

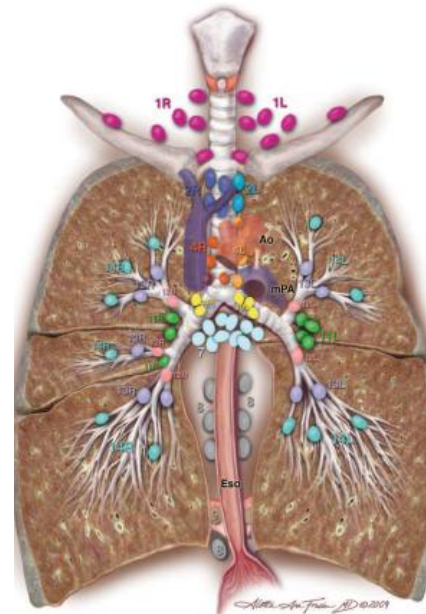
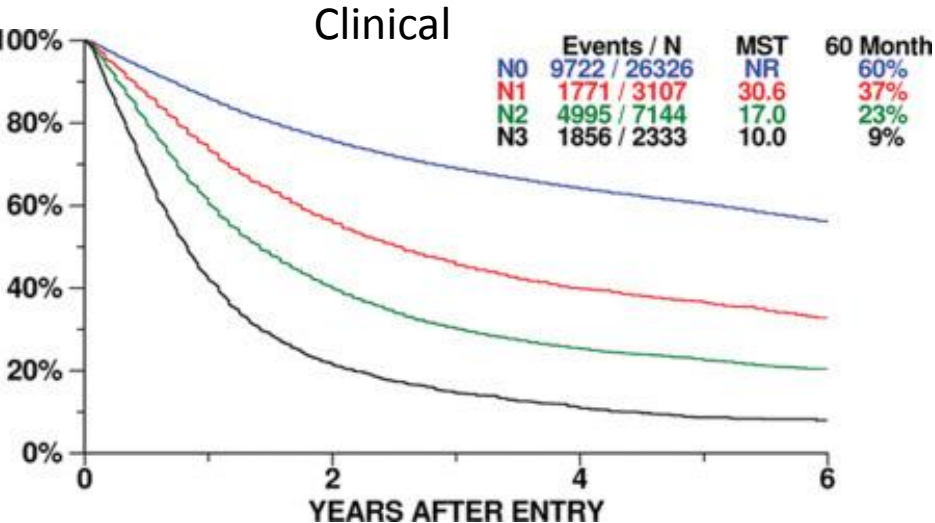
Νεότερα δεδομένα στη διάγνωση, σταδιοποίηση και θεραπεία του καρκίνου πνεύμονα

# Θωρακική υπερηχογραφία (EBUS, b EUS) και σταδιοποίηση του μεσοθωρακίου

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Πανεπιστημίου Θεσσαλίας



# International Association for the Study of Lung Cancer



**Supraclavicular zone**

1 Low cervical, supraclavicular, and sternal notch nodes

## SUPERIOR MEDIASTINAL NODES

**Upper zone**

2R Upper Paratracheal (right)  
 2L Upper Paratracheal (left)  
 3a Prevascular  
 3p Retrotracheal  
 4R Lower Paratracheal (right)  
 4L Lower Paratracheal (left)

## AORTIC NODES

**AP zone**

5 Subaortic  
 6 Para-aortic (ascending aorta or phrenic)

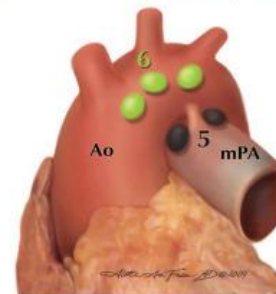
## INFERIOR MEDIASTINAL NODES

**Subcarinal zone**

7 Subcarinal

**Lower zone**

8 Paraesophageal (below carina)  
 9 Pulmonary ligament



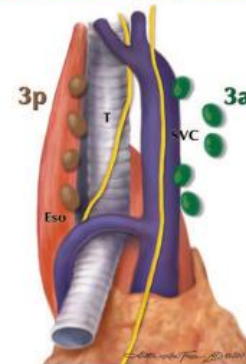
## N1 NODES

**Hilar/Interlobar zone**

10 Hilar  
 11 Interlobar

**Peripheral zone**

12 Lobar  
 13 Segmental  
 14 Subsegmental



# 8<sup>th</sup> edition Lung Cancer Stage Classification

T/M	Label	N0	N1	N2	N3
T1	T1a $\leq 1$	IA1	IIB	IIIA	IIIB
	T1b $>1-2$	IA2	IIB	IIIA	IIIB
	T1c $>2-3$	IA3	IIB	IIIA	IIIB
T2	T2a <i>Cent, Yisc Pl</i>	IB	IIB	IIIA	IIIB
	T2a $>3-4$	IB	IIB	IIIA	IIIB
	T2b $>4-5$	IIA	IIB	IIIA	IIIB
T3	T3 $>5-7$	IIB	IIIA	IIIB	IIIC
	T3 <i>Inv</i>	IIB	IIIA	IIIB	IIIC
	T3 <i>Satell</i>	IIB	IIIA	IIIB	IIIC
T4	T4 $>7$	IIIA	IIIA	IIIB	IIIC
	T4 <i>Inv</i>	IIIA	IIIA	IIIB	IIIC
	T4 <i>Ipsi Nod</i>	IIIA	IIIA	IIIB	IIIC
M1	M1a <i>Contr Nod</i>	IVA	IVA	IVA	IVA
	M1a <i>Pl Dissem</i>	IVA	IVA	IVA	IVA
	M1b <i>Single</i>	IVA	IVA	IVA	IVA
	M1c <i>Multi</i>	IVB	IVB	IVB	IVB

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# 8<sup>th</sup> edition Lung Cancer Stage Classification

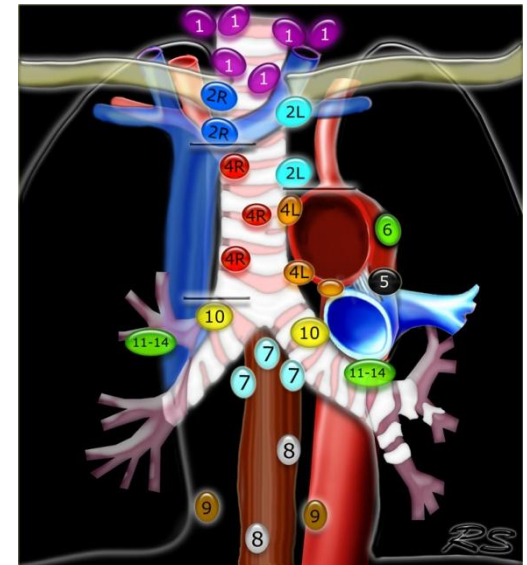
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	M1b <i>Single</i>	IVA	IVA	IVA	IVA
	M1c <i>Multi</i>	IVB	IVB	IVB	IVB

# Types of Staging Assessments

Prefix	Name	Definition
c	Clinical	Before initiation of any treatment, using any and all information available (eg, including mediastinoscopy)
p	Pathologic	After resection, made on the basis of pathologic assessment
y	Restaging	After part or all of the treatment has been given
r	Recurrence	Stage at time of a recurrence
a	Autopsy	Stage as determined by autopsy

# MEDIASTINAL LYMPH NODE STAGING

- Several techniques are available and their use depends on local availability and local expertise
- These techniques include:
  - (i) imaging techniques (CT, PET-CT)
  - (ii) endoscopic techniques (EBUS, EUS, EUB-B)
  - (iii) surgical techniques (mediastinoscopy VATS, thoracotomy)





# Mediastinoscopy vs Endosonography for Mediastinal Nodal Staging of Lung Cancer

A Randomized Trial

ASTER study

241 patients

- enlarged or FDG-avid mediastinal lymph nodes
- enlarged or FDG-avid hilar lymph nodes
- central lung lesion

## **Surgical group**

118 patients (79% sensitivity, 86% NPV)

## **Endosonography group**

123 patients 85% sensitivity –EBUS/EUS

94% sensitivity when followed by surgical staging, 93%NPV

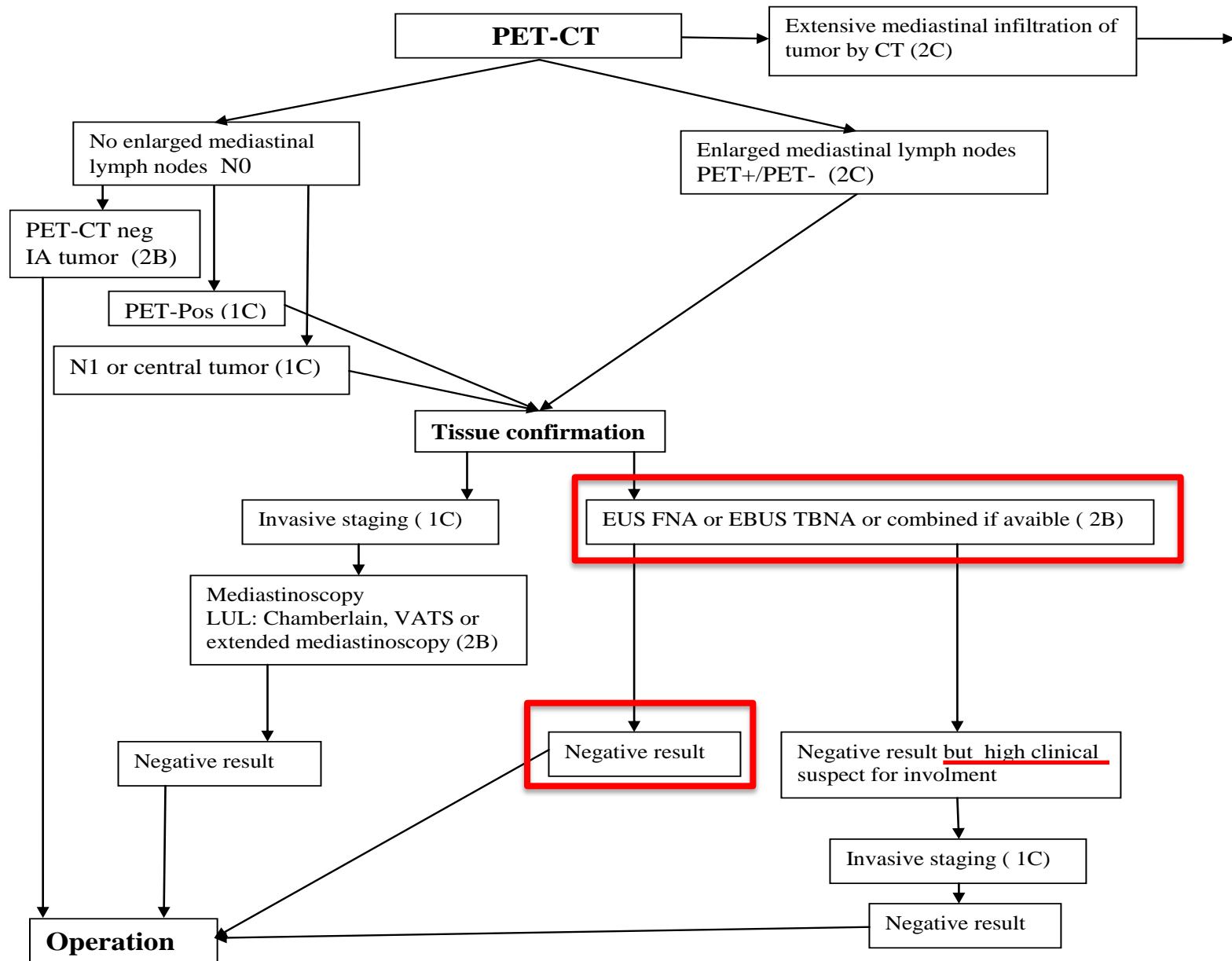
However, to detect one case of single level N2 disease, 11 patients need to undergo additional surgical staging

Endosonography and surgical staging versus immediate surgical staging reduced the percentage of unnecessary thoracotomies from 18% to 7%.

