

Transbronchial lung cryobiopsy (TBLC) for diagnosis of interstitial lung diseases (ILD)

COLDICE study results and latest CHEST guidelines

Background

The gold standard for diagnosis and classification of ILD includes HRCT (high resolution chest tomography) and a multidisciplinary diagnosis (MDD), a decision-making process involving clinicians, radiologists and pathologists¹. But in up to 30–40% of cases, definite diagnosis specifying the ILD is not possible by this strategy alone and thus, histological findings are required².

Challenges and goals

Surgical lung biopsy (SLB) until now has been the gold standard recommended in different guidelines^{3,4}, but is associated with significant morbidity, with complications including postoperative pneumothorax, pneumonia and respiratory failure, as well as significant mortality, indicated at 1.7%⁵. Given these risks and the often detrimental state of suspected ILD patients, reported SLB rates in ILD are lower than estimated necessary and in 2016 reached only 8% in Europe⁶.

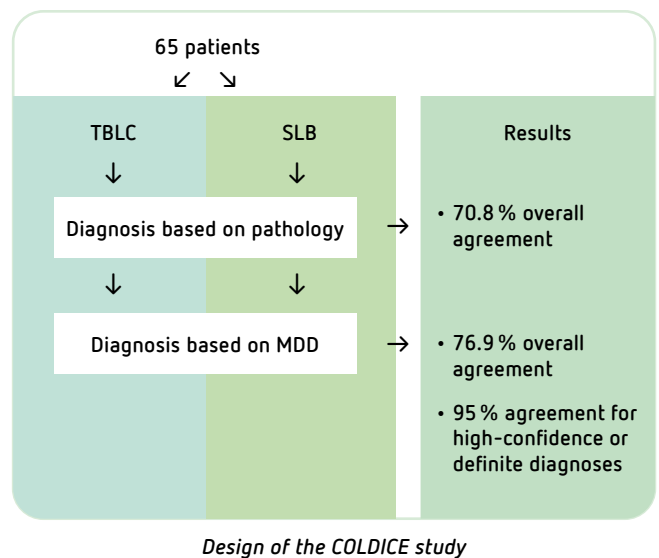
Consequently, transbronchial lung cryobiopsy (TBLC), a minimal invasive technique allowing biopsy without major surgery, is increasingly used in diagnosis of ILD⁹.

The **COLDICE study** (Cryobiopsy versus Open Lung biopsy in the Diagnosis of Interstitial lung disease) has addressed both approaches⁷.

Method

In this comparative, multicenter, prospective, investigator-initiated study, diagnostic accuracy of TBLC and SLB was compared in 65 patients, using biopsy specimens obtained sequentially from the **same patient** under **one** anesthesia.

For TBLC, 1.9 mm or 2.4 mm reusable cryoprobes (Erbe Elektromedizin, Tübingen, Germany) were used and 4 to 7 biopsy specimens were obtained from each patient. Following TBLC, two SLBs were taken from the equivalent lobes.



Results and key findings

High levels of agreement between TBLC and SLB obtained sequentially from the same patients were shown. The TBLC MDD diagnoses made with high confidence were particularly reliable, showing excellent concordance with SLB MDD diagnoses; in these cases SLB added minimal diagnostic value. For unclassifiable or low confidence TBLC MDD diagnoses, although the agreement with SLB MDD was lower, SLB provided an alternative definite or high confidence diagnosis in only a minority⁷.

This high-quality study revealed that diagnostic yield between TBLC and SLB is comparable in both cases; with histopathological assessment alone and with MDD diagnoses.

These results support the clinical utility of TBLC as a valid first-line minimally-invasive diagnostic tool for patients with ILD deemed to require lung biopsy⁷.

Implications and recommendations

Based on the results of the COLDICE study, minimally-invasive TBLC is therefore recommended for experienced bronchoscopists^{2,7,9,10}.

- ➔ As the first option in patients with ILD requiring lung biopsy
- ➔ Limiting the necessity for surgical lung biopsy to those patients in which cryobiopsy is non-diagnostic.

TBLC specimens provide data that are:

- ➔ Useful and reliable
- ➔ Particularly when high-confidence patterns are reported
- ➔ Associated with a lower mortality rate of 0.2 % compared to 1.7 % associated with VATS^{3,5}

This recommendation has also been integrated in the newest **“CHEST Guideline and Expert panel report” (2019)** on TBLC for the diagnosis of ILD, which suggests that TBLC can be used to obtain histopathological evidence for MDD diagnosis¹². Specifically, Maldonado and colleagues phrase the following recommendations:

1. In patients with suspected ILD, we suggest that TBLC can be used to provide histopathologic findings for multidisciplinary discussion (MDD) diagnosis.
2. In patients with suspected ILD undergoing TBLC, we suggest biopsy of at least two different sites (either different segments in the same lobe or different lobes).
3. In patients with suspected ILD undergoing TBLC, we suggest biopsy with the tip of the cryoprobe located 1 cm from the pleura.
4. In patients with suspected ILD undergoing TBLC, we suggest the use of fluoroscopy (Ungraded Consensus-Based Statement).
5. In patients with suspected ILD undergoing TBLC, we suggest that TBLC be performed with a bronchial blocker either through an endotracheal tube or rigid bronchoscope.
6. In patients with suspected ILD undergoing TBLC, we suggest the use of a small cryoprobe (1.9 mm) rather than a larger cryoprobe (2.4 mm).

