South African Thoracic Society consensus statement on transbronchial lung cryobiopsy for interstitial lung disease

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Background. Surgical lung biopsy (SLB), performed via open lung biopsy or video-assisted thoracoscopic surgery, has traditionally been the gold standard for diagnosing interstitial lung disease (ILD) when histological confirmation is necessary. Transbronchial forceps biopsy, while less invasive, often yields small, artifact-prone specimens that are insufficient for conclusive histopathological analysis. Transbronchial lung cryobiopsy (TBLC) has emerged as a minimally invasive alternative, offering a higher diagnostic yield and superior tissue integrity due to the retrieval of larger, *en bloc* samples. International societies currently conditionally recommended TBLC as a potential first-line diagnostic tool for ILD, citing its favourable safety profile and diagnostic performance.

Technique, procedural environment and complications. TBLC may be performed via flexible bronchoscopy with or without an artificial airway. When an artificial airway is used, general anaesthesia is administered, and a supraglottic device or endotracheal tube facilitates bronchoscope and blocker access. Without an artificial airway, the procedure is conducted under conscious sedation using an oral bite guard. A bronchial blocker is deployed to control bleeding, and biopsies are obtained under fluoroscopic guidance with freezing times of 6 - 10 seconds. At least four adequate samples (>5 mm) are collected. Post-procedure care includes positioning the patient with the biopsied lung in the dependent position and performing imaging to detect pneumothorax. While bleeding and pneumothorax are potential risks, they are generally manageable. Definitive exclusion criteria for TBLC have not yet been established, but characteristics such as severely impaired lung function, pulmonary hypertension and significant comorbidity are associated with adverse events.

Conclusion. Although TBLC yields marginally lower diagnostic rates compared with SLB, it remains a cost-effective and safer alternative, particularly in resource-limited settings. The South African Thoracic Society strongly advocates for TBLC as the first-line diagnostic modality in all cases of ILD, where histology is required, provided there are no contraindications. This recommendation is based on the lower cost and morbidity associated with TBLC compared with SLB. An exception is made for patients with non-diffuse or non-peribronchiolar disease who are suitable candidates for SLB and where the procedure is readily available. Strengthening local capacity and expertise in TBLC is crucial for improving ILD diagnostic accuracy in South Africa.

Keywords. Cryobiopsy, interstitial lung disease, interventional pulmonology.

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Executive summary

Background

- Surgical lung biopsy (SLB), via open lung biopsy or video-assisted thoracoscopic surgery, has traditionally been the gold standard for diagnosing interstitial lung disease (ILD) when histopathological diagnosis is considered critical.
- Transbronchial forceps biopsy (TBFB) can aid in obtaining a histological diagnosis. However, this method often provides small samples that are subject to crush artifacts and lack penetration beyond the peribronchial sheath, precluding a conclusive histopathological analysis in most cases.
- Transbronchial lung cryobiopsy (TBLC) is a more recent,

minimally invasive technique that offers a higher diagnostic yield for ILD than TBFB and retrieves larger, structurally intact tissue samples removed *en bloc*, improving histopathological integrity for analysis.
- Since 2022, international societies have issued a conditional recommendation endorsing TBLC as a potential first-line option for patients with undiagnosed ILD needing histopathological diagnosis, given the high yield and favourable safety profile.
- While TBLC has a ~10 - 15% lower diagnostic yield compared with SLB, studies indicate that it offers better cost-effectiveness in resource-limited settings.

TBLC utilising flexible bronchoscopy with an artificial airway

- General anaesthesia is generally achieved using target-controlled infusions of propofol and remifentanil, with pressure-controlled mechanical ventilation by an anaesthetist.
- A supraglottic airway (SGA) or endotracheal tube (ETT) is inserted.
- Using a multiport adaptor, an endobronchial blocker (7.0 Fr/65 cm Arndt Endobronchial Blocker Set (Cook Medical, USA) is introduced through the SGA or ETT alongside the bronchoscope.
- Alternatively, a Univent endotracheal tube (AdvaCare Pharma, USA) can be used with a dedicated accessory channel that accommodates the blocker, avoiding the need for shared access.
- The TBLC is then performed as described below.

TBLC utilising flexible bronchoscopy without an artificial airway

- A flexible bronchoscope with an oral bite guard is utilised for oral intubation.
- Conscious sedation is administered by a dedicated physician.
- Prior to intubation, an endobronchial blocker is attached with an adjustable loop to the distal tip of the bronchoscope. These are then jointly introduced into a segment or subsegment of the target lobe. The balloon is inflated, and its position is endoscopically confirmed.
- The TBLC is then performed (as described below).

