EBUS, b-EUS TBNA: Διαβρογχική και διοισοφάγεια σταδιοποίηση του μεσοθωρακίου

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ΕΛΛΗΝΙΚΗ ΠΝΕΥΜΟΝΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
HELLENIC THORACIC SOCIETY

- Καρκίνος του πνεύμονα : η πιο συχνή αιτία θανάτου από καρκίνο παγκοσμίως
- 1.2 εκατομμύρια θάνατοι παγκοσμίως κάθε χρόνο.
- Στην Ευρώπη 410.000 νέες περιπτώσεις το 2012.
- Οι περισσότερες αφορούν μη μικροκυτταρικό καρκίνο (NSLC).

Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013; 49: 1374–1403

NELSON TRIAL : Η δεύτερη μεγάλη μελέτη ελέγχου με CT για καρκίνο του πνεύμονα μετά την NLST

Ο έλεγχος ρουτίνας με αξονική τομογραφία θώρακος σε άτομα σε υψηλό κίνδυνο για καρκίνο του πνεύμονα οδηγεί σε μείωση των θανάτων από τη νόσο.

- 27.000 screening CTs
- 2.503 (9.3%) μη συγκεκριμένα ευρήματα (indeterminate)- σύσταση για repeat scan σε 4-6 μήνες.
- 598 (2.2%) θετικά αποτελέσματα στη CT.
- 243 (0.9%) Καρκίνος πνεύμονα.
- 65-70% των καρκίνων στην ομάδα screening ήταν στάδιο IA-II - δηλαδή χειρουργήσιμοι.
- 70% των καρκίνων στην ομάδα ελέγχου (που δεν έκανε CT) ήταν σταδίου III-IV

Συνολική μείωση θνητότητας κατά 26% σε άνδρες και 61% γυναίκες υψηλού κινδύνου σε περίοδο 10 ετών.

De Koning H, Van Der Aalst C, Ten Haaf K, et al: 2018 World Conference on Lung Cancer. Abstract PL02.05. Presented September 25, 2018.

Σταδιοποίηση NSCLC

Αφού έχει τεθεί η υποψία ή διάγνωση NSCLC πρέπει να εκτιμήσουμε την έκταση (στάδιο) της νόσου.

1. Υπάρχει απομακρυσμένη μετάσταση ή ο όγκος περιορίζεται στο θώρακα?
2. Αν περιορίζεται στο θώρακα, υπάρχει διήθηση των μεσοθωρακικών λεμφαδένων?

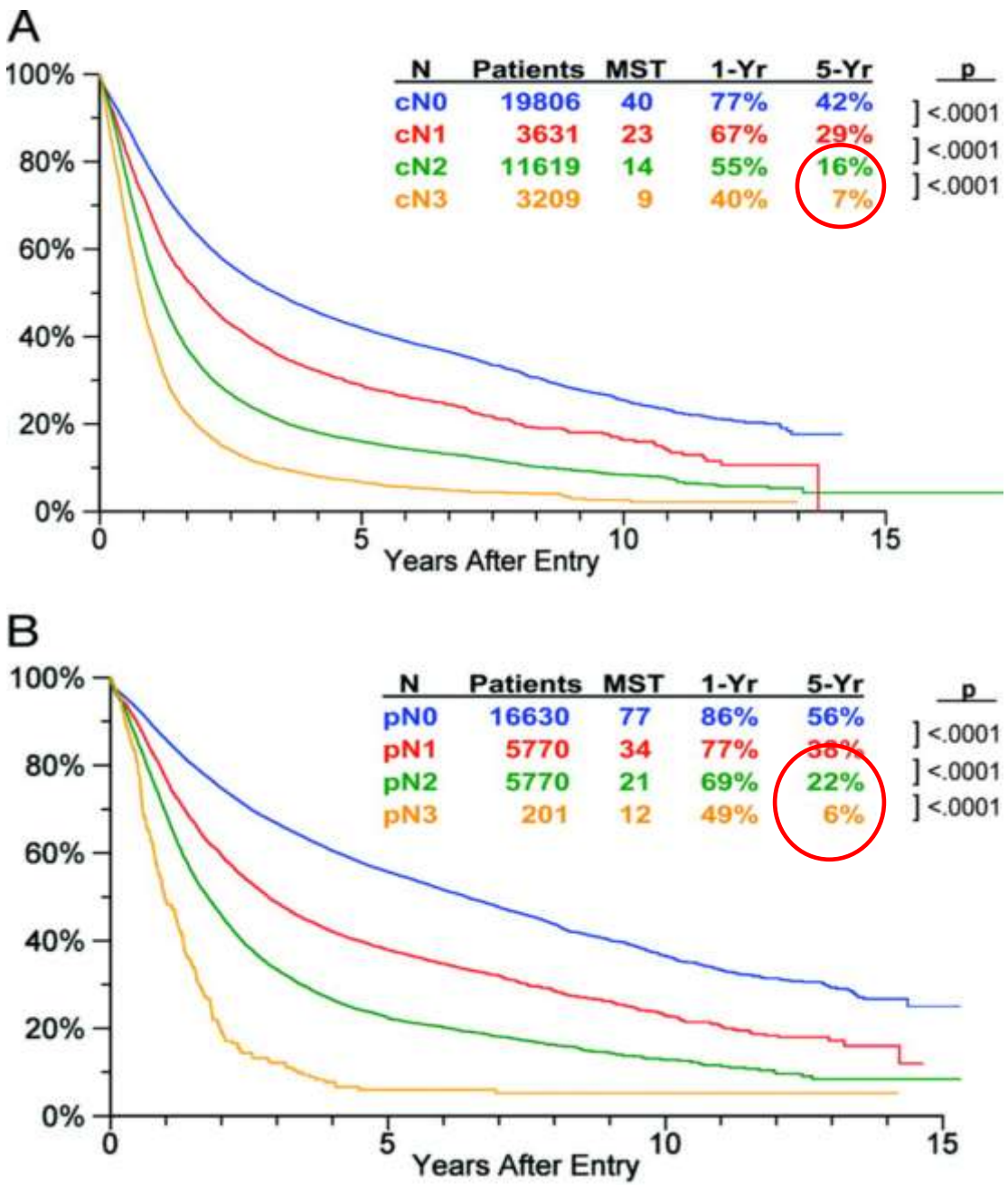
Η διήθηση του μεσοθωρακίου θα επηρεάσει την στρατηγική θεραπείας.

