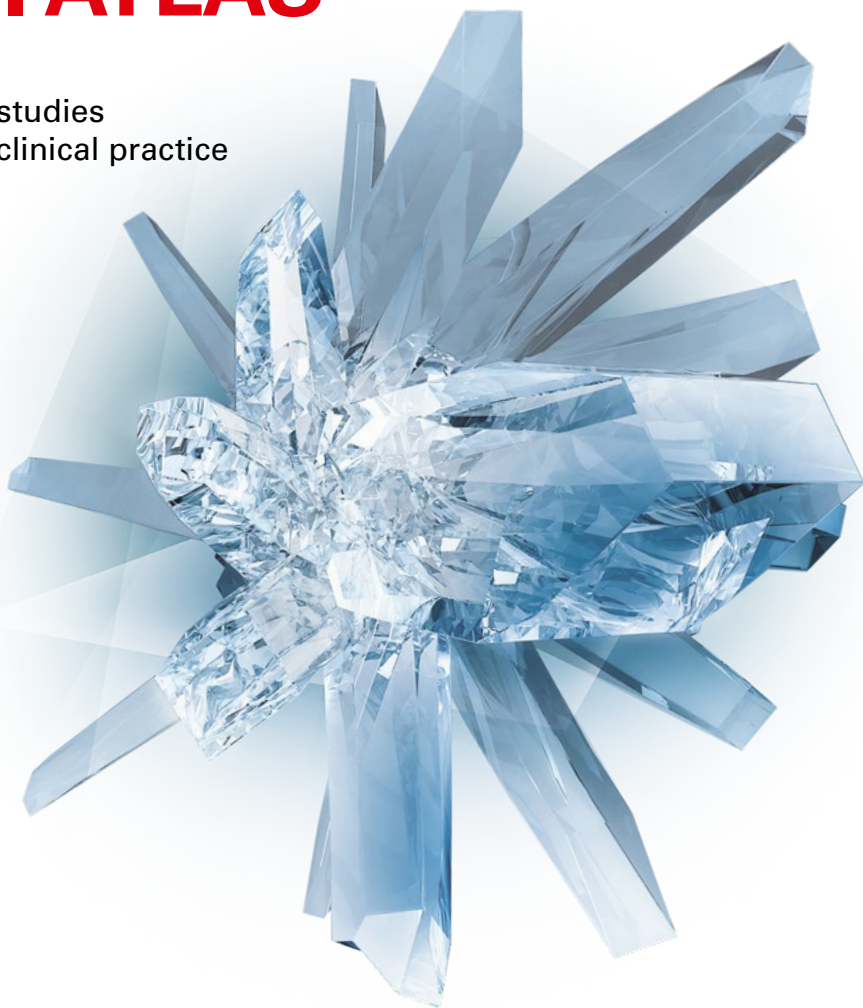
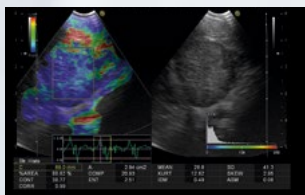


# ENDOBRONCHIAL ULTRASOUND MINI ATLAS

Case studies  
from clinical practice





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## Introduction

# Endobronchial ultrasound: new perspectives

Dear readers,

The key to a successful EBUS procedure is excellent visualization together with sufficient tissue for diagnostic and staging purposes. Almost a decade after the first generation EBUS endoscope was released, PENTAX Medical has accomplished several enhancements to improve diagnostic outcomes. The second generation PENTAX Medical Ultrasound Video Bronchoscope EB19-J10U has an enlarged working channel of 2.2mm, enabling the use of large bore needles so that bigger tissue samples can be taken. Additionally, the actual needle passage through the cartilage rings is facilitated by a steeper needle angulation, allowing sub-centimeter and deeper lying lymph nodes to be sampled more easily. The already superior ultrasound image quality has been further improved to include frequencies of up to 13MHz, enabling high-resolution imaging in the near field. Optimal orientation in the tracheobronchial tree is provided through superior optical image quality. Without a doubt, the PENTAX Medical EB19-J10U EBUS endoscope will be an important piece of equipment for your bronchoscopy practice.

In this mini atlas, several well-documented cases are presented that demonstrate the capabilities of the new PENTAX Medical EBUS endoscope. Diagnostic cases include the diagnosis and staging of lung cancer and the assessment of sarcoidosis and mediastinal lymphoma. In addition, the use of the EBUS scope in the esophagus (EUS-B) is presented. Dedicated and well-renowned endoscopic centers have contributed to this unique selection of cases. Each case follows a similar format, starting with a CT and/or PET-CT scan, followed by the EBUS and EBUS-TBNA procedure and cytopathological outcomes.

