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Reviewer A

Your study of a prototype carbon nanotube radiation enabled stationary digital chest tomosynthesis system is well designed to methodologically clarify relationships between nodules characteristics and the ability of the image interpreters to identify the nodules, with some limitations inherent in the study.

I would like to ask the following questions for better clarification of the data and also make some comments:

1-Were the readers in the study tasked to comment on clarity of image by s-DCT or just the identification? Are the authors able to comment on ability of s-DCT to detect nodules from background changes that might be seen during bronchoscopy? Background atelectasis and/or mucus plugging, airway blood clotting, etc. are known to happen frequently during bronchoscopy. And most importantly is s-DCT imaging powerful enough to distinguish the nodule from those background artifacts?

Reply 1 – The readers were not asked to comment on clarity of the s-DCT imaging. This study was not designed to assess nodule identification during procedures and the attendant changes that occur during these procedures, as such, we cannot comment experimentally on the ability of s-DCT to distinguish between background artifacts and nodules. The data set was collected as part of a nodule tracking clinical trial, however this was a negative trial likely due to the poorer identification rate of smaller (<8mm) nodules. A follow up reader study is underway in a population of patients who had CT scans with nodules and whom where targeted for biopsy. The technology is being optimized with a wider angular span carbon nanotube x-ray source as part of ongoing preclinical animal model studies.

Text adjustments – lines 248-260 in the Discussion.

2-Real time confirmation of tools in target has been recognized as one of the challenges in bronchoscopic biopsy of lung nodules. The authors have shown using s-DCT may improve detection rate for nodules ≥ 8mm. However, it is equally important to have real time imaging during navigation and not just real time confirmation at the end of navigation.

Do the authors think s-DCT can be used to guide bronchoscope in a real time fashion toward the target? In other terms, when the tool is found not to be in target, how s-DCT imaging can help to re-route the bronchoscope to the target? Unless the imaging is live while the bronchoscope is moving, it is hard to re-direct the scope toward the target.

Currently none of the advanced modalities including CBCT guided bronchoscopy or mobile 3D fluoroscopy permit the operator to maneuver the bronchoscope at the same time of real time imaging, due to high dose of radiation which necessitate the operator to leave the room. Meaning none of the above technologies are a real time navigation tool, but only a confirmation tool. Only modalities with possibility of real time imaging during navigation (to this reviewer's knowledge) are illumisite and LungVision platform, however the processing time to capture a real time imaging is at least about 30 seconds which may not be ideal, and their outcome data and quality of imaging data is limited so far.

I assume, s-DCT does not require the operator to leave the room while they maneuver the bronchoscope? Please clarify if it is possible for s-DCT with the fast-processing time (as reported by authors of about ~2 seconds) to help navigate the scope and re-position the tools while real time imaging is in process. That will be an extra advantage of the system which I believe has not been reported elsewhere.

Reply 2 – You are correct, s-DCT does not require the operator to leave the room, and will operate similarly to a fluoroscopy C-arm.

While beyond the scope of this paper, the DCT approach enables both "live" bi-plane imaging, as well as repeated 3-D tomosynthesis imaging, which can be used in combination for intra-procedural guidance. This work is currently being studied. This will likely take shape as an initial wide angular scan that will be used to create

the navigational pathways. During the procedure, a region of interest can be brought into plain, allowing for real time registration throughout the navigational process, providing 3 deminsional feedback for final tool position adjustment in real time.

Text adjustments – lines 269-275 for clarification

3-I also ask the authors to please clarify the quality of images in patient with high BMI. More study is needed for patient with high BMI in order to assess the quality of image in those population.

Reply 3 – Agreed. Text adjusted as such.

Text adjustments to clarify 3 – Line 276-278, added citation and reasoning for the exclusion criteria.

4-It is important to assess the quality of imaging during bronchoscopy. The study only focused on imaging in situation similar to a CT scan. As it is well known, atelectasis is commonly happening during bronchoscopy (due to different reasons such as sedation, occlusion of airways with bronchoscope, impairment of natural airway clearance during procedure, etc.) and it may affect the quality of imaging by s-DCT. Studies during bronchoscopy are needed to imitate the real-life situation.

