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First bronchoscopy with cryobiopsy and argon plasma coagulation at Indonesia national referral hospital: Case series

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Case Report

ABSTRACT

Cryobiopsy has emerged as a superior method for diagnostic endobronchial tissue sampling, offering more extensive and diagnostically valuable specimens than traditional techniques. Argon plasma coagulation (APC), a form of cryoablation, facilitates effective tumour resection and haemostasis with minimal complications. At Dr. Soetomo General Academic Hospital, conventional methods have predominantly been used for lung tumour sampling. These case reports introduced the novel application of cryobiopsy and APC in our institution, showcasing our expertise in advanced bronchoscopic techniques. We report on a 55-year-old male with a T3N1Mx stage IIIA left lung tumour and a 65-year-old male with a T4N2M1b stage IVA right lung cancer. Diagnoses were small-cell lung carcinoma and adenocarcinoma with wild-type EGFR mutation, respectively. Procedures were performed with minimal complications, demonstrating the effectiveness and safety of these techniques. These case reports underscored the potential of cryobiopsy and APC to enhance diagnostic accuracy and therapeutic outcomes, advancing pulmonary oncology care. These techniques provide superior diagnostic accuracy and therapeutic benefits with minimal complications. Our findings support the broader adoption of these advanced bronchoscopic interventions, particularly in settings where traditional methods may fall short.

INTRODUCTION

Lung cancer is the second most diagnosed type of cancer in both men and women. GLOBOCAN data from 2020 shows that lung cancer has an estimated number of new cases of 11.4%, below breast cancer (11.7%). In Indonesia, lung cancer is the second most common type of malignancy in men after nasopharyngeal cancer and is the leading cause of death in men. Data from Persahabatan Hospital in Jakarta shows that more than 80% of diagnosed cancer cases are lung cancer, with the number of cases increasing more than fivefold in the last 10 years. Persahabatan Hospital data also shows that most lung cancer patients come in advanced stages (IIIB/IV), with more than 1,000 new cases per year.[1] Fast and precise techniques are needed to determine a lung cancer diagnosis. Bronchoscopy forceps biopsy is one of the gold standard diagnostic tools used to obtain tissue samples in lung cancer. However, sometimes the sample taken from the forceps biopsy is insufficient or not representative, so other diagnostic techniques are needed to obtain a larger sample size and sufficient for confirming a tumour diagnosis.[2]

Cryobiopsy has emerged as a pivotal diagnostic method for endobronchial tissue sampling, offering significant advantages over traditional techniques. With a diagnostic yield of approximately 95%, cryobiopsy outperforms conventional forceps biopsy, which has an 85.1% yield. This higher efficacy is mainly due to the larger specimen sizes obtained, which maintain structural integrity and exhibit fewer crush artefacts. Comparative studies have demonstrated that the average specimen size from cryobiopsy is around 5 mm, significantly larger than the 2-3

mm specimens typically obtained from forceps biopsies.[3-6] Despite its advantages, cryobiopsy carries a higher risk of bleeding complications. Moderate bleeding occurs in approximately 6.5% of cryobiopsy cases, compared to 0.8% for forceps biopsy.[7-9] Additionally, the risk of pneumothorax with cryobiopsy is around 10%, necessitating careful patient selection and procedural expertise.[8,9,10] Nonetheless, cryobiopsy is invaluable for obtaining high-quality samples from central, mediastinal, and peripheral lung lesions, especially in cases where conventional biopsy techniques fall short.[11-15]

Argon plasma coagulation (APC) complements cryobiopsy by providing effective tumour resection and haemostasis. The APC is a monopolar electrosurgical technique that transfers electrical energy through ionised argon gas to the target tissue, causing coagulation necrosis without damaging surrounding tissues. This method is particularly beneficial for treating superficial tumours and managing haemoptysis, offering immediate coagulation and good visual control.[16,17] Studies have shown that APC can effectively reduce tumour size and control bleeding, mainly when used in conjunction with chemotherapy for small-cell lung cancer.[16] The APC has successfully controlled bleeding in up to 85% of endobronchial metastasis cases in clinical practice.[18] However, monitoring the coagulation time carefully is crucial to avoid potential complications such as airway burns and perforation.[19] The combined use of cryobiopsy and APC has shown promising results, offering diagnostic and therapeutic benefits with minimal complications.