TBLC procedure

- A cryoprobe attached to the controller is inserted past the deflated balloon to the periphery of the lung, and its position is confirmed using fluoroscopy.
- The operator should aim to keep the probe at least 2 cm away from the visceral pleura and use fluoroscopy to guide the cryoprobe into different subsegments.
- Freezing time of 6 - 10 seconds is applied, whereafter the bronchoscope, together with the TBLC, is removed *en bloc*.
- A dedicated balloon operator inflates the bronchial blocker as soon as this manoeuvre is completed, tamponading the target segment or subsegment.
- All TBLC specimens should be taken from the same lung in the case of an artificial airway, but without an artificial airway only a single lobe should be targeted (different segments or subsegments).
- Once the specimen is retrieved from the tip of the probe, the endoscopist re-intubates the patient and rapidly navigates the bronchoscope back to the target segment using the bronchial balloon blocker as a physical guide.
- The bronchoscope camera can be opposed against the balloon to inspect for bleeding distal to the inflation point.
- The procedure should be repeated until at least four to five macroscopically acceptable samples (>5 mm) are obtained.
- The endoscopist then inspects the segments from which the TBLCs were performed and only removes the bronchoscope once no active bleeding is observed.

Post-procedure care and complications

- The patient should recover in a position with the biopsied lung in the dependent position.
- Routine imaging (ultrasound, fluoroscopy or chest radiography) is recommended to detect pneumothorax.
- If complications are suspected, immediate imaging should be performed before the patient leaves the theatre.
- Bleeding is a significant risk, although it is generally manageable with bronchoscopic interventions and is seldom life-threatening.
- Reported pneumothorax rates range from <1% to as high as 30%, but only a small minority require intervention.

Patient selection

- Patient safety is paramount when selecting individuals for TBLC, and a thorough risk assessment is essential to weigh the benefits of increased diagnostic certainty against potential adverse events for each patient.
- Definitive safety exclusion criteria for TBLC have not yet been established, but certain characteristics have been consistently highlighted as potential contributory factors. These include severely impaired lung function (forced vital capacity <50% or diffusing capacity for carbon monoxide <30 - 35% of predicted values), pulmonary hypertension (systolic pulmonary artery pressure on echocardiography >50 mmHg), and significant comorbidities such as severe cardiac, renal or liver disease.

Conclusion

- The South African Thoracic Society strongly advocates for TBLC as the first-line diagnostic modality in all cases of ILD, where histology is required, provided there are no contraindications. This recommendation is based on the lower cost and morbidity associated with TBLC compared with SLB. An exception is made for patients with non-diffuse or non-peribronchiolar disease who are suitable candidates for SLB, provided SLB is readily available.

Introduction and background

Interstitial lung diseases (ILDs) encompass a broad group of disorders that involve inflammation and fibrosis of lung parenchyma with variable severity.[1] While many ILDs share similar clinical presentations, they differ substantially in aetiology, pathology, treatment response and prognosis.[1]

The complexity of ILD diagnosis

Initial diagnostics for suspected ILD typically include clinical assessment and chest radiography; however, these methods lack specificity. High-resolution computed tomography (HRCT) is integral

to improving diagnostic accuracy by providing detailed imaging of parenchymal and airway structures to help discriminate between ILD subtypes.[2] Effective diagnosis of ILDs requires integrating clinical, laboratory and radiological findings, best achieved through a multidisciplinary team (MDT) approach.[2] The significance of MDT discussions for ILD diagnosis has been emphasised over the past two decades, with the 2013 American Thoracic Society (ATS)/European Respiratory Society (ERS) update on idiopathic interstitial pneumonias underscoring this approach as the gold standard for diagnosis.[3] Despite the most robust MDT discussions, a definitive diagnosis remains elusive in ~30% of patients, especially in cases with atypical presentations or inconclusive radiological and serological findings.[4,5] Recent data from large randomised controlled trials suggest that histological information is required in as many as 30 - 40% of idiopathic pulmonary fibrosis (IPF) patients in order to meet diagnostic criteria as outlined in the 2018 IPF guidelines.[6] Importantly, HRCT findings definitive for usual interstitial pneumonia (UIP) are only present in ~50% of cases.[5,7] In patients for whom a final diagnosis cannot be made, the entity of 'unclassifiable ILD' is associated with major management uncertainties.[5] In these cases, high-quality biopsy specimens can provide critical histopathological insights, enhancing diagnostic accuracy, guiding therapeutic options, and reducing the number of 'unclassified ILDs'.[1,2,5]