TNM: Lung cancer

T/M	Subgroup	N0	N1	N2	N3
T1	T1a	Ia	IIa	IIIa	IIIb
	T1b	Ia	IIa	IIIa	IIIb
T2	T2a	Ib	IIa	IIIa	IIIb
	T2b	IIa	IIb	IIIa	IIIb
T3	$T3_{>7}$	IIb	IIIa	IIIa	IIIb
	$T3_{Inv}$	IIb	IIIa	IIIa	IIIb
	$T3_{Satell}$	IIb	IIIa	IIIa	IIIb
T4	$T4_{Inv}$	IIIa	IIIa	IIIb	IIIb
	$T4_{Ipsi\ Nod}$	IIIa	IIIa	IIIb	IIIb
M1	$M1a_{Contra\ Nod}$	IV	IV	IV	IV
	$M1a_{Pl\ Disem}$	IV	IV	IV	IV
	M1b	IV	IV	IV	IV

AJCC TNM Staging System, 7th Ed. (2010)

Η Σταδιοποίηση προβλέπει την επιβίωση

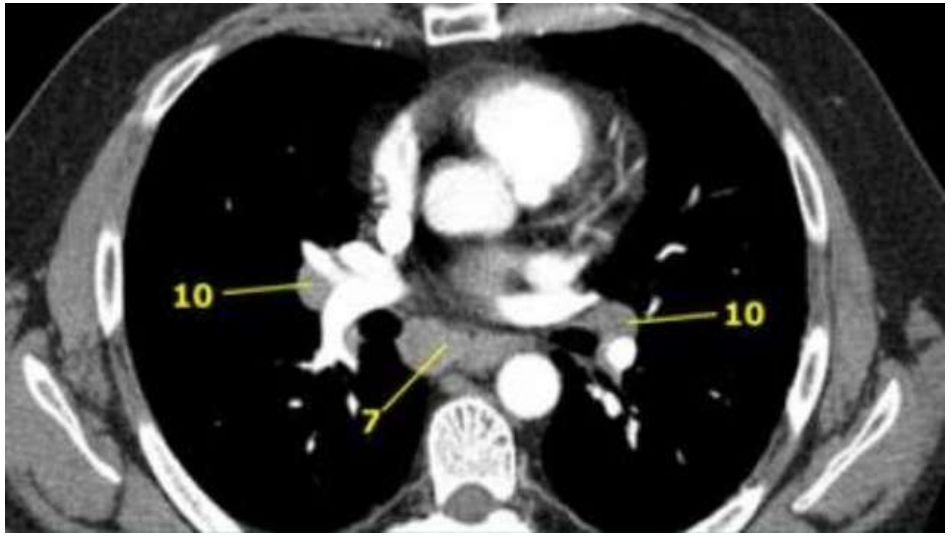


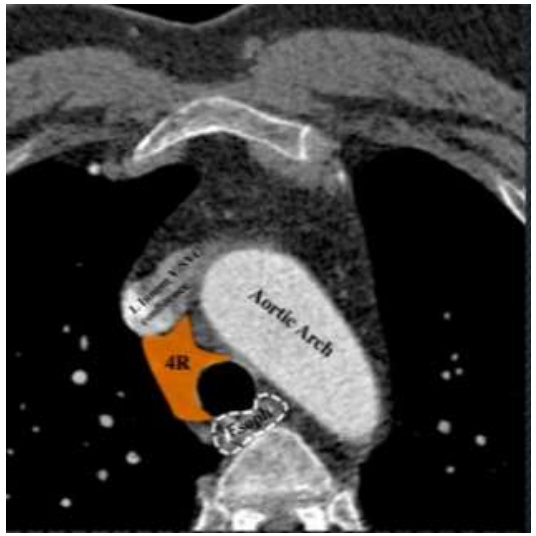
Chest. 2009;136(1):260-271. doi:10.1378/chest.08-0978

Προσδιορισμός του σταδίου (N):

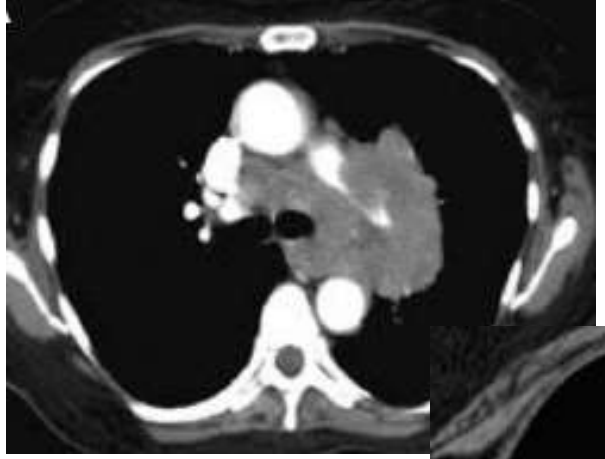
- **N1:** Ομόπλευροι (της εξεργασίας) περιβρογχικοί, πυλαίοι και ενδοπνευμονικοί λεμφαδένες.
- **N2:** Ομόπλευροι μεσοθωρακικοί και/ή υποτροπιδικοί λεμφαδένες
- **N3:** -Ετερόπλευροι μεσοθωρακικοί και πυλαίοι
  -Ομόπλευροι ή ετερόπλευροι τραχηλικοί ή υπερκλείδιοι λεμφαδένες

- **Λεμφαδενική διόγκωση ορίζεται η αύξηση του μεγέθους ενός καλά διακριτού λεμφαδένα στον κοντό άξονα > 1 cm.**





Chest. 2013;143(5_suppl):e211S-e250S. doi:10.1378/chest.12-2355



Radiographic group A: patients with mediastinal infiltration so extensive that the discrete lymph nodes can no longer be discerned or measured

Radiographic group B: patients with measurable discrete mediastinal node enlargements.

Radiographic group C: the presence of a central tumor or suspected N1 disease makes the chance of N2,3 nodal involvement high (20%-25%) despite normal-sized nodes. Further confirmation is needed

Radiographic group D: patients with a peripheral clinical stage I tumor, where the chance of either distant metastases or mediastinal involvement is quite low (6-10% with regards to T1 or T2 stage)

Accuracy of CT scanning for staging of the mediastinum in patients with lung cancer (ACCP guidelines 2013).

