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Diagnostic yield of rapid on-site cytology evaluation on fluoroscopic-guided transbronchial biopsy in a private hospital in Jakarta: a one-year retrospective study

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Abstract

Rapid on-site cytology examination (ROSE) with a fluoroscopic-guided transbronchial biopsy (TBLB) involves the immediate evaluation of cytological specimens during a diagnostic procedure. This research aims to investigate the potential yield of this diagnostic technique, shedding light on its benefits, limitations, and the evidence supporting its efficacy. A retrospective analysis of the data was conducted on 26 patients who underwent ROSE and TBLB procedures in the hospital between July 2022 and August 2023. A total of 21 patients met the requirements for the inclusion criteria: patients with peripheral pulmonary lesions found by chest X-rays or chest computed tomography scans consented to have a bronchoscopy with both ROSE and TBLB examination. A total of 5 patients were excluded because of the exclusion criteria: patients who only took either ROSE or TBLB examination and were noncompliance with bronchoscopy. The statistical software SPSS 29.0 was used for the analyses. The chi-square test was employed to evaluate differences between two groups of categorical variables and was considered significant when the p-value was under 0.05. ROSE evaluated 21 lesions and followed up with the final pathological biopsy. Malignant tumors were identified in 12 cases by ROSE and TBLB procedures. One case was benign by the biopsy results but was malignant by ROSE examination. Similarly, 8 cases were benign, as determined by ROSE examination and TBLB. Between ROSE and TBLB, there was a statistical difference with $p<0.001$. The sensitivity is 100%, and the specificity is 11.1%. However, high sensitivity was proven by ROSE compared to biopsy, which is the gold standard in this study. No significant complications were observed after the procedure. According to this study, ROSE has a high diagnostic value with high sensitivity values for real-time diagnosis but still has not been able to replace the biopsy function as the gold standard. ROSE should only be considered for screening and sample adequacy in the bronchoscopy suite.

Key words: rapid on-site examination, transbronchial lung biopsy, cytology evaluation, lung tumor, peripheral pulmonary lesions.

Introduction

Bronchoscopy is a vital medical procedure used to diagnose various respiratory conditions, particularly peripheral pulmonary lesions (PPLs) [1,2]. Pulmonary lesions are classified as nodules if it has a diameter less than 3 cm and as lung mass if greater than 3 cm [3]. According to earlier research, Transbronchial Biopsy (TBLB) has a diagnosis accuracy of more than 80% for peripheral pulmonary lesions [4-6].

However, advancements in technology have revolutionized the diagnostic process by implementing rapid on-site examination (ROSE) and TBLB. By using a bronchoscopy, doctors can get a close-up look at the airways and collect samples for further analysis from suspicious areas. This non-surgical approach provides valuable diagnostic data, reduces patient discomfort, and lowers the chance of consequences [7].

The percentage of biopsy data that supported a benign or malignant diagnosis was known as the ROSE and TBLB diagnostic yield. Nowadays, biopsy of the tissues has been regarded as the gold standard for diagnosing cancer [8,9]. TBLB is a minimally invasive diagnostic method used to collect lung tissue samples for histopathological and cytological examinations [10,11]. Traditionally, TBLB samples are collected without immediate evaluation, leading to inherent delays in diagnosis.

A real-time imaging method called fluoroscopy improves TBLB even more by directing the process and raising sample collection accuracy overall [2,7] Integrating fluoroscopy into the TBLB process also has many benefits [4]. First, it allows real-time visualization of the bronchial tree, reducing the chance of sampling errors and allowing for precise lesion targeting [11].

Fluoroscopy also assists in identifying potential problems during the procedure, like pneumothorax, and provides timely support when needed. Furthermore, by making it possible to sample smaller peripheral lesions that might not be apparent with bronchoscopic guidance alone, fluoroscopic guiding can increase the yield of TBLB [4,12].