These case reports presented the first cryobiopsy and APC performed at Dr. Soetomo General Academic Hospital. We describe the cases of two patients with advanced lung cancer who underwent these procedures. The first patient, a 55-year-old male with a T3N1Mx stage IIIA left lung tumour, and the second, a 65-year-old male with a T4N3M1b stage IVA right lung tumour, both benefited from these advanced techniques. The diagnostic yield and safety profile observed in these cases underscore the potential of cryobiopsy and APC as superior alternatives to conventional biopsy methods.

CASE REPORT 1

A 55-year-old male was admitted to Dr. Soetomo General Academic Hospital in Surabaya with multiple respiratory and systemic complaints. The patient reported experiencing shortness of breath for one week, accompanied by left-sided chest pain that was described as stabbing in nature. This pain had persisted for three months and had worsened over the last two weeks. Additionally, the patient had been coughing for the past eight months, producing blood spots for the past three months. He also reported intermittent fever for the past two months, along with a significant decrease in appetite and unintentional weight loss over the past three months. Despite these severe symptoms, the patient had not previously sought extensive medical evaluation until this admission. He also had a history of smoking 80 pack years.

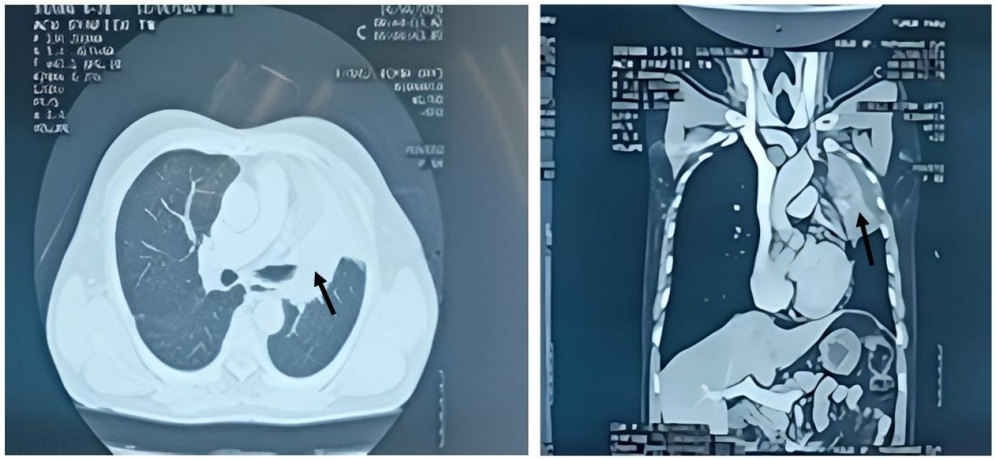

Figure 1. A contrast-enhanced CT scan revealed a mass in the lingular segment of the left lung's superior lobe (black arrow).

Physical examination revealed significant findings, including dullness on percussion over the upper one-third of the left hemithorax, suggestive of underlying pathology. A contrast-enhanced computed tomography (CT) scan of the chest identified a sizable mass measuring 4.3 x 3.8 x 6.7 cm in the lingular segment of the superior lobe of the left lung with left lower paratracheal lymphadenopathy (Figure 1). Metastatic process was not found from the CT scan, and the patient had not undergone another diagnostic examination to determine metastasis in another organ, such as bone survey, abdominal ultrasonography (USG) and brain CT scan. Hence, this mass was staged as T3N1Mx, corresponding to stage IIIA lung cancer according to the International Association for the Study of Lung Cancer (IASLC) Tumour, Node, and Metastasis (TNM) stage 9th edition. The patient's pain severity was assessed with a Visual Analog Scale (VAS) score of 3, and his performance status was recorded as 1, indicating that he was symptomatic but ambulatory and capable of self-care.