Options for obtaining tissue

Surgical lung biopsy (SLB), via open lung biopsy or video-assisted thoracoscopic surgery (VATS), has historically been the gold standard for diagnosing ILD, with a diagnostic yield of >95%.[6,8] VATS is generally preferred owing to its minimally invasive nature.[6,8] However, SLB carries significant morbidity and mortality risks, with an in-hospital mortality rate of 17% and a complication rate of 30%, including pneumothorax, pneumonia and respiratory failure.[9] These risks are particularly concerning for older patients and those with advanced lung disease, often precluding SLB in high-risk cohorts.[9]

In certain patient populations, transbronchial forceps biopsy (TBFB) can aid in obtaining a histological diagnosis.[10] However, this method often provides small samples that are subject to crush artifacts and lack of penetration beyond the peribronchial sheath, precluding a conclusive histopathological analysis in many instances.[6,8] TBFB is not very sensitive for diagnosing complex histopathological patterns such as UIP.[11] Overall diagnostic yield for all ILDs ranges between 20% and 30% for TBFB, with many specimens lacking suitable diagnostic tissue.[10] The complication rate for pneumothorax is ~10%, and for bleeding 3 - 5%.[10,12] It is for these reasons that guidelines do not recommend TBFB as a first-line investigation for the histopathological diagnosis of ILD.

Transbronchial lung cryobiopsy (TBLC) is a more recent, minimally invasive technique that offers a higher diagnostic yield for ILD than the conventional forceps-based biopsy.[8,13] Using a cryoprobe, rapidly cooled by carbon dioxide or nitrous oxide, TBLC retrieves larger, structurally intact tissue samples removed *en bloc*, which greatly improve histopathological integrity for analysis.[4,11-13] Compared with VATS, TBLC reduces morbidity and healthcare resource use, and often allows same-day discharge with minimal recovery time.[1,2,13-17] Studies show that TBLC has a diagnostic yield between 80% and 91%, while SLB has a diagnostic yield of ~95%.[5,10,12,18] A meta-analysis found that the pooled diagnostic yield after MDT was 77% for TBLC and 94% for SLB, with an increase in diagnostic yield to 81% in experienced centres.[1] A retrospective comparative review by Freund *et al.*[10] showed a diagnostic yield for TBLC of 74% in fibrotic and 88% in non-fibrotic lung diseases compared with <50% in either category for TBFB.[10] Despite the greater quantity of tissue biopsied with TBLC, there was little difference in the overall complication rates.[10]

Current recommendations for TBLC

In 2022, the ERS issued a conditional recommendation endorsing TBLC as a potential first-line option for patients with undiagnosed ILD needing histopathological diagnosis, given the high yield and favourable safety profile.[11] Despite increasing evidence supporting TBLC, the technique remains unstandardised, and its precise role within the diagnostic framework of ILD continues to evolve.[5,8,11,19] The variation in procedural techniques across centres and practitioners highlights the need for standardised competency criteria to enhance the diagnostic yield and safety of TBLC.

While TBLC has rapidly gained acceptance worldwide, there are currently no established guidelines or recommendations for its use in ILD in Africa, including South Africa (SA). This opinion statement by the South African Thoracic Society (SATS) therefore aims to review available data and suggest an evidence-based, safe and practical approach in SA. Cryotechnology has many other indications, e.g. sampling nodules, foreign body removal and tumour debulking, but these indications fall outside the scope of this statement.

Technique and procedural environment

TBLC shares similarities with traditional TBFB and may be performed using either a flexible or rigid bronchoscope under various procedural conditions.[5,12,20] Owing to the potential for airway and bleeding complications, TBLC should be reserved for experienced bronchoscopists proficient in managing such risks.[5,12,21] The target lobe and segment(s) for sampling should be identified in advance. The procedure should be conducted in a bronchoscopy suite or operating theatre equipped with standard emergency equipment and medications for interventional bronchoscopy.[5,12,21] Fluoroscopic guidance is strongly recommended for all cases.[5,12,21] Two flexible bronchoscopy techniques have been safely utilised in SA: flexible bronchoscopy with an artificial airway (the preferred technique globally) or without an artificial airway.[21,22]

Flexible bronchoscopy with an artificial airway

If this procedure is performed under general anaesthesia, intravenous anaesthesia using target-controlled infusions of propofol and remifentanil, with pressure-controlled mechanical ventilation, is administered by an anaesthetist. A supraglottic airway (SGA) or endotracheal tube (ETT) is inserted. Using a multiport adaptor, an endobronchial blocker (7.0 Fr/65 cm Arndt Endobronchial Blocker Set; Cook Medical, USA) is introduced through the SGA or ETT alongside the bronchoscope (Fig. 1). Alternatively, a Univent endotracheal tube (AdvaCare Pharma, USA) can be used (Fig. 2) with a dedicated accessory channel that accommodates the blocker, avoiding the need for shared access. The TBLC is then performed as described below.

