



## DIAGNOSING A PERIPHERAL LUNG LESION

## Respiratory Medicine

Dr Kunal Luthra Assistant Professor, Rajiv Gandhi Superspeciality Hospital, Delhi

## ABSTRACT

**Introduction:** Flexible bronchoscopy is valuable procedure in diagnosing lung lesions. Bronchoscopy can be done under fluoroscopy guidance for diagnosing peripheral lung lesions. **Methods:** Retrospective analysis of the bronchoscopy procedures done for peripheral lung lesions under fluoroscopy guidance. The nondiagnostic cases undergoes surgical biopsy/follow up for radiological progression/CT guided biopsy/repeat bronchoscopy as decided by the multi-disciplinary discussion and patient preference. **Results:** Out of 15 patients; bronchoscopy done with fluoroscopy guidance was diagnostic in 11 patients, while 3 patients were diagnosed with video-assisted thoracoscopic surgery procedure. One patient was lost on follow up. The most common diagnosis obtained was malignancy lung (9 patients), followed by metastatic carcinoma breast (2 patients), and tuberculosis in 2 patients. The sensitivity, and negative predictive value of the fluoroscopy guidance bronchoscopy procedure were 71%, and 20%. **Conclusion:** In a resource constrained setting, peripheral lung lesions can be evaluated initially using conventional bronchoscope biopsy under fluoroscopy guidance.

## KEYWORDS

Peripheral lung lesions, bronchoscopy, Fluoroscopy, Video-assisted thoracoscopic surgery

## INTRODUCTION

Flexible bronchoscopy is valuable procedure in diagnosing lung lesions. The sensitivity of bronchoscopy for central lesion is higher than peripheral lung lesion. Peripheral lung lesions are defined as lesion not visible beyond the segmental bronchi i.e. not visualized by flexible bronchoscope. The sensitivity of bronchoscopy is affected by size of the lesion; higher for peripheral tumors with diameter >2cm than lesion <2cm.<sup>[1]</sup> The sensitivity is higher if bronchus extends to peripheral lesion, as seen in CT scanning.<sup>[2,3]</sup>

Another technique, radial endobronchial ultrasound aids in diagnosing peripheral lung lesions. Recent meta-analysis showed significant between study heterogeneity with overall sensitivity of radial ebus as 72% in diagnosing peripheral lung lesions.<sup>[4]</sup>

Due to heterogenous data regarding radial EBUS studies, and nonavailability of r-ebus at our institute, we decided to evaluate peripheral lung lesions with conventional bronchoscopy with fluoroscopy guidance. The false negative rate of bronchoscopy in peripheral lung lesion is not defined.<sup>[1]</sup> The objective of this study is to detect sensitivity, false negative rate of bronchoscopy procedure done under fluoroscopy guidance in peripheral lung lesions.

## METHODOLOGY

Retrospective analysis of the data of Bronchoscopy (BAL, biopsy, brush) done for lung lesions under fluoroscopy guidance at our institute.

## Inclusion Criteria

Lung nodules/mass not approachable by conventional bronchoscopy or CT guided biopsy are included for bronchoscopy done with fluoroscopy guidance after multidisciplinary discussion (oncologist, radiologist, and pulmonologist) regarding need and procedure for the histopathological diagnosis.

**Fluoroscopy Protocol Followed For Bronchoscopy:** CT planning via MDCT virtual bronchoscopy with flythrough is done to assess the approach or path by bronchoscopy under fluoroscopy guidance.<sup>[5]</sup>

Once bronchoscope reaches the target segment, biopsy forceps is introduced into subsegment under fluoroscopy guidance till it reaches the lesion, multiple biopsies are then taken.(Figure 1) The distance from the scope to the lesion is marked externally on the biopsy forceps. For lesions invisible on fluoroscopy (behind the cardiac shadow or rib shadow) marking on external surface of patient is done with lead marker via CT thorax on the day of procedure.<sup>[6]</sup>(Figure 2)

The nondiagnostic cases undergoes surgical biopsy/ follow up for radiological progression/ repeat bronchoscopy/ CT guided biopsy as decided by the multi-disciplinary discussion and patient preference

Statistic analysis was done using frequency tables. Means, range, diagnostic accuracy, sensitivity etc. were calculated.