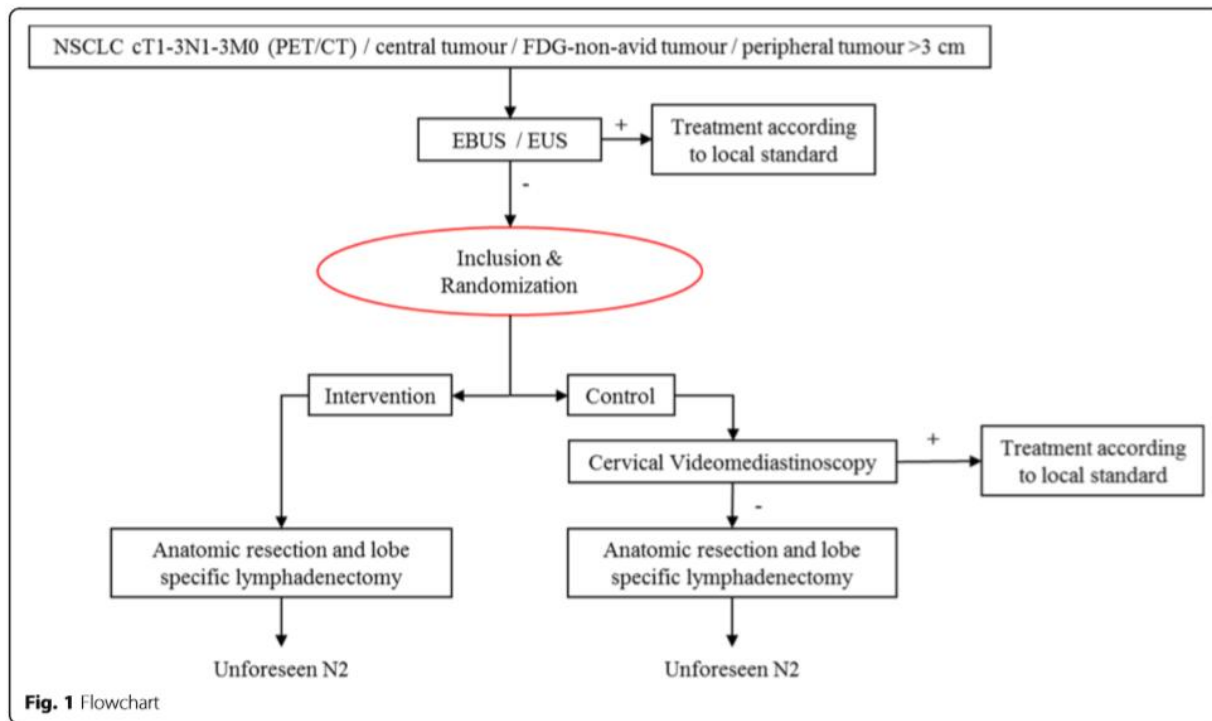
*Annema JT, JAMA 2010*



# Staging of the mediastinum ( no distal metastases)



# Το μέλλον θα (απο)δείξει....



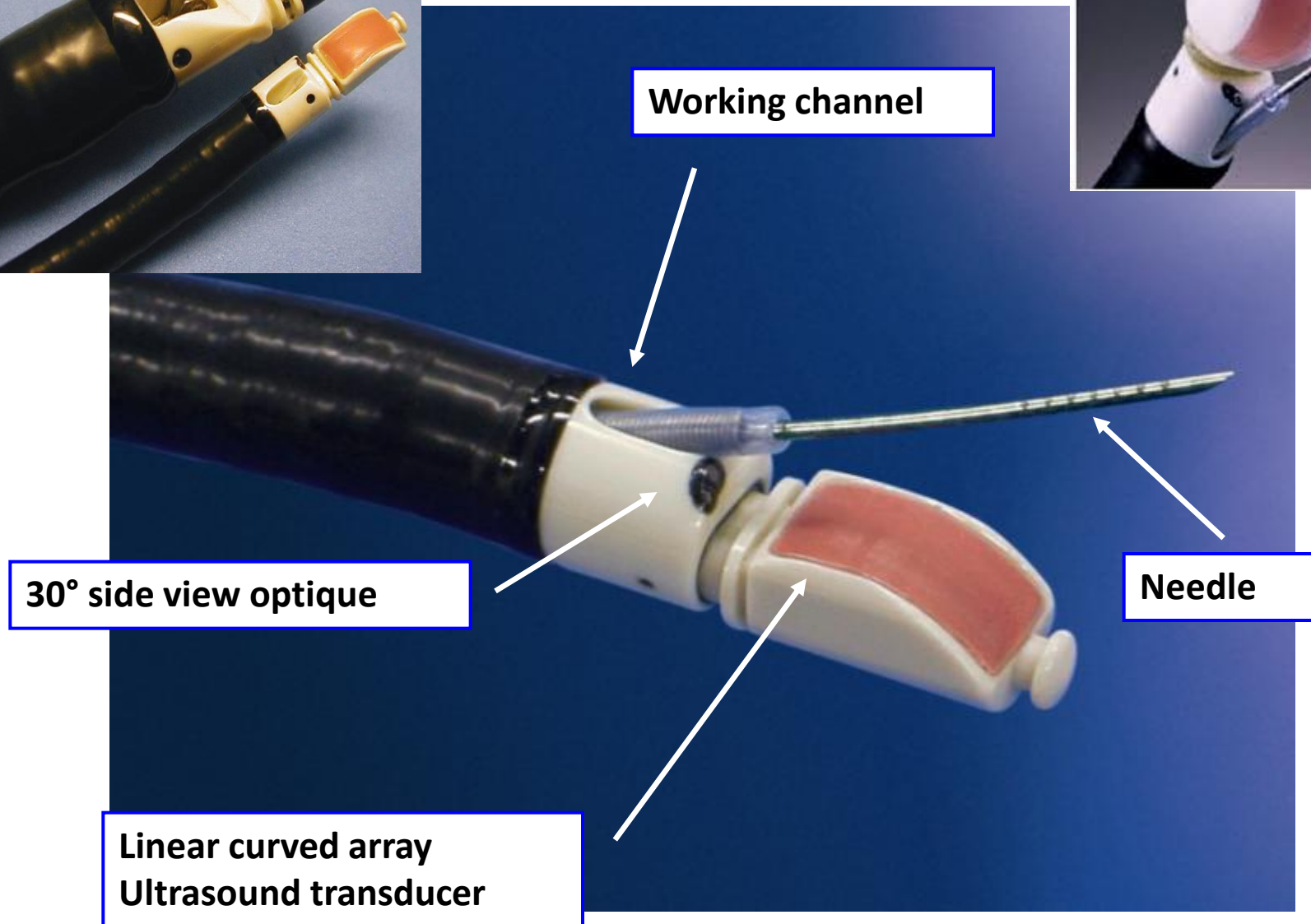
Main objective: to compare the **cost-effectiveness** and **cost-utility of mediastinal staging strategies** including and excluding mediastinoscopy, provided that non-inferiority of excluding mediastinoscopy regarding unforeseen N2 disease can be demonstrated.

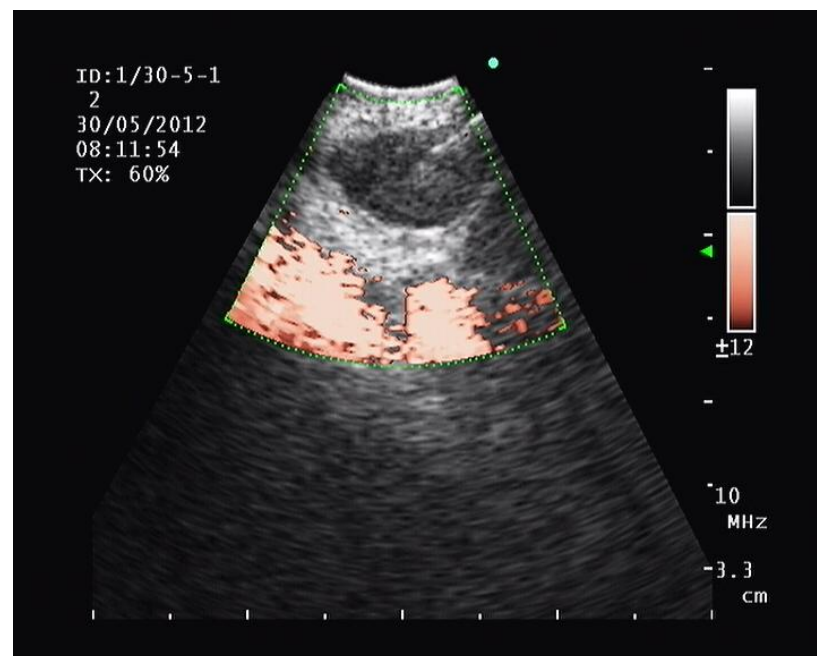
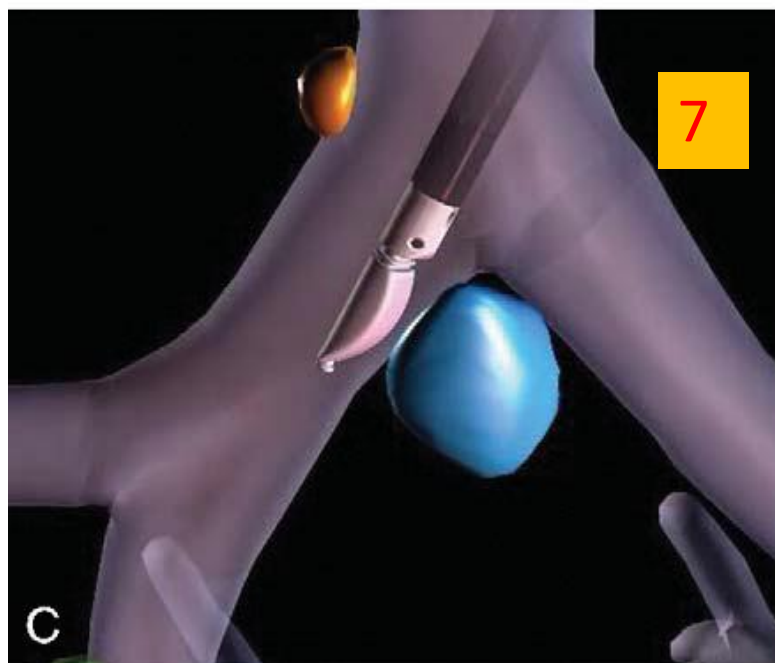


### Methods for Staging Non-small Cell Lung Cancer

Diagnosis and Management of Lung Cancer,  
3rd ed: American College of Chest Physicians  
Evidence-Based Clinical Practice Guidelines

