Original Article

Cone beam computed tomography-guided bronchoscopic sampling of peripheral pulmonary lesions: The first Indian experience

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ABSTRACT

Background: Conventional bronchoscopic approaches have a lower diagnostic yield (DY) compared to transthoracic biopsy for sampling peripheral pulmonary lesions (PPLs). Cone-beam computed tomography (CBCT)-guided bronchoscopy overcomes the limitations of conventional bronchoscopy techniques. This study evaluates DY, predictors of success, and safety of CBCT-guided bronchoscopy for PPL biopsy. **Materials and Methods:** This single-center retrospective study included all consecutive patients who underwent CBCT-guided biopsy for PPLs between November 2023 and November 2024. Clinico-radiologic and procedural details, tool-in-lesion (TIL) relationships, DY, factors predicting DY, and complications were assessed. **Results:** Of the 183 patients who underwent bronchoscopic sampling of PPL during study period, 50 patients underwent CBCT-guided biopsy. The overall DY of CBCT biopsy was 88% (44/50). A type 1 TIL (tool within lesion) was obtained in 57% (28/49), type 2 TIL (tool touch lesion) in 35% (17/49), and a type 3 TIL (tool away from lesion) in four cases. The factors predicting DY were size of lesion and the tool–lesion relationship. DY increased with increasing size of PPL and decreased the farther the tool was from the center of the target. The DY was 100%, 82%, and 25% for lesions with type 1, type 2, and type 3 TIL, respectively ($P = 0.024$). CBCT biopsy was safe with no procedural mortality, no pneumothorax, and moderate to severe bleed in seven cases. **Conclusion:** CBCT-guided biopsy for peripheral pulmonary lesions is safe and has a DY of 88%. DY is higher for lesions ≥2 cm and when the tool is within the lesion (type 1 TIL) on CBCT spin.

KEY WORDS: Bronchoscopy, cone-beam CT scan, navigational bronchoscopy, peripheral pulmonary lesion, radial EBUS

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INTRODUCTION

The detection of peripheral pulmonary lesions (PPLs) has increased with the widespread use of computed tomography (CT). Early diagnosis and management of intermediate- to high-risk nodules is essential for improving patient outcomes.The primary goal in sampling PPLs is to achieve a high diagnostic yield using the safest modality available.[1] While transthoracic needle biopsy (TTNB) has a superior diagnostic accuracy

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compared to bronchoscopy-guided methods, it carries a higher risk of complications, particularly pneumothorax and bleeding.[2] Other drawbacks of a TTNB are inability to perform simultaneous mediastinal staging and inability to perform a simultaneous broncho-alveolar lavage (BAL). In several centres, guided bronchoscopic approaches are hence preferred as the initial diagnostic strategy.

Despite advancements in bronchoscopy, the diagnostic yield (DY) for PPLs with conventional bronchoscopic tools such as radial endo-bronchial ultrasonography (R-EBUS) remains around 70% due to limitations such as (a) CT-to-body divergence, (b) lack of real-time tool in lesion (TIL) confirmation, (c) challenges in navigation, and (d) positional changes when passing biopsy instruments through the bronchoscope.[3] Cone-beam computed tomography (CBCT)-guided bronchoscopy offers a promising solution by overcoming CT-to-body divergence, enabling navigation using augmented fluoroscopy, and providing a three-dimensional tool in lesion confirmation.[4] Use of a CBCT guidance for PPL sampling has been shown to improve the diagnostic outcomes.[5]

Since the first publication of CBCT-guided PPL sampling by Wolfgang *et al*.,[6] in 2014, this approach has been widely used in several countries, both for diagnosing PPLs and for nodule ablation. However, till date, access to CBCT equipment is limited, and this approach is underutilized in many developing countries. In this single-center retrospective study, we reviewed our initial experience of CBCT-guided biopsies for PPLs. We assessed the DY, predictors of success, and safety of this technique for diagnosing PPLs.

MATERIALS AND METHODS

This is a single-centre retrospective observational study conducted at the department of pulmonary medicine of a tertiary care referral institute. All consecutive patients who underwent CBCT-guided bronchoscopic biopsy for PPLs between November 2023 and November 2024 were included. PPLs were defined as lesions (nodules, masses, and consolidation) that were within the lung parenchyma, not visible endobronchially, and not accessible by linear EBUS.

