

Peer review file

Article information: <https://dx.doi.org/10.21037/jtd-21-1032>

Reviewer A

Dr Kim and colleagues have submitted a manuscript describing the use of digital tomosynthesis in the setting of patients who have undergone rigid bronchoscopy for benign and malignant central airway obstruction and potentially placement of a silicone stent.

The manuscript is well written, detailed and examines several data points that compare plain CXR with DTS for the detection of complications associated with silicone stenting including granulation tissue and migration.

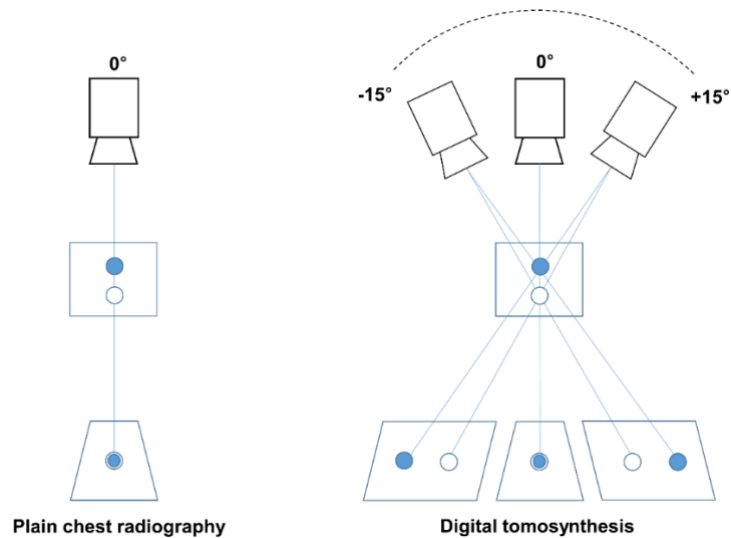
Comment 1. The authors should include a more detailed explanation of digital tomosynthesis as the pulmonary and thoracic community are not generally familiar with the specifics of DTS and how it differs from standard chest radiographs. A diagram may be helpful in this introductory section.

Reply 1. Thanks for your suggestion. We added the detailed explanation and figure for DTS to the INTRODUCTION section.

[INTRODUCTION, page 4, line 67 - 70]

In the DTS, the tube performs a caudo-cranial sweep $\pm 15^\circ$ around the standard PA plane, collecting around 60 low-dose projections for 10-12 seconds. (5) The angular movement of the tube enables the separation of overlapping anatomy in the DTS, but not in the CXR (**Supplementary figure 1**).

[Supplementary figure 1]



Supplementary figure 1. Principle of CXR and DTS image acquisition

Reviewer B

Easy to read,

but descriptive article only, not on clinical interest of DTS.

Comment 1. what was the reason to execute these exams? I have the impression that patients seem to be asymptomatic, i do not know their bronchial status; asymptomatic migration or granulomas detected by CXR or DTS must be tolerated. they must precise clinical status of population studied.

- in our center, we rarely use CT before bronchoscopy: if hemoptysis, dyspnea, patient undergo flexible and/or bronchoscopy. So, DTS might have an interest against CXR only, but not against CT. DTS doesn't give any information about lung status, pleural status, for example.

in conclusion, only a descriptive interest for this article. But, authors should define the place of this exam in follow up: to detect early and asymptomatic lesions? to anticipate bronchoscopic intervention? to avoid a bronchoscopy intervention, if symptoms are not related to stent complication?

Reply 1. Thanks for your comment.

First, when DTS was used for other lung diseases and comparative studies with CXR came out, our institution started using DTS for the first time that DTS might be better than CXR in the evaluation of airway diseases or airway stents. We hypothesized that the anatomy of the central airway overlapping the mediastinum could be better detected through DTS.