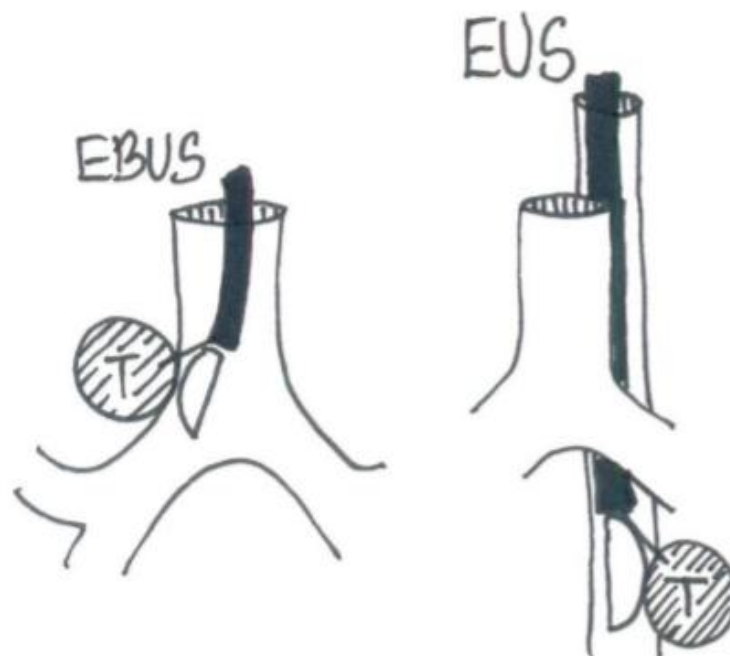
Method	N	Sensitivity (%)	Specificity (%)	NPV
CT	7368	55	81	83
PET-CT	2014	62	90	90
MES	10648	81	100	91
EUS	2756	89	100	86
EBUS	2347	89	100	91
EBUS/EUS	811	91	100	96





# Endosonographic nodal staging

- 1991: EUS-FNA
- 2003: Endobronchial ultrasound (EBUS)
- 2007: Esophageal ultrasound (EUS) with EBUS scope (EUS-B)

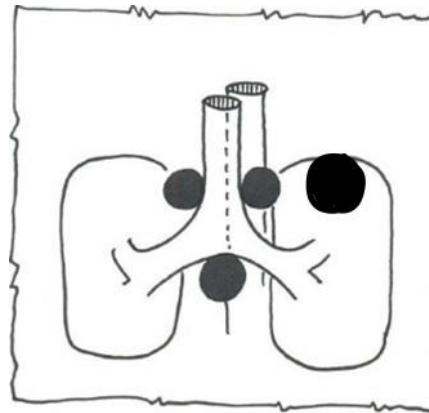


**This combined EBUS scope approach can be performed in one endoscopy session by a single operator which facilitates staging.**

Combined endobronchial and esophageal 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)



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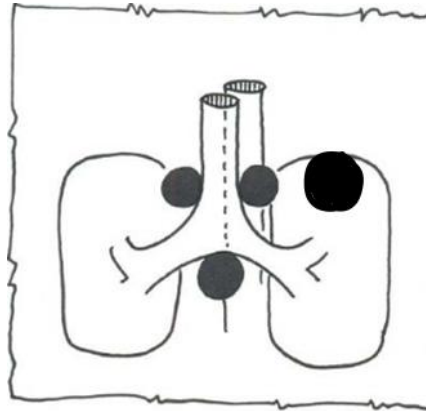
For mediastinal nodal staging in patients with suspected or proven NSCLC with abnormal mediastinal and/or hilar nodes at CT and/or PET, **endosonography** is recommended over surgical staging as the initial procedure (Recommendation grade A).



Combined endobronchial and esophageal 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)

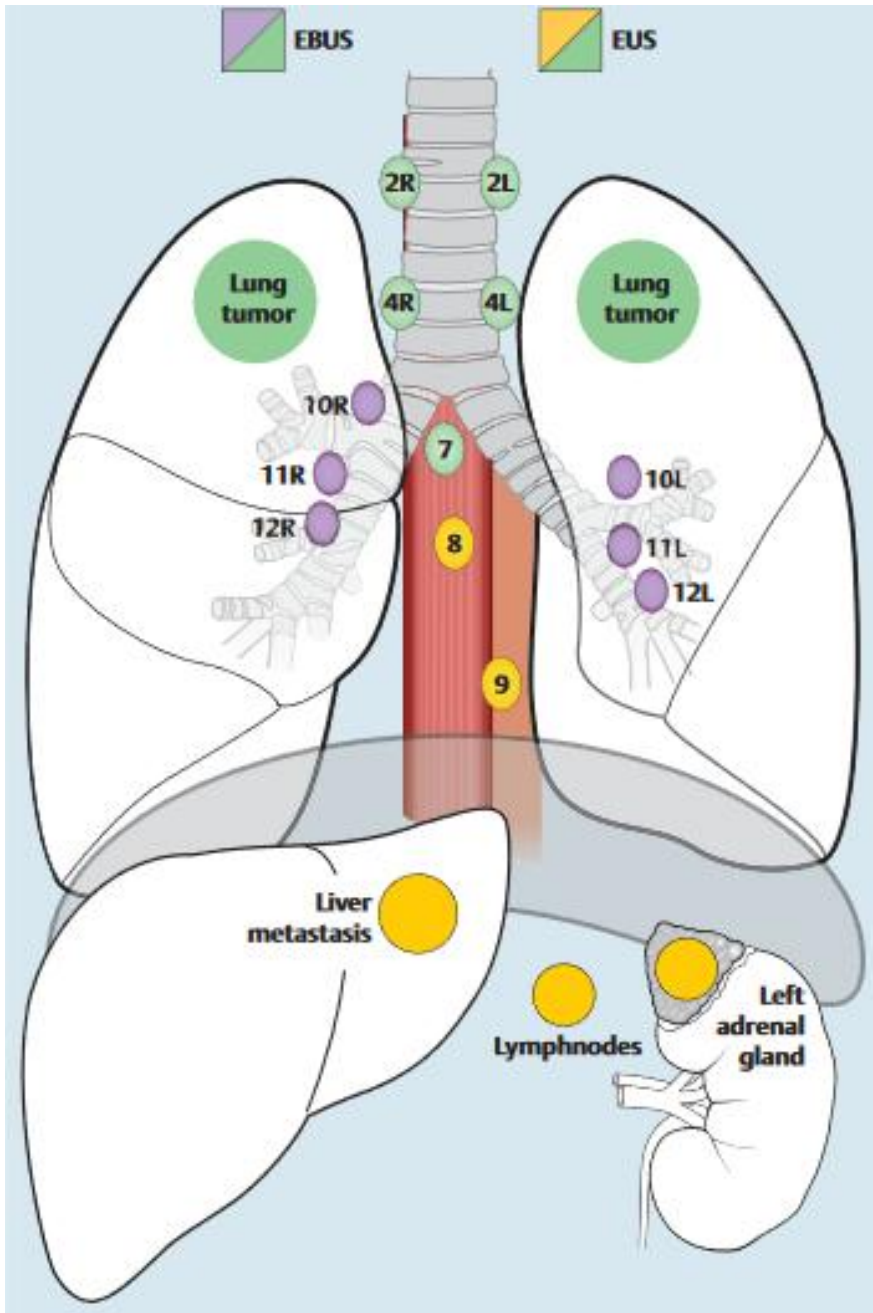


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The **combination of EBUS-TBNA and EUS-FNA or EBUS (EUS-B-FNA)** scope is preferred over either test alone (Recommendation grade C).

If the combination of EBUS and EUS-(B) is not available, we suggest that **EBUS alone** is acceptable (Recommendation grade C).



## EBUS alone:

- 10R, 11R
- 10L, 11L

## EUS alone

- 5, 8, 9, left adrenal

## EBUS/EUS

- 2L, 4L, 7, (2R, 4R)

VATS  
for  
5, 6 LN

# Utility and Safety of Endoscopic Ultrasound With Bronchoscope-Guided Fine-Needle Aspiration in Mediastinal Lymph Node Sampling: Systematic Review and Meta-Analysis

- 10 studies
- 1,080 subjects with mediastinal lymphadenopathy
- The same echobronchoscope

Table 6. Summary Characteristics of EBUS-TBNA and the Combined Procedure (EBUS-TBNA and EUS-B-FNA)

Characteristic	EBUS-TBNA Alone	Combined Procedure
Sensitivity (%)	80.3 (73.7–85.9)	91 (85.8–94.8)
Specificity (%)	100 (98.7–100)	100 (98.7–100)
Positive likelihood ratio	74.9 (18.9–296.8)	88.9 (22.5–351.2)
Negative likelihood ratio	0.21 (0.09–0.49)	0.095 (0.03–0.28)
Diagnostic odds ratio	388.5 (90.9–1659.9)	1323.5 (278.3–6293.6)

All values are pooled values with 95% confidence intervals in parentheses.  
EBUS-TBNA = endobronchial ultrasound-guided transbronchial needle aspiration  
EUS-B-FNA = endoscopic ultrasound with bronchoscope-guided fine-needle aspiration

**The additional diagnostic gain of EUS-B-FNA over EBUS-TBNA was 7.6% in the diagnosis of mediastinal adenopathy.**

**No serious complication of EUS-B-FNA procedure was reported.**

# Utility and Safety of Endoscopic Ultrasound With Bronchoscope-Guided Fine-Needle Aspiration in Mediastinal Lymph Node Sampling: Systematic Review and Meta-Analysis

Table 7. Individual Studies Reporting the Reasons for Performing EUS-B-FNA

First Author	Reasons for Performing EUS-B-FNA
Hwangbo <sup>11</sup>	<u>Inaccessible by EBUS-TBNA</u> , technical difficulty of EBUS-TBNA, intolerance of bronchoscopy due to cough or dyspnea, brain metastasis with mass effect, medical condition precluding bronchoscopy (ischemic heart disease)
Hwangbo <sup>24</sup>	Inaccessible by EBUS-TBNA, well visualized areas by EUS-B-FNA, technical difficulty of EBUS-TBNA
Herth <sup>25</sup>	Inaccessible by EBUS-TBNA
Szulobowski <sup>26</sup>	Inaccessible by EBUS-TBNA, patient comfort
Bugalho <sup>27</sup>	Inaccessible by EBUS-TBNA
Araya <sup>28</sup>	Inaccessible by EBUS-TBNA, poor performance status, poor respiratory condition
Oki <sup>29</sup>	Not reported
Szulubowski <sup>30</sup>	Not reported
Lee <sup>31</sup>	Inaccessible by EBUS-TBNA
Oki <sup>32</sup>	Inaccessible by EBUS-TBNA, technical difficulty of EBUS-TBNA

- LN: 9, 8, 7, 4L, 5
- No cough
- No cartilage to hit during FNA
- Preferred by patients?
- More time for ROSE

# Από ποιους λεμφαδένες θα πάρω υλικό;

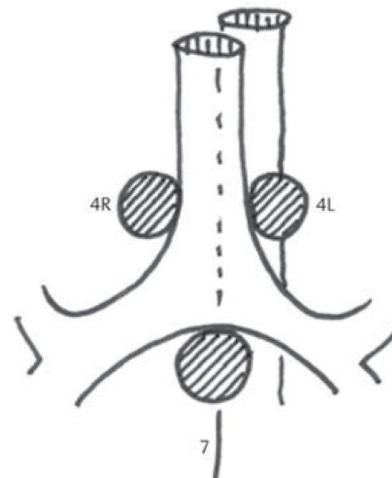
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- complete sampling (all visible lymph nodes)
- systematic sampling (each nodal station)
- selective sampling ('hit-and-run' suspicious nodes only)
- limited or no sampling

Combined endobronchial and esophageal 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)