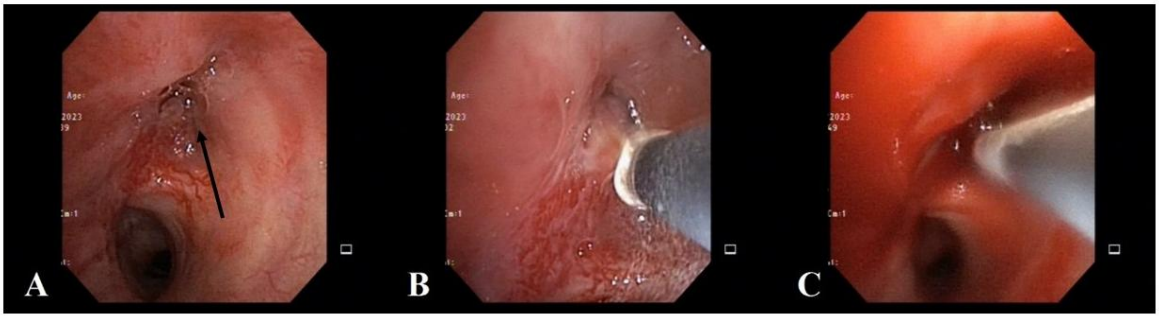

Figure 2. A. Hyperemic mucosal mass obstructing the upper portion of the left main bronchus (black arrow); B. First cryobiopsy samples from the masses; C. Second cryobiopsy samples

The bronchoscopic examination further elucidated the extent of the disease. The procedure revealed an obstructive mass with hyperemic mucosa occupying the upper portion of the left main bronchus (Figure 2A). Additionally, paraseptal emphysema was observed in the apical segment of the upper lobe of the lung. The decision was made to perform a cryobiopsy to obtain a more substantial and diagnostically valuable tissue sample. The cryobiopsy procedure was carried out using a flexible bronchoscope equipped with a cryoprobe. The first and second cryobiopsy samples obtained from the mass were significant in size and quality, providing sample tissue for histopathological examination (Figure 2B and 2C). Histopathological analysis confirmed the diagnosis of small cell lung cancer (SCLC), a highly malignant and aggressive form of lung cancer characterised by rapid growth and early metastasis (Figure 3) with final TNM staging T3N1Mx limited disease.

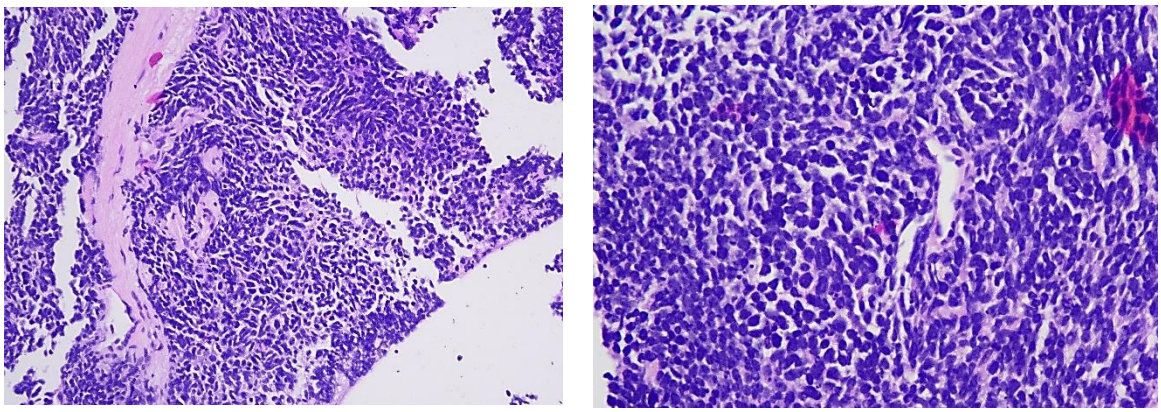

Figure 3. Histopathology confirming small cell lung cancer.

Following the cryobiopsy, the patient underwent six cycles of chemotherapy with etoposide-carboplatin, a regimen commonly used in the treatment of SCLC. The post-chemotherapy evaluation included a follow-up contrast-enhanced CT scan of the thorax, which demonstrated stable disease according to the Response Evaluation Criteria in Solid Tumours (RECIST) criteria (Figure 4). This indicated that the tumour had not progressed significantly during the treatment period, a favourable outcome given the aggressive nature of SCLC.

