# Endobronchial ultrasound EBUS – a new method for the diagnosis and staging of lung cancer

## *Ecobronhoscopia EBUS - o nouă metodă de diagnostic și stadializare a cancerului bronhopulmonar*

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**Abstract**

*In this paper we present a new method, endobronchial ultrasound (EBUS), which appeared recently among the tools of the pulmonologist for the diagnosis and staging of lung cancer. Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) provides the opportunity for obtaining tissue samples required for the histologic and cytologic diagnosis of lung cancer. The advantages of EBUS have to be made popular as it is a minimally invasive method, safe, simple, fast, also with a superior cost/ benefit ratio compared to any previously used methods.*

***Keywords:*** *EBUS, EBUS-TBNA, ROSE*

**Rezumat**

*În lucrarea de față prezentăm o nouă metodă, ecobronhoscopia (EBUS), ce a apărut în arsenalul medicului pneumolog pentru diagnosticul și stadializarea neoplasmului bronhopulmonar (NBP). Puncția transbronșică ecoghidată (EBUS-TBNA) oferă posibilitatea efectuării examinării histopatologice și citologice în NBP. Avantajele EBUS trebuie cunoscute deoarece reprezintă o metodă nouă, minim invazivă, sigură, simplă, rapidă, având de asemenea un raport cost/beneficiu superior oricărei metode folosite anterior.*

***Cuvinte-cheie:*** *EBUS, EBUS-TBNA, ROSE*

## Introduction

Bronchoscopy is a key method in the diagnosis process in pulmonology, and interventional bronchoscopy has rapidly evolved in the last decade worldwide. In our country, these techniques also develop in small steps. Initially, bronchoscopy was limited to the evaluation of the interior aspects of the airways, allowing the diagnosis of endobronchial tumors. The introduction of EBUS (endobronchial ultrasound) enabled the approach of structures adjacent to the airways, i.e. mediastinal tumors and peribronchial lymph nodes. EBUS allows the performing in real-time of mediastinal and hilar puncture of enlarged lymph nodes (Transbronchial needle aspiration-TBNA), thus contributing to tumor diagnosis and staging of lung cancer.

## Lung cancer: a global morbidity and mortality problem

Lung cancer remains one of the major public health problems in the world and one of the main causes of death. Early diagnosis is synonymous with early treatment of lung cancer, a major factor for the final outcome. The five year survival in patients with lung cancer vary according to the stage of the disease, being 61% in stage IA and 1% in stage IV[1]. Correct staging of lung cancer plays an important role in the management of these cases and guides the therapeutic conduct: radical surgery, chemotherapy or radiotherapy. Mediastinal lymph node involvement is present in 26% of newly diagnosed lung cancers and represents one of the major prognostic factors, marking the boundary between stage IIIA and IIIB, ie the boundary between operable and inoperable cases of lung cancer[1].

## The limits of imaging studies in staging of lung cancer and the "classical" staging methods

Computed tomography (CT) and positron emission tomography (PET- CT scan) remain the main imaging methods for diagnosis and staging of lung cancer, but they do not provide histopathological confirmation, mandatory for the choice of treatment. Although the radiological methods of staging are useful in lung cancer, a change is required in the staging methods as CT and PET-CT have a low specificity[2,3]. The limit of 1 cm for suspicious adenopathy proved to be an insufficient criterion for discriminating between the malignant or reactive nature of the lymph nodes enlargement. In other words, patients with primary tumors or patients with N1 invasion on imaging studies or who have unremarkable

lymph nodes on CT or PET examinations may actually have nodal tumor dissemination and are exposed to understaging[3]. Moreover, *The American College of Chest Physicians* (ACCP) and *European Thoracic Society* (ETS) guidelines state the need for preoperative staging by EBUS in these patients[4,5].

Mediastinoscopy and thoracotomy were considered the "gold standard" methods for obtaining tissue samples from the primary tumors or from suspicious mediastinal lymph nodes, allowing the histopathological examination and staging of these cases. These methods have the disadvantage of an invasive approach, which brings a certain degree of risk and also a high level of discomfort to the patients.

## EBUS: the new gold standard in lung cancer staging

EBUS is a minimally invasive method for the diagnosis and staging of patients with lung cancer, introduced in pulmonology practice for more than a decade, and is now available in our country. This technique combines the advantages of bronchoscopy and ultrasound examination for the diagnosis and visualization of peribronchial structures, including vascular structures using the Doppler function. This technique allows real-time TBNA, avoiding vascular elements, and is supported by the rapid on-site cytological examination (ROSE) which allows a quick on-site diagnosis[6].
According to the construction of the ultrasound probe, there are 2 types of EBUS: radial and linear (convex). Both types of endoscopic ultrasonography have a processor and a transducer. The transducer sends and receives ultrasound (US). The processor processes the US and thus creating an US-tissue image.