Eligible patients were those who had a PPL requiring biopsy as part of routine clinical care. At our center, bronchoscopic sampling is the predominant sampling technique for PPLs which were not abutting the pleura. Lesions which are larger and are easily accessible without advanced navigation/imaging modalities were approached using a standard bronchoscope (BF-1TH190; Olympus, Tokyo, Japan) or a thin bronchoscope (BF-P190; Olympus, Tokyo, Japan) and a radial EBUS probe (Olympus, Tokyo, Japan) imaging. These procedures were conducted outside the CBCT suite and were excluded from the current analysis. CBCT-derived augmented fluoroscopy (CBCT-AF) guidance was the preferred approach for smaller lesions (<3 cm in diameter). All procedures were performed by any one of two interventional pulmonologists (VNM, VPP), each with more than 10 years' experience in performing bronchoscopies. Written informed consent was obtained from all patients. Institutional ethical clearance was obtained for the study (Ref No: RP/PP/12-2024).

CBCT procedure

All procedures were performed in CBCT suite under general anesthesia using a lung navigation ventilation protocol.[7] Patients were intubated using an 8–8.5 size endotracheal tube (ETT) and ventilated with high positive end-expiratory pressure (10–12 cm H_2O), a low fraction of inspired oxygen (FiO_2 ≤0.30), and a high tidal volume (8–10 mL/kg) throughout the procedure to prevent atelectasis. All procedures were performed in supine position. Recruitment maneuvers were not routinely applied after induction and were used only when CBCT scan showed atelectasis obscuring the target PPL.

All patients underwent initial CBCT scan for procedural planning and guidance using a floor-mounted CBCT system (Allura Xper FD20, Philips, Netherlands). The target lesion was then marked with crosshairs in axial, sagittal, and coronal views on CBCT console. Whenever feasible, the path to the nodule was also manually marked on the console using bread-crumbs. Subsequently, live fluoroscopic images with augmented fluoroscopy (AF) overlay were obtained. In addition, for patients where the preprocedure CT was compatible, the airway path leading to the target was mapped using the virtual bronchoscopic navigation (VBN) system (Archimedes, Broncus, China).

A thin (BF-P 190; Olympus, Tokyo, Japan) or an ultrathin (BF-MP 190; Olympus, Tokyo, Japan) flexible video-bronchoscope was then introduced through the ETT for initial airway inspection. Using AF (with or without VBN) guidance, the bronchoscope was advanced to the target lesion. The lesion was then visualised using a 20 MHz radial EBUS probe (Olympus UM-S20-17S). Once the lesion was identified with radial EBUS, the bronchoscope was stabilized with a bronchoscope stabilisation system (Mediflex, NewYork, USA), and a second CBCT spin performed to confirm the tool-in-lesion (TIL) position. TIL was defined based on the location of probe in relation to the PPL in three orthogonal planes (axial, sagittal, and coronal): type 1 lesion (tool is in the lesion in all three planes), type 2 lesion (tool is at the edge of lesion in one or more planes), and type 3 lesion (tool is away from lesion in all planes). "Center Strike" was defined as a subset of type 1 TIL when the probe was in the exact centre of target in all three orthogonal planes.

After confirmation of the tool in lesion, a 1.1 mm cryo probe (Erbe, Germany) without sheath was inserted through the working channel of scope and advanced to the lesion under AF guidance. After reconfirmation

of cryo-probe position using AF, a cryobiopsy was performed using an cryo-activation time between 8 and 10 seconds. All samples were analyzed using rapid on-site evaluation (ROSE) of the imprint smears. Additional cryobiopsies (usually 3–4) were obtained and sent for histopathological examination (HPE) and other ancillary tests, as deemed necessary. When necessary, BAL was also obtained from the lesion.

DY was determined in accordance to STARD (Standards for Reporting Diagnostic Accuracy Studies) guidelines.[8] Patients with a diagnosis (benign or malignant) that is sufficient to decide patient care at the end of the index procedure were considered diagnostic. Atelectasis during the initial CBCT scan was noted and graded using the ASSESS score.[9] The number of CBCT spins obtained, time taken to localize the lesion, and total time taken for the procedure were noted.

All patients underwent a post-procedural chest radiograph to assess for pneumothorax. Post-procedural bleed was categorised as mild (requiring no intervention), moderate (required instillation of topical epinephrine or an occlusion balloon tamponade), or severe (bleeding which leads to hypotension, intra-procedural hypoxemia, which necessitated selective lung ventilation, or leads to mortality).

Statistical analysis

Statistical analysis was performed using the SPSS software (version 24.0). Categorical and continuous variables were expressed as frequency (percentage) and mean ± S.D., respectively. Descriptive statistics were used to summarise the demographics and procedural details of the study population. Associations between two or more qualitative variables were assessed using the Chi square or Fischer exact test as appropriate. A P value of < 0.05 was considered statistically significant, and all P values presented are two-tailed. Univariate logistic regression analyses were used to determine the factors predicting DY.