The use of general anaesthesia is believed to improve patient comfort and may reduce the risk of iatrogenic complications owing to

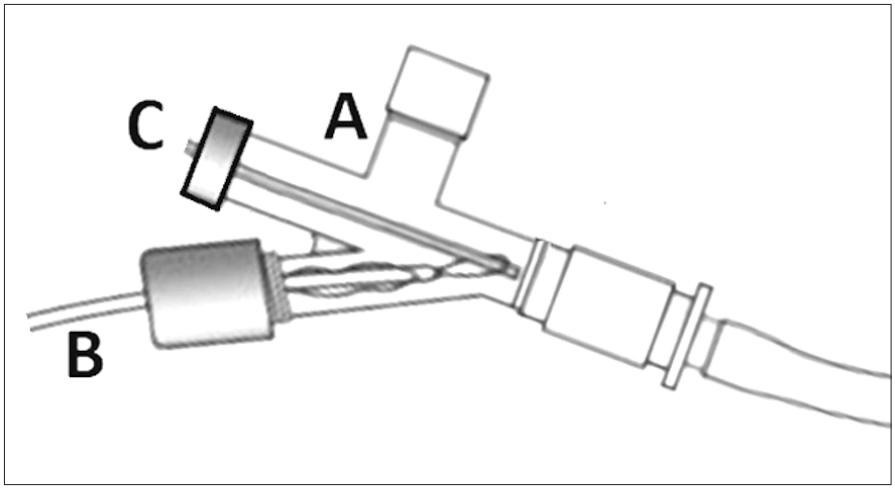

Fig. 1. Using a multiport adaptor (A), an endobronchial blocker (B) is introduced through an endotracheal tube alongside the bronchoscope (C).

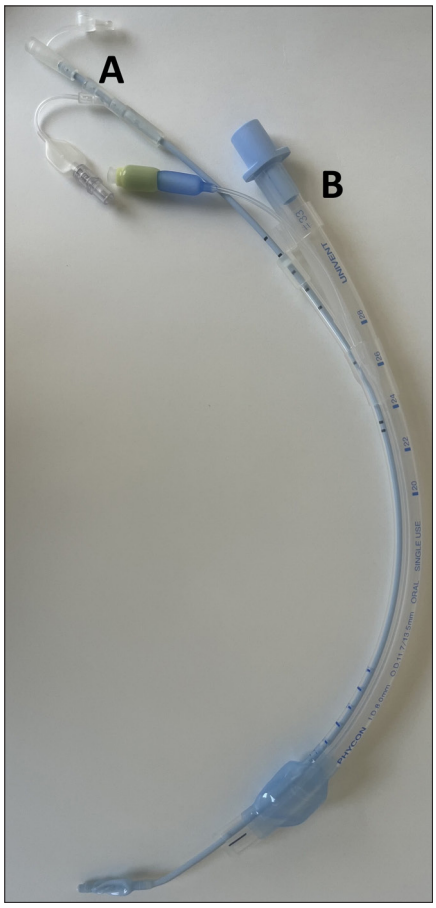

Fig. 2. When using a Univent endotracheal tube, a dedicated accessory channel allows an endobronchial blocker (A) to be introduced through the endotracheal tube (B).

less movement and coughing, better control of the airway, and immediate access in the event of major bleeding, as well as providing a convenient conduit for re-intubation with the bronchoscope. Randomised trials will be required to demonstrate the superiority of either technique, as this has not conclusively been shown in the literature; however, most guidelines recommend that cryobiopsy be performed using an artificial airway.

Flexible bronchoscopy without an artificial airway

When using conscious sedation rather than general anaesthesia, a flexible bronchoscope with a 2.8 or 3.2 mm working channel is preferred, and an oral bite guard (Fig. 3) is inserted for oral intubation.[5,12,21] Supplementary oxygen is routinely given via nasal prongs at 5 - 15 L/min.[5,21] Conscious sedation is administered by a dedicated physician, typically using an opioid (e.g. fentanyl) and propofol-based protocols in accordance with institutional guidelines. An endobronchial blocker is attached with an adjustable loop to the distal tip of the bronchoscope (Fig. 4) and introduced into a segment or subsegment of the targeted lobe.[21]

TBLC technique

Once the bronchial blocker is in the target segment, the balloon is inflated, and its position is endoscopically confirmed (Fig. 5). All TBLC specimens should be taken from the same lung in the case of an artificial airway, but without an artificial airway only a single lobe should be targeted (different segments or subsegments). A cryoprobe attached to the controller (ERBECRYO 2; Erbe Elektromedizine GmbH, Germany) is then inserted past the deflated balloon to the periphery of the lung, and its position is confirmed using fluoroscopy (Fig. 6). The

Fig. 3. Transbronchial lung cryobiopsy performed with a flexible bronchoscope, and oral intubation via a plastic bite guard. Supplementary nasal oxygen is routinely administered.