Recent studies have demonstrated the potential of ROSE, a method that allows a pathologist to assess bronchoscopic specimens in real time. Because of this instant input, the bronchoscopist may maximize the diagnostic output and guarantee sample adequacy [13,14]. ROSE, allows us to get quick feedback on the quality and sufficiency of the biopsy samples [10,11].

ROSE can potentially improve diagnostic process efficiency and accuracy by rapidly assessing if the collected sample is adequate for appropriate analysis [1,15].

This research aims to explore the diagnostic yield of ROSE on the fluoroscopic-guided transbronchial biopsy, shedding light on its benefits, limitations, and the evidence supporting its efficacy.

Materials and Methods

Patient selection and eligibility criteria

Patients who were diagnosed with PPLs between July 2022 – August 2023, who got combined fluoroscopy-guided TBLB and ROSE testing.

This study is a retrospective study, we retrospectively reviewed the medical records.

Inclusion criteria were as follows: cases with PPLs discovered by chest X-rays or chest CT scan, those who are not contraindicated for general anaesthesia and bronchoscopy, and consent to do a bronchoscopy with ROSE and TBLB evaluation.

Exclusion criteria were as follows: patients who only took either ROSE or TBLB examination, had bleeding tendencies and were noncompliant with bronchoscopy. The primary objective of this retrospective study is to compare the diagnostic yield of peripheral pulmonary lesions between transbronchial lung biopsy (TBLB) and rapid on- site examination (ROSE) on the same sample.

TBLB procedure

Every patient had fasted for six hours before doing the procedure. Propofol and fentanyl were used to induce conscious sedation during the surgeries.

Three different pulmonologists with specialized training conducted bronchoscopy using a flexible bronchoscope to examine the tracheobronchial tree for intraluminal pathology.

When bronchoscopy successfully localized the target lesion in all patients with PPLs, we collected data from those patients. Fluoroscopy allows real-time visualization of the bronchial tree, enabling precise targeting of lesions and reducing the risk of sampling errors.

By fluoroscopic guidance, we can enhance the yield of TBLB by enabling the sampling of smaller peripheral lesions that might not be visible under bronchoscopic guidance alone.

Rapid on-site cytology evaluation of specimens

We perform the ROSE procedure on patients who have undergone TBLB. The sample was quickly and uniformly spread across numbered glass slides.

ROSE immediately evaluated one specimen while the other was sent to the main laboratory for biopsy. The ROSE sample was fixed, stained in Diff-Quick A solution, and examined under the microscope to determine a preliminary diagnosis based on cytology.

A cytopathologist screened the stain and regularly reported the results. Based on the pathologist's information, the bronchoscopist changed location or stopped the sample procedure. If the sample proved to have no diagnostic value, the bronchoscopist collected a new sample at the original location or different site, with appropriate additional

modalities (brush, biopsy forceps, and bronchial wash).

Evaluation of TBLB and final diagnosis

The other slide was delivered to the main laboratory for biopsy examination. Based on the histological and cytological studies, all results from the ROSE and biopsy were categorized into three groups: i) malignant or potentially malignant (the samples had cancerous cells or signs that might be malignant); ii) benign (the results revealed benign tumours, a special infection, or a non-neoplastic condition such as chronic inflammation, fibrosis, necrosis or inflammation); iii) not diagnostic (the specimens contained only blood, histiocytes, lung parenchyma, and respiratory epithelial cells). The final diagnosis was made based on clinical symptoms, imaging results, ROSE and histopathologic analysis, expert judgment, and therapy impact observation. After the procedure was finished, we did the fluoroscopy to identify potential complications during the procedure, such as pneumothorax, providing immediate intervention if necessary.

Statistical analysis

The statistical analyses were conducted utilizing IBM Corp.'s SPSS 29.0 software. Chi-square was used to compare the differences between two groups of categorical variables. P-values under 0.05 are indicated statistical significance differences.