## RESULTS

Fifteen patients underwent bronchoscopy under fluoroscopy guidance at our institute. Out of 15 patients, 9 were male. The most common presenting complaint was cough, followed by chest pain, anorexia, weight loss, and hoarseness. The underlying lung disease was present in three patients; emphysema in two and fibro-bronchiectasis in one. Three patients had history of cancer; all of them were carcinoma breast. Six patients had history of smoking. (Table 1)

The smallest lesion sampled was 10mm; and the largest was 57mm. Seven lesions were nodules i.e.  $\leq 30$ mm while 8 were mass. Majority of the patients (10/15) evaluated had single lesion only. Most of the lesions were located in upper lobe (11/15). CT bronchus sign was present in 9 lesions. (Table 2)

The most common diagnosis obtained was malignancy lung (9 patients), followed by metastatic carcinoma breast (2 patients), and tuberculosis in 2 patients. Bronchoscopy done with fluoroscopy guidance was diagnostic in 11 patients, while 3 patients were diagnosed with VATS guided procedure.

The procedures that were done under VATS guidance are lobectomy, thoracotomy-wedge resection, and thoracotomy-pleural biopsy. The diagnosis obtained were metastatic carcinoma breast, squamous cell carcinoma lung, and adenocarcinoma lung respectively.

The two lesions diagnosed as tuberculosis were lobulated and smooth respectively. Out of 11 lesions that were diagnosed as metastatic/malignancy; 9 were spiculated, and 2 were lobulated. The lesion diagnosed benign was smooth shape. One spiculated lesion that was lost on follow up was considered false negative for the procedure. (Table 3) Overall, the diagnostic accuracy, sensitivity, and negative predictive value of the fluoroscopy guidance bronchoscopy procedure were 73%, 71%, and 20% respectively.

Table 1 Baseline Characteristics

Total patients	15
Gender (Male/Female)	9/6
Mean Age (Range)	52.8 (26-75)
Complaints	
Cough (dry/productive)	8 (5/3)
Chest pain	6
Anorexia	6
Weight loss	4
Hoarseness	4
Hemoptysis	3
Shortness of breath	3
Comorbidity	
Diabetes	3
Hypertension	2
Fibro-bronchiectasis	1
Hypothyroid	1

Emphysema (centrilobular/paraseptal)	2 (1/1)
Smokers (>20 packyears)	6 (6)
History of cancer (site)	3 (Carcinoma breast)

**Table 2 Lesion Characteristics**

Number of lesions	15
Mean long axis diameter (range)	30mm (10-57)
<20mm	5
21-30mm	2
31-40mm	4
41-50mm	2
>50mm	2
Location (Right/Left)	(8/7)
Right upper lobe	7
Right lower lobe	1
Left upper lobe	4
Left lower lobe	3
Shape	
Spiculated	10
Lobulated	3
Smooth	2
Bronchus sign	9

**Table 3 Procedure Details And Diagnosis**

Lesions visible on fluoroscopy/number of lesions	14/15
Sedation (conscious/deep)	13/2
BAL	7
Brush	4
Biopsy	14
Diagnostic procedure	
Bronchoscopy (fluoroscopy guided)	11 (TP 10; TN 1)
VATS guided	3 (TP 3)
Final diagnosis	
NSCLC (NOS)	3
Adenocarcinoma lung	3
Carcinoma (NOS)	2
Tuberculosis	2
Metastatic Carcinoma breast	2
Squamous cell carcinoma lung	1
Benign	1
Lost to follow up	1

Abbreviations: BAL (Broncho-alveolar lavage), NSCLC (Non small cell lung carcinoma), NOS (not otherwise specified)

**Table 4 Characteristics And Diagnosis Of Peripheral Pulmonary Lesions < 25 mm Size**

Size(in mm)	Shape	Location	Diagnosis	Diagnostic procedure
10	Spiculated	Apical segment Right upper lobe	Metastatic Adenocarcinoma breast	VATS Lobectomy
13	Smooth	Posterior segment Right upper lobe	Benign lesion	Follow up after Bronchoscopy biopsy
14	Spiculated	Anterior segment Right upper lobe	NSCLS (NOS)	Bronchoscopy Biopsy
18	Lobulated	Superior segment Right lower lobe	Mucin secreting Adenocarcinoma	Bronchoscopy Biopsy
19	Spiculated	Lateral basal segment Left lower lobe	Metastatic Carcinoma breast	Bronchoscopy Biopsy, Brush
23	Spiculated	Superior segment Left lower lobe	Carcinoma (NOS)	Bronchoscopy Brush
24	Smooth	Anterior segment Right upper lobe	Tuberculosis	Bronchoscopy Biopsy BAL

Abbreviations: VATS-Video assisted thoroscopic surgery; NSCLS (NOS)- Non-small cell lung carcinoma (not otherwise specified); BAL-Bronchoalveolar lavage

**DISCUSSION**

Tumour tissue biopsy is essential for accurate diagnosis, and determining the histological subtype. Tissue is still the issue in personalized care of lung cancer.<sup>[7]</sup> In our study, we tried to obtain biopsy specimen in majority (14/15) of patients. Overall, biopsy yielded a specific histopathologic diagnosis in nine patients, bronchoalveolar lavage and brush cytology were diagnostic in one, and two patients respectively.