After gaining experience in patients' evaluation with DTS, our institution routinely conducts DTS immediately after stent insertion, 1 month after, and 3 months after follow-up. After that, if the patient does not have any additional problems, we follow-up the patient's airway stent status with DTS every 6 months. At each DTS test, pulmonary function test and CAT score for patient symptom check are measured together. This is our routine workflow. However, in an early outpatient clinic visit with complaints of symptoms or an emergency room visit, the stent status is evaluated by DTS, chest CT, or flexible bronchoscopy, considering the patient's condition. Then a decision is made on bronchoscopic intervention.

In this study, cases were included only when the results of three tests (CXR, DTS, and bronchoscopy) were present. The fact that even bronchoscopic intervention was carried out means that the patients complained of symptoms above a certain level requiring intervention. Even for patients not included in this study, stent status was routinely evaluated with DTS instead of CXR. So, we actually consider the DTS as a primary screening test in order to 1) detect early and asymptomatic lesions, 2) determine whether additional bronchoscopy intervention is needed, and 3) avoid bronchoscopy intervention when symptoms are not related to stent complications. In some cases, airway or stent status evaluation is performed through chest CT or flexible bronchoscopy considering the patient's condition or the interval with the previous chest CT. However, recently, DTS is conducted as a routine test based on the advantages mentioned in this study

In addition, DTS has demonstrated its usefulness to detect pulmonary lesions such as nodules, ILD, and Mycobacterial disease. (1- 4) In the case of patients with airway disease, obstructive pneumonia caused by airway obstruction, or coexisting pulmonary tuberculosis in patients with post tuberculosis bronchial stenosis could also be identified through DTS.

The routine workflow and DTS utilization of our institution mentioned above were summarized and added to the DISCUSSION section.

[DISCUSSION, page 12, line 270 - 275]

Our institution routinely conducts DTS immediately after stent insertion, 1 month after, and 3 months after follow-up. After that, if the patient does not have any additional problems, we follow-up the patient's airway stent status with DTS every 6 months. However, in an early outpatient clinic visit with complaints of symptoms or an emergency room visit, the stent status is evaluated by DTS, chest CT, or flexible bronchoscopy, considering the patient's condition. Then a decision is made on bronchoscopic intervention.

[Reference]

1. James TD, McAdams HP, Song JW, et al. Digital tomosynthesis of the chest for lung nodule detection: interim sensitivity results from an ongoing NIH-sponsored trial. Med

- Phys 2008;35:2554-7.
2. Kruamak T, Edwards R, Cheng S, et al. Accuracy of Digital Tomosynthesis of the Chest in Detection of Interstitial Lung Disease Comparison With Digital Chest Radiography. *J Comput Assist Tomogr* 2019;43:109-14.
 3. Gunnell ET, Franceschi DK, Inscoe CR, et al. Initial clinical evaluation of stationary digital chest tomosynthesis in adult patients with cystic fibrosis. *Eur Radiol* 2019;29:1665-73.
 4. Kim EY, Chung MJ, Lee HY, et al. Pulmonary mycobacterial disease: diagnostic performance of low-dose digital tomosynthesis as compared with chest radiography. *Radiology* 2010;257:269-77.

Reviewer C

The authors address an important area. Clearly there are limitations with DTS and authors appropriately highlight in their discussion.

Comment 1. Supplementary table 2 provides good information. it may be good idea to simplify the table to include the conclusions.

Reply 1. Thank you for the comments.

We already presented diagnostic performance calculated based on 2x2 contingency table through Tables 2 and 3 and briefly presented the information of **Supplementary table 2** by marking the "n/N" fraction together.

The presentation of information in the 2x2 table once again as supplementary data was intended to show the number of cases used to calculate each diagnostic performance in detail. In addition, the 2x2 table itself is bulky and it was difficult to shorten it to more than this, so it was marked as "n/N" in main table.

Reviewer D

In this article, Kim et al conducted a retrospective study of patients who underwent bronchoscopic intervention after chest radiography (CXR) and digital tomosynthesis (DTS) examinations from September 2013 to August 2020. CXR and DTS were done on the same day. The bronchoscopic intervention was done within 10 days after CXR and DTS. Images modalities were evaluated using a bronchoscopic view as a reference with sensitivity, specificity, accuracy, positive predictive value, and negative predictive value for assessing the diagnostic performance.