First Author	Year	No.	Tech	Prev	Sens	Spec	PPV	NPV
Eggeling[137]	2002	73	CE	70	82	50	79	55
Wallace[143]	2001	121	CE	69	87	35	75	54
Marom[88]	1999	79	CE	56	59	86	84	63
Vansteenkiste[150]	1998	56	CE	50	86	79	80	85
Aaby[156]	1995	57	…	44	72	91	86	81
Schillaci[136]	2003	83	CE	42	69	75	67	77
Vansteenkiste[151]	1998	68	CE	41	75	63	58	78
Primack[157]	1994	159	CE	38	63	86	73	79
Turkmen[130]	2007	59	CE	36	43	66	41	68
Laudanski[141]	2001	92	CE	33	60	73	51	79
Yokoi1[58]	1994	113	CE	33	62	80	61	81
Gdeedo[153]	1997	100	CE	32	63	57	41	76
Bury[155]	1996	53	CE	32	71	81	63	85
McLoud[159]	1992	143	CE	31	64	62	44	79
Pieterman[90]	2000	102	CE	31	75	66	50	85
Yen[127]	2008	96	CE	31	47	80	52	77
Osada[146]	2001	335	CE	30	56	93	77	83
Jolly[160]	1991	336	CE	30	71	86	69	87
Subedi[47]	2009	91	CE	29	50	86	59	81
Buccheri[154]	1996	80	CE	28	64	74	48	84
Pozo-Rodriguez[24]	2004	132	CE	27	86	67	49	93
Kiernan[138]	2002	92	CE	27	64	94	80	88
Reed[19]	2003	302	CE	25	37	91	58	81
Nosotti[139]	2002	87	CE	25	64	88	64	88
Dunagan[144]	2001	72	CE	25	50	87	56	84
Kimura[135]	2003	203	CE	24	63	97	88	89
Yi1[29]	2007	143	CE	24	65	89	65	89
Suzuki[149]	1999	440	CE	23	33	92	56	82
Bury[152]	1997	64	CE	22	79	84	58	93
De Wever[44]	2007	50	CE	22	91	72	48	97
Webb[162]	1991	154	CE	21	52	69	31	84
Cole[161]	1993	150	…	21	26	81	26	81
Takamochi[132]	2005	71	CE	21	20	89	33	81
Kamiyoshihara[145]	2001	546	CE	20	33	90	46	84
Takamochi[147]	2000	401	CE	20	30	82	30	83
Lee[126]	2009	182	CE	20	36	79	30	83
Yang[128]	2008	122	CE	20	52	73	33	86
Kelly[134]	2004	69	CE	19	46	86	(43)[a]	87
Saunders[148]	1999	84	…	18	20	90	(30)[a]	84
Nomori[133]	2004	80	…	18	50	95	(70)[a]	90
Ebihara[131]	2006	205	CE	15	32	83	(26)[a]	87
Poncelet[142]	2001	62	CE	15	56	68	(23)[a]	90
Von Haag[140]	2002	52	CE	12	50	65	(16)[a]	91
Median: prevalence > 30					**67**	**74**	**62**	**79**
Median: prevalence 21-30					**63**	**87**	**58**	**84**
Median: prevalence ≤ 20					**41**	**83**	**30**	**87**
Summary: Median		**7,368**		**30**	**55**	**81**	**58**	**83**

			Sens	Spec	PPV	NPV
Median: prevalence > 30			**67**	**74**	**62**	**79**
Median: prevalence 21-30			**63**	**87**	**58**	**84**
Median: prevalence ≤ 20			**41**	**83**	**30**	**87**
Summary: Median	**7,368**	**30**	**55**	**81**	**58**	**83**

Chest. 2013;143(5_suppl):e211S-e250S. doi:10.1378/chest.12-2355

Accuracy of integrated PET-CT scanning for staging of the mediastinum in patients with lung cancer (ACCP guidelines 2013).

First Author	Year	No.	Prev	Sens	Spec	PPV	NPV
Cerfolio[200]	2004	40	100	75	…	…	…
Plathow[204]	2008	52	73	100	100	100	100
Fischer[361]	2011	79	33	85	100	100	93
Lee[202]	2009	41	32	38	89	63	76
Yi[209]	2008	150	30	62	94	82	85
Maziak[29]	2009	167	29	48	93	74	82
Subedi[47]	2009	91	26	92	85	69	97
Yi[129]	2007	143	24	56	100	100	88
Carnochan[76]	2009	194	23	42	87	50	83
Lee[40]	2007	126	22	86	81	56	95
De Wever[44]	2007	50	22	73	82	53	91
Lee[126]	2009	182	20	81	73	42	94
Yang[128]	2008	122	20	52	73	33	86
Perigaud[203]	2009	51	20	40	85	40	85
Billé[199]	2009	159	19	48	93	(63)[a]	88
Toba[207]	2010	42	19	100	88	(67)[a]	100
Usuda[208]	2011	63	17	36	92	(50)[a]	87
Sanli[205]	2009	78	14	82	90	(56)[a]	97
Shin[206]	2008	184	13	48	95	(58)[a]	93
Summary: median		**2,014**	**22**	**62**	**90**	**63**	**90**

Chest. 2013;143(5_suppl):e211S-e250S. doi:10.1378/chest.12-2355

Πλεονεκτήματα vs. Μειονεκτήματα του PET CT

- Συνολικά 20% παραπάνω ασθενείς χαρακτηρίζονται σωστά ως έχοντες απομακρυσμένες (M1) ή λεμφαδενικές (N2,N3) μεταστάσεις συγκριτικά με την σταδιοποίηση με CT.
- Αν δεν επιβεβαιωθούν ιστολογικά, τα ευρήματα του PET CT μπορεί λανθασμένα να απομακρύνουν ασθενείς από πιθανή ριζική χειρουργική αντιμετώπιση.
- Στις κλινικές μελέτες με PET scan αυτό συνέβη σε ποσοστό 5-42%
- Το PET CT είναι λιγότερο ευαίσθητο σε βλάβες < 7-10 mm.