RESULTS

Study population demographics and nodule characteristics

Between November 2023 and November 2024, a total of 183 patients underwent bronchoscopic sampling of PPLs. Of these 183 patients, only 50 patients underwent CBCT-guided sampling, and the rest underwent non-CBCT-guided sampling using radial EBUS under conventional fluoroscopy guidance. Of the 50 patients who underwent CBCT, a biopsy was performed in 47 cases [Figure 1]. In two cases, the probe could not be navigated close to the target lesion, and in one case, the lesion was found to be resolved in initial CBCT spin.

Patient demographics and lesion characteristics are summarised in Table 1. The mean age of patients was 56 years, with 60% of the cohort being men. Lesions were predominantly located in upper lobes (56%), with only 40% demonstrating a positive bronchus sign on CT. The mean lesion diameter was 21.7 ± 1.2 mm, and 48% (24/50) of lesions were ≤20 mm in diameter.

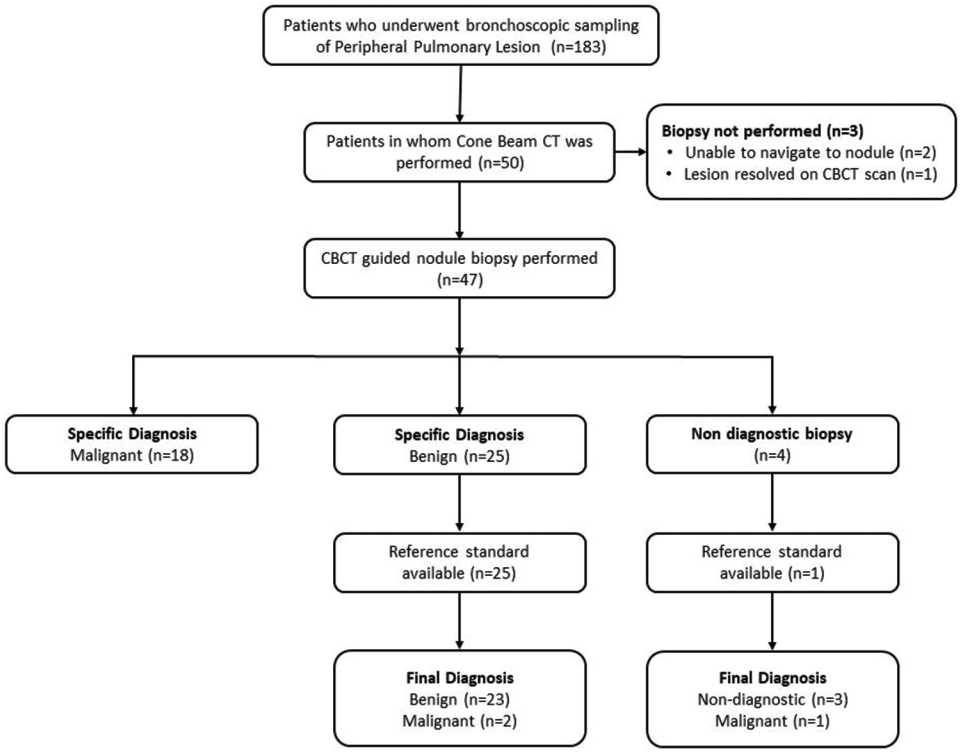

Figure 1: Flow of patients in the study reported in accordance to "Standards for Reporting Diagnostic Accuracy Studies-inspired flow diagram", adapted for studies of minimally invasive diagnostic procedures for peripheral pulmonary nodules

CBCT procedural details

The average time to navigate to lesion was 7.7 ± 4.7 minutes. The mean total procedure time, measured from anaesthesia induction to scope removal (excluding staging linear EBUS), was 76.2 ± 20.7 minutes.

Virtual bronchoscopy navigation (VBN) was utilized in 72% (36/50) of cases, with a direct pathway identified in 52.7% (19/36) of cases. A thin bronchoscope was used in 60% (30/50) of the cases, and an ultra-thin scope was used in the remaining. An average of 2.04 CBCT spins were performed per procedure. Only 54% (27/50) of lesions were visible on fluoroscopy. AF was used in all cases, and multi-planar AF images were obtained in 50% (25/50). Most lesions (44/50; 88%) could be visualised on r-EBUS, with the image being concentric in 41% (18/44) and eccentric/adjacent in 59% (26/44) of cases [Figure 2].