A big thank-you to all authors and people involved in the creation of this mini atlas of cases. The following clinical cases show the enhanced capabilities you achieve when using the EB19-J10U and support you in obtaining the best clinical outcomes for your patients.

Kind regards,

Jouke T. Annema, MD PhD  
Professor of Pulmonary Endoscopy  
Amsterdam, The Netherlands





# EBUS in pulmonary practice

EBUS is regarded as the greatest innovation in pulmonary endoscopy, following the invention of flexible bronchoscopy in the late 1960s. Numerous studies have proven the value of EBUS as a diagnostic tool for various common pulmonary diseases. Guidelines advocate EBUS as the initial tissue sampling technique of choice – over mediastinoscopy – for lung cancer staging.<sup>1)</sup> Virtually all mediastinal nodes – with the exception of the aorto pulmonary/aortic nodes – can be reached. Additionally, the hilar nodal stations can be evaluated. In those patients with suspected lung cancer without endobronchial abnormalities – but a centrally located tumor adjacent to the major airways – EBUS-guided TBNA can safely aspirate intra-pulmonary tumors.

EBUS is increasingly used to stage the mediastinum for cases other than lung tumors; for example mediastinal and hilar staging for esophageal cancer, breast, or renal cancer.

EBUS is also the diagnostic technique with the highest rate in granuloma detection in patients with sarcoidosis stage I/II.<sup>2)</sup> Additionally, its safety profile is superior to transbronchial lung biopsies.

The EBUS endoscope is also intended for use in the esophagus. Mediastinal evaluation with the EBUS endoscope (EUS-B) is increasingly used for several reasons. An esophageal examination is generally tolerated better by patients due to the absence of coughing in the examination; and easier tissue sampling due to the lack of cartilage rings. Especially for the evaluation of lymph node stations 4L and 7, EUS-B is an alternative for EBUS. An additional advantage is the access to the lower mediastinum and the left adrenal gland. The addition of EUS-B to EBUS improves the local regional staging of lung cancer and a recent guideline recommends the consideration of EUS-B following EBUS.<sup>3)</sup>

1) Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Silvestri GA et al. Chest. 2013 May;143(5 Suppl):e211S-e250S

2) Endosonography vs. conventional bronchoscopy for the diagnosis of sarcoidosis: the GRANULOMA randomized clinical trial. von Bartheld MB et al. JAMA. 2013 Jun 19;309(23):2457-64

3) Combined endobronchial and oesophageal endosonography for the diagnosis and staging of lung cancer. European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). Vilmann P et al. Eur Respir J. 2015 Jul;46(1):40-60

## **The PENTAX Medical EB19-J10U Ultrasound Video Bronchoscope**

# **Discover new facts of vision**

The PENTAX Medical Ultrasound Video Bronchoscope EB19-J10U is designed to improve diagnostic outcomes. It features crystal clear ultrasound imaging to support diagnostic accuracy, contributes to a smooth facilitation of the EBUS-TBNA, and is ergonomically designed for ease of operation and high working comfort.

### **Crystal clear imaging for precise visualization**

Offers state-of-the-art ultrasound image quality for clear visualization of the airway wall, surrounding lymph nodes, and adjacent structures. It supports orientation and navigation in the airways by the sharpened HD endoscopic view.

### **Reliable tissue acquisition**

The combination of outstanding ultrasound imaging and an enlarged working channel contribute to an accurate and easier real-time ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for the diagnosis and staging of lung diseases through the use of a wide range of needles.

### **Unmatched ergonomic design for ease of operation**

Optimal working comfort for users and high patient tolerance provided by the small ultrasound transducer, the slim endoscope outer diameter, and the unique ergonomics of the control body.





## **Equipment and approach for the EBUS mini atlas case collection**

In combination with Ultrasound systems (ARIETTA V70, HI VISION Preirus and Noblus) and PENTAX Medical video processors (DEFINA EPK-3000 and EPK-i5000), the ultrasound and endoscopic images taken with the EB19-J10U offer crystal clear resolution for precise imaging of the airways. The equipment was used to capture clinical ultrasound and endoscopic images shown in the following cases. For further information about these products, please refer to PENTAX Medical.

The EBUS cases were collected in hospitals across Europe. All cases were documented in the same structure: patient history and differential diagnosis, EBUS findings, cytopathological diagnosis, and patient follow-up.