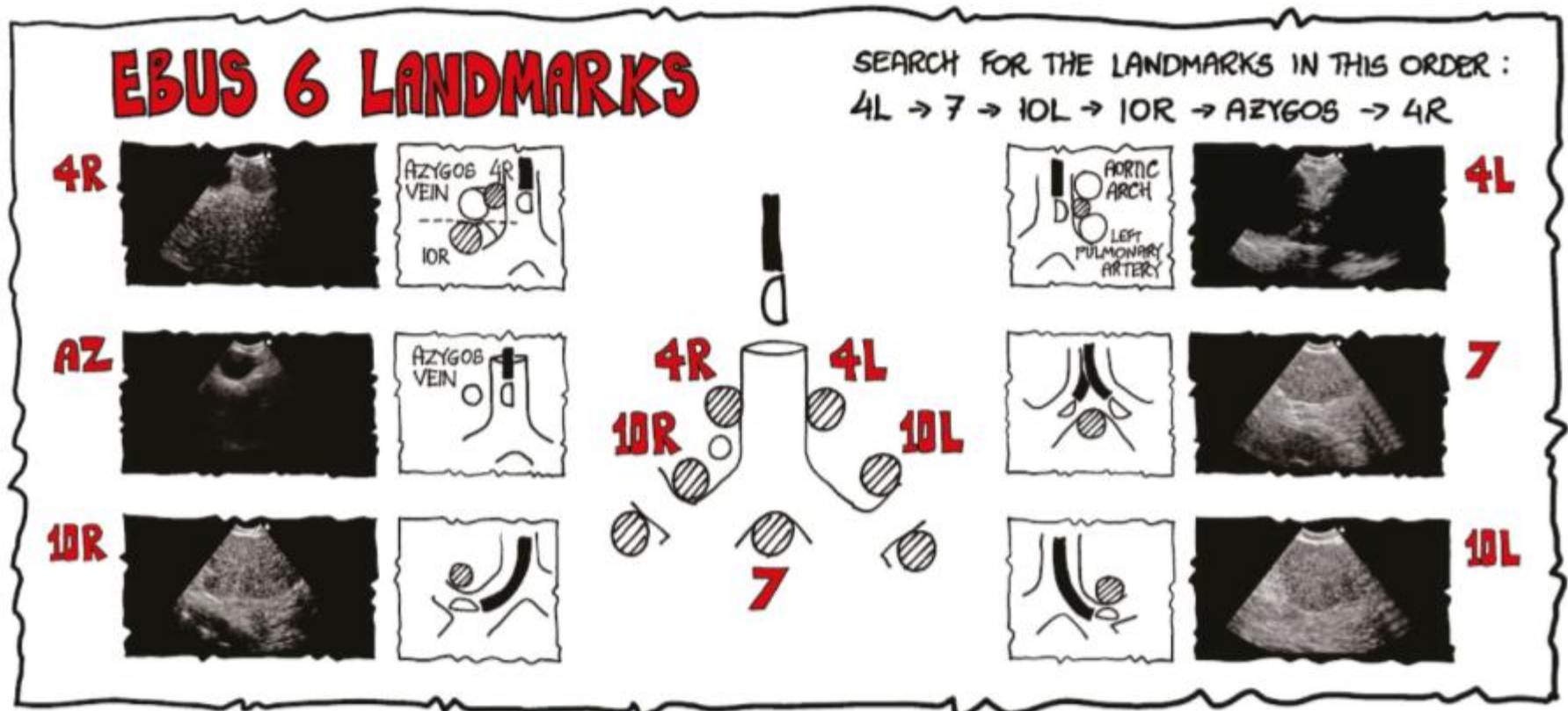
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A complete assessment of mediastinal and hilar nodal stations, and sampling **of at least three different mediastinal nodal stations** (4R, 4L, 7) is suggested in patients with NSCLC and an abnormal mediastinum by CT or CT-PET (Recommendation grade D).