Products

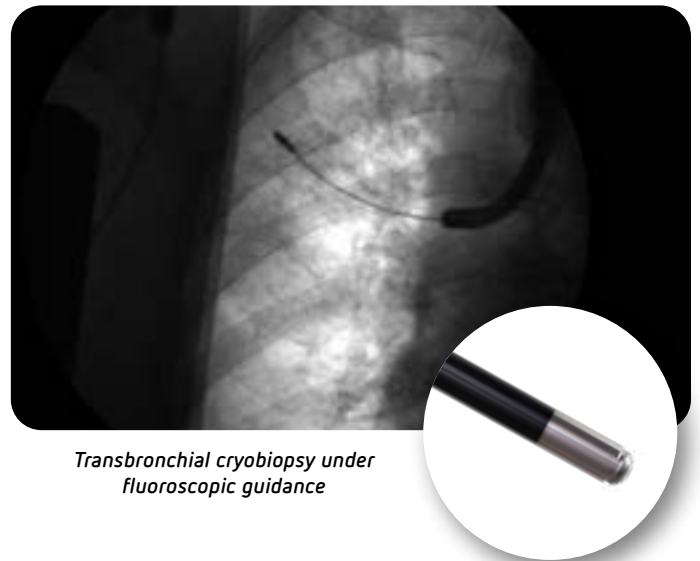
The COLDICE study was performed with the 1.9 mm reusable cryoprobe and the ERBECRYO® 2 system.

Our new portfolio includes three flexible single-use cryoprobes with diameters of 1.1, 1.7 (see pic.) and 2.4 mm. Several advantages are offered by the new portfolio such as enhanced ergonomics and handling characteristics through patented elements^{15,16}.

The consistent technical performance supports

- ➔ Consistent target tissue effects
- ➔ Superior reproducibility
- ➔ Improved standardization^{13,14}

Besides tissue biopsies, our flexible single-use cryoprobes allow further clinical applications. These include tissue devitalization and the extraction of tissue tumors, as well as foreign bodies.



Transbronchial cryobiopsy under fluoroscopic guidance

References

- 1 Travis WD, Costabel U, Hansell DM et al. An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013; 188: 733–748
- 2 Hetzel J, Maldonado F, Ravaglia C et al. Transbronchial Cryobiopsies for the Diagnosis of Diffuse Parenchymal Lung Diseases: Expert Statement from the Cryobiopsy Working Group on Safety and Utility and a Call for Standardization of the Procedure. *Respiration* 2018; 95: 188–200
- 3 Raghu G, Remy-Jardin M, Myers JL et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med* 2018; 198: e44–e68
- 4 Behr J, Günther A, Bonella F et al. S2k-Leitlinie Idiopathische Lungenfibrose – Update zur medikamentösen Therapie 2017. *Pneumologie* 2017; 71: 460–474
- 5 Hutchinson JP, McKeever TM, Fogarty AW et al. Surgical lung biopsy for the diagnosis of interstitial lung disease in England: 1997–2008. *Eur Respir J* 2016; 48: 1453–1461
- 6 Guenther A, Krauss E, Tello S et al. The European IPF registry (eurIPFreg): baseline characteristics and survival of patients with idiopathic pulmonary fibrosis. *Respir Res* 2018; 19: 141
- 7 Troy LK, Grainge C, Corte TJ et al. Diagnostic accuracy of transbronchial lung cryobiopsy for interstitial lung disease diagnosis (COLDICE): a prospective, comparative study. *The Lancet Respiratory Medicine* 2019
- 9 Cavazza A, Colby TV, Dubini A et al. Transbronchial Cryobiopsy in the Diagnosis of Diffuse Lung Disease. *Surg Pathol Clin* 2020; 13: 197–208
- 10 Troy LK. Direct Communication 2019
- 12 Maldonado F, Danoff SK, Wells AU et al. Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Diseases: CHEST Guideline and Expert Panel Report. *Chest* 2019
- 13 Internal measurements D144193
- 14 Internal test report D147320
- 15 Internal measurements D099747
- 16 Usability report D129848
- 17 User acceptance test report D162230