Our special thanks goes to the editor of this EBUS mini atlas, Prof. Jouke T. Annema of Academic Medical Centre, University of Amsterdam, The Netherlands.

# 1 Suspected lung cancer

## Patient history & differential diagnosis

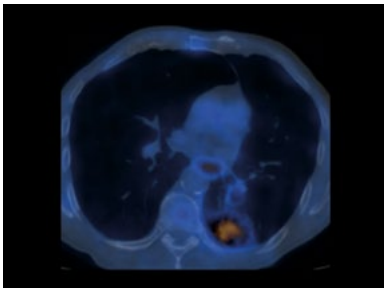
A 76-year-old male, a former construction worker and current smoker (40 pack-years) presented with hemoptysis. The chest CT scan showed a mass in the left lower lobe and an enlarged lymph node station 10L. The PET-CT revealed FGD uptake in the lung mass, LN 10L, and in multiple bone lesions.

Differential diagnosis:

- Pulmonary carcinoma (NSCLC, SCLC)

## EBUS findings

The EBUS confirmed the presence of an enlarged hilar lymph node 10L (short axis 14x12mm) with a round shape and sharp borders with hypo-echoic texture. Real-time Elastography showed a predominantly blue pattern, indicating stiffness of the node suggesting malignant involvement. An EBUS-TBNA of the 10L lymph node was performed.



**Image 1** – FDG avid mass in the LLL and an enlarged LN 10L

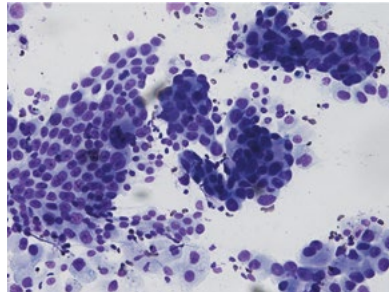


**Image 2** – Enlarged LN 10L 14 x 12 mm

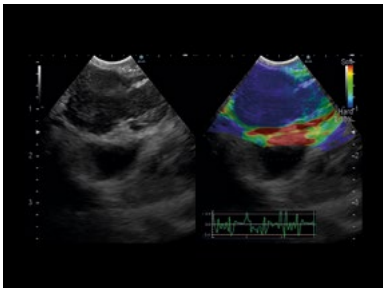
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### Diagnosis & follow-up

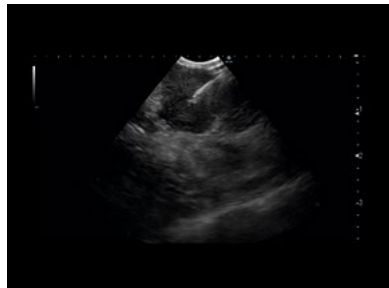
The EBUS-TBNA samples revealed a lymph node metastasis from an adenocarcinoma. Genotyping was performed but no mutations were found in the genes EGRF, KRAS, ALK, and ROS1. In conclusion, this patient with a final diagnosis of pulmonary adenocarcinoma of the left lower lobe (stage IV) was treated with cisplatin and pemetrexed chemotherapy.



**Image 5** – EBUS-TBNA aspirates showing groups of adenocarcinoma cells (papanocolau smear)



**Image 3** – Elastography of LN 10L demonstrating a predominantly blue pattern



**Image 4** – EBUS-TBNA of LN 10L using a 25G COOK needle

# 2

## Lung cancer staging

### Patient history & differential diagnosis

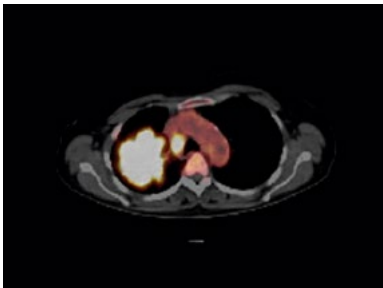
A 60-year-old female, a never smoker, was referred with a cough and hemoptysis. A chest CT scan revealed an 8cm mass in the right upper lobe and a secondary mass in the middle lobe as well as enlarged nodes in the right hilum and paratracheal to the right (station 4R). A PET-CT revealed intense FDG uptake in the RUL mass and lymph nodes, avid lymph nodes 2R, 4R and 7, as well as a single lesion in the pelvis.