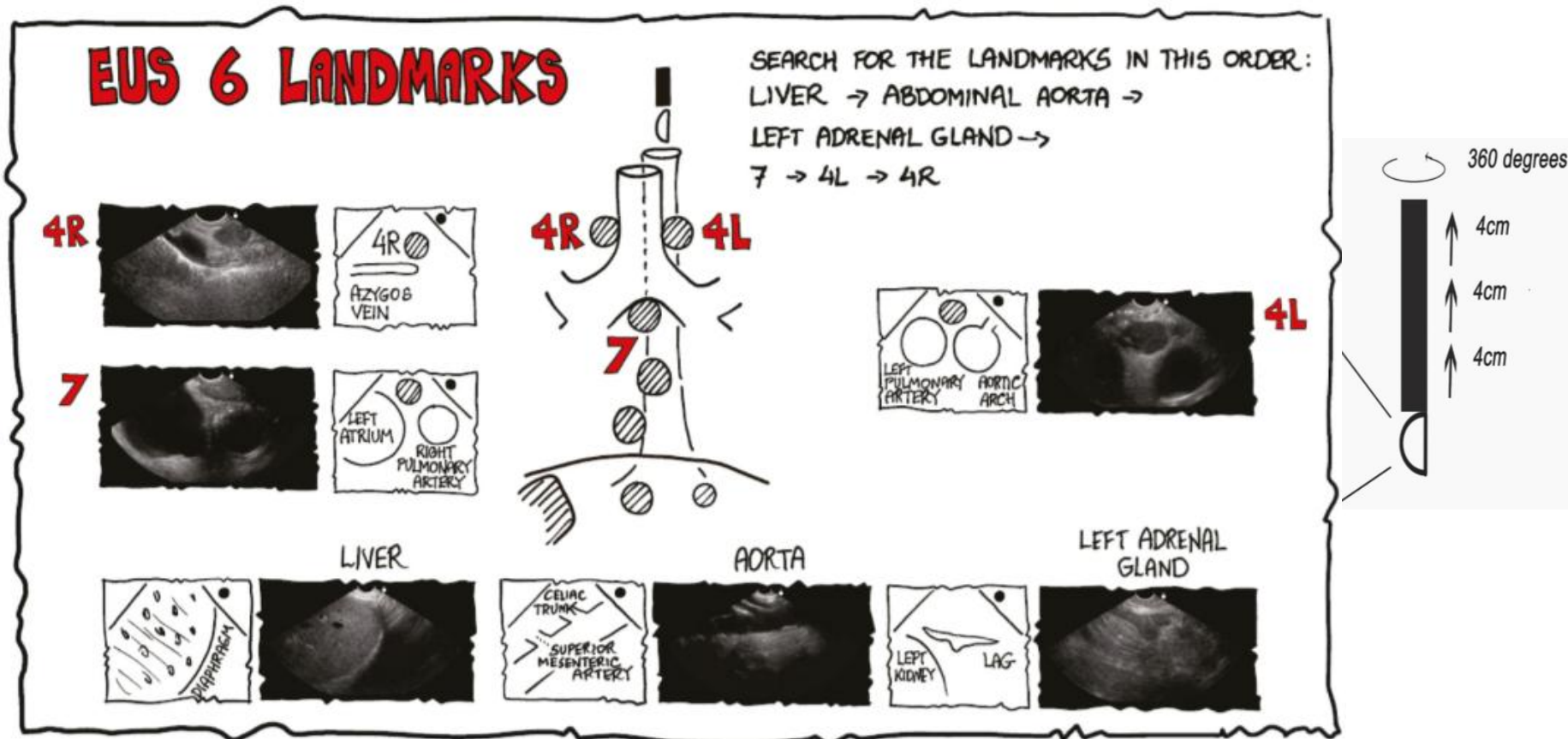


# Συστηματικός έλεγχος των λεμφαδένων



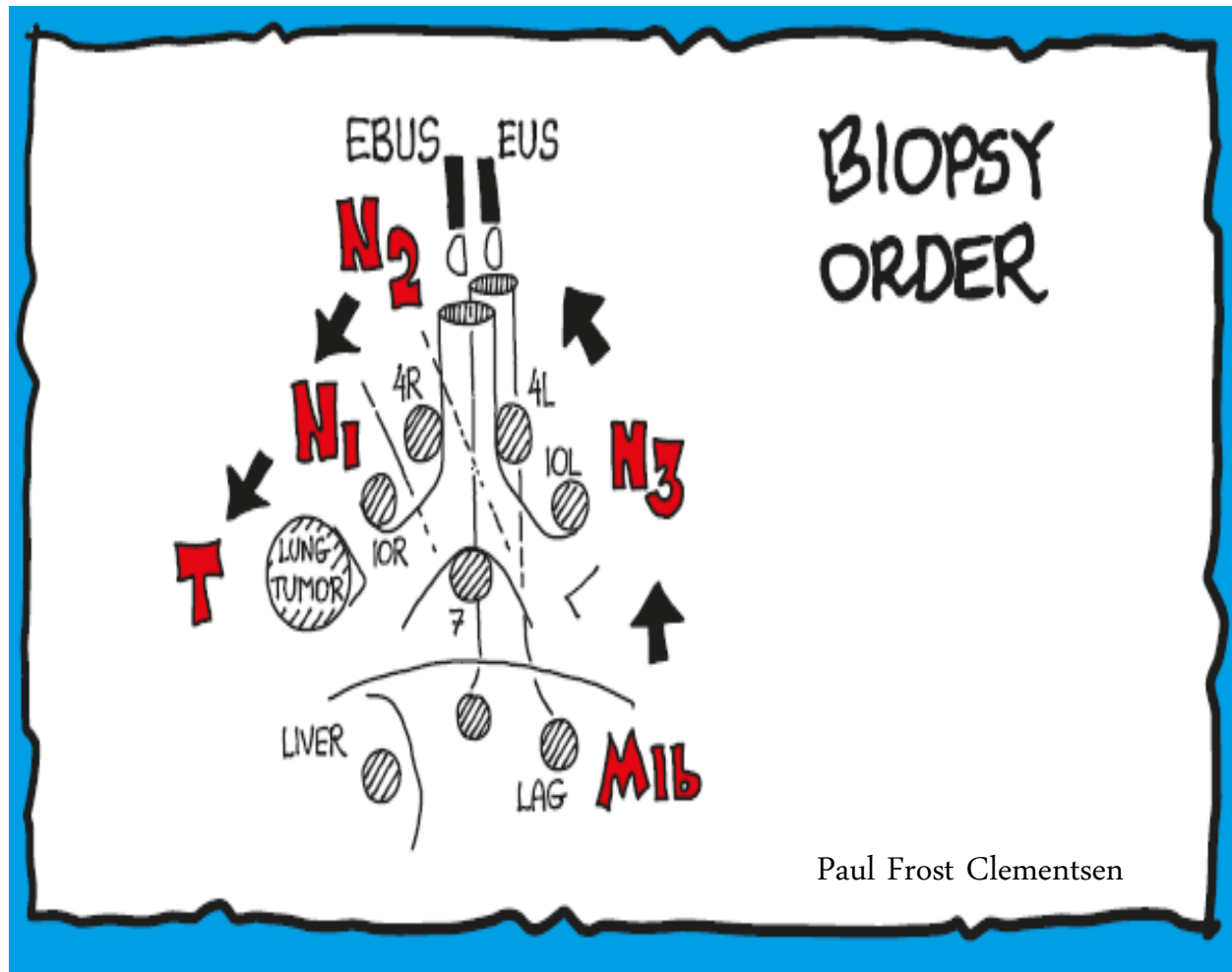


# Συστηματικός έλεγχος των λεμφαδένων



Paul Frost Clementsen 2015

# Sampling order: N3- N2- N1



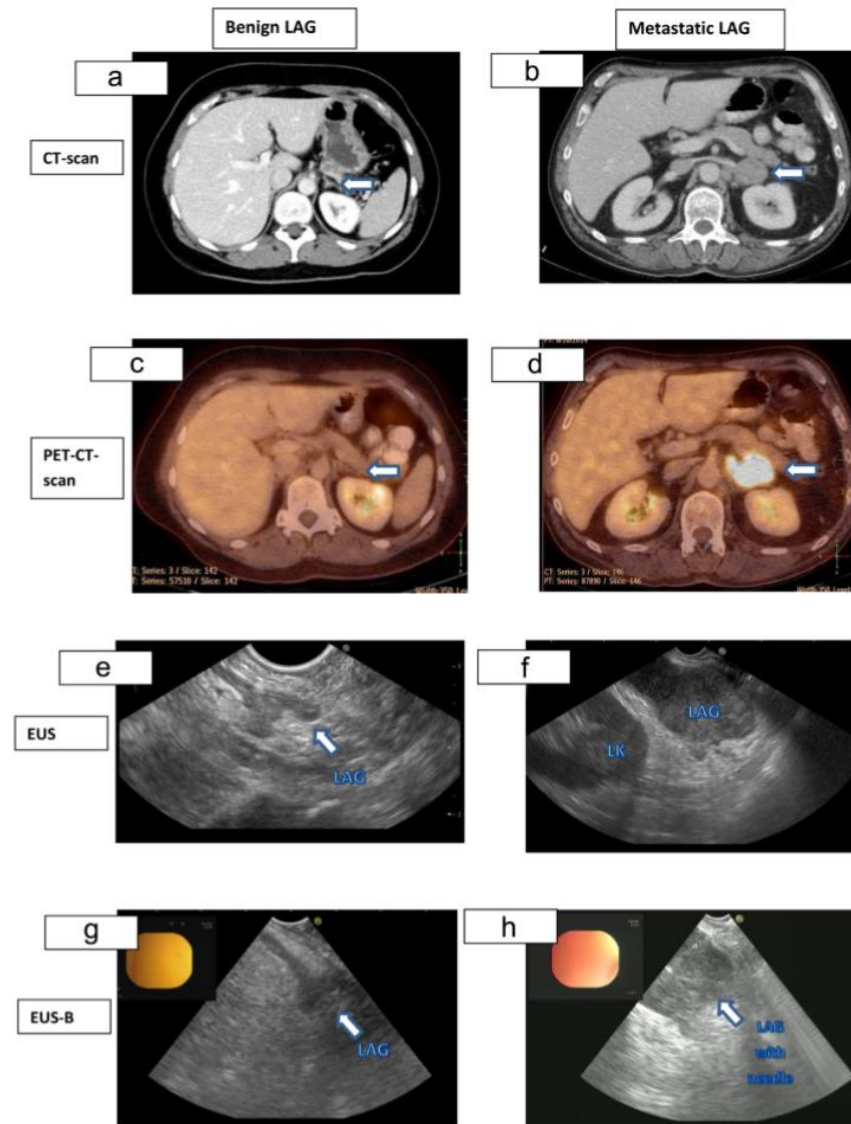
# Endosonography for left adrenal gland staging of lung cancer

Prospective trial (44 patients with (suspected) lung cancer and suspected mediastinal and LAG metastases.

Following complete mediastinal staging using the EBUS scope (EBUS+EUS-B), the LAG was evaluated and sampled by both EUS-B (experimental procedure) and conventional EUS (current standard of care).

## RESULTS:

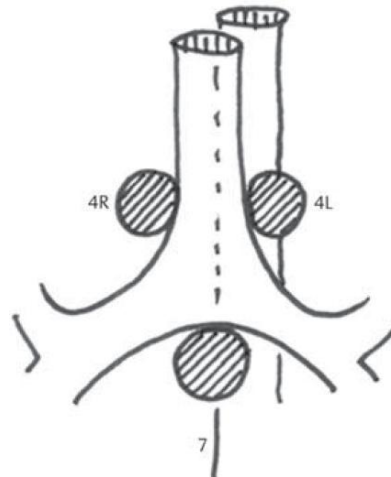
- The success rate for LAG analysis (visualized, sampled and adequate tissue obtained)
- 89% for EUS-B-FNA
- 93% for EUS-FNA



Combined endobronchial and esophageal 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)



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For optimal endosonographic staging of lung cancer, we suggest that individual endoscopists should be trained in **both EBUS and EUS-B** in order to perform **complete endoscopic staging in one session** (Recommendation grade D).

**Complete E(B)US staging**

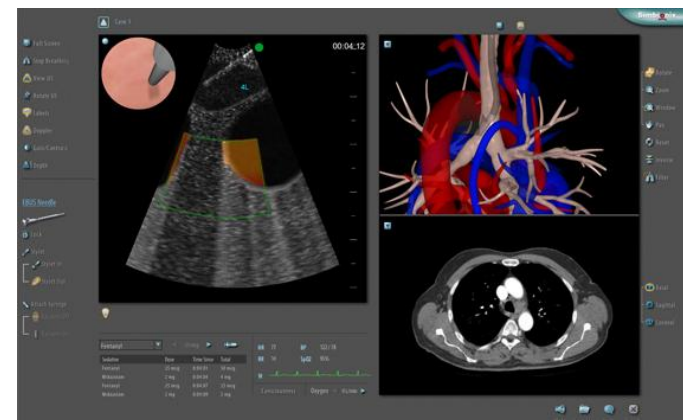
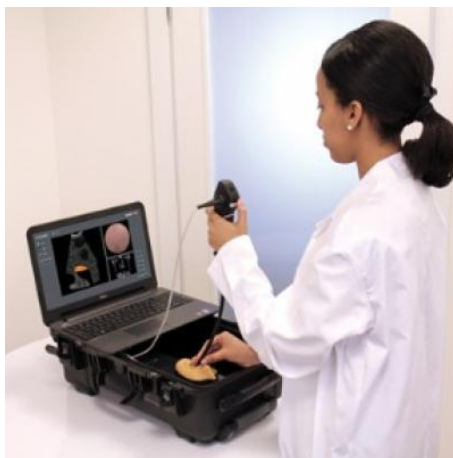
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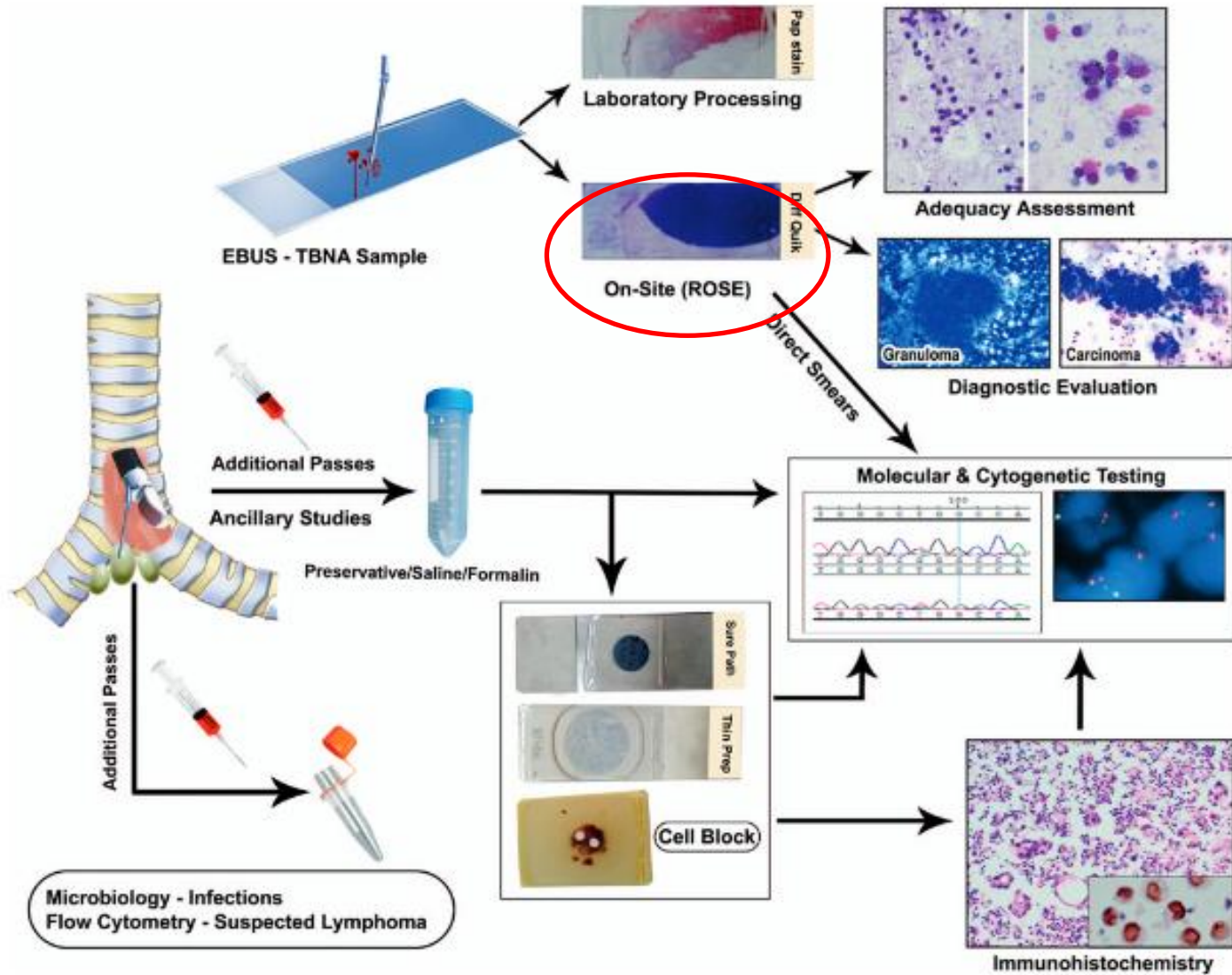
- We suggest that new trainees in endosonography should follow a structured training curriculum consisting of **simulation-based training** followed by **supervised practice** on patients (Recommendation grade D).
- We suggest that competency in EBUS-TBNA and EUS-(B)FNA for staging lung cancer be assessed using available **validated assessment tools** (Recommendation Grade D).



