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Diagnostic yield of Virtual Bronchoscopic Navigation (VBN) guided Bronchoalveolar Lavage (BAL) in peripheral pulmonary infections: a prospective pilot study

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Research Article

Keywords: virtual bronchoscopy navigation, VBN, broncho alveolar lavage, BAL, peripheral pulmonary infections

Posted Date: November 3rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11583846/v1

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Additional Declarations: No competing interests reported.

Abstract

Background: Bronchoalveolar lavage (BAL) is a key diagnostic tool in evaluating pulmonary infections and infiltrative lung diseases. However, conventional BAL relies on operator-dependent segment selection, potentially limiting diagnostic yield in peripheral pulmonary lesions. Virtual Bronchoscopic Navigation (VBN) has been shown to improve localization in biopsy procedures but its role in guiding BAL remains unexplored.

Objectives: To evaluate the diagnostic yield of VBN-guided BAL in patients with clinical features of pulmonary infection having peripheral pulmonary lesions on radiology.

Methods: This prospective observational pilot study included 50 adult patients with features of pulmonary infection having peripheral pulmonary lesions on radiology. All patients underwent VBN-guided BAL. Samples were analyzed using microbiological, molecular, and cytological techniques. Diagnostic yield and impact on clinical diagnosis were assessed.

Results: A definitive diagnosis was achieved in 42/50 patients (84%). Diagnostic yield was higher in immunocompromised patients (92.9%) compared to non-immunocompromised patients (80.6%), though not statistically significant (p=0.414). The final diagnosis differed from the initial clinical diagnosis in 62% of cases. Common diagnoses included bacterial pneumonia (36%), tuberculosis (28%), and fungal infections (16%).

Conclusion:VBN-guided BAL demonstrates high diagnostic yield in peripheral pulmonary lesions and may significantly alter clinical management. Larger comparative studies are required to validate these findings.

Introduction

Lower respiratory tract infections remain a major cause of global morbidity and mortality, with the diagnostic burden being especially pronounced in vulnerable populations, where timely and accurate pathogen identification is critical for optimal outcomes. Although non-invasive microbiological sampling, such as induced sputum analysis, is routinely employed as an initial diagnostic approach, it frequently fails to yield definitive or actionable results.

Flexible bronchoscopy with bronchoalveolar lavage (BAL) has therefore been established as a cornerstone diagnostic modality for evaluating pulmonary infections, malignancy, alveolar hemorrhage, and diffuse parenchymal lung diseases such as eosinophilic pneumonia and hypersensitivity pneumonitis. However, the diagnostic yield of BAL is highly dependent on accurate segmental targeting, which is typically guided by operator interpretation of computed tomography (CT) imaging. This reliance introduces variability and may limit diagnostic accuracy, particularly for small or peripherally located lesions.

Virtual bronchoscopic navigation (VBN) is an advanced imaging-based technology that utilizes CT-derived three-dimensional reconstruction to guide bronchoscopic procedures with enhanced spatial precision. Navigational bronchoscopy systems employ dedicated software to identify target lesions and generate a virtual bronchial pathway, enabling more accurate localization of peripheral and otherwise difficult-to-access lung lesions. While VBN has been extensively validated for improving diagnostic yield in bronchoscopic biopsy of peripheral pulmonary nodules, its application in guiding BAL has not been systematically explored. Virtual bronchoscopic navigation (VBN) is an advanced imaging-based technology that utilizes CT-derived three-dimensional reconstruction to guide bronchoscopic procedures with enhanced spatial precision. Navigational bronchoscopy systems employ dedicated software to identify target lesions and generate a virtual bronchial pathway, enabling more accurate localization of peripheral and otherwise difficult-to-access lung lesions. While VBN has been extensively validated for improving diagnostic yield in bronchoscopic biopsy of peripheral pulmonary nodules, its application in guiding BAL has not been systematically explored.

Given that BAL involves fluid instillation and retrieval rather than direct tissue sampling, the potential role of VBN in optimizing segmental targeting represents a novel and under-investigated area. We therefore conducted a prospective observational study to evaluate the diagnostic yield of VBN-guided BAL in patients undergoing bronchoscopic evaluation for suspected pulmonary infections and to assess its impact on clinical decision-making.