Differential diagnosis:

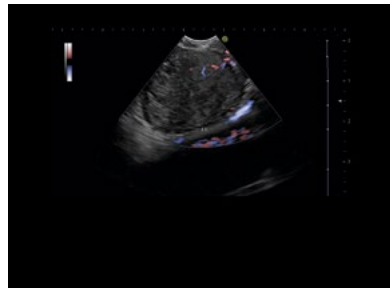
- Pulmonary carcinoma (NSCLC, SCLC)
- Lymphoma
- Pulmonary, lymphogenic, and distant metastasis from extra thoracic tumor (sarcoma)
- Infectious disease (tuberculosis, nocardia, fungi)

### EBUS findings

The EBUS showed a normal appearance of left-sided lymph nodes. It delineated enlarged lymph nodes 2R, 4R, 7 and 10R. FineFlow imaging of LN 4R showed a well vascularized node. Elastography imaging showed a predominantly blue pattern in the right side paratracheal nodes (2R and 4R) suggesting malignant involvement. An EBUS-TBNA was performed.



**Image 1** – PET-CT showing FDG avid mass in the RUL and uptake in LN 4R



**Image 2** – Very well demarcated and vascularized LN 4R with an inhomogeneous echo texture

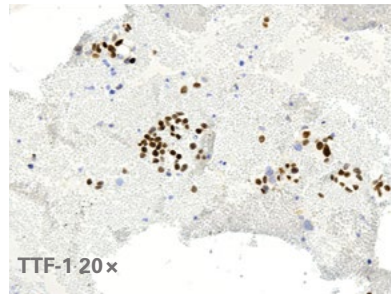
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## Diagnosis & follow-up

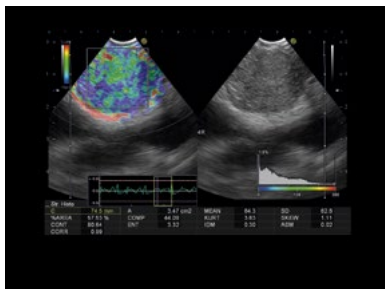
The EBUS-TBNA samples of the 4R showed adenocarcinoma. Molecular analysis on EBUS cytology was performed with the following outcomes:

- EGFR/ROS1/ALK/MET/ERB no abnormalities
- KRAS mutation c.34G>C (p.(Gly12Arg))  
56 % mutant allele

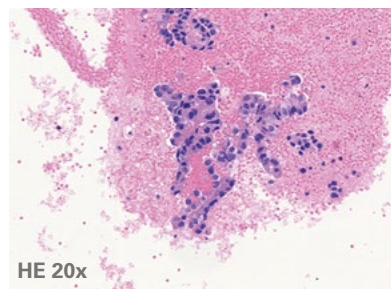
In conclusion, this patient with lung adenocarcinoma of the RLL, cT4N2M1c (bone metastasis pelvis), was treated with cisplatin and pemetrexed.



**Image 5** – TTF1 positive compatible with adenocarcinoma; next generation sequencing showed a KRAS mutation



**Image 3** – Conventional image (right panel) and Elastography image (left panel) of LN 4R demonstrating a mixed but predominantly blue pattern



**Image 4** – Cell block of EBUS-TBNA aspirate demonstrating clearly atypical cells with nuclei of different form and gross chromatine with prominent nucleoli

# 3

## Hilar lymph node relapse

### Patient history & differential diagnosis

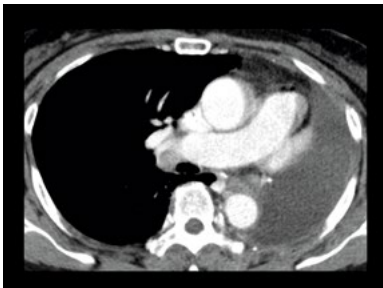
A 45-year-old, non-smoking Chinese male with prior left-sided pneumonectomy (pT4N1Mo, adenocarcinoma) was admitted to the hospital. A chest CT scan performed four months after pneumonectomy showed a new lesion in the right hilum. The patient was referred for an EBUS examination.

Differential diagnosis:

- Recurrence of NSCLC (adenocarcinoma)
- Reactive node post-pneumonectomy

### EBUS findings

The EBUS confirmed the presence of a hilar lymph node 11R (short axis 11mm) which was oval shaped with an inhomogeneous echo texture and sharp borders. Elastography was suggestive of malignant involvement showing a predominantly blue pattern. An EBUS-TBNA of the 11R lymph node was performed.