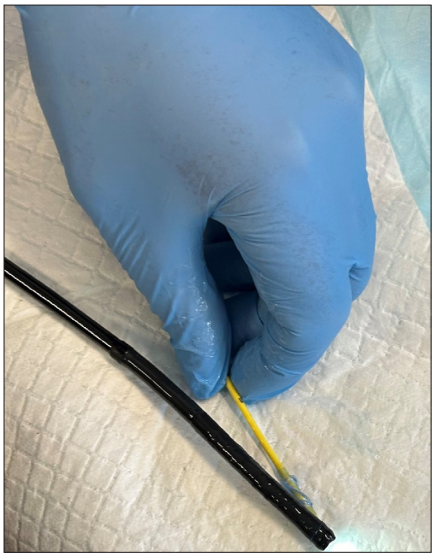

Fig. 4. A bronchial blocker attached to the distal tip of the bronchoscope prior to insertion. The balloon is only inflated once the target segment is identified.

operator should aim to keep the probe at least 2 cm away from the visceral pleura and use fluoroscopy to guide the cryoprobe into different subsegments.[5,12,22] A freezing time of 6 - 10 seconds is applied, whereafter the bronchoscope, together with the TBLC, is removed *en bloc*.[5,12,20-22] A dedicated balloon operator inflates the bronchial blocker as soon as this manoeuvre is completed, tamponading the target segment or subsegment.[5,20-22] Once the specimen is retrieved from the tip of the

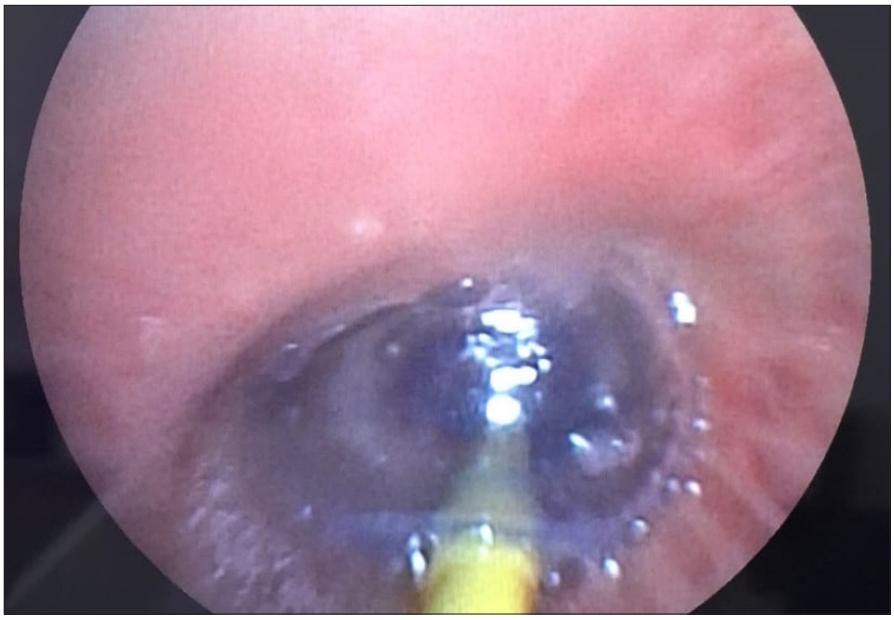

Fig. 5. The bronchial blocker with the balloon inflated, providing endoscopic confirmation that it is correctly positioned.

probe, the endoscopist reintubates the patient and rapidly navigates the bronchoscope back to the target segment using the bronchial balloon blocker as a physical guide. The bronchoscope camera can be placed against the balloon to inspect for bleeding distal to the inflation point (Fig. 7). The balloon should only deflate if it is deemed safe (no excessive bleeding).

The procedure should be repeated until at least four to five macroscopically acceptable samples (>5 mm) are obtained (Fig. 8).[5,12,18,23] Diagnostic yield improves significantly with more biopsies – from 67.6% (a single) to 91% – while additional samples beyond four offer diminishing returns.[15] It is therefore suggested to obtain four to five samples to reduce the risk of a non-diagnostic procedure.[5,15,23] Finally, the endoscopist inspects the segments from which the TBLCs were taken, and only removes the bronchoscope and bronchial blocker once no active bleeding is observed.

Post-procedure care

After the procedure, the patient should recover in a position with the biopsied lung in the dependent position. Routine imaging (ultrasound, fluoroscopy or chest radiography) is recommended to detect pneumothorax; some advocate waiting up to 20 minutes to detect slow air leaks. If complications are suspected, immediate imaging should be performed. If no complications are apparent, imaging should still be completed before discharge from the recovery area or return to the ward after an adequate period of recovery (60 minutes).