Reply 4 – We whole heartedly agree. In its current iteration, the s-DCT prototype is preclinical and limited by the 80kVp imaging energy and power capability of this current, repururposed secruity tube initially designed for carry-on baggage screening. Higher energies and powers with a wider angle x-ray tube that has been recently obtained are underway with animal studies. The large animal model is known to have atelectasis during procedures and attention will be focused on degradation of image quality during the procedure. The intent of the current study was to show the ability of proceduralists to identify nodules with the technology, because if the targets are not visible on s-DCT, then the technology would not be feasible as a real time intraprocedural adjunct to modern robotic and navigational bronchoscopy systems.

Text adjustments to clarify 4 – lines 249-260 and 269-275.

5-Author may consider clarification in conclusion section about improvement only in nodules with sizes of ≥ 8mm and limitation on non-solid lesions. Also, the need for additional study during bronchoscopy as well as need for study in populations with higher BMI.

Reply 5 – Agreed, text adjusted as below.

Text adjustments to clarify 5 –Lines 254-258 and 281-283.

Reviewer B

I reviewed the manuscript entitled "Feasibility of a Prototype Carbon Nanotube Enabled Stationary Digital Chest Tomosynthesis System for Identification of Pulmonary Nodules by Pulmonologists" This report was interesting for me because the number of the patients who have indeterminate nodules have increased with CT check-up, and pulmonologists and thoracic surgeons always consider this problem; although it has a few limitations.

Major comments

1. I understood that this article contained a new modality for tumor identification. However, it is difficult to judge whether this paper is appropriate for this journal because it is thought that the main insistence of this article is a feasibility of a prototype carbon nanotube used for tomosynthesis, and it is associated with radiological and physical themes, although, of course, I understood that a tumor more than 8 mm could be detected by s-DCT.

Reply 1 – This article is intented to show that the novel s-DCT technology, in a non-optimized, prototypical form, can feasibly be used by proceduralists to identify targets of bronchoscopic biopsy (nodules >8mm in size). If proceduralists were unable to use the s-DCT images to identify biopsy targets, then the technology would not have feasibility as a real time intraprocedural imaging system.

Text adjustments 1 for clarity – Lines 115-117 and 218-219

2. Although s-DCT may become a feasible modality to identify nodules being considered for biopsy, isn't a conventional CT finally needed for the assessment and planning before biopsy? Because recent approaches have applied three-dimensional CT navigation-- in such a case, isn't this method wasteful in the end? Furthermore, doesn't this increase the possibility of radiation exposure? I wonder if it is important to also discuss a plan on how this method can be used; such as a follow-up method for small sized tumor, and so on.

Reply 2 – The s-DCT system is meant to serve as an intra-procedural device with low radiation dose. With the wider angle system under development, it is also conceivable that the planning CT (required for all procedural approaches) will be unnecessary. Once the initial detailed scan is obtained and navigational plan established, the system is then used similar to moving gantry c-arm systems, "augmented fluoroscopy" as it has been called in the literatures, with a foot petal to obtain real time images of the region of interest, thus allowing for real time registration and tool positional fine tuning.

Text adjustment to clarify – Line 87-88, lines115-117, lines 255-260

3. I think that it is better to emphasize the usefulness of a prototype carbon nanotube s-DCT in not only the introduction section but also the discussion section.

Reply 3 – Agreed, text adjusted as such.

Text adjustment to clarify – Line 211-217

Minor comments

1. Although the authors described the postoperative complications in the introduction section, the reference (6) seems not to reflect the recent surgical data. I think that

more recent papers should be supplied in references.

Reply 1 – We will adjust as suggested.

Text adjustment – line 73-74, added new complication rates for VATS and open thoracotomy and adjusted the reference to match.

2. Although the authors described a low diagnosis rate with bronchoscopy, it is thought that the recent innovations (EBAS-TBNA, and so on) have been increasing the diagnostic rate of pulmonary nodules.

Reply 2 -- This is true, it is hoped that robotic bronchoscopy will lead to improved diagnostic, however the literature has not yet established this to be the case, and these innovations continue to rely on adjunct radiographic confirmatory modalities (such as cone-beam CT, c-arm fluoroscopy, moving gantry tomosynthesis ("augmented fluoroscopy"). As such, we are seeking to develop a low dose, stationary, real time imaging modality that can also be used as a navigational platform.

Text adjustment -- lines115-117, lines 255-260

3. In line 127, why did the gathering of the reader study data take such a long time from when the images were obtained?

Reply 3 – This was a retrospective study using imaging data from a separate study that was aimed at using this technology for nodule follow up in lung cancer screening programs, therefore the discrepancy between time of image acquisition and this current reader study.

Text adjustment – Lines 127-128 and Line 134.