



## Convex endobronchial ultrasound: same coin, two faces. Challenging biopsy and staging for non-small-cell lung cancer

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### Practice points

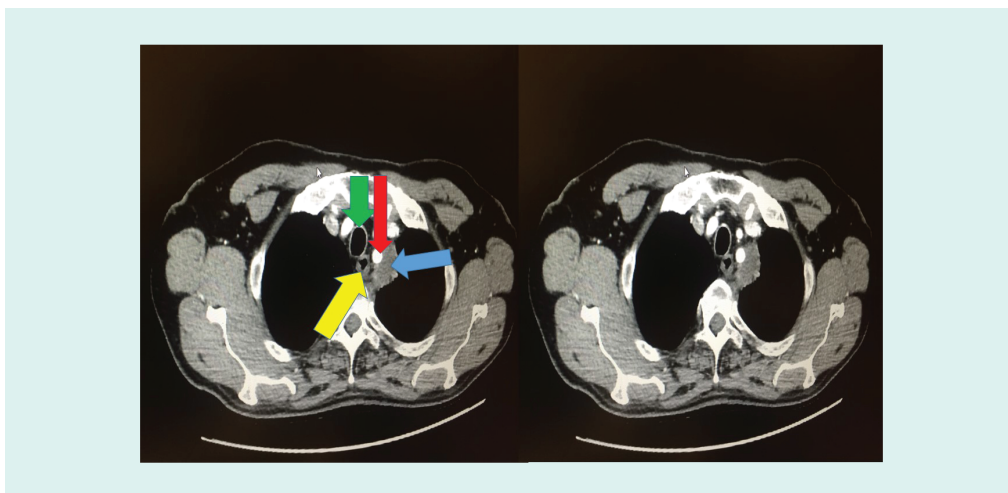
- Transbronchial needle aspiration with endobronchial ultrasounds for paraesophageal masses.
- General anesthesia with intubation makes the access of the esophagus very easy.
- General anesthesia with jet-ventilation makes the diagnostic process easier and safer for patients with chronic obstructive pulmonary disease.
- There is practically no major difference between the different ultrasound endoscopic equipment.
- Paraesophageal masses are easily accessible with transbronchial needle aspiration with endobronchial ultrasounds.
- It is not always necessary to use general anesthesia in order to obtain tissue sample.

Lung cancer is still diagnosed at a late stage due to lack of early disease symptoms. Despite the development of new diagnostic endoscopic tools, such as radial/convex endobronchial ultrasounds (EBUS) and electromagnetic navigation, most patients are still diagnosed at advanced stage disease. Most of the patients refer to their doctor only if they cough blood or their cough changes character. There are challenging cases in the diagnosis and staging of a patient, such as the one that we will present. We present a case of lung cancer that was diagnosed through a biopsy from the main lesion, with access from the esophagus, through transbronchial needle aspiration with EBUS, under general anesthesia and intubation. Staging with transbronchial needle aspiration with EBUS was also performed at the same session.

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Nowadays, we have novel diagnostic tools for lung cancer with radial/convex endobronchial ultrasounds (EBUS) and electromagnetic navigation [1–3]. The radial probe is used for peripheral lesions while the convex probe is used for central and lymph node staging. Esophageal ultrasound (EUS), on the other hand, is used for the diagnosis of gastrointestinal lesions and lymph node staging of gastrointestinal disease. However, there are cases where the EUS endoscopic technique can be used to obtain a sample within the mediastinum and the convex-EBUS system can be used to obtain sample from paraesophageal lesions. The new convex-EBUS system has a larger working



**Figure 1. Computed tomography scan of the thorax with intravenous contrast administration on the day the endoscopy was performed.** The green arrow indicates the trachea; the yellow arrow indicates the esophagus; the red arrow indicates the vessel; and the blue arrow indicates the mass.