Materials and methods

This prospective study was designed to assess the diagnostic yield of bronchoalveolar lavage (BAL) performed under virtual bronchoscopic navigation (VBN) guidance in patients with clinical and radiological features suggestive of peripheral pulmonary infection. The study was prospectively registered with the Clinical Trials Registry–India (CTRI) (Registration No: CTRI/2023/08/056256). The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Armed Forces Medical College (Approval No: IEC/2023/255). Written informed consent was obtained from all participants prior to enrollment. Patients were prospectively enrolled based on the following predefined inclusion and exclusion criteria.

Inclusion Criteria

- Age ≥18 years
- Presence of symptoms suggestive of pulmonary infection (e.g., fever, cough)
- Peripheral pulmonary lesion defined as a lesion located in the outer half of the lung field on axial computed tomography (CT) imaging, confined to a single segment and measuring <2 cm in size (including consolidation, nodules, ground-glass opacities, or cavitary lesions)
- Provision of informed consent

Exclusion Criteria

- Extensive pulmonary involvement on chest imaging
- Central pulmonary lesions (defined as those occupying the medial half of the lung field on axial CT imaging)
- SpO2 of < 90% on room air
- Hemodynamic instability, uncontrolled arrthymias
- Refusal or inability to provide informed consent

Eligible patients underwent a high-resolution CT (HRCT) chest scan compatible with the LungPoint system. CT images were uploaded into the navigation software, which reconstructed a virtual bronchial tree and identified the target lesion along with the optimal bronchial pathway. All bronchoscopic procedures were performed by a single experienced respiratory physician to ensure procedural consistency and minimize inter-operator variability. BAL was conducted by advancing the bronchoscope to the target segment as determined by VBN guidance, followed by instillation and retrieval of sterile saline as per standard protocol. A diagnosis was considered “definite” if after treatment for the etiology as diagnosed using VBN-guided BAL, the patient showed clinical resolution of symptoms and repeat CT chest done during follow up showed resolution.

Clinical, radiological, and microbiological data were prospectively collected for all enrolled patients. Descriptive statistical methods were used to analyze the data and evaluate the diagnostic yield of VBN-guided BAL.

Results and analysis

A total of 50 patients were included in the study. The cohort was male-predominant, consisting of 31 males (62%) and 19 females (38%). The age distribution was broad, with a mean age of 43.42 years (SD - 18.66 years), reflecting a heterogeneous adult population.

Radiological characteristics

Analysis of the CT scans (Figure 1) revealed that the targeted pulmonary lesions were most frequently located in the upper lobes, specifically the left upper lobe (n = 17, 34%), followed by the right lower lobe (n = 13, 26%), right upper lobe (n = 12, 24), left lower lobe (n = 5, 10%), and right middle lobe (n = 3,6%). The predominant radiological patterns observed (Figure 2) included nodules (n = 29, 58%), consolidation (n = 11, 22%), cavitary lesions (n = 9, 18%), and ground-glass opacities (n = 8, 16%).

Microbiological, molecular finding and diagnostic yield

BAL fluid was sent for microbiological, molecular and cytological analysis. BAL for gram stain and culture was positive in 6 patients (12%), Ziehl-Nelsen (ZN) stain was positive in 5 patients (10%), MTB GeneXpert was positive in 14 patients (28%), BAL galactomannan was raised in 8 patients (16%), BAL for BioFire respiratory panel ® was diagnostic in 18 patients (36%).

A definitive diagnosis was achieved in 41 patients, corresponding to an overall diagnostic yield of 82% for VBN guided BAL in patients with peripheral pulmonary infections. The definitive diagnosis (Figure 3) included bacterial pneumonia (n=18, 36%), pulmonary tuberculosis (n=14, 28%), fungal pneumonia (n=8, 16%) and viral pneumonia (n=1, 2%). Representative CT images are provided in Figure 4.

Among the 50 patients, 14 were immunocompromised. A definitive diagnosis was established in 13 of these patients, demonstrating a diagnostic yield of 92.9% for VBN guided BAL in immunocompromised patients with peripheral pulmonary infections.

Stratification based on baseline chest X-ray findings demonstrated a diagnostic yield of 93.8% (15 out of 16 patients) in patients with abnormal chest radiographs, compared to 79.4% (27 out of 34 patients) in those with normal chest radiographs but abnormal CT findings. Although this difference did not reach statistical significance (Fisher's exact test, $p = 0.409$), the high yields across both groups suggest that VBN-guided BAL may be effective irrespective of initial radiographic presentation.

