with floor-mounted CBCT. We apologize that comparison with SABR cannot be thoroughly discussed in the very limited word count of this article type "Letter to the Editor".

Changes to the text: nil

Reviewer D

Comment 1: Line 78-80: the abstract seems to indicate that 10 ablations were performed but

later on this is clarified to only be 10. Please reword: “We 36 respond by presenting our 10-case series of mobile C-arm-guided ENB biopsy and 37 microwave ablation of lung nodules.” To make clear that not all nodules underwent ablation.
Reply 1: Thank you for your comment and clarifications. We have performed 10 ENB procedures with Cios Spin, but only 4 were ENB ablations.
Changes to the text: Please see Line 51 where “and” has been changed to “and/or” in the abstract. Details regarding the type of ENB procedures performed can now be clearly seen in the newly added “Table 1”.

Comment 2: 82 – how is navigational success defined?
Reply 2: “Navigation success” is defined as the CT confirmation of placement of ENB tools at or adjacent to target lung nodule such that desired procedure can be carried out. For biopsy cases, the biopsy needle must be placed within the nodule. For ENB ablation cases, the ablation catheter must be placed into or adjacent to the nodule such that a predicted margin of 5mm is obtained upon calculation of predicted ablation zone.
Changes in the text: nil

Comment 3: Please include a table listing all procedures in the case series. Please include nodule size, location, presence of air bronochogram and histology obtained. Distance from pleural and 1/3rd of lung would be value as well if available. Please include pertinent follow up histology for those who went to resection. Please include radiographic follow up if performed for benign histology.
Reply 3: Thank you for your helpful suggestions. A table with nodule and procedural details have been added.
Changes to the text: “Table 1” has been added.

Comment 4: Procedural methods: Please include details regarding ventilator techniques if aplicable vs. conscious sedation. procedures time?
Reply 4: Thank you for your question. All of our cases were performed under general anaesthesia (please kindly see Line 132). In future, when the technology and technique matures, we may be able to perform this procedure under conscious sedation which would further reduce the general anaesthetic risk to these patients.
Changes to the text: nil

Comment 5: If you have follow up data for the 4 nodule that were ablated please include the duration of follow up and clinical status of the patients.
Reply 5: Thank you for your interest in our work. Of the 4 ablated nodules, the longest follow up is at 9 months currently. Recent follow up CTs of the 4 nodules all showed no evidence of recurrence and patients have been clinically well. Since our article mainly focus on technical feasibility and short term outcome of the new mobile C-arm machine, the mid- or long-term follow up results may be slightly out of scope and limited by the word count of this article type. We look forward to publishing our mid- to long-term results and local control rates of all our ENB ablation cases with or without mobile C-arm CT (currently more than 80 cases) in the upcoming future.

Changes to the text: nil

Comment 6: How much radiation is emitted in this procedure? How does it compare to cone beam CTs. How does it compare to digital tomosynthesis?
Reply 6: Thank you for your enquiry. The radiation dose of mobile C-arm machine is lower than that of floor-mounted CBCT, as a smaller 16x16x16cm 3D volume is scanned compared to 19x25x25cm in DynaCT. The effective dose of 1 CT by Cios Spin is 0.14 mSv (for low dose CBCT), 0.26 mSv (for standard CBCT), and 0.84 mSv for (for high-quality Cios Spin CBCT). Dose area product ranges from 3700-4100 μGym2 per CBCT. Due to the very limited word count of this article type "Letter to the Editor", we are sorry that we not able to insert all clinical details.
Changes to the text: nil

Reviewer E

Comment 1: The authors conclude that in their view this 'light-version' is able to perform sufficient image quality and 3D information for most lesions (solid, and relatively large), and that this system could be used instead of a hybrid OR. I would like to add an additional warning that this may be the case in experienced hands, but I doubt that it would suffice for 'starters'. A recent paper by Verhoeven etal in JOBIP 2021 showed a significant learning curve using top-level imaging. But with less good imaging quality and software tools, this learning curve may be much longer, and more difficult to overcome than stepping down from with ample experience on toplevel image guidance to a lesser quality guidance as these authors have done. So my fear is that this Cios system in the hands of a less experienced team may not be as safe as it appears from this work.
With these considerations in mind, additional further research is warranted and needed. I would like to advise the authors to revise their conclusion section accordingly.
Reply 1: Thank you for your insightful comments regarding this new technique. It did indeed take us many cases to integrate CBCT and ENB navigation, and optimize the workflow. As you pointed out, we would perhaps expect the learning curve to be steeper for those starting off with a mobile C-arm system (rather than CBCT) to perform ENB. "Starters" using mobile C-arm (without prior experience in the hybrid operating room) should probably build their experience with easier cases first, eg. larger and predominantly solid nodules, positive bronchus sign, and should start with biopsy rather than ENB ablation. We apologize that due to the limited word count of this "letter to the editor" article type, detailed discussion on learning curve issue is not possible.
Changes to the text: Conclusion has been modified, please see Lines 143-151.