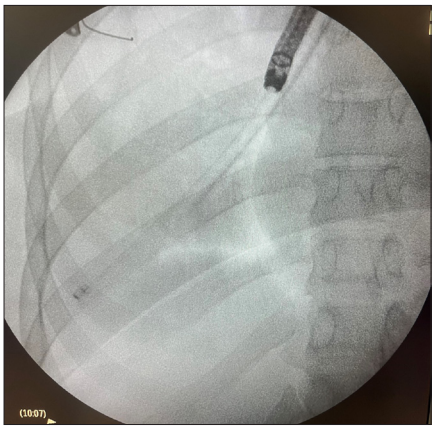

Fig. 6. An example of fluoroscopy. In this case the operator retracted the probe by 2 - 3 cm prior to confirming its position again and performing the biopsy.

Complications

TBLC is a minimally invasive procedure, but it is nonetheless associated with several risks, the most significant being bleeding and pneumothorax.[11,12,16] Although TBLC is generally considered safer than SLB, it is important to understand its specific risks.

Bleeding

Bleeding rates vary widely in the literature, which is attributed to differences in procedural techniques, such as freeze time and probe size, and positioning. In addition, the definitions of bleeding severity are variably reported in the literature. Bleeding is generally manageable with bronchoscopic interventions, including balloon tamponade.[5,15,24]

A recent meta-analysis identified the mean overall incidence of bleeding as 27%, with a range of 0% to 78%, although only a small minority required any intervention.[2] A larger meta-analysis reported the pooled incidence of moderate to severe bleeding after TBLC as 10%; however, this rate decreased to 7% in experienced centres that had performed ≥70 procedures.[1] Smaller individual studies observed moderate bleeding in 17 - 20% of patients after TBLC.[15,22,24]

Several techniques and strategies may mitigate the risk and severity of bleeding during TBLC.

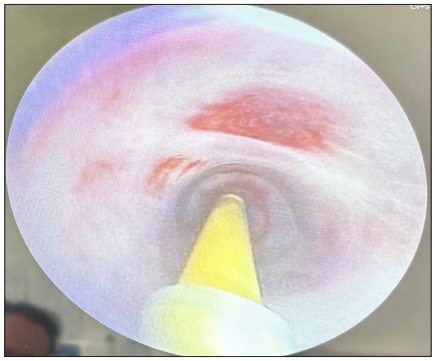

Fig. 7. An example of the endoscopic view when the bronchoscope's tip is placed against the balloon to inspect for bleeding (in this case very minor).

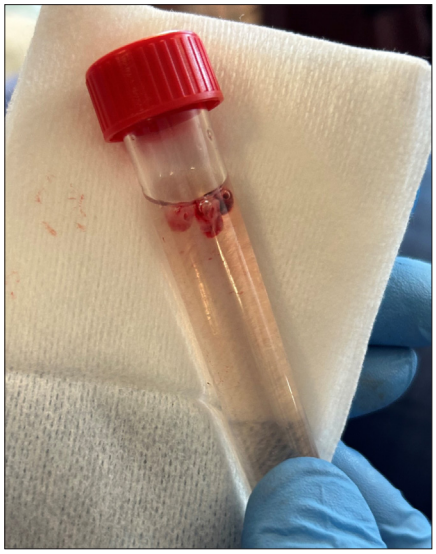

Fig. 8. Transbronchial cryobiopsy specimens obtained with a 1.7 mm probe.