Results

Clinical characteristics

During this study period, 26 patients had fluoroscopy-guided TBLB to diagnose PPLs discovered by chest X-rays or a chest CT scan (Figure 1). This study included 21 patients, and 5 participants who only received a biopsy or ROSE were eliminated. The clinical characteristics of patients are mentioned in Table 1. Thirteen patients were diagnosed with malignant tumours, which is adenocarcinoma (61.9%), and 2 patients with metastatic tumours (9.5%). (Figure 2) The other final diagnosis was benign diseases, which are tuberculosis (14.3%) and pneumonia (14.3%). 14 patients feel no complications after the procedure (66.7%). The other complications after the bronchoscopy procedure were mild hemoptysis (14.3%), bleeding (4.8), cough (4.8%), and sore throat (9.5%). Eight patients received chemotherapy, and three patients who had a final tuberculosis diagnosis were given antituberculosis medication. Two patients were already receiving palliative care, two patients had passed away, and five patients had received antibiotics. One patient was referred to a different hospital (Figure 3).

The association of ROSE with pathological results of biopsy

ROSE assessed 21 lesions in total, and the final pathological biopsy was performed for further investigation. 12 cases had both ROSE and biopsy results showing malignant tumours. One case was benign by the biopsy result but was malignant by ROSE examination. Furthermore, 8 cases were benign by ROSE examination and the biopsy.

Between ROSE and biopsy, a statistically significant difference was observed (p-value <0.001) (Table 2). The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of ROSE were 100%, 11.1%, 92.3%, and 100%. The likelihood ratio analysis shows that the positive test result increases the patient's probability of having an illness by about 1.1 times. However, high sensitivity proven by ROSE compared to biopsy as the gold standard was found in this study (100%) (Table 3).

Discussion

PPLs are diagnosed using various methods, including biopsy and rapid on-site examination (ROSE) [1]. According to this study, ROSE has a high diagnostic value with high sensitivity values for real-time diagnosis. Thus, ROSE should only be considered for screening and sample adequacy in the bronchoscopy. This study shows a statistically significant difference between ROSE and biopsy (p-value <0.001). In an earlier study, diagnostic sensitivity and specificity of TBLB were 59.57%, 100% [6].

We usually perform the ROSE procedure on patients undergoing TBLB examination. ROSE involves the immediate evaluation of specimens obtained during a biopsy procedure, such as transbronchial brushings or needle aspirations [16,17]. The method helps diagnose by providing real-time results on the sample's sufficiency and quality [18]. ROSE can shorten the duration of bronchoscopy, and the number of biopsies, and minimize complications. It can also provide a safe and feasible method for diagnosing PPL [11]. ROSE can also detect other specific infections, such as mycobacterium tuberculosis [1,18]. Mycobacterium tuberculosis was discovered in three patients by cytology investigation, allowing for early diagnosis and treatment beginning. One of three techniques was used to verify tuberculosis: positive culture of Mycobacterium tuberculosis on a respiratory specimen, acid-fast bacilli staining, or PCR [18].

However, there are some limitations on ROSE's use in PPL diagnosis. Pathologists must be on-site at all times to conduct assessments, which may not be feasible in all medical settings. This is one potential drawback. Interobserver variability may therefore impact the accuracy of the immediate evaluation, resulting in false-positive or false-negative results. We acknowledge a single discrepancy: a lesion that was first identified as benign on ROSE turned out to be malignant on histology. This case highlights a known

limitation of ROSE, which, although an excellent tool for rapid evaluation, may not always accurately distinguish between benign and malignant lesions in certain circumstances. This misinterpretation could be caused by cytologic atypia, poor sample quality, or the presence of benign tissue components inside a malignant lesion.