Impact on clinical decision making

A key finding of this study was the discrepancy between provisional clinical diagnoses and final diagnoses established through VBN-guided BAL. Concordance between the initial provisional diagnosis and final diagnosis was observed in only 19 of 50 patients (38%). In contrast, the diagnosis was revised in 31 patients (62%) following VBN-guided BAL. This finding underscores the limitations of relying solely on clinical assessment, imaging, and non-invasive testing. VBN-guided BAL facilitated more accurate etiological diagnosis, enabling a shift from empirical to targeted therapy in a substantial proportion of patients.

Discussion

The evaluation of peripheral pulmonary lesions (PPLs) and complex pulmonary infiltrates continues to pose a diagnostic challenge in respiratory medicine. While percutaneous biopsy offers high diagnostic accuracy, it is associated with procedure-related risks, including pneumothorax and hemorrhage (4). In contrast, conventional flexible bronchoscopy is safer but has limited ability to access distal airways, resulting in lower diagnostic yields for peripheral lesions (5). The sampling techniques employed in flexible bronchoscopy includes bronchioalveolar lavage (BAL), forceps biopsy, brush biopsy and cryobiopsy. While biopsy techniques are extensively used for evaluation of malignant and infiltrative lung diseases, the evaluation of suspected infective lesions in peripheral lung can mostly be done with BAL.

BAL is a minimally invasive and targeted sampling technique that enables evaluation of the physiological and pathophysiological milieu of the lower respiratory tract. Compared with sputum analysis, BAL provides higher-quality samples from the alveolar space with reduced contamination from the upper airway (2). The retrieved fluid can be subjected to a wide range of investigations including cytological analysis, microbiological cultures, acid-fast bacilli (AFB) staining and molecular diagnostic tests like polymerase chain reaction (PCR). Furthermore, whole-genome sequencing and real-time metagenomic

sequencing of BAL fluid are now increasingly being deployed to diagnose viral, bacterial, and fungal pneumonias in critically ill patients (3).

BAL for evaluation of peripheral pulmonary infiltrates was mostly a blind procedure with the conventional flexible bronchoscope having a visualization of upto fourth to sixth airway generation, until the introduction of virtual bronchoscopic navigation (VBN). VBN utilizes pre-procedural computed tomography (CT) data to generate a three-dimensional reconstruction of the bronchial tree, enabling accurate navigation to target lesions (6)(7). VBN has been demonstrated to be superior to non-navigational bronchoscopy in the assessment of peripheral pulmonary lesions measuring 20 mm or less in diameter and has been shown to significantly shorten the total examination time, improving patient tolerance and overall procedural efficiency (4). Though VBN has been extensively studied for evaluation of peripheral pulmonary malignant lesions its role in improving the diagnostic yield of BAL for suspected peripheral pulmonary infections is largely unexplored.

The diagnostic yield of conventional (unguided) BAL is variable and depends on disease type and patient population, with reported yields ranging from approximately 31% to 83% (1). In specific conditions such as sputum-negative pulmonary tuberculosis, the yield may be substantially lower (32 to 38%), whereas higher yields (84.6%) have been reported in sputum positive pulmonary tuberculosis. (10)(11)

The importance of BAL is particularly pronounced in immunocompromised patients, where pulmonary infections are often paucibacillary, severe, rapidly progressive, and caused by a broad spectrum of pathogens. In such populations, early and accurate diagnosis is critical, as empirical therapy may be inadequate or inappropriate. In a prospective longitudinal study of 2,666 immunocompromised cases, conventional BAL led to a direct change in medical management in 52.36% of all cases, highlighting its pivotal role in clinical decision-making (13). Similarly, in non-HIV immunocompromised adults presenting with pulmonary infiltrates, conventional unguided BAL achieved an overall diagnostic yield of 52.4% and altered the management plan in 43.7% of patients (1).