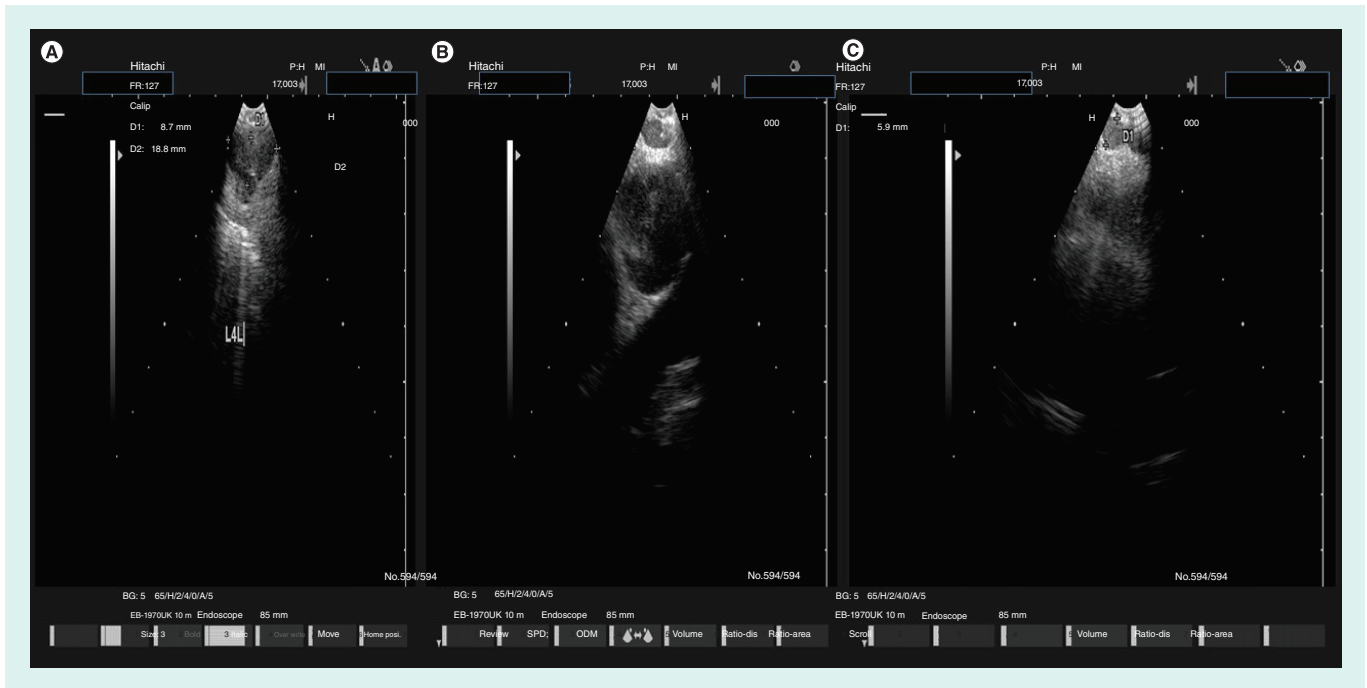
**Figure 2. Positron emission computed tomography scan.** Lymph node stations 10 R, 7 and 10 L are positive and therefore the N status of the disease was 3.

channel and, nowadays, the operator can use a larger, 19G needle without damaging the equipment (working channel). Until now, we used 21 and 22G needles and, by making patents, we used 19G out of the indications of the equipment.