Η σύσταση της ACCP είναι:

3.1.2. In patients with an imaging finding (eg, by PET) suggestive of a metastasis, further evaluation of the abnormality with tissue sampling to pathologically confirm the clinical stage is recommended prior to choosing treatment (Grade 1B)**.**

Chest. 2013;143(5_suppl):e211S-e250S. doi:10.1378/chest.12-2355

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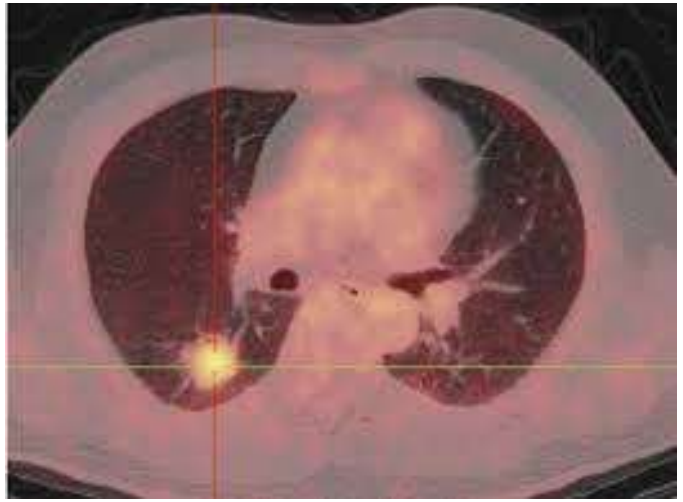
- In patients with suspected or proven <3cm peripheral NSCLC with normal mediastinal and hilar nodes at CT and/or PET, we suggest initiation of therapy **without further mediastinal staging** (Recommendation grade C).



- For mediastinal nodal staging in patients with suspected or proven non-small-cell peripheral lung cancer without mediastinal involvement at CT or CT-PET, 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 fluorodeoxyglucose (FDG)-PET-avid **ipsilateral hilar nodes (N1)**;
(ii) primary tumor **without** FDG uptake; (pulmonary carcinoid, pulmonary adenocarcinoma in situ).
(iii) Tumor size **≥3cm** (Recommendation grade C).

Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer. Endoscopy 2015; 47: 545–559

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 non-small-cell lung cancer (NSCLC) with abnormal mediastinal and/or hilar nodes at computed tomography (CT) and/or positron emission tomography (PET), **endosonography is recommended over surgical staging as the initial procedure (Recommendation grade A).**

- **If endosonography does not show malignant nodal involvement, we suggest that mediastinoscopy is considered, especially in suspected N1 disease (Recommendation grade C).**

Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

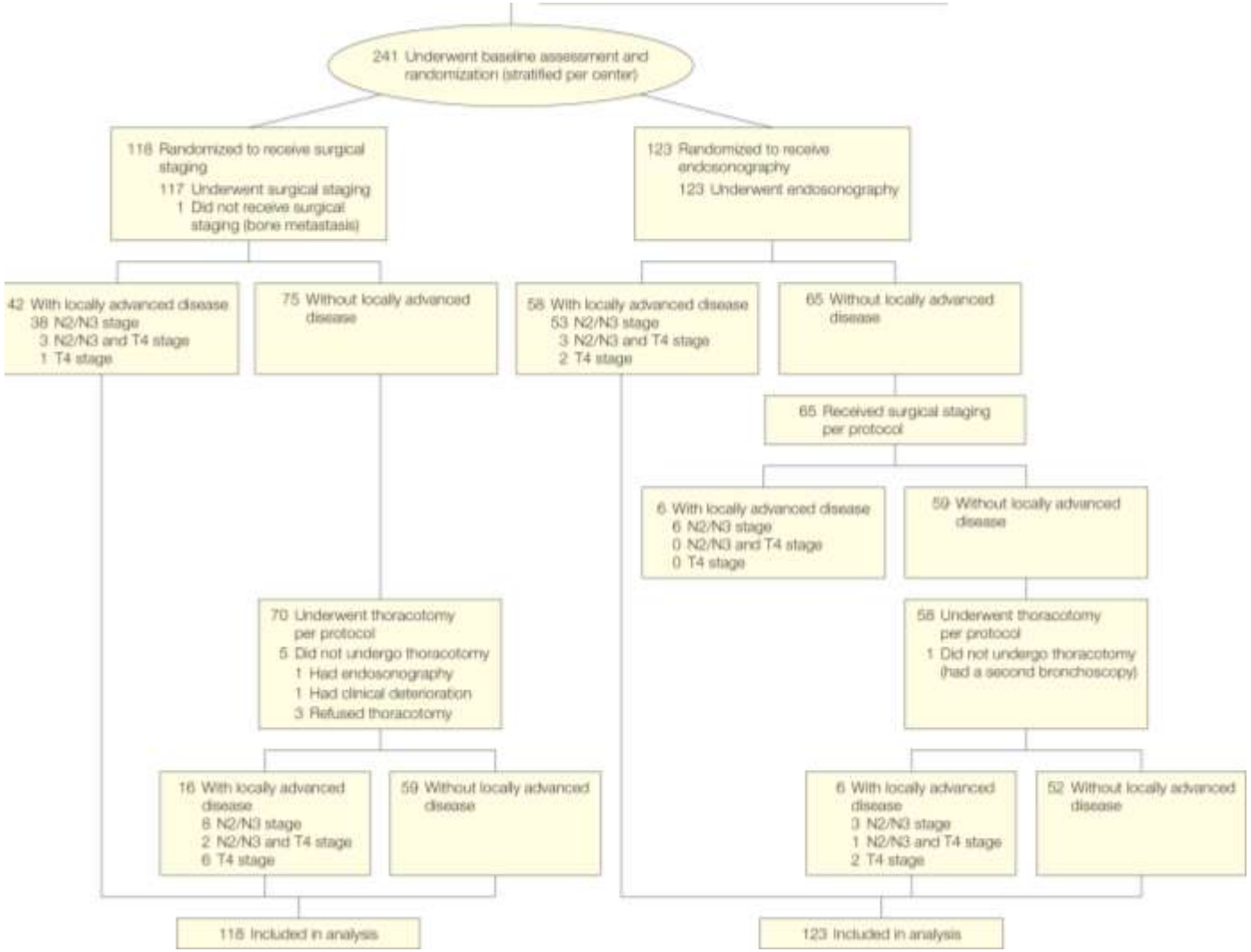
The ASTER study (Assessment of Surgical sTaging versus Endobronchial and endoscopic ultrasound in lung cancer: a Randomized controlled trial

- 241 patients with enlarged or FDG-avid mediastinal lymph nodes, enlarged or FDG-avid hilar lymph nodes, or a central lung lesion were randomized.