**Image 1** – Right hilar lesion (11R) and a fluid-filled cavity after left-sided pneumonectomy



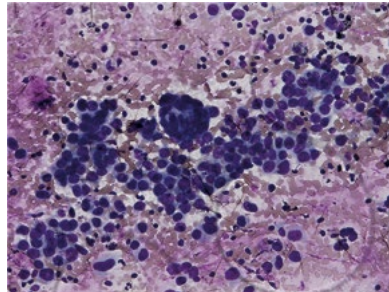
**Image 2** – EBUS showing two sharply demarcated, iso-echoic hilar lymph nodes (11R)



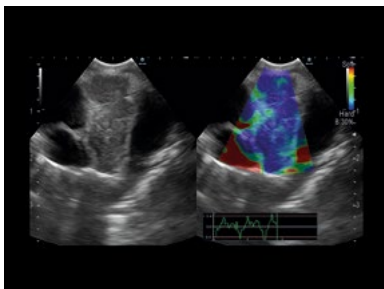
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### **Diagnosis & follow-up**

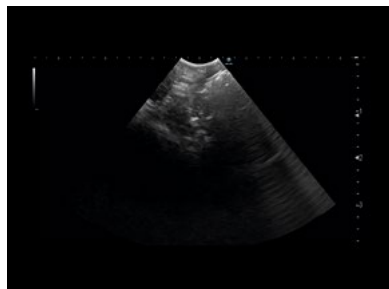
The EBUS-TBNA samples of LN 11R showed an adenocarcinoma with a lymphatic background. Genotyping didn't reveal EGFR or other mutations. This patient unfortunately presented with recurrent adenocarcinoma and started chemotherapy with cisplatin and pemetrexed.



**Image 5** – EBUS-TNA sample showing groups of adenocarcinoma cells



**Image 3** – Elastography image (right panel) of LN 11R demonstrating a predominantly blue pattern



**Image 4** – EBUS-TBNA of LN 11R using a 22G COOK needle

# 4 Small cell lung cancer

## Patient history & differential diagnosis

A 72-year-old female, former smoker (45 pack-years) with weight loss and impaired food passage was referred for analysis of a left upper lobe mass as well as enlarged lymph nodes in the left hilum (station 11L) and the subcarinal region (station 7). The PET-CT showed a FDG avid left upper lobe lesion and the two nodules with compression of the esophagus.

Differential diagnosis:

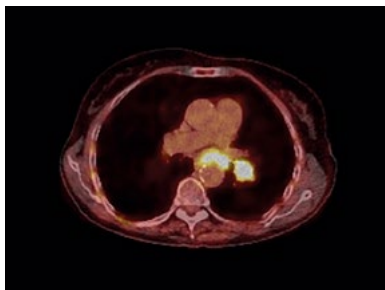
- Pulmonary carcinoma (NSCLC/SCLC)
- Esophageal carcinoma with regional metastases

## EBUS findings

An enlarged hypo-echogenic LN 7 (18 mm) and an enlarged well-demarcated LN 11L (11 mm) were found during the EBUS examination. Elastography of LN 7 clearly distinguished the malignant area from the reactive tissue. EBUS-TBNA was performed.



**Image 1** – CT scan of the chest showing enlarged lymph nodes 7 and 11L

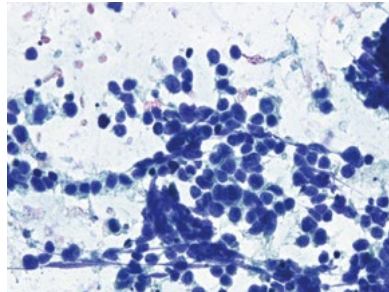


**Image 2** – PET-CT showing FDG uptake in lymph nodes 7 and 11L

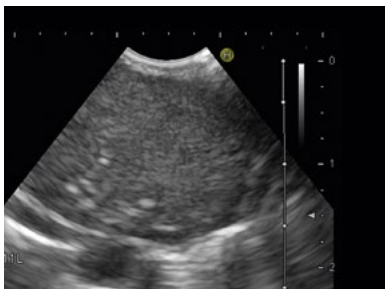
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### Diagnosis & follow-up

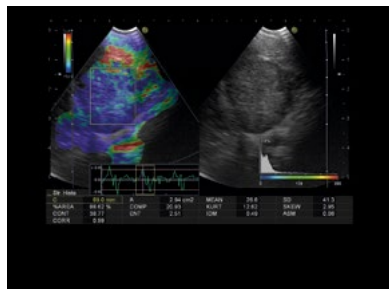
Small cell lung cancer was found in the LN 7 tissue acquired by EBUS-TBNA. Chemotherapy with cisplatin and etoposide was given.



