


Transbronchial lung cryobiopsy under real-time radial EBUS: First report on a novel twist of the classical technique

Nektarios Anagnostopoulos¹ | Simone Petrarulo²  | Claudia Ravaglia^{2,3} |
Alessandra Dubini⁴ | Sara Piciocchi⁵ | Grigoris Stratakos¹ | Venerino Poletti^{2,3,6}

¹Interventional Pulmonology Unit of the 1st Respiratory Medicine Department National and Kapodistrian, University of Athens, "Sotiria" Hospital, Athens, Greece

²Department of Medical Specialities, Pulmonology Unit, GB Morgagni—L. Pierantoni Hospital, Forlì, Italy

³Department of Medical and Surgical Sciences (DIMEC), University of Bologna/Forlì Campus, Forlì, Italy

⁴Department of Pathology, GB Morgagni—L. Pierantoni Hospital, Forlì, Italy

⁵Department of Radiology, GB Morgagni—L. Pierantoni Hospital, Forlì, Italy

⁶Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Aarhus, Denmark

Correspondence

Venerino Poletti, Department of Medical Specialities, Pulmonology Unit, GB Morgagni – L. Pierantoni Hospital, Via Carlo Forlanini, 34, 47121 Forlì FC, Italy.
Email: venerino.poletti@gmail.com

Associate Editor: Johnny Chan

Abstract

Transbronchial lung cryobiopsy (TBLC) is a relatively new technique for obtaining lung biopsies, known for being the least invasive method while offering a high diagnostic yield, a favourable safety profile, and a significant reduction in morbidity, mortality, and hospital stay length compared to surgical lung biopsy. Radial-EBUS (r-EBUS) represent a cornerstone modality for accessing 'invisible' peripheral pulmonary lesions. However, a major drawback of these techniques is the lack of 'real-time' visualization of the biopsy being obtained. In this case report, we present a young woman who was referred to us with a cough, haemoptysis, and a non-resolving lung consolidation. She underwent TBLC under real-time rEBUS guidance. This clinical case demonstrates that, in specific clinical scenarios, TBLC with real-time rEBUS is an excellent diagnostic tool.

KEYWORDS

interventional pulmonology, radial EBUS, transbronchial lung cryobiopsy

INTRODUCTION

Pneumonia is an acute infection of the lower respiratory tract and a leading cause of mortality globally. Despite modern advances, several organisms are implicated in the disease, which often remain difficult to identify microbiologically. Pneumonia can have various radiological manifestations, necessitating numerous differential diagnoses within a clinical-microbiological framework (e.g., inflammatory pathology, infectious diseases, neoplasms, lymphoproliferative disorders, and others). In certain contexts, histological examination remains essential for excluding alternative diagnoses.¹

Transbronchial lung cryobiopsy (TBLC) is a relatively new technique for obtaining lung biopsies, considered the least invasive method with high diagnostic yield, a safety profile, and significant reduction in morbidity, mortality, and length of hospital stay compared to surgical lung biopsy. The technique not only proven useful in the diagnostic approach of patients with interstitial lung disease (ILDs), but also in patients with pulmonary lesions of benign or malignant origin especially when combined with other modalities such as radial EBUS (rEBUS), fluoroscopy, navigation bronchoscopy, cone beam-CT (CBCT), robots or to sample mediastinal lesions near the airways.^{2–4} rEBUS on the other hand is the cornerstone modality used for reaching

Nektarios Anagnostopoulos and Simone Petrarulo have contributed equally to the work.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Author(s). *Respirology Case Reports* published by John Wiley & Sons Australia, Ltd on behalf of The Asian Pacific Society of Respirology.