- Sensitivity for mediastinal lymph node metastasis was **79% for surgical staging versus 94% for endosonography followed by surgical staging** (P=0.04)

- **Sensitivity of the combination of EUS and EBUS alone–without subsequent surgical staging- 85%;** not significantly different from immediate surgical staging.

- Reduction of unnecessary thoracotomies from **18% to 7%** (P=0.02)



Jouke T. Annema, MD, PhD; JAMA. 2010;304(20):2245-2252. doi:10.1001/jama.2010.1705

Preoperative Staging by EBUS in cN0/N1 Lung Cancer: Systematic Review and Meta-Analysis.

- Sensitivity of systematic staging using EBUS-TBNA for detection of radiologically occult mediastinal metastases in cN0/N1 lung cancer.
- **Mean prevalence of N2/N3 disease was 15%.**

- EBUS-TBNA had pooled sensitivity of 49% [95% confidence interval (CI), 41%-57%], pooled specificity of 100% (95% CI, 99%-100%), mean negative predictive value 91% (82% to 100%) for detection of unsuspected N2/N3 metastases.

- Number needed to test to detect occult N2/N3 disease was 14 (95% CI, 10.8-16.3), which halved with addition of per-esophageal endoscopic ultrasound.

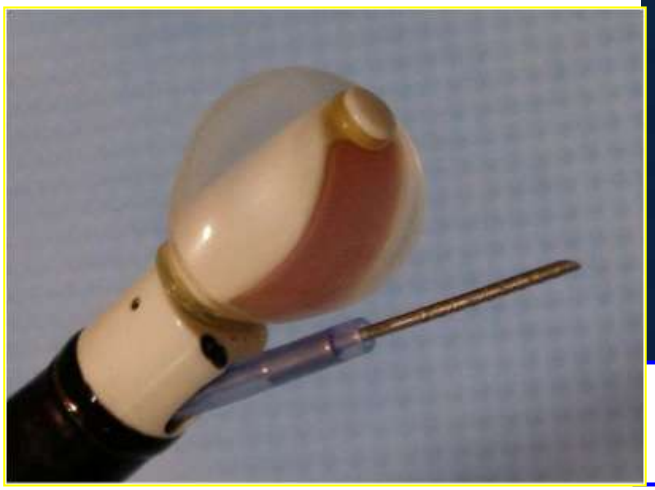
- Preoperative systematic staging by EBUS-TBNA of early lung cancer can reduce postoperative upstaging.

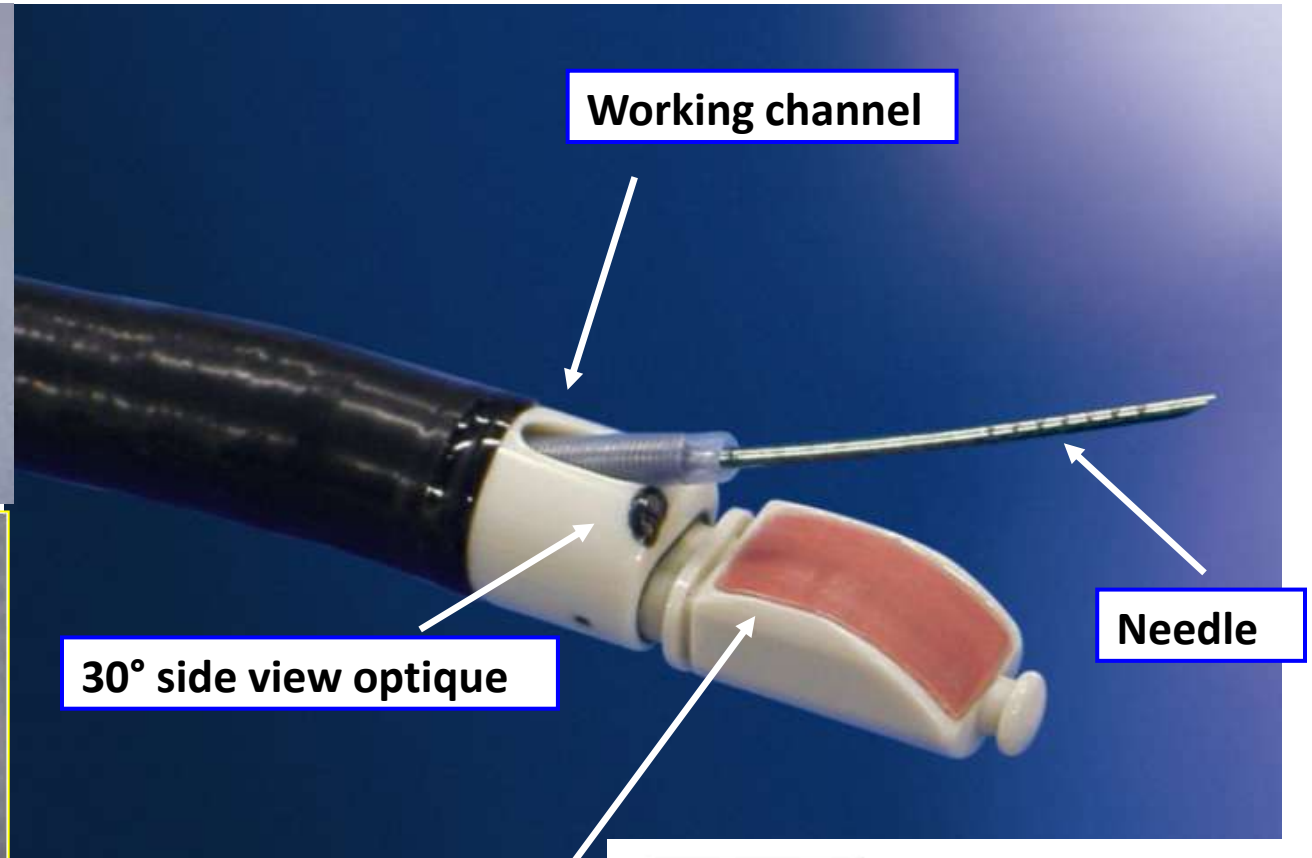
- Verification of negative results by mediastinoscopy in selected cases remains of value.