Table 1: Demographics and clinico-radiologic characteristics of patients

	Patients (*N*=50)*
Age (years)	56.16±13.6
Gender	
Male	30/50 (60.0)
Female	20/50 (40.0)
Past history of malignancy	7/50 (14.0)
Past history of tuberculosis	3/50 (6.0)
Type of lesion on HRCT chest	
Nodule/Mass	42/50 (84.0)
Consolidation	8/50 (16.0)
Average lesion diameter	
<10 mm	6/50 (12.0)
10.1-20 mm	18/50 (36.0)
20.1-30 mm	17/50 (34.0)
>30 mm	9/50 (18.0)
Mean volume of lesion (mL)	5.44±8.17
Pulmonary lesion location	
Right upper lobe	13/50 (26.0)
Right middle lobe	5/50 (10.0)
Right lower lobe	9/50 (18.0)
Left upper lobe	15/50 (30.0)
Left lower lobe	8/50 (16.0)
CT bronchus sign	
Present	20/50 (40.0)
Absent	30/50 (60.0)

*Values expressed as mean±SD or *n*/*N* (%)

CBCT-AF navigation achieved a navigational success rate of 92% (45/49), with tool inside lesion (Type 1 CBCT-TIL) obtained in 57% (28/49) of cases. Of these 28 cases, 23/28 (82.1%) of lesions demonstrated center strikes. A tool touch lesion (Type 2 CBCT-TIL) was obtained in 35% (17/49) of cases [Figure 3]. The tool was away from target in four cases (Type 3 CBCT-TIL). Of these four cases, the tool was close to the target in two cases, and a cryobiopsy was performed with an extended freeze time of 12 seconds. Intra-procedural atelectasis was noted in 42% (21/50) of cases, but it was mild (ASSESS 1 Grade) and did not obscure the lesion. ASSESS grade 2 and 3 atelectasis were not observed in our study [Table 2].

Diagnostic performance of CBCT-guided biopsy

Of the 47 cases where a biopsy was obtained, HPE revealed that 38% (18/47) of lesions were malignant, 53% (25/47) were benign, and 8% (4/47) were non-diagnostic [Table 3]. The most common malignant subtype was lung adenocarcinoma, and the most common benign diagnosis was organising pneumonia (OP).

Four biopsies were non-diagnostic, with histopathology showing non-specific inflammation/normal lung parenchyma [Supplementary Table 1]. Of the nine patients with OP on histopathology, clinico-radiologic and serologic profiles confirmed the final clinical diagnosis as

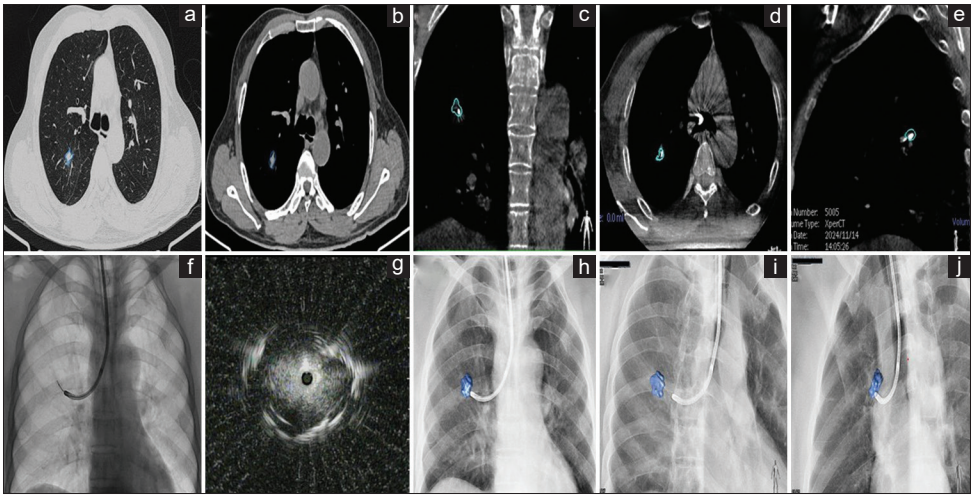

Figure 2: CBCT-guided biopsy using augmented fluoroscopy and multiplanar imaging. (a and b) Preprocedural CT scans showing a soft tissue nodule measuring 1.34 × 0.85 mm in the right upper lobe. (c-e) CBCT images confirming tool-in-lesion (type 1) in the coronal, axial, and sagittal planes, respectively. (f) Conventional fluoroscopy not demonstrating the target lesion. (g) Radial EBUS demonstrating a concentric image. (h-j) Multiplanar augmented fluoroscopy images verifying the tool within the lesion in three planes (anteroposterior, right anterior oblique and left anterior oblique views, respectively). Histopathological analysis of biopsy specimens revealed granulomatous inflammation. CBCT: cone-beam computed tomography, CT: computed tomography, EBUS: Endobronchial ultrasonography

