

MEDICAL INSIGHTS

Transbronchial cryobiopsy for sampling of mediastinal lesions¹

Evaluation of transbronchial needle aspiration and the flexible single-use 1.1 mm cryoprobe for sampling of mediastinal lesions

Background

Targeted therapies and immunotherapy are becoming increasingly important for treatment of lung malignancies². The current standard of mediastinal and perihilar lesion sampling is transbronchial needle aspiration (TBNA)¹. TBNA guided by endobronchial ultrasound (EBUS) delivers cytologic samples only, which may be insufficient when material for histopathologic, genetic or immunologic assessment is needed¹.

For peripheral lung nodules, transbronchial cryobiopsy has already become an accepted diagnostic modality³. Known advantages over forceps biopsy or TBNA include sampling with fewer artifacts and the ability to provide material to perform a sufficient molecular testing^{1,4,6}. To date, few cases of mediastinal lesion sampling have been reported⁵.

Challenges and goals

In their present publication *Transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: a randomised trial*, the working groups from Thoraxklinik Heidelberg, Germany and Third Military Medical University Chongqing, People's Republic of China, assess the safety and efficacy of linear EBUS-guided transbronchial mediastinal cryobiopsy¹.

Method

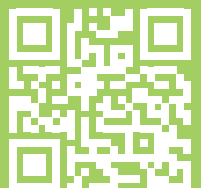
In the prospective comparative dual-center clinical trial, 196 patients with a mediastinal lesion were enrolled. A CT or PET scan was conducted before diagnostic bronchoscopy. Patients were included when at least one mediastinal lesion, other than cyst or abscess, with a minimum length of 1 cm in the short axis was found.

Both, TBNA and transbronchial mediastinal cryobiopsy guided by linear EBUS were conducted in the same patient. Patients were randomised for either TBNA or cryobiopsy to be performed first¹.

For transbronchial mediastinal cryobiopsy, the airway wall adjacent to the lesion was opened with a needle-knife using electro-surgical current. The flexible single-use 1.1 mm cryoprobe was inserted, placed in the lesion and activated for 7 seconds of freezing before extraction.

Diagnostic yield and adverse event rate were the primary endpoints¹.

CRYO.ERBE-MED.COM



Results and key findings

The overall diagnostic yield with transbronchial mediastinal cryobiopsy was significantly higher compared to TBNA (91.8 % vs. 79.9 %; analysis by subgroups see tab. 1). The percentage of samples from NSCLC sufficient for PCR testing for transbronchial mediastinal cryobiopsy was significantly higher compared to TBNA (93.3 % vs. 73.5 %; $p < .001$).

Lymphadenopathy	Diagnostic yield TBNA	Diagnostic yield Cryo	p-value
Common malignancy	94.1%	95.6%	Non-significant
Uncommon malignancy	25.0%	91.7%	Significant
Benign disease	53.2%	80.9%	Significant

For all lymphomas detected, cryobiopsy was able to deliver an accurate subclassification. The likelihood of retrieving a diagnostic cryobiopsy specimen was independent of the lesion size, lymph node station and patient characteristics¹.

Cryobiopsy samples had a mean diameter of 4.6 mm and a mean area of 10.7 mm². Minor bleeding was the most common adverse event, and required no further intervention in all cases. Two patients had a pneumothorax and one patient had a pneumomediastinum. All three patients recovered spontaneously without drainage or any other intervention. The duration of the procedure was longer for cryobiopsy (11.7 vs. 9.4 min; $p < .001$)¹.

Implications

The results of this study demonstrate that transbronchial mediastinal cryobiopsy is a safe procedure with high diagnostic yield¹.

Compared to forceps biopsy, samples of three times the size were harvested¹.

Earlier trials have underlined the importance of sample size and adequacy for molecular target testing with regards to diagnosis and subsequent therapeutic decisions, especially in the subtypes of NSCLC (e.g. PCR, NGS, immunohistochemistry, fluorescence in-situ hybridization)^{1,2,4,6}. In addition, previous studies have also pointed out that larger samples may also help to mitigate the negative effect of necrotic areas within the mass on diagnostic yield (e.g. in SCLC)⁶.

No major complications occurred during the procedure or in the 4-week follow-up period. Due to the study design, the complications cannot be confidently attributed to either of the biopsy techniques, as both of them were conducted in the same patient¹. In this study, the investigators have used a needle knife and electro-surgical current to gain access to the lymphnode¹. Other authors described access through the puncture channel of a TBNA-needle⁸.

Facing high diagnostic yield, good quality for molecular analysis and an independence of the diagnostic yield from patient and lesion characteristics, transbronchial mediastinal cryobiopsy, in the hands of an experienced bronchoscopist, may provide a readily implementable strategy to the current diagnostic process¹.

The authors emphasize, that the benefits of transbronchial mediastinal cryobiopsy justify the longer procedure time compared to TBNA¹.

Products

The flexible single-use 1.1 mm cryoprobe (20402-401) was operated with the ERBECRYO® 2 in this trial. Freezing was activated for 7 seconds before extraction¹. Depending on the clinical setting, freezing times of 3 seconds have also been found to acquire adequate samples⁸. For electrosurgical airway incision the autoCUT-mode of the VIO® 200 D generator was used (Effect 2, 50 W max.)¹. Alternatively, the use of endoCUT® I-mode for incision in the airway using needle knives has been reported (endoCUT® I Effect 1 – Duration 3 – Interval 3), providing fractionated cutting and coagulation⁷.



Flexible cryoprobe for single use, 1.1 mm (20402-401)

References

1. Zhang J, Guo J-R, Huang Z-S, et al. Transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: a randomised trial. *Eur Respir J* 2021; in press (<https://doi.org/10.1183/13993003.00055-2021>).
2. Tone M et al. Comparison of adequacy between transbronchial lung cryobiopsy samples and endobronchial ultrasound-guided transbronchial needle aspiration samples for next-generation sequencing analysis. *Thorac Cancer*. 2021 Jan;12(2):251-258. doi: 10.1111/1759-7714.13770.
3. Simon M et al. Cryobiopsy in Lung Cancer Diagnosis-A Literature Review. *Medicina (Kaunas)*. 2021 Apr 19;57(4):393. doi: 10.3390/medicina57040393.
4. Haentschel M et al. Cryobiopsy increases the EGFR detection rate in non-small cell lung cancer. *Lung Cancer*. 2020 Mar;141:56-63. doi: 10.1016/j.lungcan.2019.12.008.
5. Zhang J et al. Primary Mediastinal Seminoma Achieved by Transbronchial Mediastinal Cryobiopsy. *Respiration*. 2020;99(5):426-430. doi: 10.1159/000505936.
6. Hetzel J et al. Cryobiopsy increases the diagnostic yield of endobronchial biopsy: a multicentre trial. *Eur Respir J*. 2012 Mar;39(3):685-90. doi: 10.1183/09031936.00033011.
7. Amat B et al. The electrosurgical knife in an optimized intermittent cutting mode for the endoscopic treatment of benign web-like tracheobronchial stenosis. *Arch Bronconeumol*. 2012 Jan;48(1):14-21. English, Spanish. doi: 10.1016/j.arbres.2011.07.001.
8. Gonuguntla HK et al. (2021) Endobronchial ultrasound-guided transbronchial cryo-nodal biopsy: a novel approach for mediastinal lymph node sampling. *Respirology Case Reports*, 9(8), e00808. <https://doi.org/10.1002/rcr2.808>