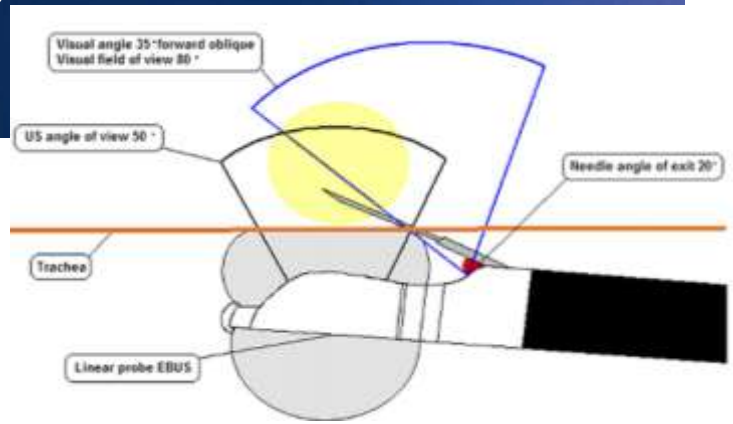
Journal of Bronchology & Interventional Pulmonology

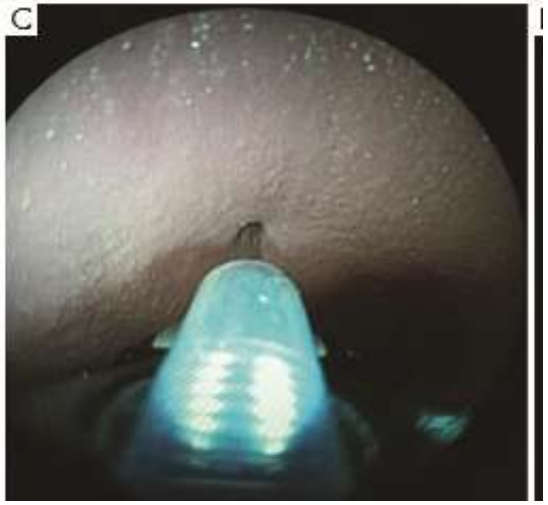
Leong TL. Preoperative Staging by EBUS in cN0/N1 Lung Cancer: Systematic Review and Meta-Analysis.
J Bronchology Interv Pulmonol. 2018 Aug 22.

EBUS-TBNA, EUS- B, EUS-FNA

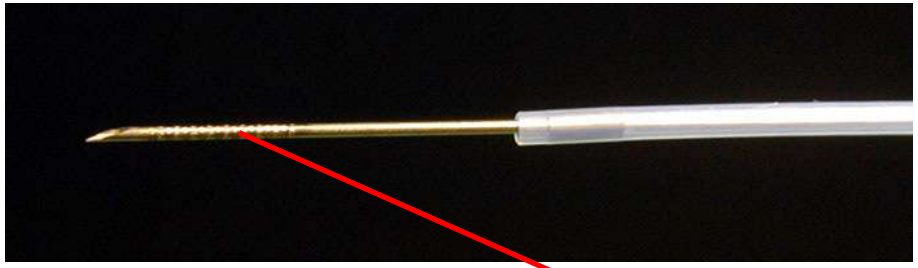








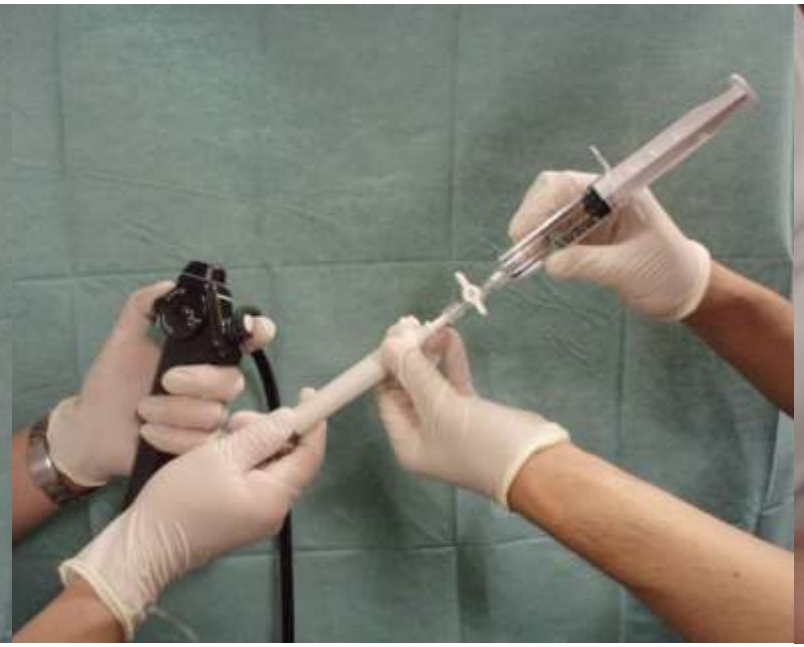
Βελόνα 22Gauge



Η άγρια επιφάνεια επιτρέπει στη βελόνα να φαίνεται στον US και να αποκόπτει ιστικό κύλινδρο