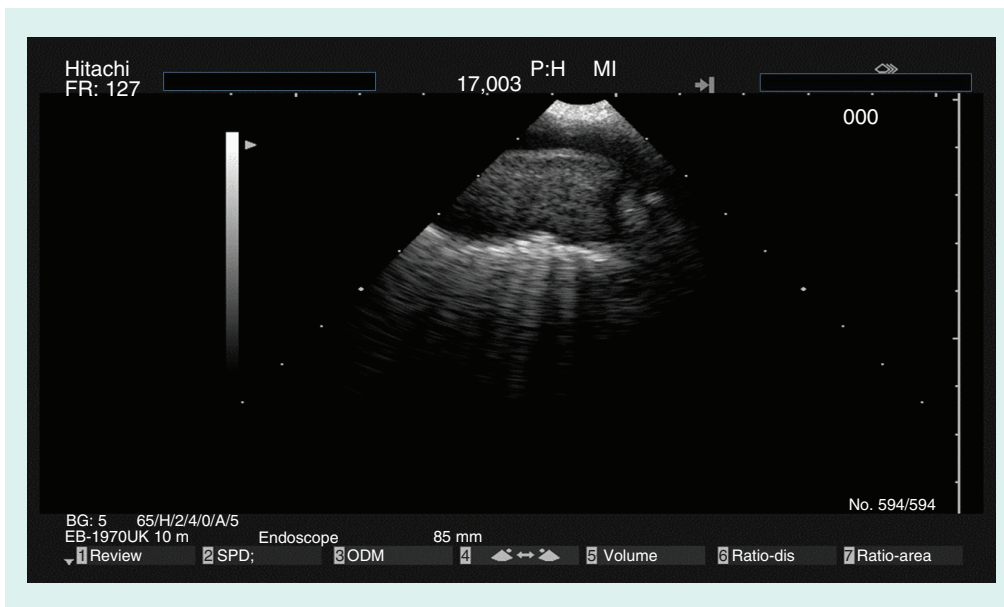
On the other hand, due to the large working channel, the EUS system can use all three diameters: 19, 21 and 22G. We avoid using 19G needle for lesions  $\leq 2$  cm and for stations 4L, 4R, 10L and 10R, due to the high probability of causing severe adverse effects [4]. In order to make better use of the material obtained from the 21 and 22G needle, we make cell blocks, but this is not necessary for the 19G needles, as they obtain larger tissue chunks [5]. Cell blocks can be used to investigate epidermal growth factor expression, anaplastic lymphoma kinase expression, programmed death-ligand, proto-oncogene B-Raf and proto-oncogene tyrosine-protein kinase [6–8]. Convex probe EBUS (CP-EBUS) is used both as a diagnostic tool for thoracic lesions and for non-small-cell lung cancer staging in conjunction with positron emission computed tomography (PET-CT) [9]. There are challenging cases, like the one that we present, where one instrument is used for both diagnosis and staging.

### Case presentation

We present the case of a 50-year-old man referred to our interventional pulmonary department from our oncology department. The patient had a PET-CT scan and a CT scan of the thorax, which revealed a paraesophageal mass and that lymph nodes in the mediastinum were slightly positive  $\geq 3$ SUV (Figures 1 & 2). We intubated the patient and performed staging (stations 2R/L, 4R/L, 7, 10R/L and 11R/L) (Figure 3) and afterward, while the patient was still intubated, we inserted the CP-EBUS (PENTAX EB-1970UK, PENTAX Medical, Tokyo, Japan) through



**Figure 3.** Ultrasound pictures taken during the procedure. We observe with the EUB 6500HV the ultrasound figures/lymph nodes, per station: (A) lymph node 4L, (B) lymph node 7 and (C) lymph node 11L.



**Figure 4.** Paraesophageal mass imaged with the EUB-6500HV.

the esophagus and performed biopsy of the paraesophageal mass with a 22G needle (Figure 4). The patient did not have any intrabronchial lesions (Figure 5).

The patient was diagnosed with lung adenocarcinoma (Figure 6) with an unfortunate N category of N3, but he had *PD-L1* expression of 90% and received pembrolisumab as first-line treatment (Figure 7). We used the following staining protocol for PD-L1 IHC 22C3pharmDx DAKO. After deparaffinization and rehydration, tissue specimens were led in Target Retrieval Procedure with Target Retrieval Solution, Low pH (Code RT100/PT101/PT200,

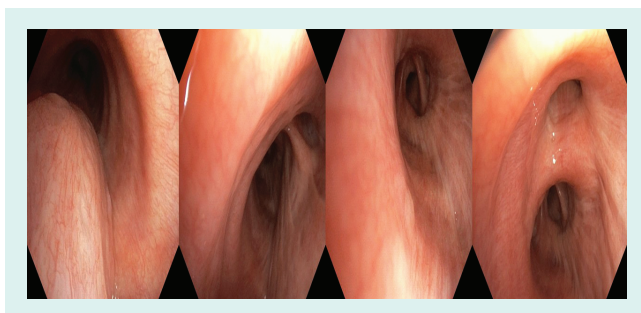


Figure 5. Representative bronchoscopic figures.