Comprehensive hands-on training of EBUS-TBNA procedure

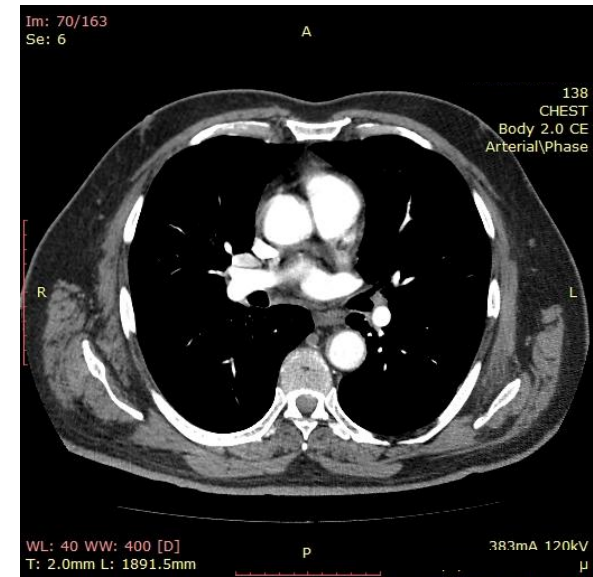
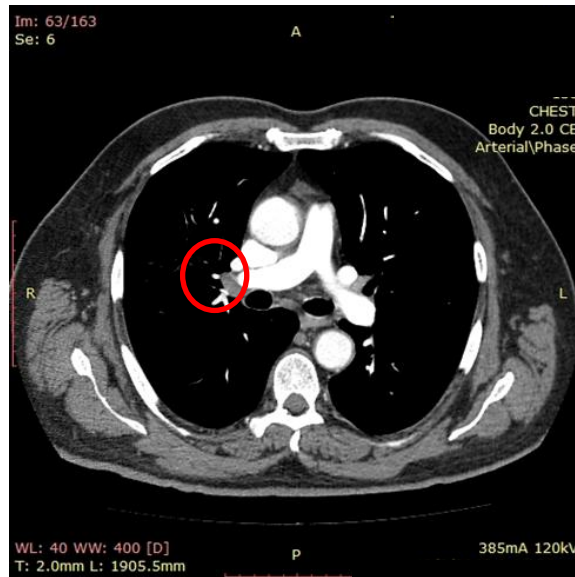
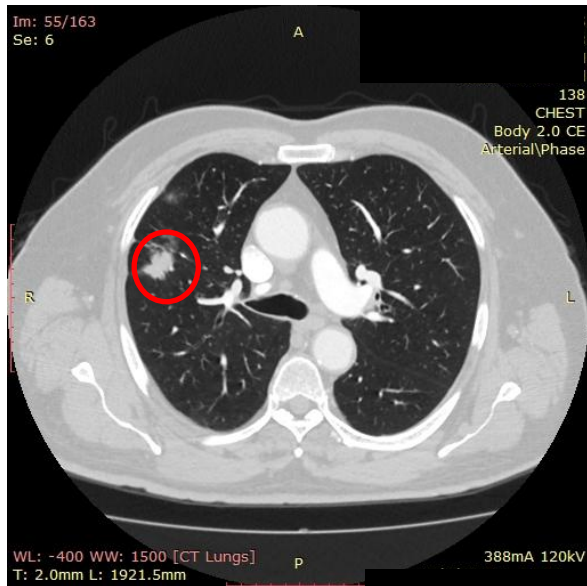


# Διαχείριση υλικού (EBUS-TBNA)



# Πιθανό Ca πνεύμονα – σταδιοποίηση μεσοθωρακίου

64 ετών, καπνιστής (60pys), όζος 1,8cm ΔΑΛ – τυχαίο εύρημα



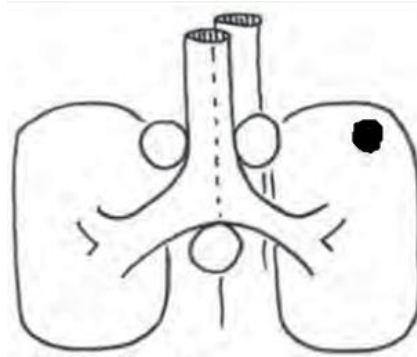
PET-CT όζος ΔΑΛ SUVmax=6.8, Πυλαίοι άμφω SUV=3.2



**Combined endobronchial and esophageal 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)**



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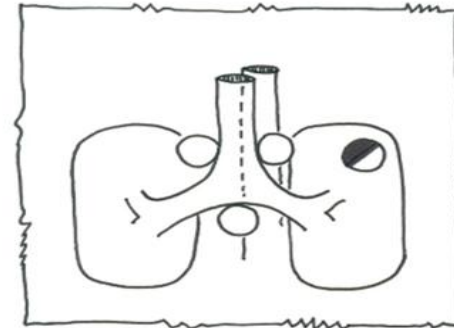
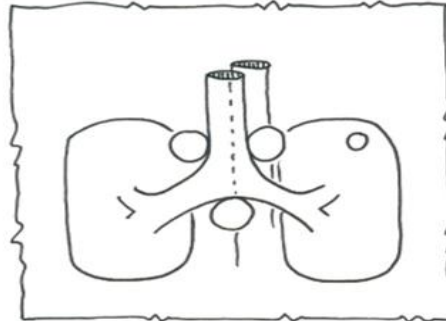
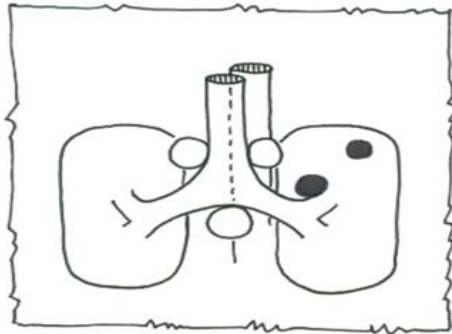


In patients with suspected or proven **<3cm peripheral NSCLC** with normal mediastinal and hilar nodes at CT and/or PET, we suggest initiation of therapy without further mediastinal staging (Recommendation grade C).

Combined endobronchial and esophageal 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)

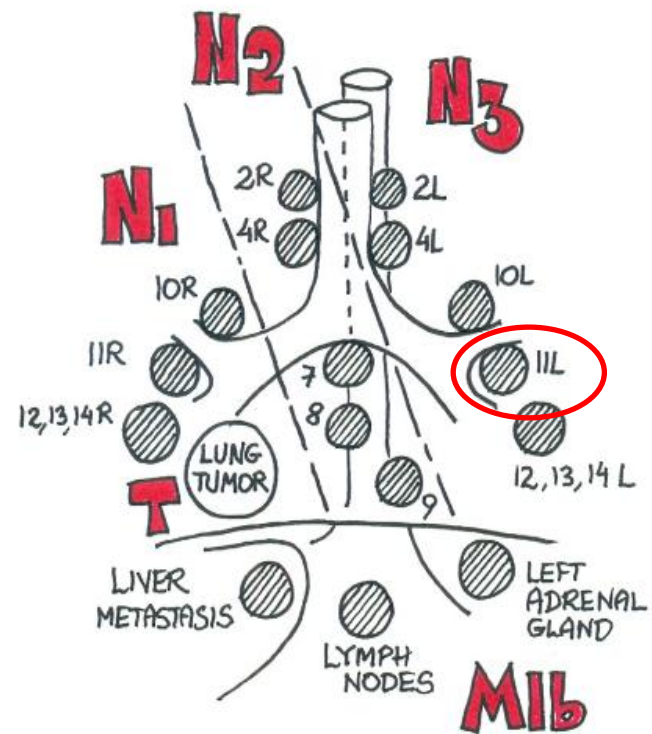
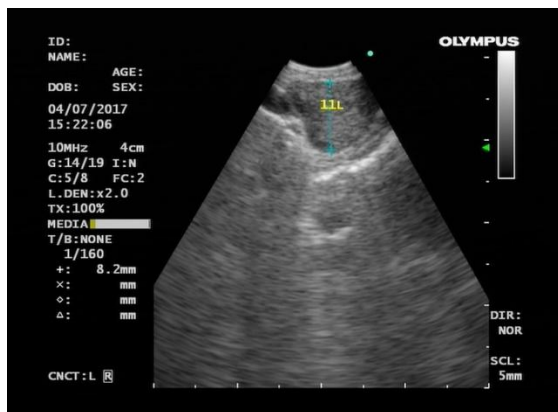


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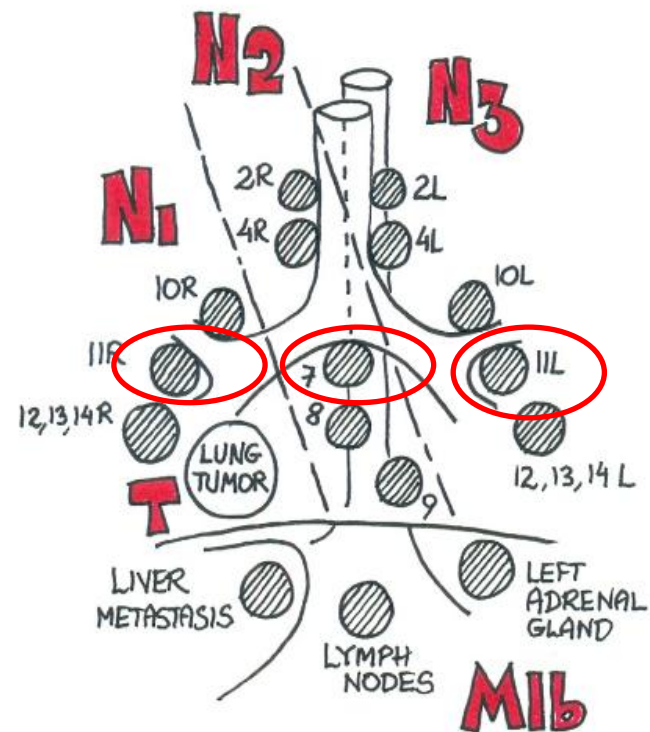
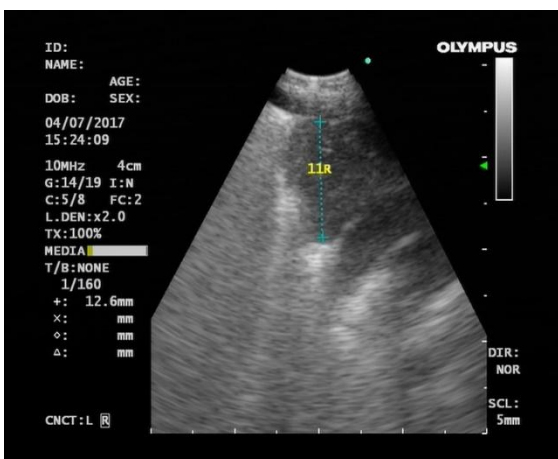
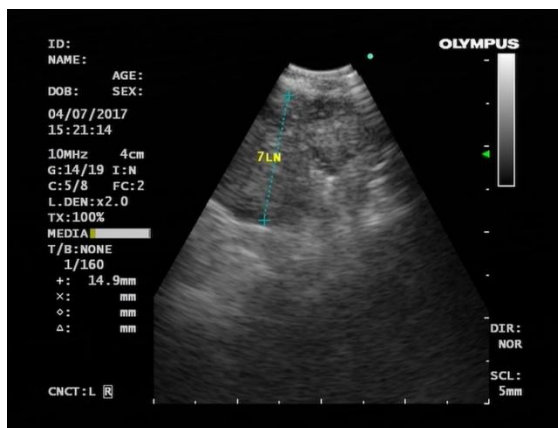


For mediastinal nodal staging in patients with suspected or proven peripheral NSCLC without mediastinal involvement at CT or CTPET, we suggest that **EBUS-TBNA and/or EUS-(B)-FNA** should be performed before therapy, provided that one or more of the following conditions is present:

- (i) enlarged or (FDG)-PET-avid ipsilateral hilar nodes
- (ii) primary tumor without FDG uptake;
- (iii) tumor size  $\geq 3$  cm ( grade C)