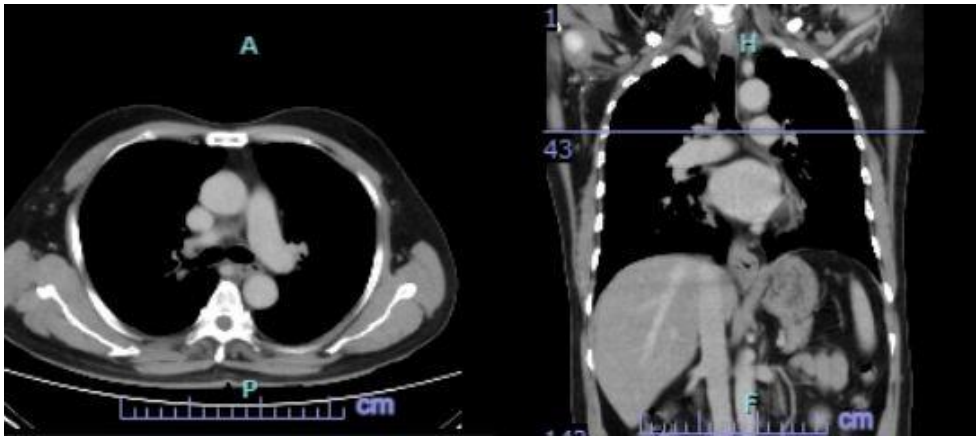

Figure 4. Post-chemotherapy CT scan showing stable disease according to RECIST criteria.

The use of cryobiopsy in this patient was particularly beneficial. The larger tissue samples obtained gave a more accurate diagnosis, enabling the healthcare team to tailor the treatment plan effectively. The cryobiopsy procedure was performed without any immediate complications, such as significant bleeding or pneumothorax, which are potential risks associated with this technique. The absence of complications in this case underscores the importance of procedural expertise and careful patient selection when employing advanced diagnostic methods like cryobiopsy.

In summary, the application of cryobiopsy in this case provided critical diagnostic information that guided effective treatment. The procedure's success in obtaining high-quality tissue samples and its safe execution highlight its utility in managing complex lung cancer cases. This case also underscores the potential benefits of integrating advanced diagnostic and therapeutic techniques in routine clinical practice to improve patient outcomes.

CASE REPORT 2

A 65-year-old male presented to Dr. Soetomo General Academic Hospital with a chief complaint of haemoptysis, having coughed up blood spots for two days. He also reported significant weight loss of 7 kg over the last six months, decreased appetite, and nausea, though without vomiting. The patient had a substantial smoking history of 50 pack years.

Physical examination revealed decreased vesicular breath sounds in the lower two-thirds of the right hemithorax, indicating potential underlying pathology. The patient also exhibited notable lymphadenopathy, with an approximately 5 cm hard, immobile lymph node in the right shoulder region and additional lymphadenopathy in the right supraclavicular area. This patient already had a Fine Needle Aspiration Biopsy (FNAB) for shoulder lymphadenopathy with a result suggestive of metastatic adenocarcinoma. A contrast-enhanced CT scan of the chest revealed a mass measuring 5.3 x 4.3 x 4.8 cm in the anterobasal segment of the inferior lobe of the right lung (Figure 5). Hence, this mass was staged as T3N3M1b, corresponding to stage IVA lung cancer according to IASLC TNM 9th staging, indicating advanced disease with metastasis.

Bronchoscopic examination further detailed the extent of the tumour. The procedure showed that the lumen of the upper portion of the lower right lobe was obstructed by a mass with smooth, hyperemic mucosa that bled easily upon contact (Figure 6A). Given the location and friable nature of the tumour, obtaining a biopsy posed a risk of significant bleeding.

