



## Editorial

# The Latest in Endobronchial Ultrasound and Lung Cancer<sup>☆</sup>

## Novedades en ultrasonografía endobronquial y cáncer de pulmón

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Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was introduced in Spain over 12 years ago.<sup>1</sup> Since then, its use has become generalized, and it is now the technique of choice in the hilar and mediastinal nodal staging of lung cancer. More burning issues in recent times include standardization of staging, endoscopic ultrasound guided fine-needle aspiration (EUS-FNA) using the EBUS scope, transvascular access, molecular studies, elastography, and advances in echo-bronchoscopes.

The accuracy of EBUS-TBNA in lung cancer staging depends on the thoroughness of the methodology used, and requires the sampling of lymph node stations 4R, 4L, and 7, at least, if these contain lymph nodes measuring more than 5 mm.<sup>2</sup> When these conditions are met, the rate of false negatives is less than 5%, while more scant sampling results in false negatives in up to 15% of cases.<sup>3</sup> EBUS-TBNA has difficulty reaching some potentially affected regions in the left lymph node stations, and it cannot be used to obtain samples from the para-aortic (6) or subaortic (5) stations in general, and sampling of the hilar and interlobar stations (10 and 11) is occasionally prevented by intervening large vessels. It must be said, however, that situations in which a diagnosis depends on sampling from these sites are extremely rare.

When EBUS-TBNA is combined with EUS-FNA, the diagnostic yield increases by 12% (95% confidence interval: 8%–18%) compared to use of the endobronchial route alone.<sup>4</sup> This increase is attributed mainly to the proportion of suboptimal transbronchial procedures reported in all series. The transesophageal route does not present technical difficulties for pulmonologists, and offers some advantages, such as less interference with ventilation and greater ease of sampling, due to the absence of cartilage. In clinical practice, the systematic sampling of all stations via both routes is unnecessary, and the transesophageal approach can be restricted to stations in which EBUS is less effective (primarily station 4L), and to those

which cannot be accessed by this technique, such as stations 8 and 9.<sup>5</sup> The left adrenal approach is technically possible with the EBUS scope, and has a similar yield to that of the standard EUS (89% vs 93%, respectively).<sup>6</sup>

Only around 50 cases of transvascular biopsy with EBUS-TBNA have been reported in the literature, the vast majority of which were performed via the pulmonary artery or one of its branches. The biopsy technique is not difficult in itself and the diagnostic yield is similar to that of standard procedures.<sup>7,8</sup> The potential risks of passing a needle through a blood vessel are basically laceration of the vessel wall, embolization of the tumor or clots in both the pulmonary and systemic bloodstream, and the release of atheromatous plaques into the bloodstream. However, with the exception of discreet hematomas visualized by ultrasonography at the site of the biopsy, no major complications have been described in the literature. To avoid downplaying the risks, and until more cases and guidelines are available, this technique must be approached with caution: it should be attempted only by bronchoscopists with expertise in the use of EBUS, the patient should be closely evaluated, and information must be shared among specialists. Specific informed consent must be obtained, and intubation and mechanical ventilation, biopsy with a 25G needle, and pathology evaluation in situ or rapid on-site evaluation (ROSE) are all required.

Currently, sampling using EBUS-TBNA needs to provide enough material not only for diagnostic, but also for cell block preparation and molecular marker testing.<sup>9</sup> Consequently, EBUS-TBNA is useful for examining not only epidermal growth factor receptor (EGFR) mutations in the tumor cell,<sup>10</sup> but also a wide range of markers that have demonstrated their value in disease prognosis and prediction of response to adjuvant treatment, areas that are still under investigation.<sup>11</sup>

The latest ultrasound processors have improved the basic functions of B-mode ultrasound imaging, and include advanced endobronchial ultrasound technologies, such as elastography, a function that provides additional diagnostic information on the biomechanical characteristics of a tissue, by measuring the changes in elasticity caused by a mechanical force (compression or shear wave). These changes generate color images that show the relative elasticity or stiffness of the tissue, and can be used to classify lymph

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nodes as benign or malignant<sup>12</sup> (sensitivity: 81%–100%, specificity: 76.9%–92.3%). Elastography can be used in diagnostic procedures and in ultrasound-guided lymph node staging to identify the most suspicious lymph nodes in a specific station and/or circumscribed areas of stiffness within a node as a target for EBUS-guided biopsy.<sup>13</sup> The suspicion and site of nodal metastases can potentially affect clinical decisions by minimizing unnecessary biopsies, thus reducing invasiveness and procedure time, and the risk of false negatives on cytology.