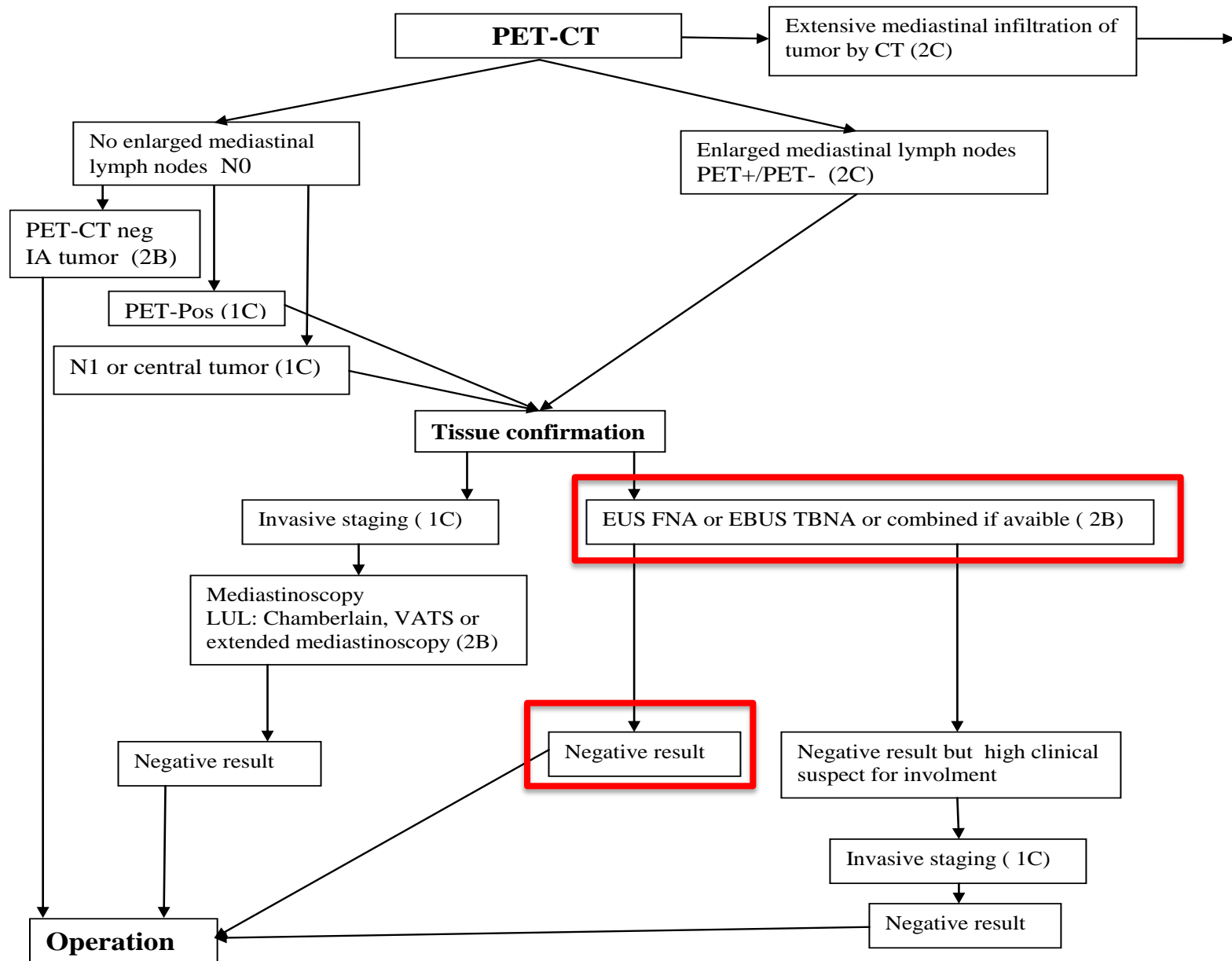


- **Διάγνωση:** λεμφαδένες χωρίς στοιχεία κακοήθειας

T/M	Label	N0	N1	N2	N3
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T4	T4 $>7$	IIIA	IIIA	IIIB	IIIC
	T4 <i>Inv</i>	IIIA	IIIA	IIIB	IIIC
	T4 <i>Ipsi Nod</i>	IIIA	IIIA	IIIB	IIIC
M1	M1a <i>Contr Nod</i>	IVA	IVA	IVA	IVA
	M1a <i>Pl Dissem</i>	IVA	IVA	IVA	IVA
	M1b <i>Single</i>	IVA	IVA	IVA	IVA
	M1c <i>Multi</i>	IVB	IVB	IVB	IVB



# Staging of the mediastinum ( no distal metastases)



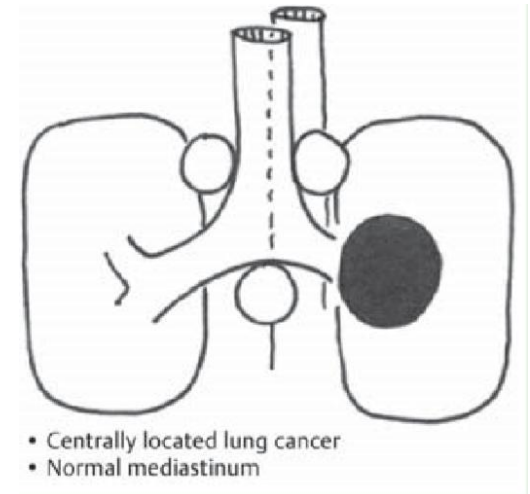


## Centrally located tumor

False-negative rates:

CT 20%–25%

PET 24%–83%



For mediastinal staging in patients with **centrally located** suspected or proven NSCLC without mediastinal or hilar involvement at CT and/or CT-PET, we suggest performance of EBUS-TBNA, with or without EUS-(B)-FNA, in preference to surgical staging

# Επανασταδιοποίηση NSCLC

Mediastinal re-staging can be performed with:

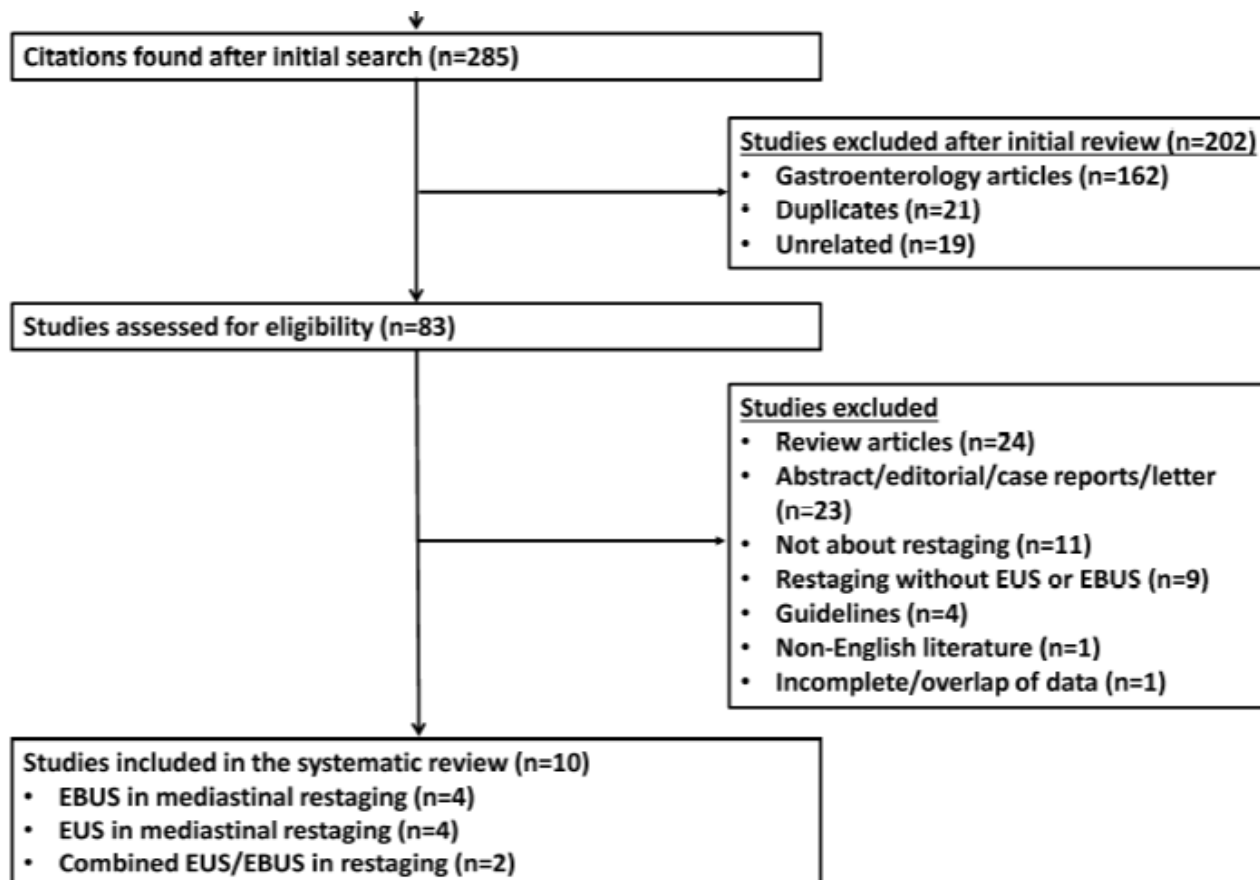
- imaging

CT *false negative 33%, false positive 25%*

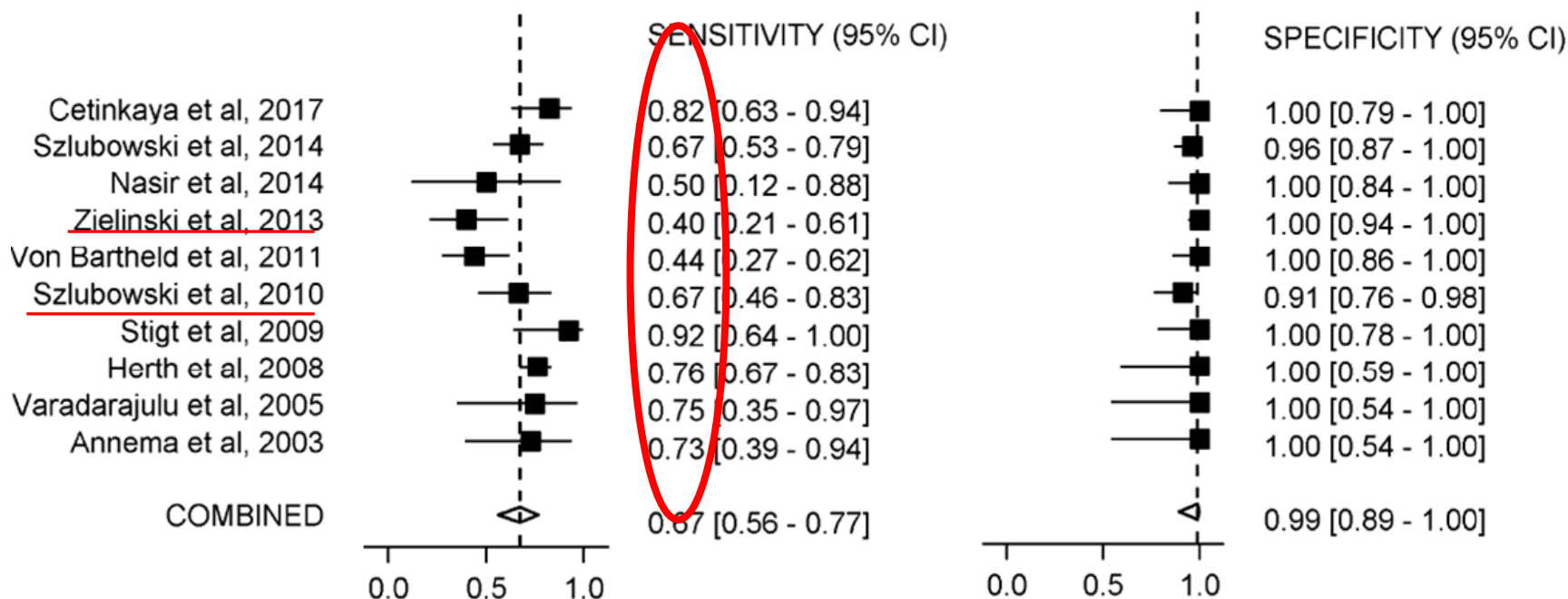
PET *false negative 33%, false positive 33%*

- invasive surgical procedures (mediastinoscopy, thoracotomy)  
*false negative of repeat mediastinoscopy 22%*
- minimally invasive endosonographic procedures
- or a combination of the above

# Efficacy of endosonographic procedures in mediastinal re-staging of lung cancer after neoadjuvant therapy: A systematic review and diagnostic accuracy meta-analysis



# Efficacy of endosonographic procedures in mediastinal re-staging of lung cancer after neoadjuvant therapy: A systematic review and diagnostic accuracy meta-analysis



**Conclusions:** Endosonographic procedures are safe and highly specific in mediastinal re-staging of lung cancer.

## Restaging

For mediastinal nodal restaging following neoadjuvant therapy, EBUS-TBNA and/or EUS-(B)-FNA is suggested for detection of persistent nodal disease, but, if this is negative, subsequent surgical staging is indicated (Recommendation grade C).