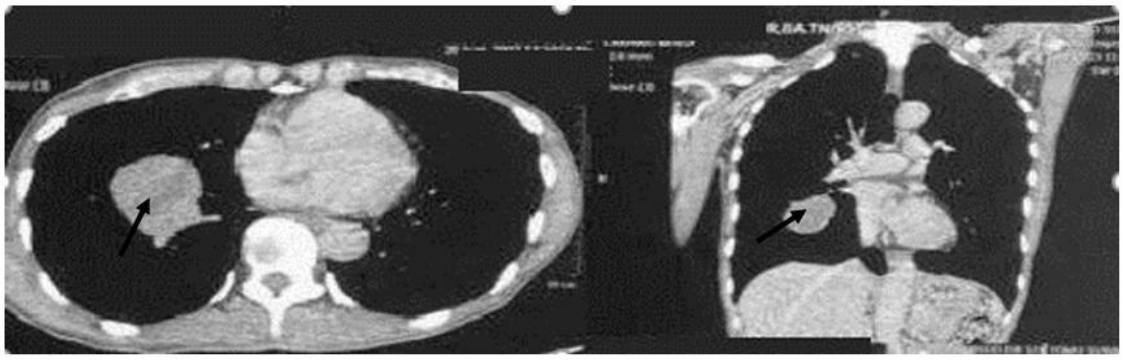

Figure 5. Contrast-enhanced CT scan revealing a mass in the anterobasal segment of the right lung's inferior lobe (black arrow).

The team decided to perform cryobiopsy with APC to manage this risk and obtain an adequate tissue sample for diagnosis. The cryobiopsy allowed for the extraction of larger and more diagnostically valuable tissue samples, while the APC was used to control the bleeding associated with the biopsy procedure. The first and second cryobiopsy samples obtained from the mass were substantial and maintained excellent structural integrity, providing sample tissue for histopathological examination (Figure 6B-D).

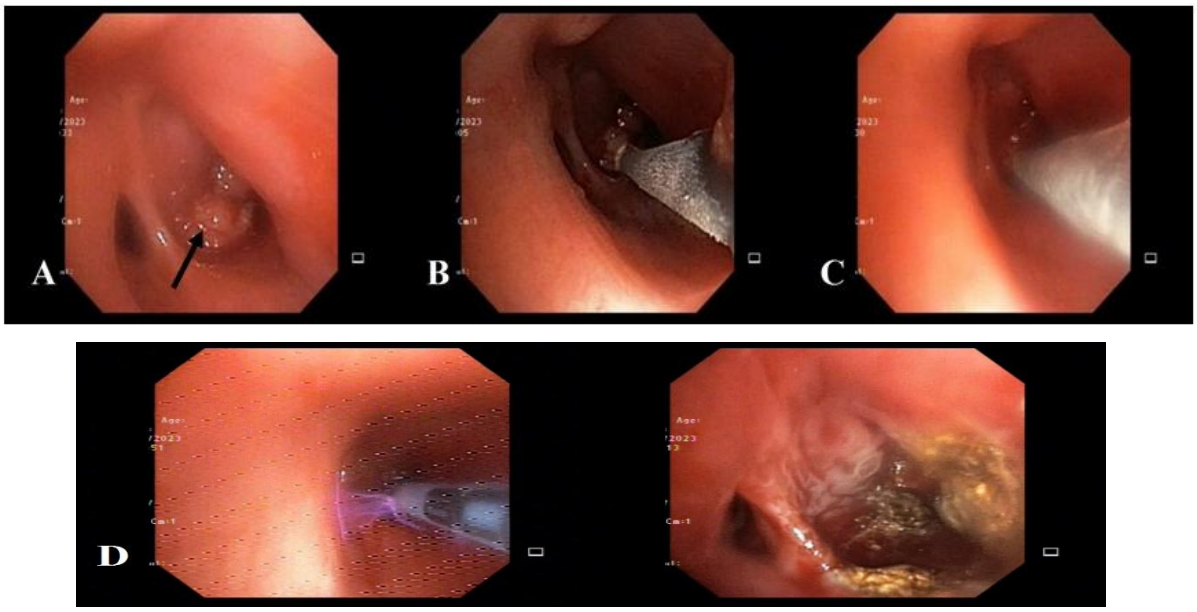

Figure 6. A. Mass with hyperemic mucosa obstructing the lumen of the lower right lobe (black arrow); B. First cryobiopsy samples from the masses; C. Second cryobiopsy samples; D. Argon plasma coagulation treatment on the mass.

The histopathological analysis revealed adenocarcinoma (Figure 7) with a wild-type EGFR mutation, which is a subtype of non-small cell lung cancer (NSCLC) that lacks mutations in the epidermal growth factor receptor, often influencing treatment decisions.