**Image 5** – EBUS-TBNA sample of LN 7 showing malignant cells with molding and a characteristic cytoplasm to nuclei ratio as seen in small cell lung cancer



**Image 3** – LN station 11L showing an isoechogenic texture with intense reflections



**Image 4** – LN station 7 (subcarinal) oval shaped with sharp borders and hypo-echoic texture (right panel). Elastography (left panel) clearly distinguishes the malignant (blue) area from the reactive (red) tissue

# 5 Mediastinal mass

## Patient history & differential diagnosis

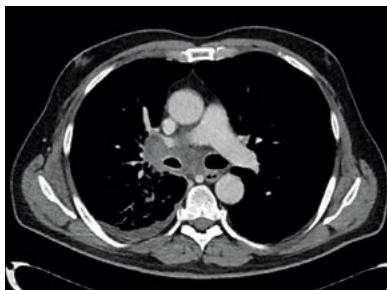
A 61-year-old male, a former smoker (35 pack-years), presented with thoracic pain. His chest CT scan showed a right hilar mass surrounding the hilar vessel and compressing the intermediate bronchus. A post-obstruction pneumonia was found, in addition to multiple enlarged lymph nodes 11R, 10R, 7, 4R, 2R and 2L.

Differential diagnosis:

- Pulmonary carcinoma (NSCLC/SCLC)
- Lymphoma

## EBUS findings

During the bronchoscopy the right main bronchus was compressed without mucosal abnormalities. An EBUS was performed and confirmed the presence of multiple enlarged LN stations 4R, 10R, 7, and 2L. For diagnostic and staging purposes, an EBUS-TBNA was carried out.



**Image 1** – CT showing an enlarged mass in the right hilum compressing and invading the right pulmonary artery and an enlarged subcarinal lymph node

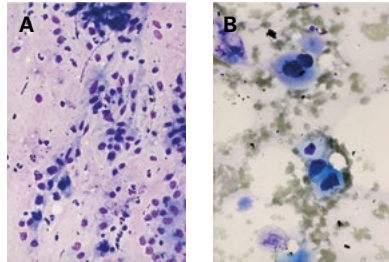


**Image 2** – Well-demarcated, inhomogeneous lesions in the right hilum (station 10R) pressing the pulmonary artery

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### Diagnosis & follow-up

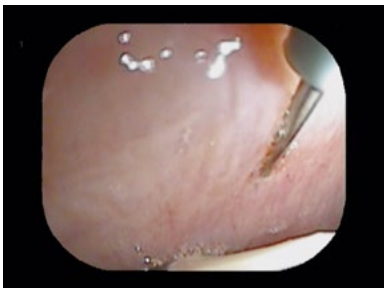
The EBUS-TBNA samples showed a squamous cell carcinoma with a necrotic background. In conclusion, this patient had an extensive stage III squamous cell cancer of the right lower lobe. The treatment advice was chemotherapy consisting of a doublet including platinum.



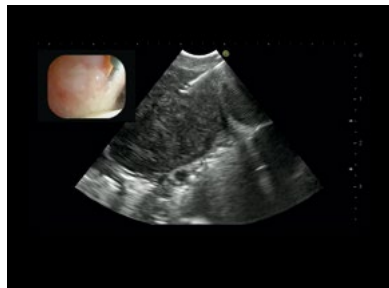
**Image 5 –**

**A** Squamous cell carcinoma  
(Giemsa staining)

**B** Typical bright blue cytoplasm in the  
Giemsa staining



**Image 3 –** Optical image during EBUS-TBNA showing the blue sheath, the needle, and the ultrasound transducer at the bottom right



**Image 4 –** EBUS-TBNA of the right hilar lesion

# 6 Intrapulmonary tumor

## Patient history & differential diagnosis

A 69-year-old male, former smoker (30 pack-years) was referred with severe lower back pain. CT scan of the chest and abdomen showed a centrally located left upper lobe lesion (4.5 cm), and several large lymph node clusters (>5 cm) in the mediastinum and a slightly enlarged LN paratracheal to the left (station 4L) and a lesion in vertebra Th12.

Differential diagnosis:

- Pulmonary carcinoma (NSCLC/SCLC)
- Metastasis of extra thoracic tumor (sarcoma, prostate, etc)

## EBUS findings

EBUS revealed an intrapulmonary left upper lobe tumor visible next to the aorta without signs of invasion (no T4). EBUS-TBNA of LN 4L was performed. EUS-B showed a visible tumor adjacent to the esophagus with no invasion in the aorta. EUS-B-FNA of LN 4L (15mm) was performed.