The radial probe is inserted through the scope's channel, along with a water balloon which allows a 360 degrees image of the structures adjacent to the bronchus around the probe tip. The balloon ensures a good contact with the bronchial wall and improves the transmission of the ultrasound image. The probe allows the visualization of the lesion, then it is withdrawn, keeping in place it's sheath, to allow the insertion of the biopsy clip and broach for tissue sampling[7,8].

The convex, linear probe is incorporated into the scope's tip and allows the collection of tumor tissue in real time. The scope's diameter is 6.9 mm, the working channel is 2 mm and the angle is 30 degrees or 50 degrees. In this technique, the airways are filled with air, which can produce a number of artifacts. In order to overcome this problem, a balloon filled with water is used, allowing a good contact with the bronchial wall and proper environment for ultrasound transmission, "an ultrasound window", that allows viewing of the tumors outside the bronchial wall. The frequency range is 5-20 MHz. A frequency of 7.5 MHz is most commonly used due to a better tissue penetration, but at the cost of a slightly reduced resolution (Fig 1. a-d)[8,9]. A standard bronchoscopy is required to be performed before EBUS, for a complete inspection of the bronchial tree.

EBUS can be performed under local anesthesia with conscious sedation or under general anesthesia (supported with JET ventilation) using a laryngeal mask (LMA) or with a endotracheal intubation tube (ETT). Real-time TBNA is performed. From the material extracted and processed on-site, a number of slides are selected for rapid-staining using the Diff-Quick method. By using ROSE, one can obtain the confirmation of the presence or absence of the tumor cells (Fig 1-e). ROSE can also confirm the nodal location by evaluating the cellularity (a smear showing more than 30% lymphocytes is considered suggestive for lymph node origin of the sampled tissue). By evaluating the cellularity, ROSE is also useful as a control method for obtaining quality tissue samples suitable for performing genetic studies. The specimens obtained can be mounted directly on slides or collected and included in a cell block allowing the supplementary studies, like immunohistochemistry.

During the examination, all mediastinal and hilar lymph node stations can be accessed, allowing the tumor staging, very important in the therapeutic decision of the case.

## The indications of EBUS

- Staging of patients with lung cancer (node stations 2, 3, 4, 7, 11, 12, 13 can be approached and punctured).
- The diagnosis of mediastinal or hilar lymphadenopathy of unknown etiology, visible on CT or PET-CT.
- The diagnosis of mediastinal tumors that have contact with the bronchial wall[7].

Herth et al. have demonstrated in a wide range of patients suspected of mediastinal lymph nodes metastasis of lung cancer, visible on CT scan, that EBUS-TBNA has a sensitivity of 94%, and specificity of 100% and a diagnostic accuracy of 94%[3]. TBNA was carried out in the nodes with an average diameter of 1.6 cm, levels 2L, 2R, 4L, 4R, 10R, 11R, and 11L[9]. Similar results have been obtained by other authors[7,10,11,12].

EBUS-TBNA is also useful in evaluating nodes that are not enlarged on chest CT scan examination. Herth et al. evaluated 100 patients with lung cancer with no lymph nodes enlargement on CT examination. For all patients, a surgical control was performed. EBUS-TBNA had a sensitivity of 92%, specificity of 100% and a negative predictive value of 96%[3,9].

Regarding the costs, EBUS-TBNA is apparently more expensive than conventional TBNA, but the costs are counterbalanced by the reduction of the number of mediastinoscopies required for the diagnosis of patients with lung cancer[12]. A number of studies in the literature consider EBUS-TBNA as the method that has the best cost/benefit ratio[9,12,13]. The sensitivity of this new method is reported to be of 94 to 95.6%, higher than the surgical methods (mediastinoscopy and exploratory thoracotomy)[6,15].

## CONCLUSIONS

EBUS, introduced as a method for the diagnosis and staging of lung cancer in the last decade, is a simple, reproducible, inexpensive technique with an increased cost/benefit ratio.

