

Cryoprobe Biopsy Improves Diagnostic Yield in Transbronchial Biopsy

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Conventional transbronchial biopsy with forceps often yields small specimens with crush artifact, limiting diagnostic accuracy for pulmonary lesions. Recent clinical trials indicate that cryoprobe biopsy provides larger, more intact specimens, leading to a higher diagnostic yield for various thoracic pathologies.

KEY TAKEAWAYS

- **The Pivot:** Cryoprobe biopsy offers superior specimen quality and diagnostic yield compared to traditional forceps biopsy.
- **The Data:** Cryoprobe use localizes freezing at the probe tip, enabling retrieval of larger, more intact biopsy specimens.
- **The Action:** Clinicians performing bronchoscopic lung biopsies should consider cryoprobe technology to enhance diagnostic success.

Bronchoscopic biopsy is a standard procedure for diagnosing pulmonary lesions. However, the conventional method using forceps can result in small specimen sizes and poor specimen quality due to crush artifact, which may compromise diagnostic accuracy.^{1,2,3} This limitation necessitates alternative approaches to improve tissue acquisition.

Clinical Context and the Need for Improved Diagnostics

Pulmonary lesions, ranging from benign inflammatory processes to malignant tumors, present a significant diagnostic challenge. Early and accurate diagnosis is crucial for effective treatment planning and improving patient outcomes. Conventional transbronchial biopsy using forceps has been a cornerstone of this diagnostic process for decades. While widely available and relatively safe, its inherent limitations often lead to inconclusive results, requiring repeat procedures, more invasive surgical biopsies, or prolonged periods of diagnostic uncertainty. These delays can be particularly detrimental in cases of rapidly progressing malignancies. The need for a method that consistently yields larger, higher-quality tissue samples is therefore paramount in respiratory medicine.

The FROSTBITE-2 Randomized Clinical Trial and Related Studies

The FROSTBITE-2 Randomized Clinical Trial, published in JAMA in 2026, investigated the efficacy of cryobiopsy versus forceps for bronchoscopic lung biopsy. The trial demonstrated that cryoprobe use localizes freezing at the probe tip, which enables the retrieval of larger, more intact biopsy specimens.¹ This mechanism directly addresses the limitations observed with forceps, where crush artifact frequently degrades specimen quality.¹

The FROSTBITE-2 trial involved a diverse patient population presenting with various types of pulmonary lesions,

including suspected malignancies and interstitial lung diseases. Patients were randomized to receive either cryobiopsy or conventional forceps biopsy. The primary outcome measured was diagnostic yield, defined as the proportion of biopsies providing a definitive diagnosis. Secondary outcomes included specimen size, quality, and complication rates. The rigorous methodology of this randomized controlled trial provides strong evidence for the superiority of cryobiopsy in improving diagnostic accuracy.

Further research supports these findings. A 2025 study in the *Journal of Visualized Experiments* examined the application value and safety of ultrafine bronchoscopy combined with frozen lung biopsy in the diagnosis of peripheral pulmonary nodules. This study similarly concluded that cryoprobe use localizes freezing at the probe tip, facilitating the retrieval of larger, more intact biopsy specimens compared to conventional forceps.² The improved specimen quality is critical for accurate histological assessment, particularly in cases of subtle or early-stage lesions.

This study focused on peripheral pulmonary nodules, which are often challenging to access and biopsy effectively with conventional methods due to their location. The combination of ultrafine bronchoscopy, allowing for navigation into smaller airways, and cryobiopsy further enhances the ability to obtain diagnostic tissue from these difficult-to-reach areas. The safety profile observed in this study also reinforces the viability of cryobiopsy as a routine diagnostic tool.

Another prospective observational study, published in *Annals of Medicine* in 2025, compared sequential cryoprobe and biopsy forceps in endobronchial ultrasound-guided transbronchial needle aspiration for mediastinal and hilar lesions. This study also reported that cryoprobe use localizes freezing at the probe tip, enabling the retrieval of larger, more intact biopsy specimens.³ The consistency across these studies highlights a clear advantage of cryoprobe technology in obtaining diagnostic tissue.

This observational study provided valuable insights into the application of cryobiopsy in conjunction with endobronchial ultrasound (EBUS), a technique commonly used for staging lung cancer and diagnosing mediastinal pathologies. By comparing sequential biopsies, researchers could directly observe the differences in specimen quality and size obtained from the same lesion using both methods. The findings underscore the versatility of cryobiopsy across different anatomical locations and its potential to complement existing advanced bronchoscopic techniques.

Mechanism of Action and Clinical Implications

The primary benefit of cryoprobe technology lies in its ability to preserve tissue architecture. By freezing the tissue, the cryoprobe minimizes mechanical distortion that is common with forceps, leading to specimens that are more amenable to pathological examination. This reduction in crush artifact and increase in specimen size directly contribute to a higher diagnostic yield, potentially reducing the need for repeat procedures and accelerating patient management.^{1,2,3}

The mechanism involves rapid freezing of the tissue at the probe tip, creating a strong adhesion between the tissue and the probe. When the probe is withdrawn, it pulls a larger, more cohesive piece of tissue compared to the shearing and crushing

action of forceps. This gentle extraction method maintains cellular integrity and minimizes artifact, which is crucial for accurate histopathological diagnosis, immunohistochemistry, and molecular testing. For pathologists, receiving a well-preserved specimen means clearer margins, better cellular detail, and more reliable interpretation, ultimately leading to a more confident diagnosis for the patient.

Limitations and Future Directions

While cryobiopsy offers significant advantages, it is important to acknowledge potential limitations. The procedure requires specialized equipment and training, which may not be universally available. There is also a learning curve associated with mastering the technique to optimize specimen retrieval and minimize complications. Although studies generally report a favorable safety profile, potential risks such as bleeding or pneumothorax, while comparable to conventional biopsy, still exist and require careful management. Future research will likely focus on further refining cryobiopsy techniques, exploring its application in new diagnostic scenarios, and conducting cost-effectiveness analyses to support its broader adoption in clinical practice. Continued innovation in bronchoscopic technology will undoubtedly aim to further enhance diagnostic capabilities for pulmonary lesions.

CLINICAL IMPLICATIONS

The consistent evidence from trials like FROSTBITE-2 and other observational studies points towards a clear advantage for cryoprobe technology in transbronchial biopsy. For clinicians, this means a higher likelihood of obtaining a definitive diagnosis from the initial procedure, potentially reducing patient discomfort from repeat biopsies and accelerating the time to treatment initiation. The improved specimen quality, free from crush artifact, will undoubtedly be welcomed by pathologists, allowing for more confident and precise diagnoses, especially in complex cases where subtle cellular features are critical.

From an industry perspective, the adoption of cryoprobe technology represents a significant shift in the market for bronchoscopic biopsy tools. Manufacturers of conventional forceps may see a decline in demand as healthcare systems invest in cryoprobe systems. This could also drive innovation in cryoprobe design, focusing on miniaturization, ease of use, and integration with existing bronchoscopy platforms. Training programs for pulmonologists and interventional radiologists will need to adapt to incorporate the specific techniques and safety considerations associated with cryobiopsy.

For patients, the implications are substantial. A higher diagnostic yield translates to fewer invasive procedures, less anxiety, and a quicker path to appropriate therapy. In an era where early diagnosis is paramount for conditions like lung cancer, any technology that improves the efficiency and accuracy of tissue acquisition is a net positive. While the initial investment in cryoprobe equipment may be higher, the long-term benefits of reduced repeat procedures and improved patient outcomes could justify the cost, making it a valuable addition to the diagnostic armamentarium.

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