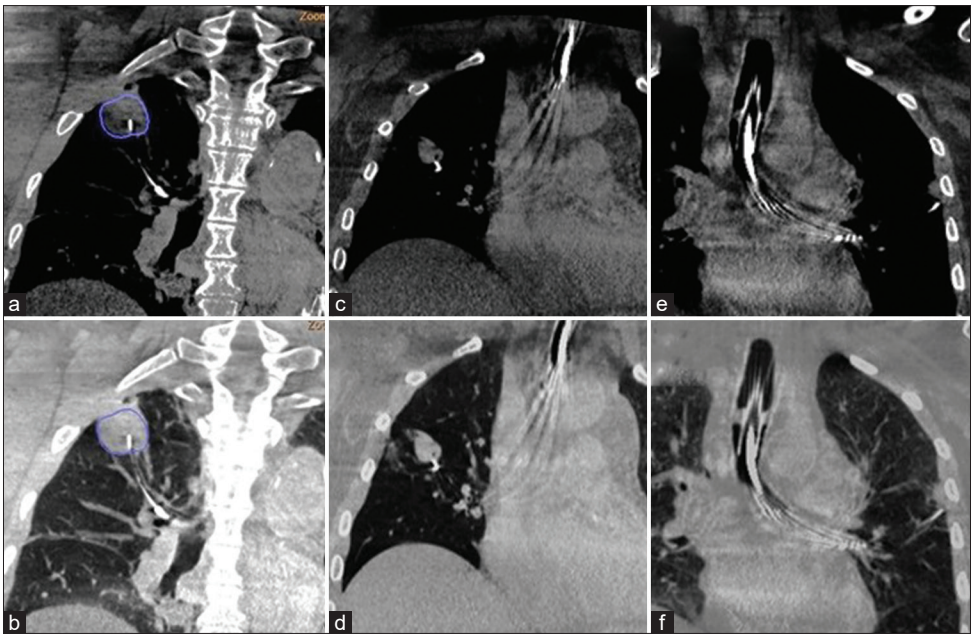

Figure 3: CBCT images showing the different types of tool-in-lesion (TIL) relationships in corresponding mediastinal and lung windows. (a and b) Type 1 (tool within the lesion), (c and d) Type 2 (tool at the lesion's edge or tool touch lesion) (e and f) Type 3 (tool away from the lesion)

Table 2: Procedural details of the patients (*N*=50)

CBCT Procedure characteristics	Number*
Average time to visualize the lesion (minutes)	7.70±4.71
Gadgets used for the procedure	
• Virtual bronchoscopic navigation (Lung Point)	36/50 (72.0)
• Radial EBUS	50/50 (100)
• Bronchoscope type	
Thin scope (Olympus *P* 190)	30/50 (60.0)
Ultra-thin scope (Olympus MP 190)	20/50 (40.0)
• Augmented fluoroscopy	50/50 (100)
CBCT Spins per procedure	
1 spin	11/50 (22.0)
2 spins	28/50 (56.0)
≥3 spins	11/50 (22.0)
Average CBCT spin per procedure	2.04
Lesion characteristics	
Visible on conventional fluoroscopy	27/50 (54.0)
Radial EBUS view	
Concentric	18/50 (36.0)
Eccentric/Adjacent	26/50 (52.0)
Not visualised	6/50 (12.0)
CBCT (Tool in lesion)	
Type 1 (Center strike/tool in lesion)	28/49 (57.14)
Type 2 (Tool touch lesion)	17/49 (34.69)
Type 3 (Tool away from lesion)	4/49 (8.16)
Atelectasis during procedure	21/50 (42.0)
ASSESS 1 (Mild)	21/21 (100)
Complications	
Bleeding	29/50 (58.0)
Mild	22/50 (44.0)
Moderate	6/50 (12.0)
Severe	1/50 (2.0)
Pneumothorax	Nil

*Values expressed as mean±SD or *n*/*N* (%). CBCT: Cone Beam Computed Tomography, EBUS: Endobronchial Ultrasonography

post-infectious OP (n = 5), auto-immune OP (n = 1), or cryptogenic OP (n = 1). In two cases of OP, the lesion did not resolve at 6 weeks, a CT guided biopsy was performed, and the diagnosis was established as malignancy. Both these cases had a Type 2 TIL relationship during the CBCT biopsy, and the initial biopsy was categorised as para-malignant OP [Supplementary Table 2].