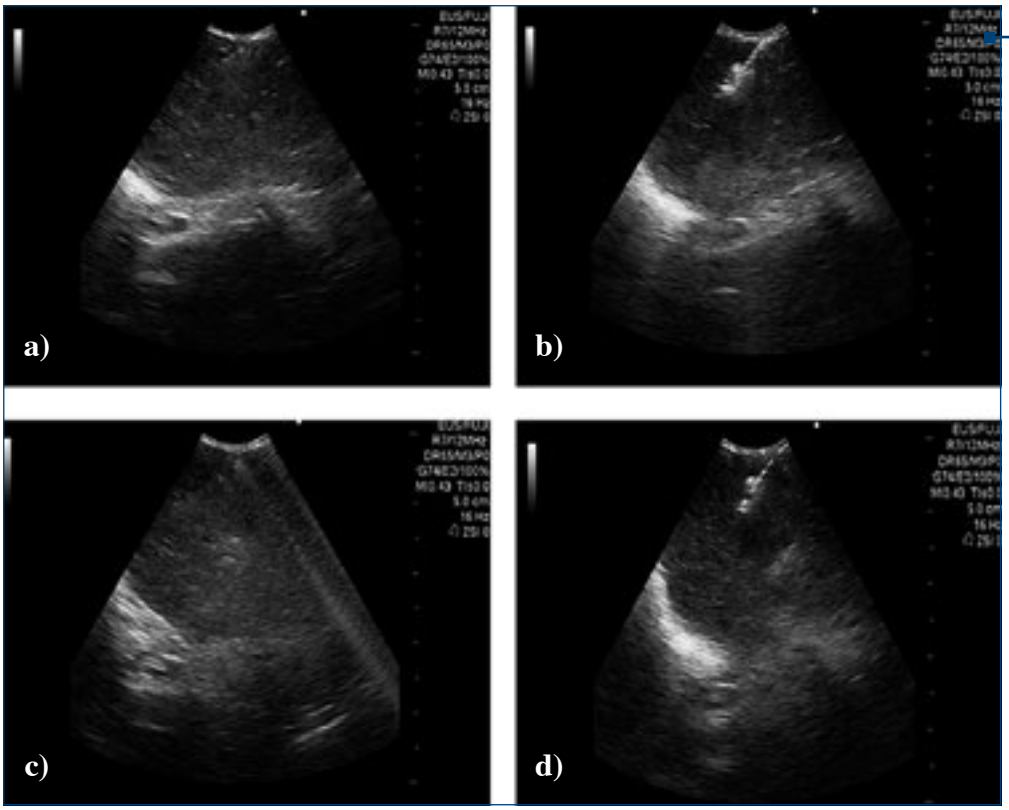
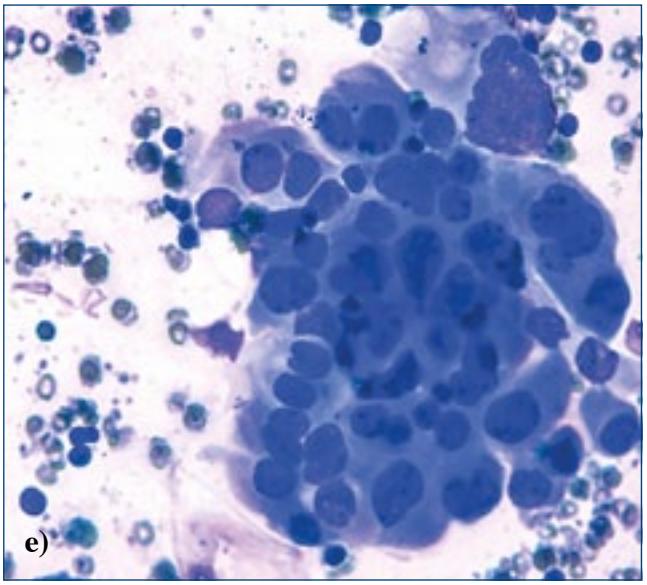



***Figure 1.*** *a), c) EBUS image of suspicious mediastinal lymph node; b), d) Lymph node TBNA performed using EBUS-note the needle inside the lymph node; e) ROSE examination – Diff. Quick stain (40x)- note the malignant cell cluster with irregular nuclei, with prominent nucleoli and the texture of the chromatin. The lymphocytic background confirms the nodal origin of the sampled tissue. The case was confirmed as an adenocarcinoma. (our casuistry).*




The increased yield of EBUS-TBNA diagnosis makes this method the first option to be offered to patients with lung cancer for diagnosis and staging. We believe that the use of EBUS in our country will reshape the current strategy to address patients with mediastinal adenopathies and lung cancer.

Lung cancer being a serious problem for diagnosis, staging and choice of the optimal treatment, there is a need for a multidisciplinary approach of these cases. It should include pulmonologists, bronchologists, oncologists, pathologists, cytologists, thoracic surgeons and anesthetists, in order to ensure a correct diagnosis and an accurate and rapid patients staging. ■

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