Comment 1. Why did the authors evaluate diagnostic performance of DTS for silicone

airway stents and related complications? Especially when non-invasive CT scan is readily available.

Reply 1. Thanks for your comment.

For the reasons mentioned in the manuscript, we prefer DTS as a routine check. Although CT can give much more information than DTS, it cannot be performed frequently in consideration of radiation exposure and cost. Complications related to airway silicone stent can occur at short intervals that we cannot predict, and it is difficult to perform CT evaluation every time. Also, it is not possible to follow up asymptomatic patients by taking chest CT every few months during outpatient follow-up. For these reasons, DTS was preferred over CT as a routine examination in our institution.

Comment 2. Authors did mention radiation exposure, why was there not direct comparison between CXR, DTS, and CT scan radiation dose in this study? It seems that the radiation dose reduction is one of the biggest arguments for use DTS instead of CT. But presumably DTS is higher radiation to CXR.

Reply 2. The advantage of DTS is that it has better diagnostic performance than CXR, and it has lower radiation exposure and cost than CT, so it can be inspected more often. As the reviewer pointed out, DTS (0.05-0.2mSv) has a higher radiation exposure than CXR (around 0.02mSv). However, there is not much information available from CXR regarding central airway related diseases or airway silicone stents. We focus more on the usefulness of DTS when all these pros and cons are taken into account.

We added the limitation of DTS, which are higher radiation exposure than CXR, in the DISCUSSION section.

[DISCUSSION, page 12, line 265 - 269]

Finally, DTS has the disadvantage of higher radiation exposure than CXR. CXR has a radiation exposure of approximately 0.02 mSv, but DTS has a higher radiation exposure than CXR. However, a method for testing with low-dose DTS has been developed.(11) It also has a higher radiation exposure than CXR, but still a significantly lower radiation exposure than CT.

Comment 3. It seems that none of imaging study can replace the gold standard of bronchoscopy evaluation, so why should we consider DTS and why not just have scheduled bronchoscopy for stent evaluation?

Reply 3. Thank you for your comment. The gold standard for evaluation of stent status is

bronchoscopy evaluation, as the reviewer said.

We also evaluated the stent status through flexible bronchoscopy in some cases during follow-up. In the case of symptom aggravation due to mucostasis, bronchoscopic toileting is performed simultaneously to relieve symptoms.

However, bronchoscopy intervention is an invasive procedure and requires the use of sedative medications for the patient. If we can obtain sufficient information through from less-invasive imaging tests, we won't have to perform invasive procedures on all patients with airway stents every time, which might be unnecessary.

Comment 4. The authors report: "Of the 167 cases with silicone stents, 53 experienced stent migration and 121 experienced stent obstructions due to granulation tissue or fibrosis." These rates of migration and obstruction appears to be higher than previous reported (10% migration and 8% granulation – Dumon, JF. Chest 1990 Feb;97(2):328-32). Why is this the case?

Reply 4. Thank you for your important comment.

In our study, we analyzed cases that underwent CXR, DTS, and bronchoscopic interventions between September 2013 and August 2020. In some cases, chest CT or flexible bronchoscopy was performed earlier than bronchoscopic intervention. In addition, some patients who have been referred to our institution for bronchoscopic intervention already received chest CT or flexible bronchoscopy at other hospitals. We set the interval between imaging tests and bronchoscopic interventions at a maximum of 10 days. Considering the real clinical situation such as delay in hospitalization date, cases exceeding 10 days were excluded from the study.

Considering these factors, the incidence of stent-related complications appears to be high because only some, but not all, patients who underwent stent procedure were selectively included in the study during the study period.

In addition, the study suggested by the reviewer (Dumon, JF. Chest 1990 Feb;97(2):328-32) had a short follow-up period, whereas our study had a long follow-up period. This might also affect the rate of stent-related complications.