# Συμπερασματικά...

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- Το πρώτο βήμα στη σταδιοποίηση του NSCLC είναι ο ενδοσκοπικός υπέρηχος (έναντι του χ/ου)
- Η συστηματική προσέγγιση των λεμφαδένων με EBUS-TBNA σε συνδυασμό με EUS-(B)-FNA αυξάνει τη διαγνωστική ακρίβεια (N3/ N2/N1) και έχει μεγαλύτερη αρνητική προγνωστική αξία από το EBUS μόνο του.
- Σε ασθενείς με περιφερική βλάβη και φυσιολογικό μεσοθωράκιο σε CT ή PET-CT, συστήνεται η χρήση **EBUS-TBNA και/ή EUS-(B)-FNA** πριν τη θεραπεία αν:
  - 1) υπάρχουν διογκωμένοι ή (FDG)-PET-avid σύστοιχοι πυλαίοι λεμφαδένες
  - 2) ο πρωτοπαθής όγκος δεν προσλαμβάνει FDG
  - 3) αν ο όγκος είναι  $\geq 3$  cm





obrigado

Dank U

Merci

mahalo

Köszí

спасибо

Grazie

Thank  
you

mauruuru

Takk

Gracias

Dziękuję

Děkuju

danke

Kiitos





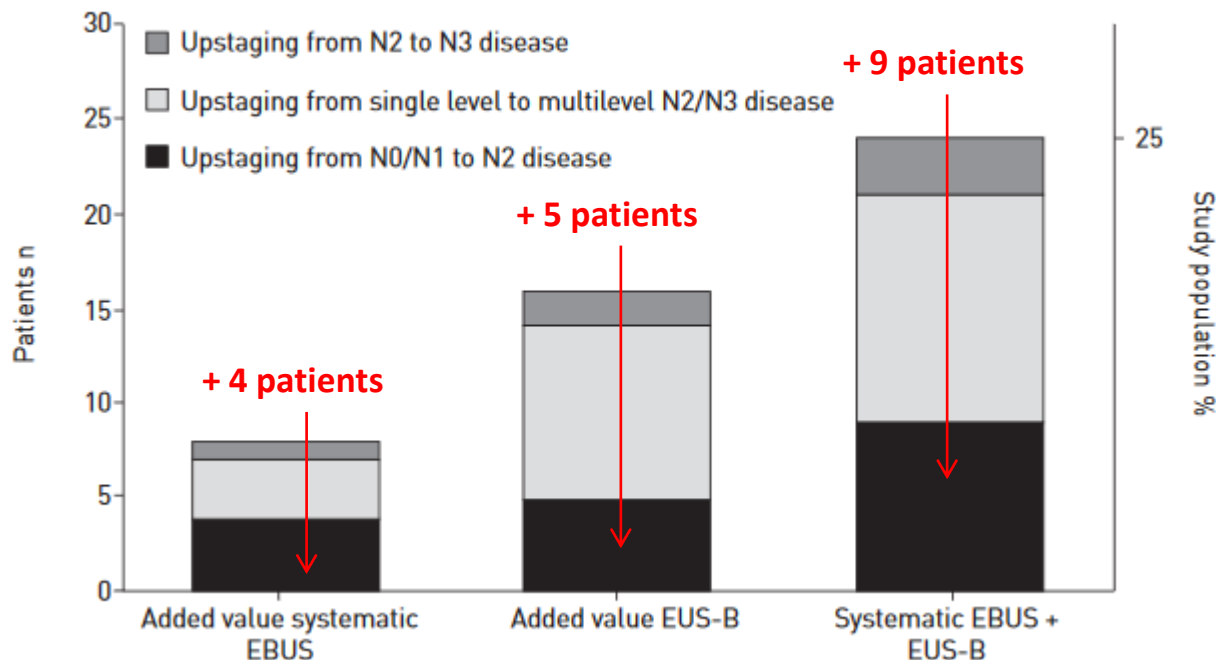
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## Systematic and combined endosonographic staging of lung cancer (SCORE study)

*Eur Respir J* 2019

Laurence M.M. Crombag<sup>1</sup>, Christophe Doooms<sup>2</sup>, Jos A. Stigt<sup>3</sup>,  
Kurt G. Tournoy<sup>4,5</sup>, Olga C.J. Schuurbijs<sup>6</sup>, Maarten K. Ninaber<sup>7</sup>,  
Wieneke A. Buikhuisen<sup>8</sup>, Sayed M.S. Hashemi<sup>9</sup>, Peter I. Bonta<sup>1</sup>,  
Daniël A. Korevaar<sup>10</sup> and Jouke T. Annema<sup>1</sup>

229 patients



Systematic EBUS followed by EUS-B increased sensitivity for the detection of N2/N3 disease by **9%** compared to PET-CT-targeted EBUS alone.



## The Role of the Pulmonologist in Rapid On-site Cytologic Evaluation of Transbronchial Needle Aspiration

### A Prospective Study

**Table 4—Sensitivity, Specificity, and Accuracy of ROSE Performed by Cytopathologist and Pulmonologist (Final Diagnosis as Gold Standard)**

Physician	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Accuracy, % (95% CI)
Pulmonologist	91 (86-94)	72 (65-78)	80 (77-90)
Cytopathologist	95 (88-95)	92 (87-95)	92 (85-94)

**Conclusions:** Training pulmonologists to have a basic knowledge of cytopathology could obviate most difficulties related to the involvement of cytopathologists in routine diagnostic activities and may reduce the costs of the procedure.

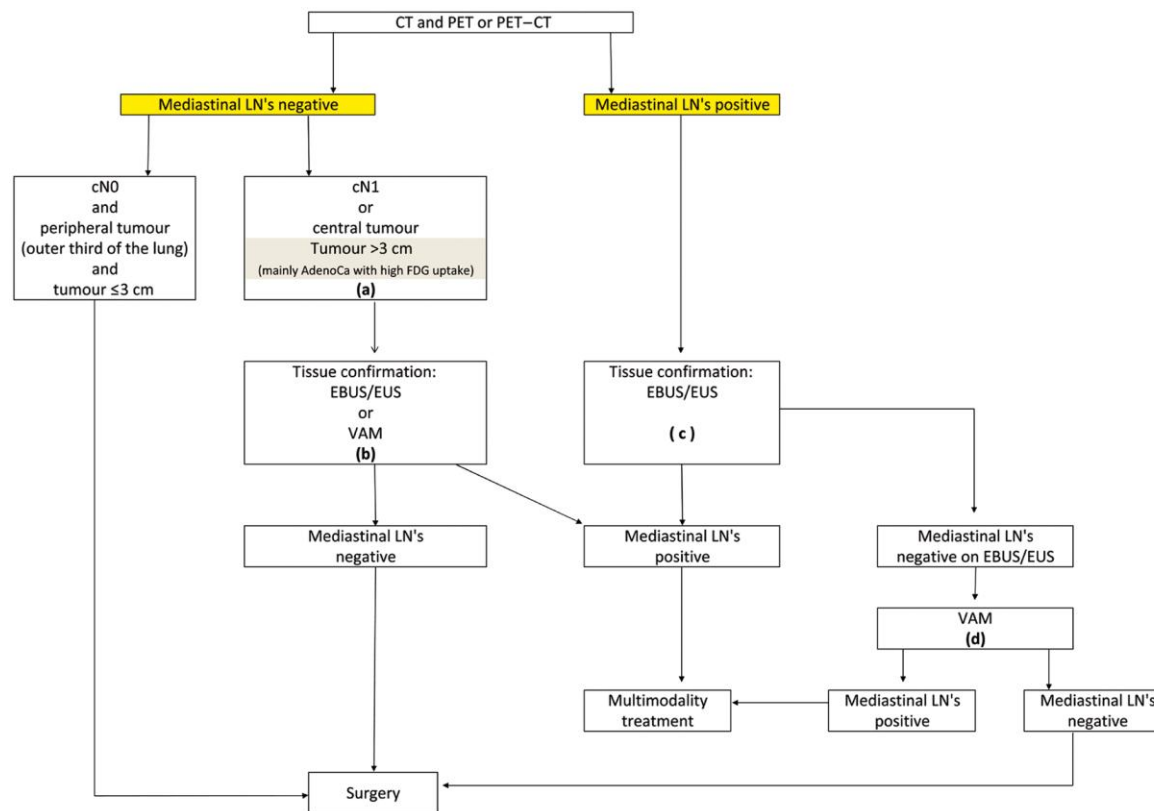
# Rapid On-Site Evaluation of Endobronchial Ultrasound–Guided Transbronchial Needle Aspirations for the Diagnosis of Lung Cancer

A Perspective From Members of the Pulmonary Pathology Society

**Table 4. Advantages and Limitations of Rapid On-Site Evaluation (ROSE)**

<b>Advantages</b>	<b>Limitations</b>
Adequacy assessment of the specimen Improved diagnostic yield Reduction of additional procedures Obtain additional passes for molecular testing, microbiology cultures, and flow cytometry Better use of laboratory resources and reduced laboratory effort because of the lower number of total slides Improved patient care	Needs an experienced cytopathologist or a dedicated trained cytotechnician Cost may not be reimbursed Time-consuming process (35–56 min) <sup>67</sup> At present, no statistically significant results for ROSE and increased diagnostic yield, fewer aspirations, decreased procedure time, and reduced rate of complications

**Figure 1.** Suggested algorithm for locoregional lymph node staging in patients with non-metastatic NSCLC. CT, computed ...



(a) : In tumours > 3 cm (mainly in adenocarcinoma with high FDG uptake) invasive staging should be considered

(b) : Depending on local expertise to adhere to minimal requirements for staging

(c) : Endoscopic techniques are minimally invasive and are the first choice if local expertise with EBUS/EUS needle aspiration is available

(d) : Due to its higher NPV, in case of PET positive or CT enlarged mediastinal LN's, videoassisted mediastinoscopy (VAM) with nodal dissection or biopsy remain indicated when endoscopic staging is negative. Nodal dissection has an increased accuracy over biopsy

# Endosonography for left adrenal gland staging of lung cancer

- Retrospective trial (143 patients)
- In **85%** of patients it was feasible to transgastrically detect the LAG with the EBUS scope.
- 9 patients punctured (6:benign adrenal tissue, 2:metastases of NSCLC, 1: pheochromocytoma)