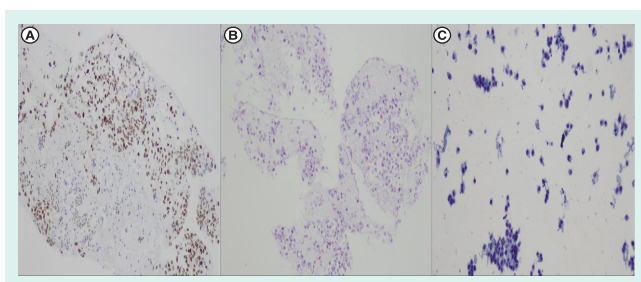


Figure 6. Tumor cells positive for (A) TTF1 x10, (B) cell block x10 and (C) pap smear x10. The cytological specimen was centrifuged and the material was placed in the cytoblock cassette. Additionally, the specimen was smeared onto glass slides. Cytologically, there were cuboidal or columnar malignant cells in low-cohesive aggregates. Single cells were also present. The nuclei were hyperchromatic and enlarged, with increased nuclear/cytoplasmic ratios. The nuclear membranes were well-defined and irregular. Immunohistochemically, the tumor cells were positive for TTF-1 and negative for p40. Based on cytomorphological and immunohistochemical findings, the final diagnosis was that of a lung adenocarcinoma.

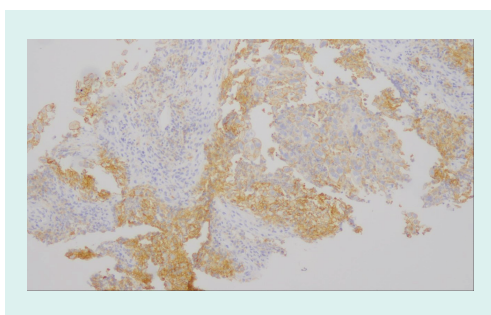


Figure 7. *PD-L1* positive case with whole membranous staining (intense 1+ and 2+) in 90% of neoplastic cells.

Dako, Agilent, CA, USA) for 20 min at 66°C. The Autostainers racks with the specimen's slides were placed on the Autostainer Link 48 (Dako). The instrument performed the staining process by applying the appropriate reagent, monitoring the incubation time and rinsing slides between reagents. The reagents times were preprogrammed in the Dako Link software. Counterstain was performed with Hematoxyline (Link) (CodeK8008) and this was mounted with nonaqueous, permanent media.

## Discussion

The CP-EBUS system can be used for the diagnosis of paraesophageal lesions and has been used on several occasions [10,11]. Based on the expertise of every pulmonary center, this approach is feasible and safe [12]. We used a 22G needle, which is known for its small diameter but is very effective for the diagnosis of several malignancies or benign lesions. Moreover, the material obtained, which is converted to cell block, can be used for the investigation of gene expression and certainly *PD-L1* expression, as in our case [13–15]. The need for proper staging is absolutely necessary and therefore a combination of PET-CT and CP-EBUS is needed in every center for lung cancer health excellence. Currently, there are centers of pulmonary medicine where the CP-EBUS is used to obtain samples from the left adrenal gland, which is again feasible in many patients, with the exception of very tall patients [16]. The EUS, on the other hand, can be used as a diagnostic tool for the mediastinum whenever a lesion can be approached more efficiently and safely [17]. In our case, it was necessary to use the CP-EBUS through the esophagus for biopsy

from the main lesion, since we could not approach it through the trachea. Moreover, we are currently investigating whether the use of EUS is necessary for the staging of mesothelioma [18]. In any case, several instruments can be used for diagnosis despite that not being their original intended purpose, as long as safety is established [19]. Advanced techniques should only be performed in centers of health excellence.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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### Ethical conduct of research

Patient consent was obtained in order to publish all relevant data of the case report.

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