Despite the established efficacy of BAL, its success inherently relies on the operator's ability to blindly wedge the bronchoscope into the correct lung segment based on mental reconstructions of two-dimensional CT scans, a navigational limitation that frequently leads to sampling healthy tissue and missing the pathological microenvironment entirely (5,7). In this context, our study demonstrates that integrating VBN guidance with BAL may enhance diagnostic performance. We observed a high overall diagnostic yield (80.6%), with particularly notable results in immunocompromised patients (92.9%). While direct comparisons with historical studies should be interpreted with caution due to differences in study design and patient populations, the findings suggest that improved segmental targeting may contribute to higher diagnostic accuracy.

An additional important observation was the discrepancy between provisional clinical diagnoses and final diagnoses established through VBN-guided BAL. The relatively low concordance rate highlights the limitations of relying solely on clinical assessment, imaging, and non-invasive testing. The use of VBN-

guided BAL facilitated more precise etiological diagnosis and supported more targeted therapeutic decision-making.

In summary, while conventional BAL remains an essential diagnostic tool in respiratory medicine, its effectiveness is constrained by limitations in segmental targeting. The integration of VBN into BAL procedures represents a promising advancement that may enhance diagnostic yield and improve clinical decision-making, particularly in patients with peripheral pulmonary lesions and in immunocompromised populations. These findings should be interpreted in light of certain limitations. This was a single-center study with a relatively small sample size, which may limit generalizability. The absence of a direct comparator arm using conventional unguided BAL precludes definitive conclusions regarding superiority. Larger, controlled studies are warranted to validate these findings and to define the precise role of VBN-guided BAL in routine clinical practice.

Declarations

Consent and institutional ethical clearance

The study was prospectively registered with the Clinical Trials Registry–India (CTRI) (Registration No: CTRI/2023/08/056256). The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Armed Forces Medical College (Approval No: IEC/2023/255. Written informed consent was obtained from all participants prior to enrollment.

Ethics approval and patient consent to participate

Consent was taken from all the patients in the study for the procedure and publication of data. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Armed Forces Medical College (Approval No: IEC/2023/255)

Patient Consent for publication - Consent was taken from all the patients for publication of data

Animal Studies: not applicable

Author contributions : S.C, R.T, P.G, S.V, M.C have made substantial contribution in conceptualization of the manuscript, analysis of data, drafting of manuscript, critical review and final approval of the version to be published. R.C, M.A and G.B were involved in data analysis. All authors agree to be accountable for all the aspects of the work

Acknowledgments: The authors would like to acknowledge the work done by all residents, nurses and technicians involved in management of the patients.

Conflict of interest: The authors have no conflict of interest to declare.

Sources of funding: There were no funds/grants received for this study. The authors have not received any financial or non-financial benefits for this case. There is no personal relationship with any organisation or person of interest by any of the authors.

Availability of data and materials: all data and materials are available with the corresponding author and can be shared on request.

Clinical trial registry number: The study was prospectively registered with the Clinical Trials Registry–India (CTRI) (Registration No: CTRI/2023/08/056256).