However, our strong PPV and NPV values demonstrate ROSE's overall diagnostic efficacy, which supports its continued usage as a useful bronchoscopy adjunct that helps doctors make decisions during the operation. Assessing tumour features, evaluating malignancy, and making a precise diagnosis are all benefits of a biopsy in PPL. By directly examining tissue samples, biopsy offers a conclusive diagnosis of PPLs [4,19]. It can assist in determining if a lesion is benign or malignant, directing subsequent therapy choices. Biopsies also make it possible to assess several tumour features, including histology, molecular markers, and genetic alterations, which can aid in developing new treatment plans [19]. Nevertheless, there are restrictions on using the biopsy in PPL. Because tissue samples from some biopsy procedures, including TBLB, are so small, they may produce crushed artefacts. ROSE has usually been used during bronchoscopy procedures in the context of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). While ROSE provides immediate feedback on sample adequacy, its effect on enhancing diagnostic accuracy remains a topic of debate. Multiple studies have found no discernible increase in diagnostic yield with ROSE during EBUS-TBNA, indicating that its main benefit is not an improvement in overall diagnostic accuracy but rather a reduction in process duration and the requirement for further passes [20-22]. This study emphasizes the possible function of ROSE in TBLB, where sample adequacy may be challenging because of the tiny and peripheral character of lesions.

There are several restrictions on this study. First, only a single center was involved in this retrospective study. Second, the sample of this study was still insufficient. ROSE is probably cost-effective, given the shorter duration and the small but considerable number of cases. However, to verify that ROSE can improve procedure diagnostic yield, a randomized multi-center study would be ideal. Bronchoscopists can give patients a prompt and accurate diagnosis that leads to the right course of treatment by providing real-time examination and precise targeting of lesions. Another study limitation is the lack of a “control group”. The inclusion of a control group could indeed have provide additional comparative data, particularly regarding procedure duration and the number of samples required. In our retrospective design, the primary focus was to evaluate the diagnostic yield of ROSE in a real-world setting where its use has become standard practice in our institution. Consequently, a control group without ROSE was not available for direct comparison.

Conclusions

In summary, ROSE's diagnostic yield on transbronchial biopsy guided by fluoroscopic imaging indicates that it has the potential to completely transform respiratory medicine. ROSE makes TBLB processes more efficient. In the bronchoscopy suite, ROSE should only be considered for screening and sample adequacy. Despite several drawbacks, this method is becoming more useful for identifying pulmonary abnormalities due to continuous study and developments in the field.

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Table 1. Clinical characteristics of the patients.

Characteristic	Value
Patients (number)	21
Sex	
Male	11 (52.4%)
Female	10 (47.6%)
Age (years)	61±2.77 (58.23-63.77)
Chief complaints	
Chronic cough	6 (28.6%)
Hemoptoe	2 (9.5%)
Dyspnea	3 (14.3%)
No complaint	10 (47.6%)
Location of lesions	
Right lung	12 (57.1%)
Left lung	7 (33.3%)
Both side of the lung	2 (9.5%)
Size of lesions	
3 cm	14 (66.7%)
3 cm	7 (33.3%)
Final Diagnosis	
Malignant tumor	
Adenocarcinoma	13 (61.9%)
Squamous cell carcinoma	0 (0%)
Small cell lung cancer	0 (0%)
Metastatic tumor	2 (9.5%)
Benign disease	
Tuberculosis	3 (14.3%)
Pneumonia	3 (14.3%)
Complication after procedure	
No complication	14 (66.7%)
Hemoptysis	3 (14.3%)
Mild bleeding (<5 mL)	1 (4.8%)
Cough	1 (4.8%)
Sore in throat	2 (9.5%)

Table 2. Comparison of ROSE results with the final pathologic diagnosis by biopsy.

	Biopsy			
ROSE	Malignant	Benign	Total	p-value
Malignant	12	1	13	<0.001*
Benign	0	8	8	
Total	12	9	21	
*Chi-square test				

Table 3. Sensitivity, negative predictive value (NPV), positive predictive value (PPV), specificity and likelihood ratio of ROSE.

Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Likelihood ratio
100	11.1	92.3	100	1.1

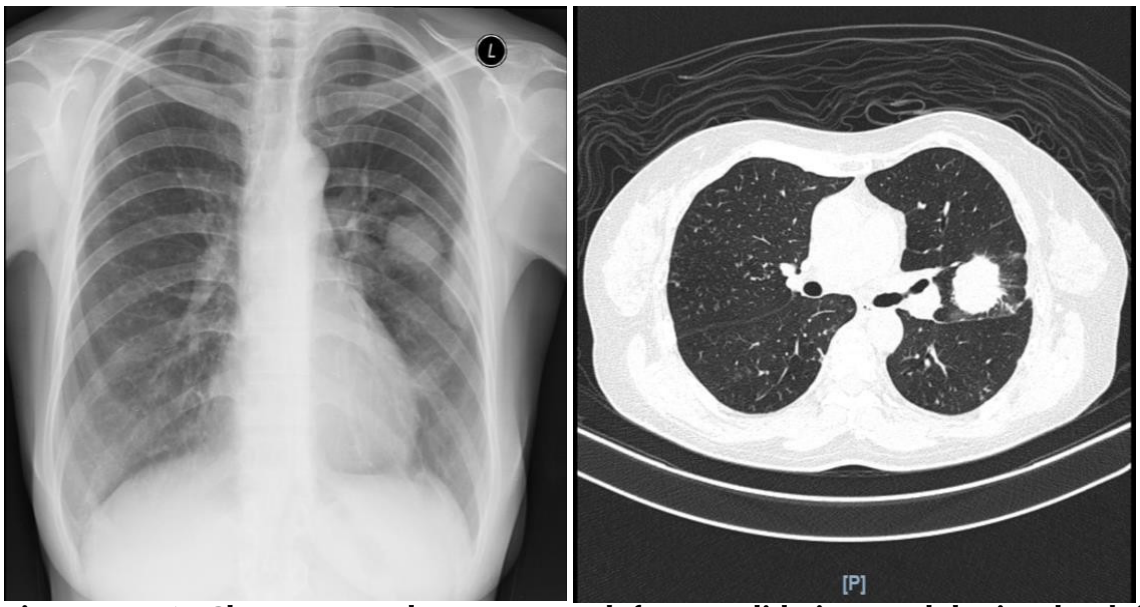

Figure 1. a) Chest X-ray demonstrates left consolidation nodule in the left lung; b) contrast-enhanced CT scan of the thorax (axial view) that shows a nodular mass measuring 3cm x AP 3.5cm x ML 3.2cm with irregular edges in the central superior lobe of the left lung was suspicious for neoplasm.