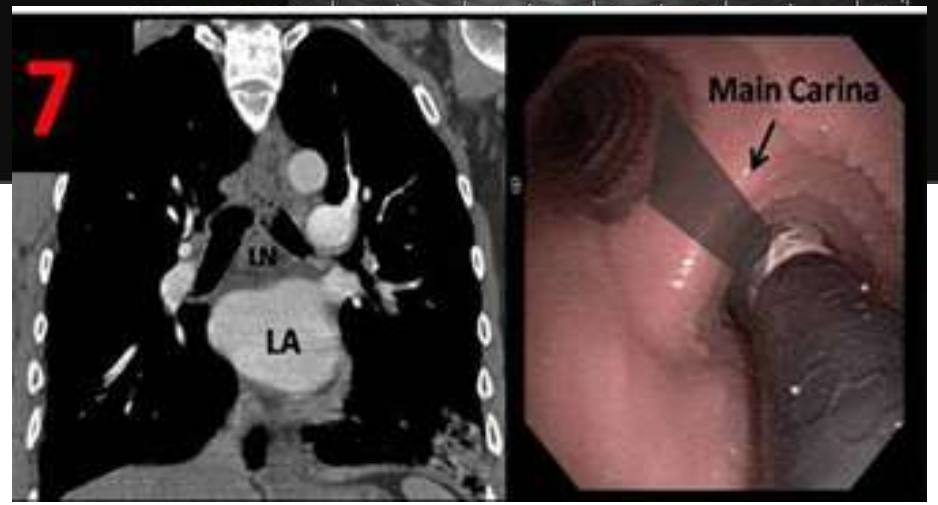
Προσαρμογή στο βρογχοσκόπιο

Δειγματοληψία

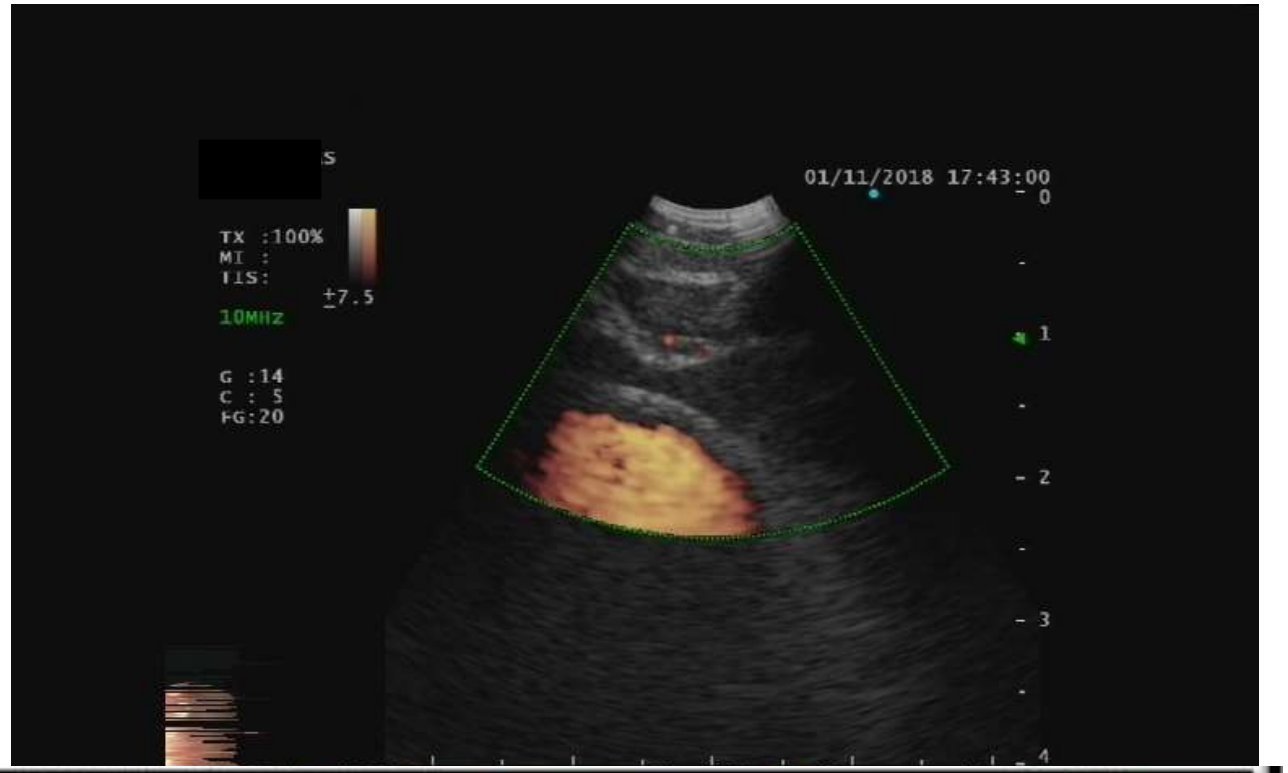


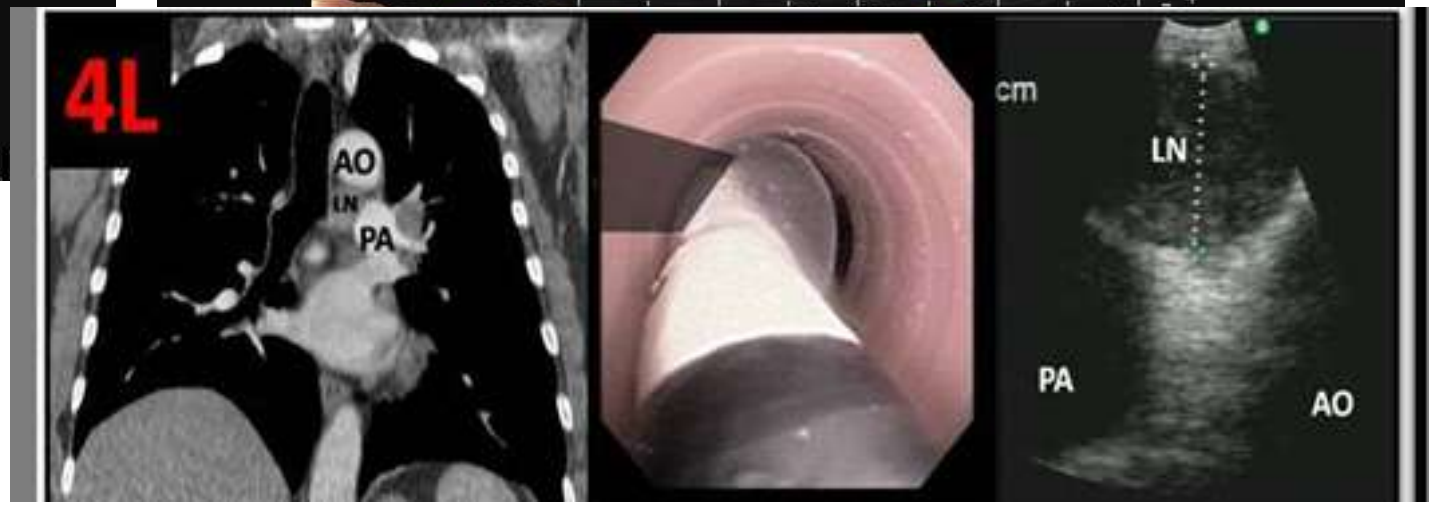
Πλακίδια και ιστικοί κύλινδροι

Σταθμός 7



Σταθμός 4L





Συστηματικός λεμφαδενικός έλεγχος

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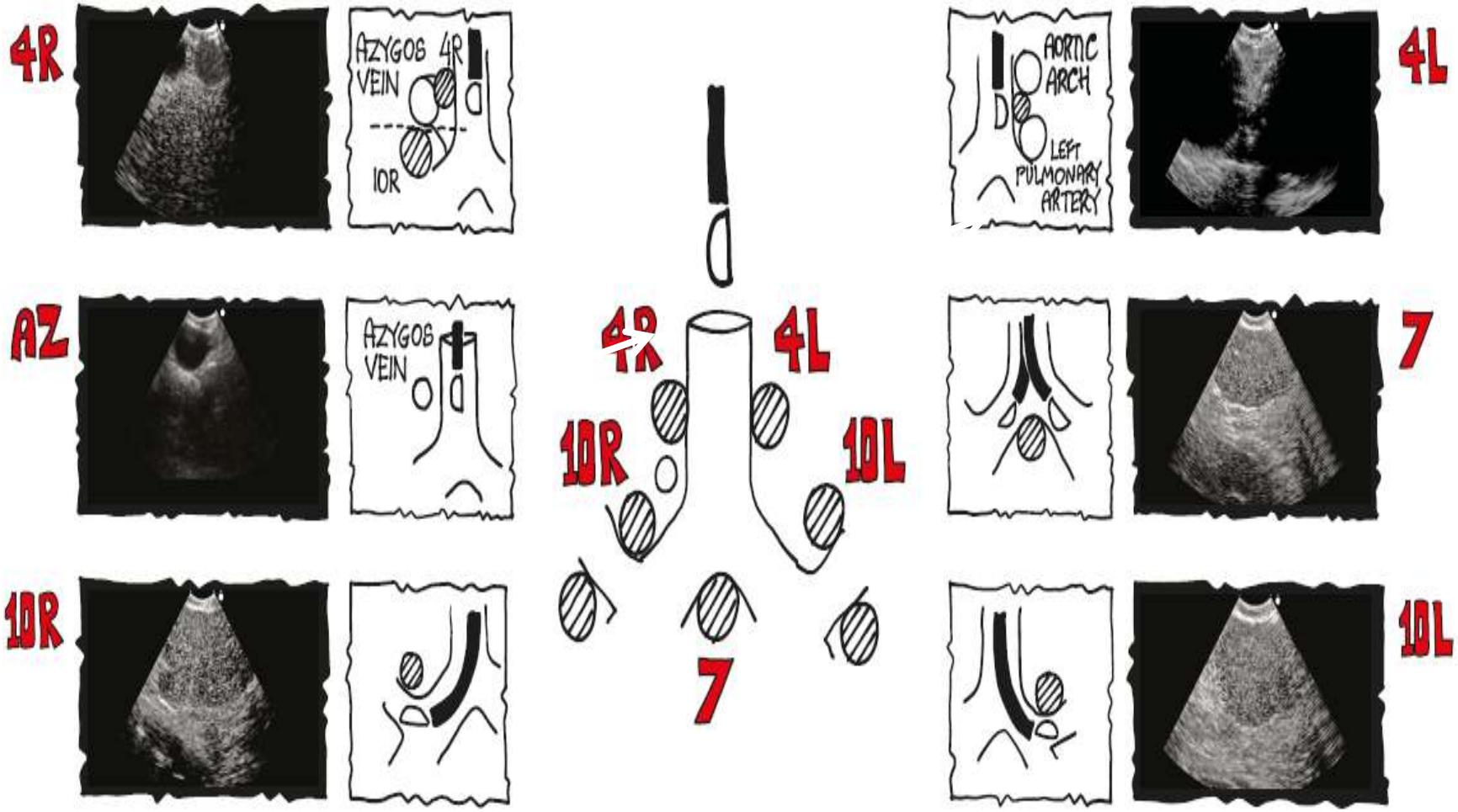
- **A complete assessment of mediastinal and hilar nodal stations, and sampling of at least three different mediastinal nodal stations (4 R, 4L, 7) is suggested** in patients with NSCLC and an abnormal mediastinum by CT or CT-PET (Recommendation grade D).

Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

EBUS 6 LANDMARKS

SEARCH FOR THE LANDMARKS IN THIS ORDER:

4L → 7 → 10L → 10R → AZYGOS → 4R



PFC 2015

FIGURE 14. [Section 4.3.2.3] Endoscopic ultrasound-guided needle aspiration of the mediastinum in patients with lung cancer.

First Author	Year	No.	Stage	Thoro	Prev	Sens	Spec	PPV	NPV
Nadarajan[310]	2010	34	cN2-3	Sel	88	100	(100)[a]	(100)[a]	(100)[b]
Tournoy[312]	2008	100	cN0-3	Sys	83	95	(100)[a]	(100)[a]	(81)[b]