PROSPERO registry number: not applicable

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Figures

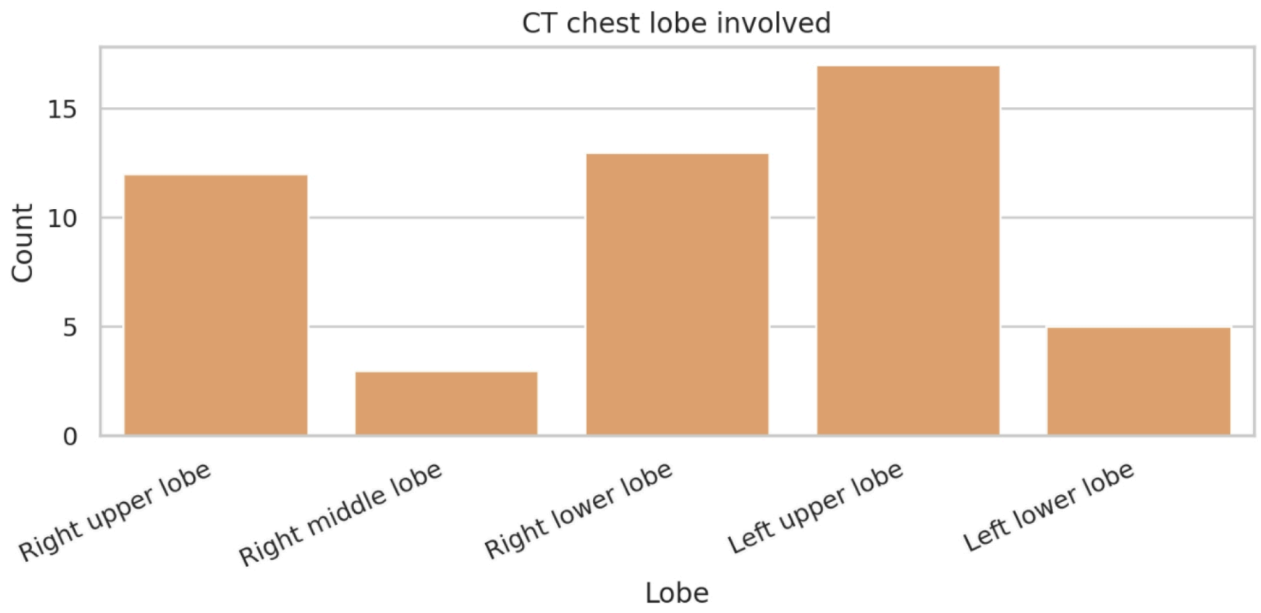


Figure 1

Radiological location of peripheral pulmonary lesion on high resolution computed tomography of chest

