Editorial

Endobronchial Ultrasound: First Choice for the Mediastinum

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The world's first curved linear array ultrasonic bronchoscope was introduced to the market by Olympus in 2004. The development of the endoscope had started more than 5 years earlier based on a request to Olympus Medical Tokyo to miniaturise existing endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) technology to be applied for diagnosis of lesions within the bronchial system. The appeal was born out of the necessity to improve mediastinal staging results.

Computed tomography (CT) and positron emission tomography (PET) are the most widely used non-invasive means for mediastinal lymph nodes. However, based on their reported specificities, CT and PET findings should be verified by cytohistologic sampling.

The 60-year-old transbronchial needle aspiration (TBNA) technology has proved its efficacy, safety and costeffectiveness particularly in diagnosing and staging lung cancer as well as in diagnosing benign granulomatous disease, but unfortunately the technique was always underused. Mainly safety concerns have been the reason.^{2,3}

The success story of endobronchial ultrasound (EBUS)-TBNA starts in 2003 with a publication in the journal Thorax by Krasnik et al.4 This article gave the first description of the principle of EBUS-TBNA. In the same journal, Herth et al.2 chronicled their study on 502 patients that showed that EBUS-TBNA resulted in 93% diagnostic yield, a sensitivity of 94%, specificity of 100% and accuracy of 94%, with a positive predictive value at 100% and negative predictive value at 11%. A further interesting outcome of the study was that no significant difference between ultrasound diagnosis under local and general anaesthesia was identified.

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With the strong acceptance of EBUS-TBNA as a reliable diagnostic tool for enlarged lymph nodes in patients with non-small cell lung cancer (NSCLC), it soon became clear that EBUS provides the best lymph nodes access.

The technique was also examined against mediastinoscopy. In a study by Ernst et al.5 it was shown that EBUS-TBNA can have a superior yield compared with cervical mediastinoscopy, which leads to the conclusion that mediastinoscopy is not necessarily of additional diagnostic benefit to evaluate negative EBUS-TBNA staged lymph nodes.

A lot of very important work was also done by Nakajima et al.⁶⁻⁹ He and his group have shown strong dedication to evaluate the benefits of EBUS-TBNA samples for immunohistochemical analysis, molecular staging and reported encouraging results with cell cycle related proteins in chemotherapy patients.

In several published meta-analysis, EBUS-TBNA has been shown to have a high-pooled sensitivity of 93% and specificity of 100%. 10-12

Multiple publications have shown that even in patients with lymph nodes <1 cm in diameter (which had been termed N0 by CT criteria), with the use of EBUS-TBNA a large percentage could still be shown to have N2/N3 disease (some despite also being negative on PET-CT). 13,14

Complications such as bleeding or infection are very rare and have only been reported as case reports.

At least it was the work of Annema et al. 15 which also convinced guidelines authorities. In a randomized controlled multicenter trial patient either underwent a surgical staging or an endosonography (combined transesophageal and [EUS-FNA and EBUS-TBNA]) followed by surgical staging in case no nodal metastases were found at endosonography. Thoracotomy with lymph node dissection was performed when there was no evidence of mediastinal tumor spread. The group showed that among patients with (suspected) NSCLC, a staging strategy combining endosonography and surgical staging compared with surgical staging alone



resulted in a greater sensitivity for mediastinal nodal metastases and fewer unnecessary thoracotomies.

All the work changed at the end of our daily doing. The recent published guideline of the American College of Chest Physicians (ACCP) is clearly pointed now. In the article by Silvestri *et al.*, ¹⁶ the ACCP recommends "In patients with high suspicion of N2 and 3 involvement, either by discrete mediastinal lymph node enlargement or PET uptake (and no distant metastases), a needle technique (EBUS-needle aspiration [NA], EUS-NA or combined EBUS/EUS-NA) is recommended over surgical staging as a best first test (Grade 1b)."

After 10 years and a lot of scientific work from several groups, a small scope becomes the state of the art.

REFERENCES

- Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013; 143: e142S-65.
- 2. Herth FJ, Eberhardt R, Vilmann P, et al. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. *Thorax* 2006; 61: 795-8.
- Holty JE, Kuschner WG, Gould MK. Accuracy of transbronchial needle aspiration for mediastinal staging of non-small cell lung cancer: A meta-analysis. *Thorax* 2005; 60: 949-55.
- Krasnik M, Vilmann P, Larsen SS, et al. Preliminary experience with a new method of endoscopic transbronchial real time ultrasound guided biopsy for diagnosis of mediastinal and hilar lesions. Thorax 2003; 58: 1083-6.
- Ernst A, Anantham D, Eberhardt R, et al. Diagnosis of mediastinal adenopathy-real-time endobronchial ultrasound guided needle aspiration versus mediastinoscopy. J Thorac Oncol 2008; 3: 577-82.
- 6. Nakajima T, Anayama T, Shingyoji M, *et al*. Vascular image patterns of lymph nodes for the prediction of metastatic disease

- during EBUS-TBNA for mediastinal staging of lung cancer. *J Thorac Oncol* 2012; 7: 1009-14.
- Nakajima T, Yasufuku K, Suzuki M, et al. Assessment of epidermal growth factor receptor mutation by endobronchial ultrasound-guided transbronchial needle aspiration. Chest 2007; 132: 597-602.
- Sakairi Y, Nakajima T, Yasufuku K, et al. EML4-ALK fusion gene assessment using metastatic lymph node samples obtained by endobronchial ultrasound-guided transbronchial needle aspiration. Clin Cancer Res 2010; 16: 4938-45.
- Mohamed S, Yasufuku K, Nakajima T, et al. Analysis of cell cycle-related proteins in mediastinal lymph nodes of patients with N2-NSCLC obtained by EBUS-TBNA: Relevance to chemotherapy response. *Thorax* 2008; 63: 642-7.
- 10. Cameron SE, Andrade RS, Pambuccian SE. Endobronchial ultrasound-guided transbronchial needle aspiration cytology: A state of the art review. *Cytopathology* 2010; 21: 6-26.
- 11. Adams K, Shah PL, Edmonds L, *et al*. Test performance of endobronchial ultrasound and transbronchial needle aspiration biopsy for mediastinal staging in patients with lung cancer: Systematic review and meta-analysis. *Thorax* 2009; 64: 757-62.
- 12. Gu P, Zhao YZ, Jiang LY, *et al*. Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: A systematic review and meta-analysis. *Eur J Cancer* 2009; 45: 1389-96.
- 13. Herth FJ, Eberhardt R, Krasnik M, *et al*. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically and positron emission tomographynormal mediastinum in patients with lung cancer. *Chest* 2008; 133: 887.01
- Herth FJ, Ernst A, Eberhardt R, et al. Endobronchial ultrasoundguided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum. Eur Respir J 2006; 28: 910-4.
- 15. Annema JT, van Meerbeeck JP, Rintoul RC, *et al*. Mediastinoscopy *vs* endosonography for mediastinal nodal staging of lung cancer: A randomized trial. *JAMA* 2010; 304: 2245-52.
- Silvestri GA, Gonzalez AV, Jantz MA, et al. Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidencebased clinical practice guidelines. Chest 2013; 143: e211S-50.