- **Endobronchial blockers.** The routine use of an endobronchial blocker has been shown to significantly reduce the occurrence of moderate to severe bleeding.[5,24] A bronchial blocker, such as the Arndt Endobronchial Blocker Set (7.0 Fr/65 cm) or the balloon blocker contained in the Univent endotracheal tube, is placed in the bronchus leading to the area to be biopsied, and inflated immediately after biopsy to isolate the biopsied segment and prevent blood from entering the central airways. This step is particularly important, since the bronchoscope must be removed from the airway to retrieve the tissue sample, leaving a period of blind time where bleeding cannot be otherwise controlled. The use of prophylactic bronchial blockers is associated with a lower rate of moderate to severe bleeding.[19] One study showed a reduction in rates of moderate to severe bleeding from 36% to 2% when using a prophylactic balloon.[20]
- **Cryoprobe size.** Use of smaller cryoprobes is suggested over a larger probe by Maldonado *et al.*,[19] who found that bleeding rates were lower using a smaller probe size and shorter freeze times. This is in contrast to Ravaglia *et al.*,[15] who in another large study showed no correlation between the bleeding risk and probe size, size or number of samples taken, or severity of impaired lung function. There are emerging data suggesting that a 1.1 mm probe may have a similar diagnostic yield compared with larger probes for the diagnosis of ILD, but with a better safety profile.[25] However, this needs to be confirmed in other prospective trials.
- **Airway management.** In the event of severe bleeding during the period in which the bronchoscope is removed, access to the airways may be difficult unless a secured airway has been established before the procedure with either an ETT or a rigid bronchoscope. However, airway management for TBLC is not yet standardised, and many centres have performed the procedure safely without a definitive airway with comparable bleeding rates using only flexible bronchoscopy and conscious sedation. Regardless of the upper airway management strategy, bronchial blockers for haemorrhage control are frequently used prophylactically. A prospective SA cohort showed a bleeding rate of 5% using flexible bronchoscopy with a prophylactic bronchial blocker and no artificial airway.[21]
- **Fluoroscopy.** Fluoroscopic guidance is recommended to help position the cryoprobe at a safe distance from the pleura, which can reduce the risk of both bleeding and pneumothorax.[5,20,26] The risk of bleeding may be higher in the more proximal region of the peripheral lung, where vessels are larger but still too distal to be protected by the cartilaginous rings of the central airway.[12] Fluoroscopy also has the advantage of guiding the tip of the probe into different subsegments.
- **Operator experience.** The risk of bleeding can be influenced by operator experience. It is recommended to have a dedicated team of bronchoscopists and nursing staff with standard monitoring equipment, intubation tools, and access to intensive care if necessary. Wherever possible, the inclusion of an anaesthesiologist skilled in airway and thoracic procedures in the procedural team will enhance patient safety and procedural performance. More experienced operators may be more proficient in techniques such as fluoroscopic guidance for proper probe placement and prophylactic bronchial blocker use, which are crucial for reducing bleeding risk.[10-12,26]
- **Additional considerations.** Patients with abnormal coagulation parameters, those with thrombocytopenia and those taking antiplatelet drugs are considered at increased risk of bleeding.[5] A conservative approach is to withhold medications associated with increased bleeding risk before the procedure. Patients with pulmonary hypertension have an increased risk of bleeding, and a pre-procedural evaluation of pulmonary artery pressure is advised.[5]

Pneumothorax

Reported pneumothorax rates range from <1% to as high as 30%.[2,5,10,12,20] Various meta-analyses report pneumothorax in the range of 10%.[5,27] A study that compared cryobiopsy with forceps biopsy reported very similar pneumothorax rates of 4.95% with TBLC v. 3.15% with TBFB.[28]

The need for intervention varies, with studies reporting that 20 - 70% of patients with pneumothorax required an intercostal chest drain.[15,28,29] A pooled analysis from studies reporting the need for a chest drain after TBLC found that only 5.6% of patients with pneumothorax required drainage.[1] The criteria to intervene were not well elucidated. Patients with a stable spontaneous pneumothorax, as defined by the British Thoracic Society (BTS) guidelines, may be managed conservatively.[30] This strategy may be applicable to selected patients with stable TBLC pneumothorax as well.

While pneumothorax is a recognised risk of TBLC, several factors can influence its occurrence:

- **Biopsy location.** Biopsies taken close to the pleura increase the risk of pneumothorax.[5] A distance of <1 cm from the pleura is associated with a significantly increased risk.[5,19] Sampling from different sites or the lower lobes can increase the risk of pneumothorax, as does the number of biopsy specimens taken.[15,17] Fluoroscopy ensures that the cryoprobe is positioned in the correct area of the lung, usually in the distal parenchyma, and allows the operator to visualise the distance between the tip of the cryoprobe and the pleura.[17,19]
- **Cryoprobe size.** The use of larger cryoprobes, such as the 1.7 mm probe, has been associated with an increased risk of pneumothorax in numerous studies.[12,15,17,19]
- **Fibrotic lung disease.** The presence of fibrotic lung disease itself seems to be associated with an increased risk of pneumothorax. Specifically, a higher radiological fibrotic score, as evaluated by the distribution of reticular abnormalities, traction bronchiectasis, and honeycombing, is associated with an increased incidence of pneumothorax.[15] Pneumothorax was also reported more frequently in patients in whom a UIP pattern was found on histological examination.[15]

Mortality rate

TBLC is associated with low mortality rates, although outcomes may vary by centre.[16] Two studies reported a 0.4% 3-month mortality rate, but the deaths were attributed to cancer and to acute exacerbations of the ILD,[15,17] while another systematic review, including 14 studies with TBLC and 16 with SLB, showed a lower 30 - 60-day mortality of 0.7% with TBLC v. 1.8% with SLB.[31]

Patient selection

Patient safety is paramount when selecting individuals for TBLC, and a thorough risk assessment is essential to weigh the benefits of increased diagnostic certainty against potential adverse events for each patient. Definitive safety exclusion criteria for TBLC have not yet been established, but certain characteristics have been consistently highlighted as potentially contributory to complications.