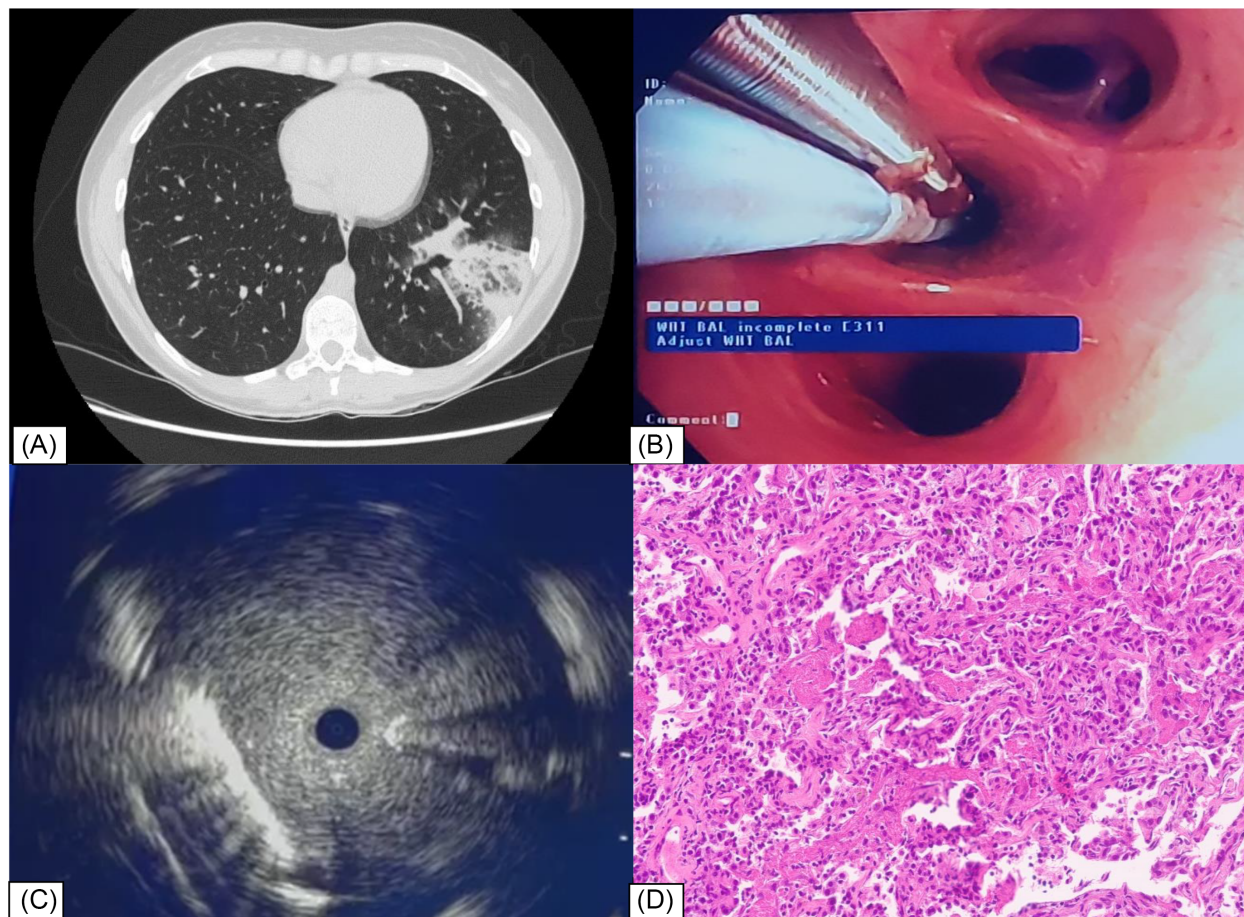


FIGURE 1 (A) CT scan with LLL consolidation. (B) Radial probe and fogarty balloon attached: Endoscopic view. (C) Radial mini probe ultrasonographic image with distinct ‘shadowing’ of the 1.1 cryoprobe. (D) Bronchiolar walls infiltrated by inflammatory cells, primarily lymphocytes, with scattered neutrophils.

‘invisible’ peripheral pulmonary lesions. Especially for those cases, the combination of thin or ultrathin bronchoscope, rEBUS with or without the use of guiding sheath (GS) and the use of 1.1 mm cryoprobe has been studied and proven an efficient combination for diagnosing PPLs.⁵ Yet the ‘Achilles heel’ of all the aforementioned techniques is the lack of ‘real-time’ visualization of the biopsy being obtained and the only up-to-date modalities that can help overcome this impediment are the CBCT, augmented fluoroscopy, confocal laser endomicroscopy and optical coherence tomography, all of them expensive equipment.

In this report, we describe a new approach of using two of the most affordable and easy-to-learn techniques to obtain an active visualization of the biopsies being taken from a pulmonary lesion, in a young patient under investigation for a non-resolving consolidation.

CASE REPORT

A 32-year-old female, non-smoker, with no significant medical history, presented to us with a persisting cough and an episode of haemoptysis. A contrast-enhanced

CT revealed a left lower lobe consolidation with ground glass opacities and some necrotic areas combined with a moderate left hilar node increase (Figure 1A). Peripheral blood analysis revealed normal haemoglobin, white blood count and an increased CRP (109 mg/L). Sputum Gram stain, culture, urine streptococcus antigen were negative. ANA, p-ANCA, c-ANCA were negative. Bronchoalveolar lavage was performed with a microbiological DNA panel negative and with marked cell count increase with normal distribution. TBLC was decided.