Larger size, spiculation, and upper lobe location are important predictors of cancer.<sup>[8]</sup>

Majority of the lesions in our study were spiculated, located in upper lobe, and larger in size. This explains the diagnosis of malignancy/metastasis as the most common diagnosis in our study. [Table2,3]

Computed tomography bronchus sign (CT-BS) is defined as CT-BS 0 that refer to absence of bronchus sign, CT-BS 1 which means airway immediately adjacent to pulmonary lesion, and CT-BS 2 is airway directly aligned with lesion.<sup>[9]</sup> For practical purpose, we considered presence or absence of bronchus sign in our study. The overall diagnostic yield of guided bronchoscopy in lesion with computed tomography bronchus sign was 74.1%.<sup>[10]</sup> In our study, diagnostic yield was 77.7% in lesion presenting with CT bronchus sign.

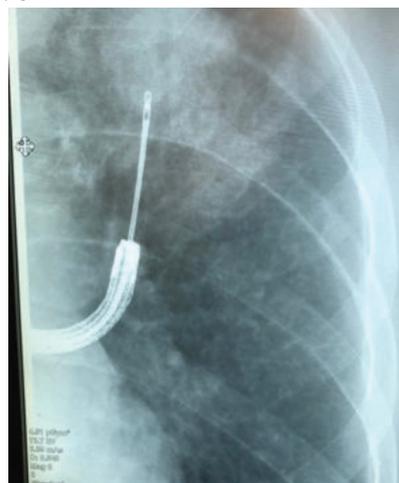
In a multicenter study, the diagnostic yield of standard bronchoscopy for peripheral lesion was 63.7%. The complications noted were rare. Pneumothorax, bleeding, respiratory failure are the complications that can occur.<sup>[11]</sup> There was no complication observed in our study. The diagnostic yield in our study was 73%.

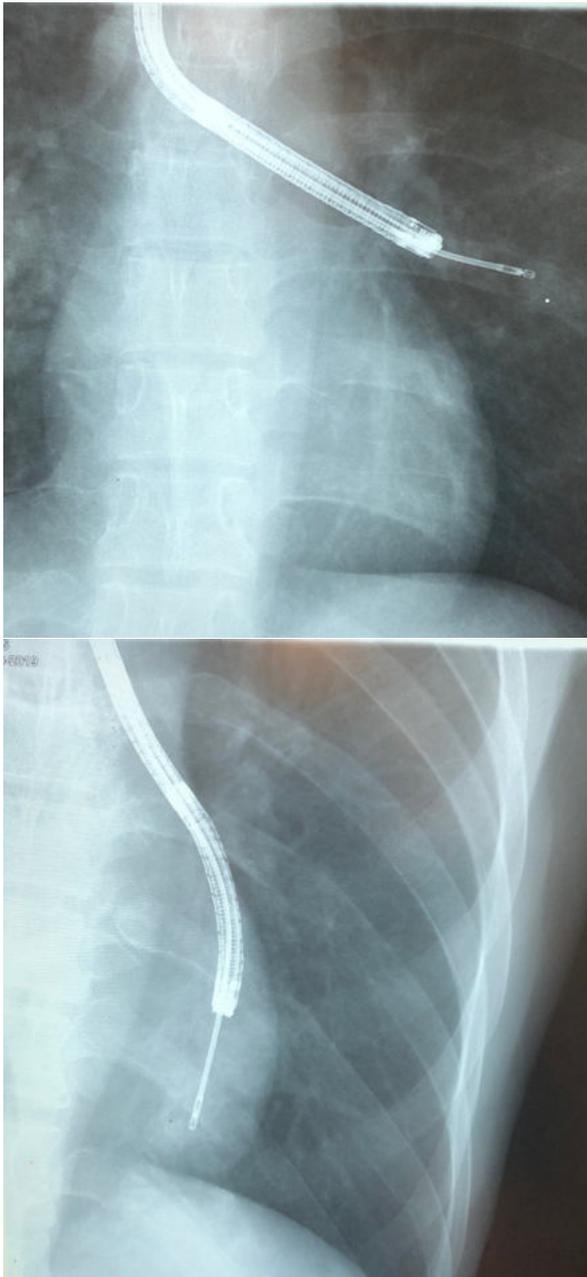
The diagnostic yield of fluoroscopy guided procedures for lesions smaller than 20mm was significantly lower than for lesions greater than 20mm (33.3% vs 72.2%).<sup>[12]</sup> In our study, there were five peripheral pulmonary lesions with size less than 20mm. Out of five, three were diagnosed with standard bronchoscopy with fluoroscopy (true positive). One lesion that could not be diagnosed was not visible on fluoroscope, hence approached after CT based lead marking.<sup>[6]</sup> The other lesion was diagnosed on follow up as benign lesion (true negative). (Table 4)