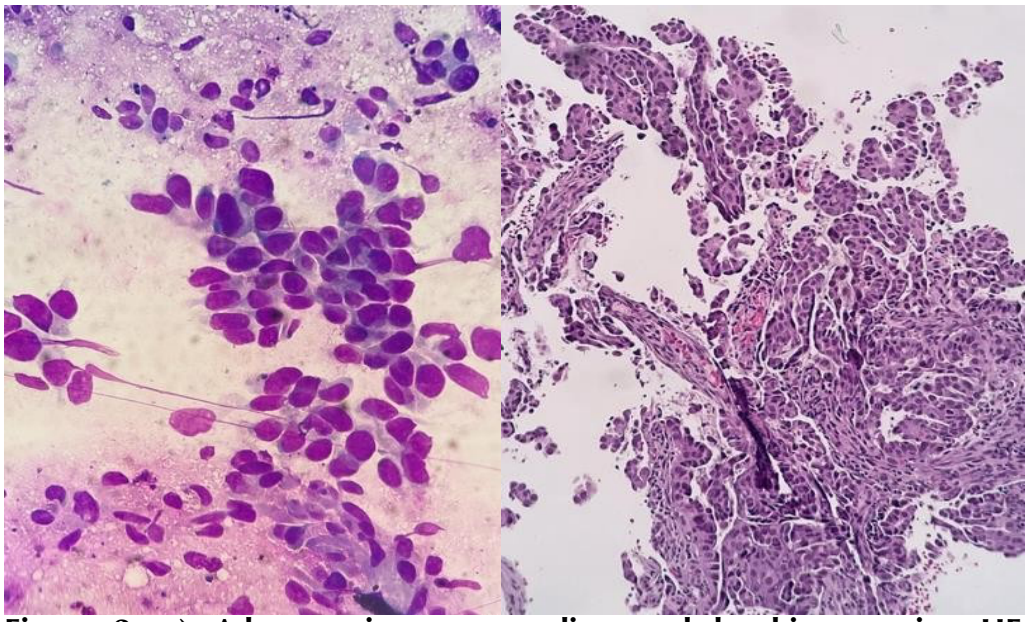

Figure 2. a) Adenocarcinoma was diagnosed by biopsy using HE staining (original magnification, 100x); b) Non-small-cell lung cancer favor adenocarcinoma was diagnosed by ROSE (Diff-Quick staining, original magnification, 400x).

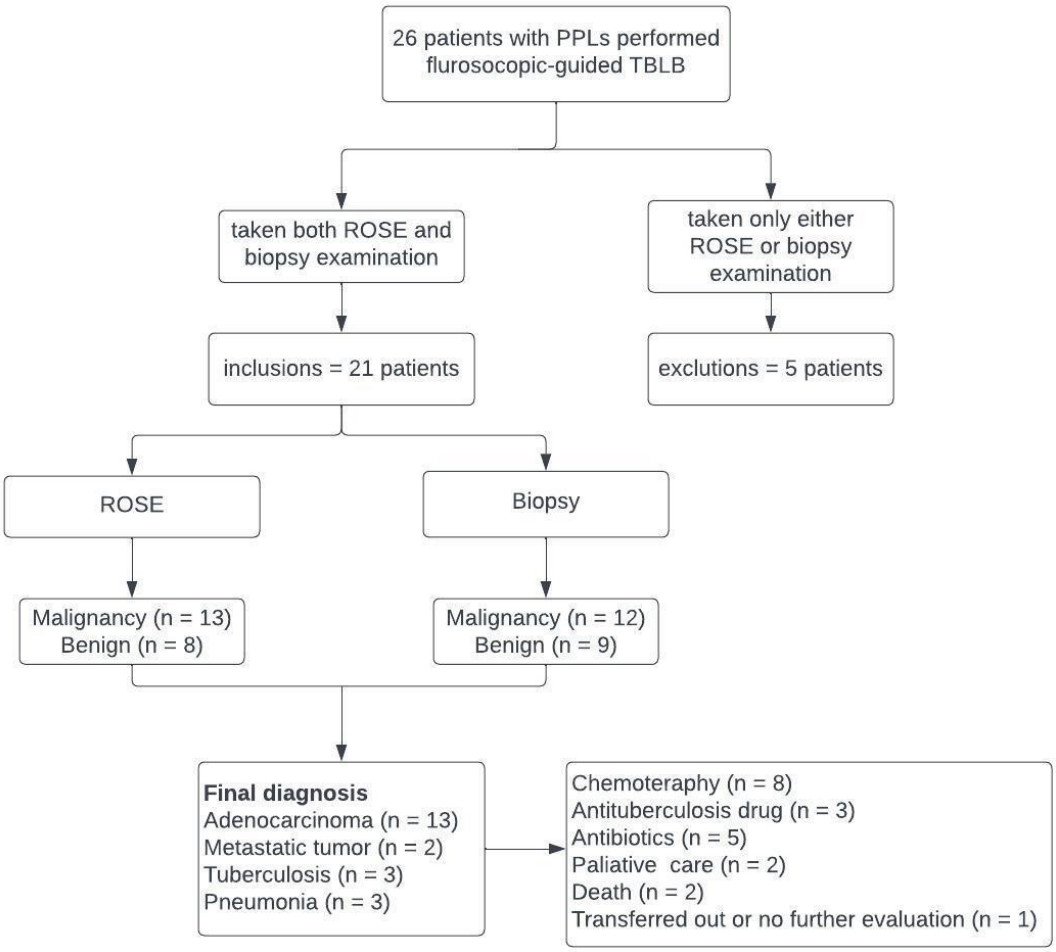

Figure 3. The diagnostic process, final diagnosis, and treatment planning.