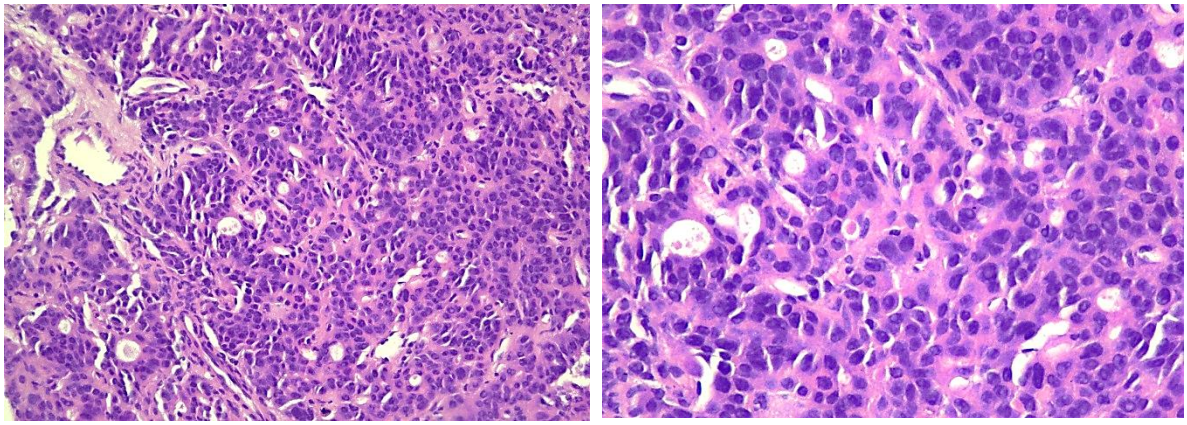

Figure 7. Histopathology confirming adenocarcinoma.

Argon plasma coagulation was particularly effective in this case. The procedure was performed immediately following the cryobiopsy to control the bleeding from the highly vascular tumour. APC utilises ionised argon gas to transfer electrical energy to the target tissue, causing coagulation necrosis. This method is effective for haemostasis in bleeding tumours. In this patient, the bleeding was successfully controlled within 10 minutes, allowing for the safe completion of the biopsy procedure without further complications.

The patient tolerated the combined cryobiopsy and APC procedure well, with no immediate complications such as significant bleeding, pneumothorax, or airway perforation. The use of APC provided immediate haemostasis, which is crucial in managing patients with friable, bleeding tumours. This combined approach facilitated a safer biopsy procedure and ensured that the patient received an accurate diagnosis, essential for tailoring an appropriate treatment plan. Post-procedural management included the administration of targeted therapy and systemic chemotherapy, considering the adenocarcinoma diagnosis and the wild-type EGFR mutation status. The patient was monitored closely for any delayed complications or signs of disease progression. Follow-up imaging and clinical evaluations indicated that the tumour remained stable, and the patient's symptoms, including haemoptysis and weight loss, showed improvement.

This case illustrates the significant benefits of integrating advanced bronchoscopic techniques such as cryobiopsy and APC in managing complex lung cancer cases. Combining these procedures provided a safe and effective method for obtaining high-quality tissue samples while managing the risk of bleeding. The successful outcome in this patient underscores the potential of these techniques to enhance diagnostic accuracy and improve patient care in cases of advanced lung cancer. In summary, integrating cryobiopsy and APC in this patient provided a dual benefit: obtaining high-quality diagnostic tissue samples and ensuring immediate haemostasis during the biopsy procedure. The absence of complications and the successful management of the patient's symptoms highlight the effectiveness of these advanced bronchoscopic techniques in the management of complex and advanced lung cancer cases.

DISCUSSION

Flexible bronchoscopy with forceps biopsy remains a cornerstone in diagnosing lung tumours. However, cryobiopsy has significantly improved diagnostic outcomes in both endobronchial and peripheral lung tumours. As highlighted in recent studies, cryobiopsy boasts a diagnostic yield of approximately 95% compared to 85.1% for conventional forceps biopsy.[3,7] This improvement is primarily attributed to the larger specimen sizes and better structural integrity provided by cryobiopsy, which minimises the occurrence of crush artefacts.[19]

Our current case reports underscore the efficacy of cryobiopsy in producing diagnostically valuable tissue samples. In the first patient, cryobiopsy facilitated the diagnosis of SCLC, while in the second patient, it confirmed adenocarcinoma with a wild-type EGFR mutation. These

outcomes align with previous findings, which have demonstrated that cryobiopsy exhibits superior diagnostic accuracy, particularly in the lower lobes of the lungs.[20,21] Despite these advantages, cryobiopsy is associated with higher rates of moderate bleeding complications (6.5%) and pneumothorax (up to 10%), necessitating careful patient selection and procedural expertise.[3,10]