The overall DY was 88% (44/50) with a diagnostic accuracy of 95.4% (42/44) at 6-month follow-up. Factors affecting the DY were assessed [Table 4]. The DY increased with increasing average lesion diameter. The DY for lesions ≤10 mm was 50%; for lesions between 10.1 mm and 20 mm, it was 83.3%; and for lesions >20 mm, it was 100% (P = 0.006). The CBCT-TIL relationship also influenced the DY. Lesions with Type 1 TIL relationship had a 100% DY; those with Type 2 TIL (Tool Touch lesion) had an 82.4% DY, and those with Type 3 TIL (Tool away from lesion) had only 25% DY (P = 0.024).

Procedural learning curve

An improvement in DY was observed with increasing procedural experience, increasing from 75% in the first quarter to 100% in the fourth quarter. The cumulative DY for the first two quarters was 79.2% (19/24), which increased to 96.1% (25/26) for the last two quarters. This difference, however, did not achieve statistical significance (P = 0.09). Also, as the procedural experience and confidence of operator increased, fewer CBCT spins were required per procedure. The average nodule size and time taken to visualise the lesion remained same throughout the study period [Table 5].

Complications

The most common procedural complication was bleeding, which was noted in 58% of the cases. It was however mild in the majority of cases (44%). Moderate bleeding was observed in six cases, and only one patient experienced

significant bleed requiring selective intubation and lung isolation. None of the patients developed pneumothorax, and there was no procedure related mortality.

Table 3: Histopathologic diagnosis of the study population (*n*=47)

Histopatholgic diagnosis	No. of patients
Malignancy	18/47 (38.3)
Adenocarcinoma	15/47 (31.9)
Metastatic Sarcoma	1/47 (2.12)
Poorly differentiated Malignancy	1/47 (2.12)
Typical carcinoid	1/47 (2.12)
Benign causes	25/47 (53.2)
Organising pneumonia	9/47 (19.14)
Tuberculosis	7/47 (14.89)
Sarcoidosis	2/47 (4.25)
Amyloidosis	2/47 (4.25)
Nocardiosis	1/47 (2.12)
Fungal Pneumonia	1/47 (2.12)
Hamartoma	1/47 (2.12)
Non Tuberculous Mycobacterium	1/47 (2.12)
Bacterial Pneumonia	1/47 (2.12)
Non-diagnostic	4/47 (8.5)

All values expressed as *n*/*N* (%)

Table 4: Factors affecting the diagnostic yield of procedure (Univariate logistic regression analysis)

Variable	Diagnostic yield	*P*
Lesion size (mm)		
<10	3/6 (50.0)	0.006
10.01-20	15/18 (83.33)	
>20.01	26/26 (100)	
Lesion location		
RUL/LUL	24/28 (85.7)	0.578
Others	20/22 (90.9)	
Type of lesion		
Nodule/mass	37/42 (88.09)	0.962
Consolidation	7/8 (87.5)	
Radial EBUS image		
Concentric	17/18 (94.4)	0.314
Non concentric	27/32 (84.37)	
CT bronchus sign		
Yes	18/20 (90)	0.723
No	26/30 (86.6)	
Bronchoscope used		
Thin bronchoscope	26/30 (86.6)	0.723
Ultra-thin bronchoscope	18/20 (90.0)	
VBN used		
Yes	31/36 (86.1)	0.518
No	13/14 (92.8)	
CBCT image type		
Type 1 (Tool within lesion)	28/28 (100)	0.024
Type 2 (Tool touch lesion)	14/17 (82.35)	
Type 3 (Tool away from lesion)	1/4 (25)	

RUL: right upper lobe, LUL: left lower lobe, EBUS: endobronchial ultrasound, CT: computed tomography, VBN: virtual bronchoscopic navigation, CBCT: cone-beam computed tomography

DISCUSSION

Our study is the first real-world observational study that assessed the DY and performance of CBCT-derived augmented fluoroscopic (CBCT-AF)-guided sampling of PPLs from India. Our study highlights that CBCT-guided bronchoscopy, in combination with R-EBUS and virtual bronchoscopic navigation (VBN), achieves a high DY of 88%, a figure that surpasses the traditionally reported yields of 50–75% for conventional bronchoscopic techniques.[10,11] These results align with an expanding body of literature that shows that CBCT-guided biopsy has a superior diagnostic yield over conventional bronchoscopic techniques.[12,13]