**Image 1** – Mass in LUL, located adjacent to the mediastinum with a close relation to the aortic arch



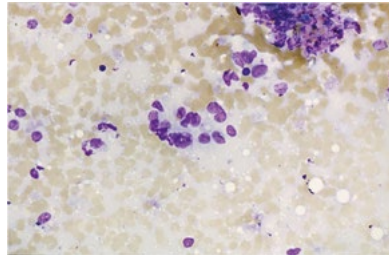
**Image 2** – Mass in the mediastinum adjacent to the ascending aortic arch; borderline sized LN 4L



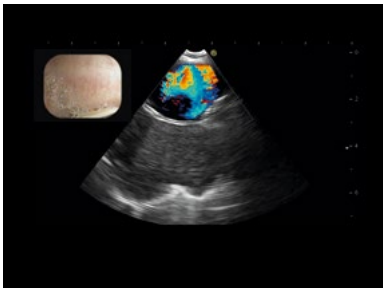
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### Diagnosis & follow-up

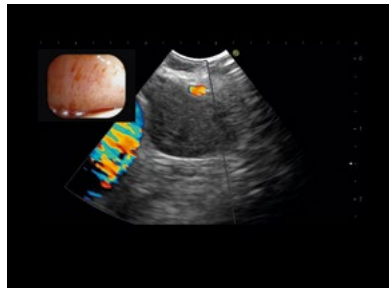
Tissue samples of EBUS-TBNA and EUS-B-FNA demonstrated adenocarcinoma. In conclusion, this patient with cT2-4N2M1 adenocarcinoma stage IV was treated by cisplatin and pemetrexed.



**Image 5** – Aspirate showing adenocarcinoma (giemsa staining) with typical light grey cytoplasm and glandular formation of the cells



**Image 3** – Color Doppler signal (main panel) depicts the aortic arch, LUL tumor showing no signs of tumor invasion; endoscopy image with airway mucosa and ultrasound head (left upper panel)



**Image 4** – Well-demarcated LN 4L, hypoechoic texture with a single vessel, with the pulmonary artery to the left

# 7

## EUS-B and the lower mediastinum

### Patient history & differential diagnosis

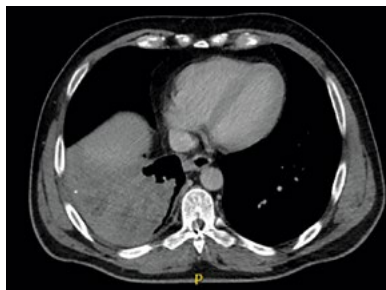
A 58-year-old construction worker, current smoker (90 pack-years) presented to the hospital with a persistent cough. A perihilar mass in the right lower lobe ( $3.8 \times 2.9$  cm) and enlarged lymph nodes 11R, 7, and 2R were found in the chest CT scan. A PET-CT revealed FDG uptake in the right lower lobe mass with signs of a post-obstruction pneumonia. FDG-uptake was also present in lymph nodes 11R, 10R, 7 and 4R.

### EBUS findings

The EBUS imaging showed well-demarcated hypoechoic lymph nodes in stations 4R and 7 (both 15 mm). Following a systematic EBUS investigation and nodal sampling, the EBUS endoscope was introduced in the esophagus for an investigation of the lower mediastinal, subcarinal, and left-sided paratracheal nodes. An oval-shaped, well-demarcated lower paraesophageal lymph node 8 was detected by EUS-B.



**Image 1** – PET-CT showing FDG uptake in mass RLL and lymph nodes 11R and 8



**Image 2** – CT scan showing mass suspected post-obstruction pneumonia and LN 8

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### Diagnosis & follow-up

The EBUS-TBNA and EUS-B-FNA tissue samples showed squamous cell carcinoma with a lymphatic background. The treatment advice for this patient with squamous cell carcinoma, RLL, cT3 N2 Mo was chemotherapy consisting of a doublet including platinum.



**Image 5** – EUS-B of LN 8, para-esophageally located in the lower mediastinum



**Image 3** – Multiple nodes in the subcarinal space adjacent to the left atrium delineated by Color Doppler



**Image 4** – EUS-B of the liver with EBUS scope positioned in the distal esophagus

# 8 Sarcoidosis

## Patient history & differential diagnosis

A 24-year-old male, a non-smoker of African origins, presented with symptoms of an uveitis, fatigue, and non-productive cough. A chest X-ray revealed bilateral hilar and mediastinal lymphadenopathy which were confirmed by a chest CT scan that showed no parenchymal involvement.