EBUS is still unable to access certain lobar and segmental nodes. A new, thinner EBUS scope (Thin Convex Probe or TCP-EBUS) might improve access to the peripheral bronchi. Preliminary studies evaluating a prototype with a tip measuring 5.9 mm and a larger bending angle (170°) in a porcine model and in human lung ex vivo, found that the equipment could visualize more bifurcations and reach all of the segmental bronchi.<sup>14,15</sup> TCP-EBUS will be able to access the N1 nodes more precisely, and possibly reach intrapulmonary lesions that have been inaccessible to date with standard EBUS.

These new developments in EBUS underline its important contribution to lung cancer diagnosis. This technique may even increase its already high diagnostic yield and the quality of the samples obtained, and its indications may continue to expand.

## References

- Monsó E, Andreo F, Rosell A, Cuellar P, Castellà E, Llatjós M. Utilidad de la ultrasonografía endobronquial con punción-aspiración en tiempo real para la estadificación de la neoplasia broncopulmonar. *Med Clin (Barc)*. 2007;128:481–5.
- García-Olivé I, Monsó E, Andreo F, Sanz J, Castellà E, Llatjós M, et al. Sensitivity of linear endobronchial ultrasonography and guided transbronchial needle aspiration for the identification of nodal metastasis in lung cancer staging. *Ultrasound Med Biol*. 2009;35:1271–7.
- Sanz-Santos J, Andreo F, Castellà E, Llatjós M, de Castro PL, Astudillo J, et al. Representativeness of nodal sampling with endobronchial ultrasonography in non-small-cell lung cancer staging. *Ultrasound Med Biol*. 2012;38:62–8.
- Korevaar DA, Crombag LM, Cohen JF, Spijker R, Bossuyt PM, Annema JT. Added value of combined endobronchial and oesophageal endosonography for mediastinal nodal staging in lung cancer: a systematic review and meta-analysis. *Lancet Respir Med*. 2016;4:960–8.
- Hwangbo B, Lee GK, Lee HS, Lim KY, Lee SH, Kim HY, et al. Transbronchial and transesophageal fine-needle aspiration using an ultrasound bronchoscope in mediastinal staging of potentially operable lung cancer. *Chest*. 2010;138:795–802.
- Crombag LMMJ, Szlubowski A, Stigt JA, Schuurbijs O, Korevaar DA, Bonta PI, et al. EUS-B-FNA vs conventional EUS-FNA for left adrenal gland analysis in lung cancer patients. *Lung Cancer*. 2017;108:38–44.
- Kazakov J, Hegde P, Tahiri M, Thiffault V, Ferraro P, Liberman M. Endobronchial and endoscopic ultrasound-guided transvascular biopsy of mediastinal, hilar, and lung lesions. *Ann Thorac Surg*. 2017;103:951–5.
- Panchabhai TS, Machuzak MS, Sethi S, Vijhani P, Gildea TR, Mehta AC, et al. Endobronchial ultrasound-guided transvascular needle aspiration: a single-center experience. *J Bronchology Interv Pulmonol*. 2015;22:306–11.
- Lourido T, Botana M, Leiro V, Núñez M, Fernández-Villar A. Diagnosis of non-nodal paratracheobronchial lesions by linear endobronchial ultrasound. *Arch Bronconeumol*. 2013;49:337–9.
- Nicholson A, Gonzalez D, Shah P, Pynegar MJ, Deshmukh M, Rice A, et al. Refining the diagnosis and EGFR status of non-small cell lung carcinoma in biopsy and cytologic material, using a panel of mucin staining, TTF-1, cytokeratin 5/6 and P63, and EGFR mutation analysis. *J Thorac Oncol*. 2010;5:436–41.
- Millares L, Serra M, Andreo F, Sanz-Santos J, Montón C, Grimau C, et al. Assessment of methylation status of locoregional lymph nodes in lung cancer using EBUS-NA. *Clin Exp Metastasis*. 2015;32:637–46.
- Andreo F, Centeno CA, Sanz J, Barturen A, Hernández A, Ruiz-Manzano J. Experiencia inicial con elastografía en tiempo real mediante ecobroncoscopia en la evaluación de ganglios linfáticos mediastínicos. *Arch Bronconeumol*. 2015;51:e8–11.
- Dietrich CF, Jenssen C, Herth FJ. Endobronchial ultrasound elastography. *Endosc Ultrasound*. 2016;5:233–8.
- Wada H, Hirohashi K, Nakajima T, Anayama T, Kato T, Grindlay A, et al. Assessment of the new thin convex probe endobronchial ultrasound bronchoscope and the dedicated aspiration needle: a preliminary study in the porcine lung. *J Bronchology Interv Pulmonol*. 2015;22:20–7.
- Patel P, Wada H, Hu HP, Hirohashi K, Kato T, Ujiie H, et al. First evaluation of the new thin convex probe endobronchial ultrasound scope: a human ex vivo lung study. *Ann Thorac Surg*. 2017;103:1158–64.