One of the findings in our study was the positive correlation between DY and tool–lesion relationship. The DY for lesions with type 1 TIL relationship was 100% and reduced to 82% and 25% for lesions with type 2 and type 3 TIL relationship, respectively. The farther the tool is from the centre of the lesion, the lower is the DY achieved. This reinforces observations by Sobieszczyk *et al*.[14] and Kheir *et al*.,[15] both of whom highlighted the importance of real-time imaging for ensuring accurate biopsy tool positioning. In the current study, a type-1 TIL was achieved in 57% of cases with a centre strike in 46% cases. This is lesser than that reported by centres with higher expertise in performing CBCT biopsies. In a recent study by Bhadra *et al*.,[16] of the 222 lesions sampled, a type 1 TIL relationship was obtained in 99% of cases, with centre strike in 68% of the cases. The higher navigational success in their study could be attributed to greater expertise of the operating team, addition of robotic bronchoscopy to CBCT imaging, and use of peripheral TBNA needles to perform peripheral airway tunneling.

Earlier studies have demonstrated that biopsies performed from the lesion periphery and from the lesion centre may have different pathologies.[6] This was observed in two of our cases where biopsy from periphery showed OP and biopsy from the centre yielded a diagnosis of malignancy. The aim of a bronchoscopist while performing advanced guided bronchoscopy is to guide the tool to as close to the centre of the target as feasible. The fact that a tool merely touching the lesion resulted in a significant drop in DY underscores the importance of precise lesion engagement.

Our findings also reaffirm that lesion size plays a crucial role in diagnostic success. The DY was the highest for lesions >20 mm (100%) and least in lesions ≤10 mm (50%).

Table 5: Procedural learning curve and changes in DY and CBCT procedure details

Procedure range (*n*)	Average lesion size (cm)	Average CBCT spins per procedure	Average time to visualize lesion (min)	Diagnostic yield*
Quartile 1 (1-12)	1.99	2.5	8.08	9/12 (75.0)
Quartile 2 (13-24)	1.86	2.16	8.91	10/12 (83.3)
Quartile 3 (25-37)	2.41	1.84	6.38	12/13 (84.6)
Quartile 4 (38-50)	2.37	1.69	7.53	13/13 (100)

*Values expressed as *n*/*N* (%)

This aligns with prior studies that have consistently shown that smaller nodules remain one of the greatest challenges in interventional pulmonology.[5,17] However, even in smaller nodules (<2 cm), CBCT significantly improved diagnostic accuracy, reinforcing findings by Casal *et al*.,[18] who showed that using CBCT improves DY, even for fluoroscopically invisible nodules. In our study also, only 58% of lesions were visible on standard fluoroscopy, and the results validate the superiority of CBCT-guided augmented fluoroscopy.[12]

In our study, all cases underwent cryobiopsy using ultrathin cryoprobes. Since introduction of cryobiopsy for PPL sampling in 2014,[19] several studies demonstrated superior yield of cryobiopsy over a forceps biopsy. The study by Kho *et al*.,[20] confirmed the superiority of cryobiopsy over forceps biopsy for lesions with eccentric/adjacent R-EBUS image orientation (75% vs 48.8%). Another study by Huang *et al*.[21] showed that while sampling ground glass nodules with CBCT, cryobiopsy increases the yield over forceps biopsy by 21.9%. Subsequent studies of CBCT biopsy also showed that ultrathin cryobiopsy increases the yield over conventional forceps biopsy.[16] While it is a routine practice at our centre to use 1.1 mm cryoprobe for biopsy of PPLs, several centers still use conventional forceps biopsy. Further studies assessing the optimal sampling strategy for PPLs are needed. Also, there is no consensus on the ideal number of cryobiopsies that need to be obtained and the optimal freeze time when performing lesion biopsy.

Another key observation from this study was the role of procedural learning in optimising CBCT workflows and improving the DY. As procedural experience increased, we noted a reduction in the number of CBCT spins required per case and an increase in DY. This reflects the learning curve associated with navigational bronchoscopy and advanced imaging integration, which has also been documented in previous studies. Cheng *et al*.[22] and Verhoeven *et al*.[17] also emphasised that operator experience plays a significant role in minimising radiation exposure and optimising workflow efficiency, and our findings echo this trend.