Differential diagnosis:

- Sarcoidosis stage 1
- Lymphoma
- Tuberculosis

## EBUS findings

Multiple enlarged, well-demarcated, isoechoic mediastinal and hilar lymph nodes at locations 4L, 5, 6, 7, 11L and 11R were found during EBUS. The EUS-B showed clustered, well-demarcated, isoechogenic lymph nodes 4L, 5, 6, 7 and 8. EBUS-guided TBNA of lymph node stations 4R and 11L was performed.



**Image 1** – Chest X-Ray showing bilateral hilar and mediastinal lymphadenopathy

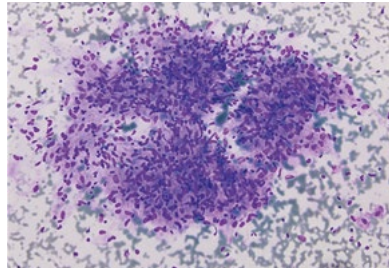


**Image 2** – CT scan of the chest with enlarged lymph nodes 7 and 11L

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### Diagnosis & follow-up

The EBUS-TBNA specimen revealed multiple granulomas with lymphatic background, with no sign of necrosis. In conclusion, this patient with sarcoidosis stage 1 needs to undergo regular intervals for clinical and radiological follow-up. This uveitis was treated with topical steroids.



**Image 5** – Clustered groups of giant cells with atypical-shaped nuclei, typical of granuloma, on a lymphatic background, without necrosis, compatible with the diagnosis sarcoidosis (Giemsa coloring)



**Image 3** – Clustering of isoechoic, well-demarcated lymph nodes around the pulmonary artery (station 11L)



**Image 4** – View of an enlarged LN station 6, located adjacent to the aortic arch (with Color Doppler)

# 9 Hodgkin's lymphoma

## Patient history & differential diagnosis

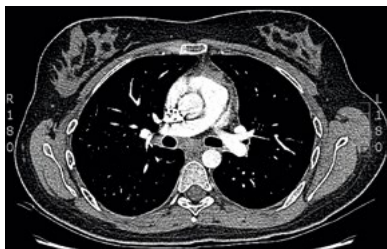
A 23-year-old female student presented with chest pain. Previous medical history revealed a stage 2A sclerosing Hodgkin's lymphoma, for which she received six cycles of ABVD chemotherapy. The CT and PET-CT were suggestive of lymphoma relapse with extensive osseous, nodal, and pulmonary involvement.

Differential diagnosis:

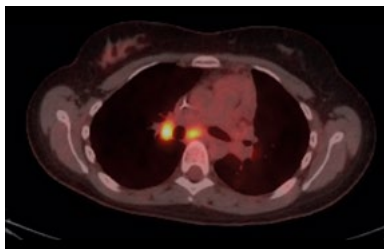
- Recurrence of Hodgkin's lymphoma

## EBUS findings

The EBUS investigation identified diffuse mediastinal and hilar nodal enlargement of lymph nodes stations 11R, 7, 4R and 4L. EBUS-TBNA samples were obtained from station 7 (20mm).



**Image 1** – Chest CT Thorax demonstrating an enlarged subcarinal node



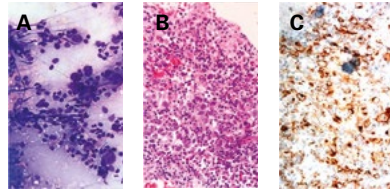
**Image 2** – Integrated PET-CT with FDG avid nodes on location 7 and 11R



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### Diagnosis & follow-up

EBUS-TBNA samples showed Reed-Sternberg cells. In conclusion, this patient with recurrence of sclerosing Hodgkin's lymphoma was referred to the hematologist for chemotherapy treatment.



**Image 5 –**

**A** Rapid Giemsa stain of EBUS-TBNA sample showing many Reed-Sternberg cells with a background of lymphoid cells, histiocytes, and eosinophils

**B** H&E stain of cell block made from the needle rinse of EBUS-TBNA showing many large Reed-Sternberg cells and scattered eosinophils

**C** CD30 stain showing many positive Reed-Sternberg cells



**Image 3 –** LN 11R inhomogeneous texture and with underlying lung and pleura



**Image 4 –** Multiple, clustered subcarinal nodes with an inhomogeneous echo texture and irregular borders

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