Comment 5. Utility of DTS in stent evaluation is of question – can you propose a clinical workflow to integrate DTS? How common is DTS in healthcare systems?

Reply 5. Our study suggests that DTS is more useful to detect silicone airway stents and stent-related complications than CXR and shows high diagnostic performance. Previous study reported that the use of DTS to verify suspected findings of pulmonary lesions on chest radiographs can reduce CT utilization by about 75% (1). Taken together, there is sufficient evidence for the usefulness of DTS for the assessment of airway silicone stent condition.

Our institution routinely conducts DTS tests immediately after stent insertion, 1 month after, and 3 months after follow-up. After that, if the patient does not have any additional problems, follow-up the patient's airway stent status with DTS every 6 months. At the time of each DTS test, pulmonary function test and CAT score for patient symptom check are measured together. This is our routine workflow. However, in the case of an early outpatient clinic visit with complaints of symptoms or an emergency room visit, the stent status is evaluated by DTS, chest CT, or flexible bronchoscopy in consideration of the patient's condition, and then a decision is made on bronchoscopic intervention.

The FDA approved DTS for diagnostic imaging in 2005. In addition to chest image, clinical uses of tomosynthesis have included vascular imaging (2), dental imaging (3), orthopedic imaging (4), and mammographic imaging (5). As in the example above, tomosynthesis is being used in various clinical areas, and our institution is using DTS as a routine test for airway evaluation.

[Reference]

1. Quايا E, Baratella E, Cernic S, et al. Analysis of the impact of digital tomosynthesis on the radiological investigation of patients with suspected pulmonary lesions on chest radiography. *Eur Radiol* 2012;22:1912-22.
2. Kruger RA, Sedaghati M, Roy DG, et al. Tomosynthesis applied to digital subtraction angiography. *Radiology* 1984;152:805-8.
3. Webber RL, Horton RA, Underhill TE, et al. Comparison of film, direct digital, and tuned-aperture computed tomography images to identify the location of crestal defects around endosseous titanium implants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:480-90.
4. Duryea J, Dobbins JT, 3rd, Lynch JA. Digital tomosynthesis of hand joints for arthritis assessment. *Med Phys* 2003;30:325-33.
5. Chong A, Weinstein SP, McDonald ES, et al. Digital Breast Tomosynthesis: Concepts and Clinical Practice. *Radiology* 2019;292:1-14.

Comment 6. Can authors elaborate why CXR and DTS was done in the first place? Was this routine stent following up care?

Reply 6. At the time when DTS was used for other lung diseases and a comparative study with CXR came out, it was first introduced with the thought that DTS could be used rather than CXR in airway disease or stent evaluation in our institution.

As DTS has proved its efficacy and accuracy in detecting other lung disease compared to CXR, we hypothesized that DTS could detect the anatomy of the central airway overlapping the mediastinum better.

As it is not easy to detect silicone stents with CXR, DTS was used to evaluate airway disease and to determine the status of airway silicone stents. (mentioned in INTRODUCTION)

section, page 4, line 80 - 82)

The clinician of our institution has been using DTS to observe the patient's condition on the outpatient clinic and continue to routinely conduct the DTS as a basic test instead of the CXR, as it is considered to be helpful in the decision of re-procedure.

And in responses to the reviewer B and previous your questions, we explained in detail the reasons why our institution conducts the DTS as a routine follow-up test and the workflow of our institution. We also added the above to the DISCUSSION section.

[DISCUSSION, page 12, line 270 - 275]

Our institution routinely conducts DTS immediately after stent insertion, 1 month after, and 3 months after follow-up. After that, if the patient does not have any additional problems, we follow-up the patient's airway stent status with DTS every 6 months. However, in an early outpatient clinic visit with complaints of symptoms or an emergency room visit, the stent status is evaluated by DTS, chest CT, or flexible bronchoscopy, considering the patient's condition. Then a decision is made on bronchoscopic intervention.