Our study also reconfirmed the safety of CBCT-AF biopsy for sampling PPLs. In our study, none developed pneumothorax. Low pneumothorax rates (0–2%) have been documented in earlier large studies of CBCT cryobiopsy.[16,21] Another study which assessed the role of cryobiopsy in interstitial lung diseases showed that use of CBCT guidance reduced pneumothorax rates when compared to use of fluoroscopy alone (9.7% vs 1.7%).[23] The lower rates of pneumothorax while performing CBCT may be attributed to real-time confirmation of the position of probe in lesion and away from pleura. Bleeding was also minimal in our study, despite universal use of cryoprobes, with moderate or severe bleed occurring in only 14% of the study population. These findings are consistent with study by Huang *et al*.,[21] in which CBCT–cryobiopsy improved DY while maintaining an acceptable safety profile. Another practical challenge in performing CBCT-guided sampling is the additional time needed for setting up the equipment and performing the procedure. This would pose a challenge in high-volume interventional pulmonology centres where time management becomes essential.

Our study despite being the first from Indian subcontinent has certain limitations. Ours is a single-centre study, and the sample size is limited. Larger studies and multi-centre studies are needed to reconfirm the findings of our study. There was significant heterogeneity in the equipment/technique used to sample the lesions (use of VBN, number of CBCT spins, use of multi-planar AF, the choice of bronchoscope, the freezing time of cryoprobe, and the number of biopsies obtained). Also, the radiation exposure, which is one of the concerns while performing CBCT-guided sampling, was not systematically collected during the study period and hence is not presented. Lastly, cost-effectiveness of these advanced diagnostics in resource-constrained settings needs to be assessed.

In conclusion, our study reinforces the growing literature that CBCT-guided sampling of PPLs represents a transformative advancement in interventional pulmonology. By providing real-time lesion localisation, reducing sampling errors, and increasing DY, CBCT significantly outperforms conventional bronchoscopic techniques, making it a highly valuable imaging adjunct for trans-bronchial biopsy of PPLs.

Author contributions

VNM: Conceptualized the idea, managed the patients, performed CBCT guided biopsy, analysed the data, reviewed and revised the manuscript. VKG: Managed the patients, collected and analysed the data, drafted the manuscript. VPP: Managed the patients, performed CBCT guided biopsy, reviewed the manuscript. RR: Managed the patients, collected and analysed the data, drafted the manuscript. KSJ: Analysed the data, reviewed and revised the manuscript. SSK: Performed rapid on-site evaluation and interpreted the biopsies.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Follow-up of cases who remained undiagnosed after CBCT guided sampling (*n*=6)

Case	Nodule size (mm)	Location of nodule	CT Bronchus sign	CBCT tool in lesion type	Biopsy result	Additional procedure performed	Lesion categorized as	Follow up
1	12.6	Left upper lobe	No	Yes (Type 2)	Reactive cells	None	Need for further follow up	Patient is lost to follow up
2	10.6	Right lower lobe	No	Yes (Type 2)	Inflammation with reactive atypia	None	Need for further follow up	Patient is lost to follow up
3	8	Right middle lobe	Yes	Yes (Type 2)	Non Diagnostic	CT Guided Biopsy	Malignant	CT guided biopsy revealed Adenocarcinoma Lung
4	6	Left upper lobe	No	No (Type 3)	Chronic inflammation	None	Benign	Under follow up
5	13.5	Right upper lobe	No	No (Type 3)	Not performed	None	Need for further follow up	Patient is lost to follow up
6	10	Right upper lobe	Yes	No (Type 3)	Not performed	None	Need for further follow up	Patient is lost to follow up

Supplementary Table 2: Follow-up of cases with organizing pneumonia on CBCT biopsy (*n*=9)

Case	Nodule size (mm)	Location of nodule	CT bronchus sign	CBCT tool in lesion type	Additional procedure performed	Final etiologic diagnosis	Follow up scan
1	21.5	Left upper lobe	No	Type 2	None	Post infectious OP	Resolution of lesion
2	14	Left upper lobe	Yes	Type 1 (center strike)	None	Post infectious OP	Resolution of lesion
3	28.3	Right lower lobe	No	Type 2	None	Post infectious OP	Resolution of lesion
4	19.9	Left lingula	No	Type 2	None	Cryptogenic OP	Resolution of lesion
5	13	Left upper lobe	No	Type 3	CT guided biopsy	Post infectious OP	Resolution of lesion
6	29	Left upper lobe	Yes	Type 2	CT guided biopsy	Para malignant OP	No resolution
7	8.5	Right upper lobe	No	Type 2	Surgical Resection	Para malignant OP	No resolution
8	24	Right upper lobe	Yes	Type 1 (center strike)	None	Auto-immune OP	Resolution of lesion
9	25	Right upper lobe	No	Type 1 (center strike)	None	Post infectious OP	Resolution of lesion