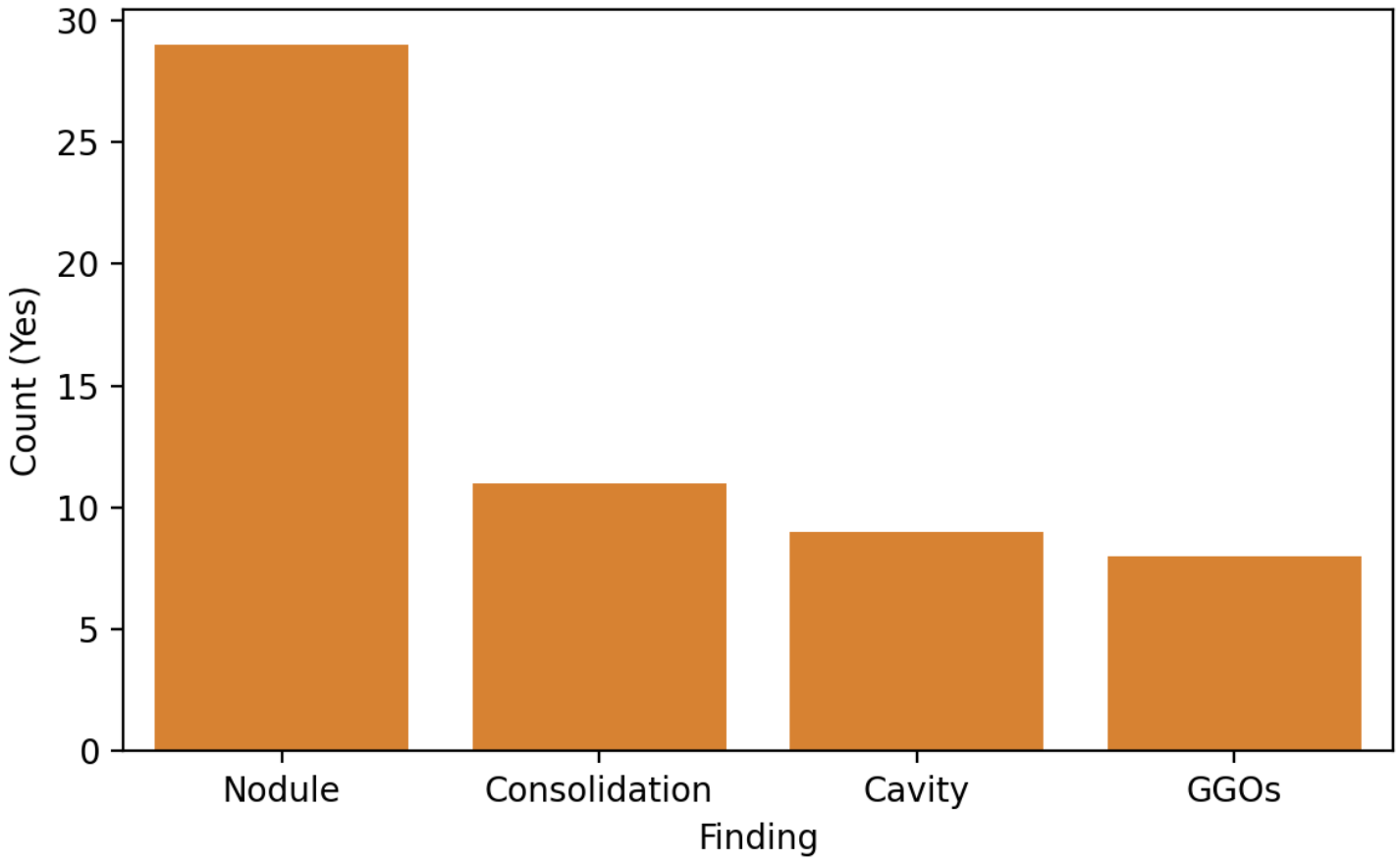


Figure 2

Peripheral pulmonary lesions on high resolution computed tomography of chest.

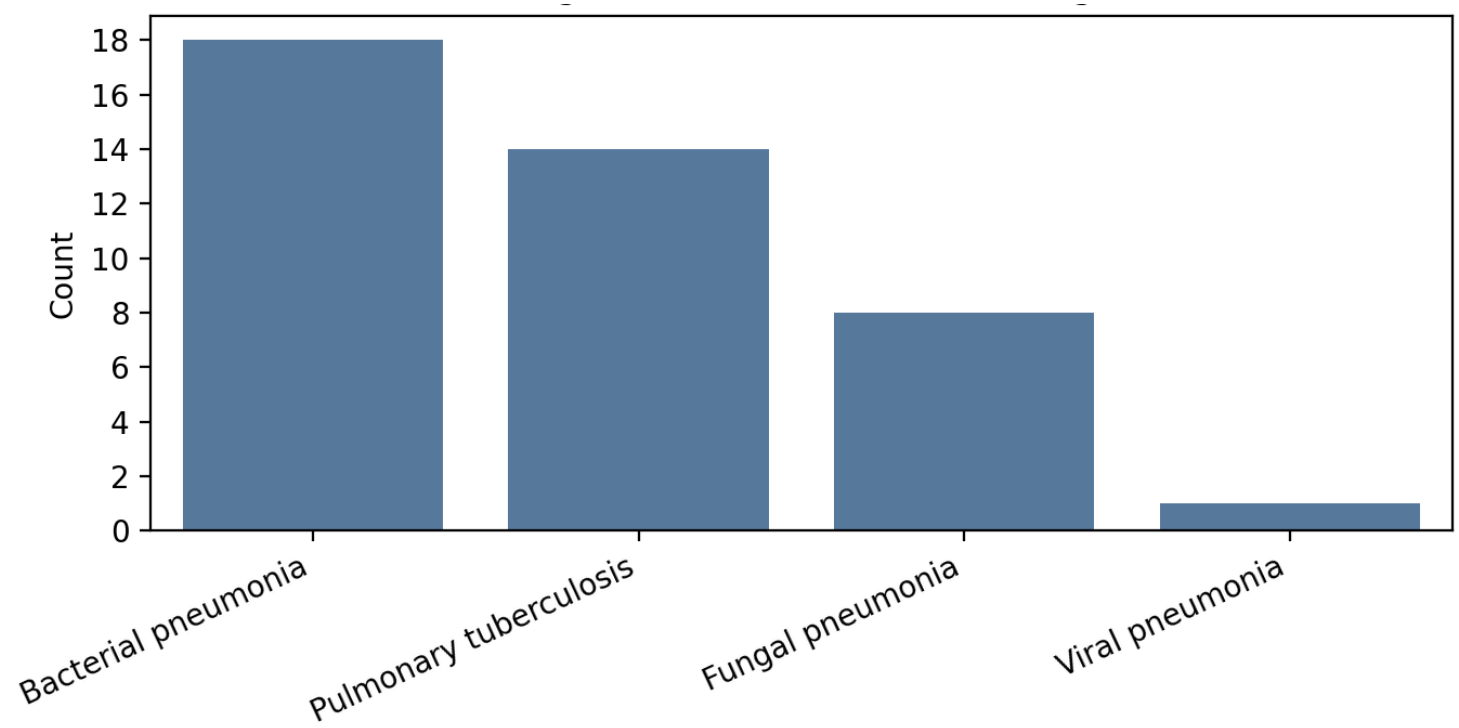


Figure 3

Definitive diagnosis of patients with peripheral pulmonary infection post VBN guided BAL.