- **Impaired lung function.** Many studies indicate that patients with severely impaired lung function, such as a forced vital capacity <50% or diffusing capacity for carbon monoxide <30 - 35% of predicted values, may face increased risks, including increased procedural complications (predominantly pneumothorax), and have higher post-procedural admission rates.[5,11,12,15,32]
- **Age.** TBLC has been performed safely in a wide age range of patients, although some studies have suggested either >65 or >75 years to be a relative contraindication to the procedure.[5,11,17,32] It may be prudent to assess individual comorbidities, fitness for procedure and therapeutic implications rather than set a defined age limitation.
- **Pulmonary hypertension.** Similarly to SLB, pulmonary hypertension can elevate bleeding risk and is considered a relative contraindication to TBLC.[5] Exact cut-off values vary, with many using the value of estimated systolic pulmonary artery pressure on echocardiography >50 mmHg to be a relative contraindication to proceed with TBLC.[5] Patients with clinical or radiological signs of pulmonary hypertension should undergo a pre-procedural evaluation of pulmonary artery pressure, ideally through echocardiography or right heart catheterisation, to stratify risk.
- **Comorbidities.** Major comorbidities such as severe cardiac, renal or liver disease should be carefully evaluated and are considered to increase procedural risk.[24] A Charlson Comorbidity Index ≥2 has been shown to be an indicator of increased hospital admission following TBLC.[32,33] Significant haemodynamic compromise is also widely considered an exclusion criterion.[32] Bleeding diathesis, significant thrombocytopenia (platelet count <70 000 per μL), or inability to stop anticoagulation or high-dose antiplatelet agents are also considered contraindications.[5,11,23,32] A high body mass index (>35 kg/m^2) may also result in procedure failure, most commonly as a result of desaturation in spontaneously breathing patients.[5,34]
- **Oxygen requirements.** Significant hypoxaemia, defined as arterial partial pressure of oxygen <7.3 kPa on room air or 8 kPa (55.8 - 60 mmHg) oxygen while receiving 2 litres per minute of nasal oxygen, puts patients at an increased risk for adverse events during or after the procedure.[8,12] Patients with pre-existing hypoxaemia have compromised reserve, and gas exchange can worsen dramatically should a complication such as a pneumothorax develop.

Practical local considerations

Many hospitals in sub-Saharan Africa lack essential equipment such as fluoroscopy, cryoprobes, and dedicated bronchoscopy suites necessary for TBLC. Additionally, limited access to cardiothoracic procedures, shortages of hospital beds, and insufficient anaesthesia availability often prevent timely access to SLB.

However, two independent SA studies have demonstrated the feasibility of performing TBLC safely, with most patients being discharged on the same day.[21,22] One study further highlighted that TBLC can be performed safely even in settings with restricted access to general anaesthesia, using conscious sedation without artificial airways.[21] Both studies advocated for the routine use of fluoroscopy to enhance procedural safety. Given that fluoroscopy is available in most major hospitals, TBLC could become more accessible than SLB as expertise in the technique expands.

Although the SA studies did not directly assess per-patient costs, avoiding operating theatre use and prolonged hospital admissions makes TBLC a more likely cost-effective alternative to SLB in under-resourced settings, even with the 5 - 10% lower diagnostic yield.[35]

Conclusion

TBLC has emerged as a valuable diagnostic tool in the evaluation of ILDs, offering a balance between diagnostic yield and procedural safety. Skilled operators and appropriate patient selection are crucial, the latter involving a careful and individualised evaluation of the procedure's risk v. benefit. The evidence suggests that obtaining at least four to five biopsy specimens significantly enhances diagnostic accuracy, with diminishing returns beyond four samples. Additionally, optimising biopsy size to at least 5 mm improves diagnostic utility, as larger specimens provide more histopathological information. Precise control of freezing time remains essential to mitigate bleeding risk and ensure procedural safety.

Despite its advantages, TBLC is not without limitations. Variability in procedural techniques, differences in operator experience, and the lack of universal guidelines pose challenges to its widespread adoption. Moreover, while TBLC reduces the need for more invasive SLB, there remains a subset of patients for whom definitive histopathological diagnosis may still require alternative approaches.

There is a great need to upskill SA pulmonologists in TBLC, and the SATS strongly advocates for TBLC as the first-line diagnostic modality in all cases of ILD, where histology is required, provided there are no contraindications.

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