An informed consent was obtained before the procedure. The patient was intubated with a 14 mm rigid tracheoscope in a deep sedation using Propofol and Remifentanyl, while maintaining spontaneous breathing. rEBUS was introduced without GS through the tracheoscope and advanced to the lateral segment of the left lower lobe (LB9) where a concentric hypoechoic area was identified. Next, a 5Fr ‘Fogarty’ bronchial blocker balloon was introduced via the rigid tracheoscope, positioned and stabilized blocking the LB9 when inflated. Once the Fogarty Balloon was in place and the radial EBUS probe activated, the 1.1 mm cryoprobe was introduced through the flexible bronchoscope and advanced to the area of interest. We were able to visualize the distal end of the cryoprobe as a

distinct artefact in the right side of ultrasound image, thus confirming its real time location within the lesion (Figure 1B,C). After 6 s of freezing time, the cryoprobe was retracted with the flexible bronchoscope 'en bloc' and the balloon inflated while maintaining imaging with the radial probe. The procedure was repeated until 4 acceptable biopsy specimens were obtained. No bleeding occurred. The chest x-ray, performed after the procedure, did not show evidence of pneumothorax.

DISCUSSION

This is the first report of a real-time visualization of 1.1 mm TBLC under rEBUS to obtain lung tissue. The procedure was successfully concluded with no adverse effects mentioned and no postoperative complications. Histological analysis revealed bronchiolar walls infiltrated by inflammatory cells, primarily lymphocytes, with scattered neutrophils. Additionally, alveolar tissue showed fibrin deposits in the alveolar lumen along with interstitial inflammatory cells (Figure 1D). A diagnosis of slowly resolving pneumonia was made. After excluding neoplasm or lymphoproliferative disease, the patient has not undergone any further pharmacological therapy. Given her good general condition, she has been placed solely on radiological follow-up. The chest x-ray performed 4 months after the procedure showed complete resolution of the pulmonary consolidation. In cases where the initial clinical or radiological presentation does not appear typical for a pulmonary infection, or when there is no clinical and/or radiological improvement after an initial attempt at empirical therapy, obtaining a definitive diagnosis becomes imperative to avoid further diagnostic delays and provide appropriate care for the patient. In this specific scenario, TBLC represents a highly valuable diagnostic method.

TBLC continue to serve as a safe alternative to SLB and is slowly becoming the first-line diagnostic procedure both in patients with ILDs or patients under investigation for PPLs. This report underlines this significance and serves as an incentive to explore the combination of available modalities to increase the diagnostic yield of interventional pulmonologist (IP) procedures. Furthermore, it proves that TBLC can be performed even without the guidance of other expensive modalities such as Navigation bronchoscopy, augmented fluoroscopic guidance or CBCT. The invaluable ability to obtain lung tissue under direct observation is highlighted in various other reports, yet the equipment and experience required are more than often prohibitory in most hospital settings. Our 'twist' on a classical, well-described

and studied technique can prove beneficial for a plethora of cases in various settings that lack the newest and more expensive IP modalities or experience.

AUTHOR CONTRIBUTIONS

All authors contributed to the manuscript, including Dr. Nektarios Anagnostopoulos and Prof. Grigoris Stratakos, who visited our Hospital and collaborated in analysing and planning the execution of this complex procedure.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID

Simone Petrarulo  <https://orcid.org/0009-0005-5860-8822>

REFERENCES

1. File TM, Ramirez JA. Community-acquired pneumonia. *N Engl J Med.* 2023;17:632–41.
2. Poletti V, Petrarulo S, Piciucchi S, Dubini A, de Grauw AJ, Sultani F, et al. EBUS-guided cryobiopsy in the diagnosis of thoracic disorders. *Pulmonology.* 2024;S2531-0437(23):223–4.
3. Petrarulo S, Ravaglia C, De Grauw AJ, et al. Endobronchial ultrasound-guided Cryobiopsy of pulmonary artery intimal sarcoma. *Am J Respir Crit Care Med.* 2024;209(12):1497–1500. doi:10.1164/rccm.202309-1633IM.
4. Calari T, Petrarulo S, Dubini A, Piciucchi S, Ravaglia C, Poletti V. Endobronchial ultrasound-guided cryobiopsy for diagnosing a case of granulomatosis with polyangiitis. *Respirol Case Rep.* 2024;12(5):e01385. <https://doi.org/10.1002/rccr.2.1385>
5. Steinfurt DP, Khor YH, Manser RL, Irving LB. Radial probe endobronchial ultrasound for the diagnosis of peripheral lung cancer: systematic review and meta-analysis. *Eur Respir J.* 2011;37(4):902–10.

How to cite this article: Anagnostopoulos N, Petrarulo S, Ravaglia C, Dubini A, Piciucchi S, Stratakos G, et al. Transbronchial lung cryobiopsy under real-time radial EBUS: First report on a novel twist of the classical technique. *Respirology Case Reports.* 2024;12(7):e01435. <https://doi.org/10.1002/rccr.2.1435>