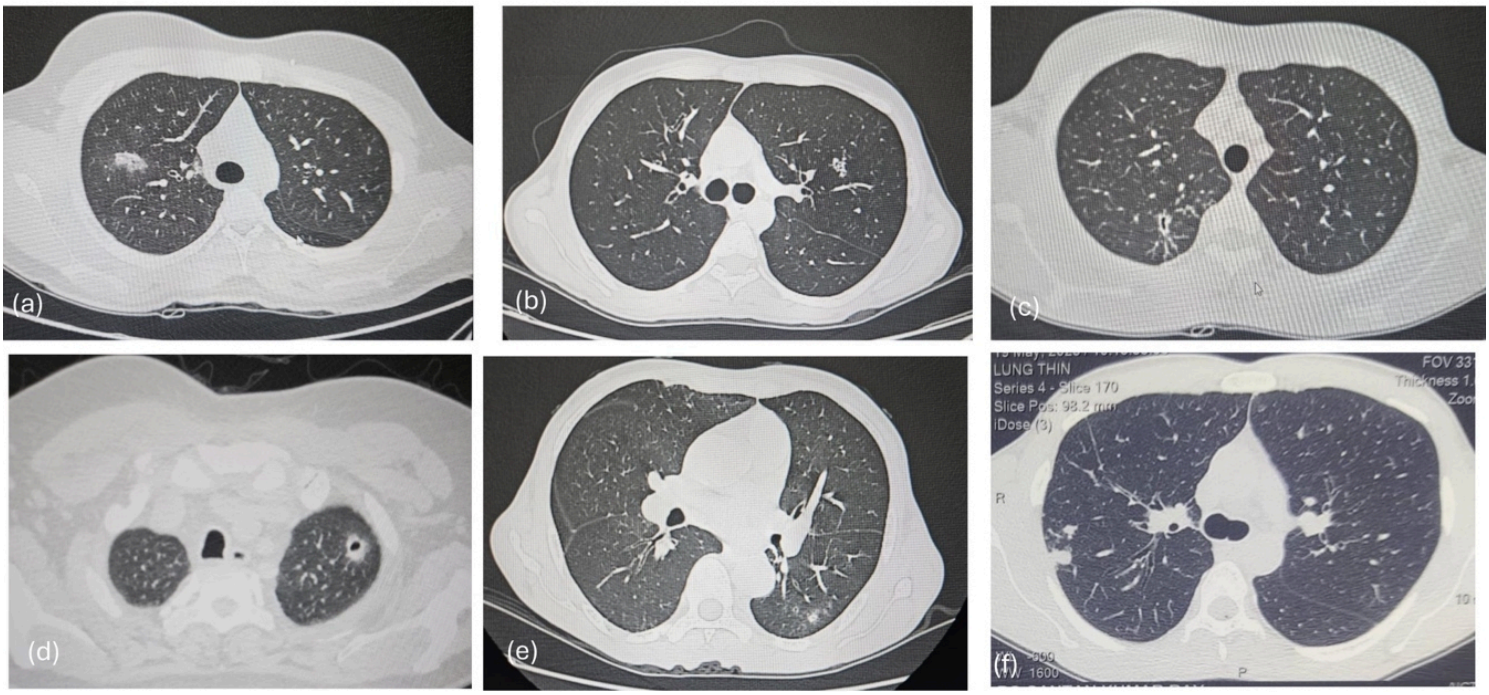


Figure 4

Computed Tomography images of patients in study **4(a)** Consolidation apical segment right upper lobe (RUL) diagnosed as Klebsiella pneumonia **4(b)** Consolidation in apico-posterior segment left upper Lobe (LUL) diagnosed as Hemophilus influenzae. **4(c)(d)** Cavitating nodules in immunocompromised patients involving posterior segment RUL and anterior segment LUL diagnosed as fungal pneumonia. **4(e)(f)** Nodular lesion in superior segment of LLL and posterior segment of RUL diagnosed as pulmonary tuberculosis