Immunohistochemistry (IHC) analysis serves as important method for differentiating primary lung cancer from metastatic cancers, and diagnosing histological subtypes of non-small cell carcinoma- not otherwise specified (NSCC-NOS).<sup>[13]</sup> GATA 3, CK7 for metastatic breast cancer; TTF1 in pulmonary adenocarcinoma; CK5, P40, P63 in primary lung squamous carcinoma are the various markers used for immunohistochemistry profiling.<sup>[14]</sup> IHC analysis was done on three biopsy specimens in our study. The details are as follows: 3.5 cm spiculated lesion diagnosed as carcinoma NOS (Ki67+ p53+), 1.9 cm spiculated lesion diagnosed as metastatic carcinoma breast (CK+ Ki67+), 1.8 cm lobulated lesion diagnosed as adenocarcinoma lung (TTF1+).

**CONCLUSION**

In a resource constrained setting; peripheral lung lesions can be evaluated initially using conventional bronchoscope biopsy under fluoroscopy guidance.





## REFERENCES

- Rivera, M. Patricia, Atul C. Mehta, Momen M. Wahidi. Establishing the Diagnosis of Lung Cancer CHEST, Volume 143, Issue 5, e142S - e165S
- Naidich DP, Sussman R, Kutcher WL, Aranda CP, Garay SM, Ettenger NA. Solitary pulmonary nodules. CT-bronchoscopic correlation. *Chest*. 1988;93(3):595-598.
- Gaeta M, Pandolfo I, Volta S, et al. Bronchus sign on CT in peripheral carcinoma of the lung: value in predicting results of transbronchial biopsy. *AJR Am J Roentgenol*. 1991;157(6):1181-1185
- Sainz Zuñiga PV, Vakil E, Molina S, Bassett RL Jr, Ost DE. Sensitivity of Radial Endobronchial Ultrasound-Guided Bronchoscopy for Lung Cancer in Patients With Peripheral Pulmonary Lesions: An Updated Meta-analysis. *Chest*. 2020 Apr;157(4):994-1011
- W. De Wever, V. Vandecaveye, S. Lanciotti, J.A. Verschakelen Multidetector CT-generated virtual bronchoscopy: an illustrated review of the potential clinical indications. *European Respiratory Journal* May 2004, 23 (5) 776-782.
- Deng C, Cao X, Wu D, Ding H, You R, Chen Q, Chen L, Zhang X, Zhang Q, Wu Y. Small lung lesions invisible under fluoroscopy are located accurately by three-dimensional localization technique on chest wall surface and performed bronchoscopy procedures to increase diagnostic yields. *BMC Pulm Med*. 2016 Nov 29;16(1):166.
- Liam CK, Mallawathantri S, Fong KM. Is tissue still the issue in detecting molecular alterations in lung cancer? *Respirology* 2020;25:933-943.
- McWilliams A, Tammemagi MC, Mayo JR, Robert H, Liu G, Soghrati K, et al. Probability of cancer in pulmonary nodules detected on first screening CT. *N Engl J Med*. 2013;369:910-9.
- Tokoro Y, Yasuo M, Kobayashi T, Hama M, Ichiyama T, Horiuchi T, et al. Computed tomography-guided bronchoscopy in the diagnosis of small peripheral pulmonary lesions: a retrospective study of 240 examinations in a single academic center. *Respir Investig* 2016;54:347-354.
- Ali MS, Sethi J, Taneja A, Musani A, Maldonado F. Computed tomography bronchus sign and the diagnostic yield of guided bronchoscopy for peripheral pulmonary lesions. A systematic review and meta-analysis. *Ann Am Thorac Soc*. 2018;15:978-87.
- Ost DE, Ernst A, Lei et al. Diagnostic Yield and Complications of Bronchoscopy for

Peripheral Lung Lesions. Results of the AQuIRE Registry. *Am J Respir Crit Care Med*. 2016;193(1):68-77.

- Boonsarngsuk V, Raweelert P, Juthakarn S. Endobronchial ultrasound plus fluoroscopy versus fluoroscopy-guided bronchoscopy: a comparison of diagnostic yields in peripheral pulmonary lesions. *Lung*. 2012;190(2):233-237.
- Lee HW, Ha SY, Roh MS. Non-Small Cell Carcinoma-Not Otherwise Specified on Cytology Specimens in Patients with Solitary Pulmonary Lesion: Primary Lung Cancer or Metastatic Cancer?. *J Cytol*. 2021;38(1):8-13.
- Vidarsdottir H, Tran L, Nodin B, et al. Immunohistochemical profiles in primary lung cancers and epithelial pulmonary metastases. *Hum Pathol*. 2019;84:221-230.