APC, a minimally invasive monopolar electrosurgical technique, complements cryobiopsy by providing effective tumour debulking and haemostasis. The APC transfers electrical energy through ionised argon gas to the target tissue, causing coagulation necrosis. This method is particularly beneficial for treating superficial tumours and managing haemoptysis, as it ensures good visual control and minimises damage to surrounding tissues.[22] The APC has been effectively used in combination with chemotherapy to reduce tumour size in cases of SCLC and to manage bleeding in endobronchial metastases.[16,18]

In our case reports, the implementation of APC demonstrated notable success. The second patient, who presented with a mass in the right lower lobe causing haemoptysis, benefited from APC treatment, which controlled the bleeding and allowed for effective tissue sampling. The combination of cryobiopsy and APC proved to be a robust approach, enhancing diagnostic yield and therapeutic outcomes with minimal complications.

Quantitative data from our case reports further validated these findings. In the first case, cryobiopsy yielded a specimen size of 5 mm, significantly larger than the average specimen size obtained via forceps biopsy, which typically ranges from 2 to 3 mm. This size advantage facilitated a more accurate histopathological assessment, confirming the diagnosis of SCLC. In the second case, APC successfully controlled bleeding within 10 minutes, a crucial factor given the 20-30% bleeding risk associated with endobronchial tumour biopsy procedures.[22] Furthermore, post-procedural follow-up showed no immediate complications such as pneumothorax or significant bleeding, reinforcing the safety profile of these combined techniques.

The literature supports the integration of cryobiopsy and APC in routine clinical practice for their combined diagnostic and therapeutic benefits. For instance, a study by Takeda et al. in 2017 demonstrated a significant reduction in tumour size and improved airway patency in patients undergoing APC alongside chemotherapy.[16] Similarly, Sancho-Chust et al. in 2019 reported effective haemostasis in 85% of cases involving endobronchial metastases treated with APC.[18]

There are some limitations of this case series. First, there is a limited number of lung cancer patients with endobronchial tumour or infiltrative mass suitable as a cryobiopsy target. Second, if an endobronchial tumour in a lung cancer patient bled easily after bronchoscopic manoeuvres (such as aspiration, brushing, and forceps) and did not stop after APC, we did not perform cryobiopsy.

CONCLUSION

Our case reports demonstrated that the combined use of cryobiopsy and APC is effective and safe for diagnosing and managing lung tumours. These techniques provide superior diagnostic accuracy and therapeutic benefits with minimal complications. Our findings support the broader adoption of these advanced bronchoscopic interventions, particularly in settings where traditional methods may fall short.

CONFLICT OF INTEREST

The authors stated that there are no conflicts of interest.

PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. Written informed consent for the medical procedures and publication of these case reports and accompanying images had been obtained from patients. The patients have given their consent for images and other clinical information to be reported in the journal for these case reports

voluntarily.

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Due to patient confidentiality and institutional ethical regulations, the clinical and imaging data that are not included in the published article are not publicly accessible.

SUPPLEMENTARY MATERIAL(S)

No supplementary materials are available for this study.

AUTHORS CONTRIBUTIONS

IAA conceptualised the case report, case interpretation, contributed to manuscript writing and manuscript finalisation. AZM collected data and drafted the manuscript. FF critically revised the manuscript for important intellectual content and manuscript finalisation.

DECLARATION OF USING AI IN THE WRITING PROCESS

The authors utilised artificial intelligence (AI) tools, such as ChatGPT by OpenAI, to assist in language refinement and grammar checking during the writing process. All intellectual content, data interpretation, critical analysis, and final decisions were solely made by the authors. The use of AI did not replace any part of the authors' original contributions or critical thinking.

LIST OF ABBREVIATIONS

APC: Argon Plasma Coagulation; CT: Computed Tomography; NSCLC: Non-Small Cell Lung Cancer; RECIST: Response Evaluation Criteria in Solid Tumors; SCLC: Small Cell Lung Cancer; VAS: Visual Analog Scale.

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