Wallace[143]	2001	121	cN2-3	Sel	79	87	(100)[a]	(100)[a]	68
Annema[323]	2004	36	cN2-3	Sys	78	93	(100)[a]	(100)[a]	80
Wiersema[305]	2001	29	cN2-3	Sel	76	100	(100)[a]	(100)[a]	100
Fritscher-Ravens[301]	2000	35	cN2-3	Lim	74	96	(100)[a]	(100)[a]	90
Annema[316]	2005	215	cN0-3	Sys	71	91	(100)[a]	(100)[a]	74
Larsen[324]	2002	29	cN2-3	Lim	69	90	(100)[a]	(100)[a]	82
Annema[306]	2010	551	cN2-3	Sys	66	83	(100)[a]	(100)[a]	75
Caddy[320]	2005	36	cN0-3	Sel	65	92	(100)[a]	(100)[a]	83
Kalade[311]	2008	33	cN1-3	Sel	64	95	(100)[a]	(100)[a]	92
Silvestri[304]	1996	26	cN0-3	Sys	62	89	(100)[a]	(100)[a]	82
Gress[302]	1998	24	cN2-3	Sel	58	93	(100)[a]	(100)[a]	90
Herth[307]	2010	139	cN1-3	Sel	52	89	(100)[a]	(100)[a]	82
Talebian[309]	2010	152	cN2-3	Sys	49	74	(100)[a]	(100)[a]	73
Sawhney[313]	2006	65	cN2-3	Sys	48	87	(100)[a]	(100)[a]	90
Fritscher-Ravens[179]	2003	33	cN0-3	Sys	48	88	(100)[a]	(100)[a]	89
Larsen[324]	2005	58	cN0-3	Sys	47	87	(100)[a]	(100)[a]	87
Eloubeidi[315]	2005	104	cN2-3	Sys	41	93	(100)[a]	(100)[a]	96
Eloubeidi[318]	2005	35	cN2-3	Sys	37	91	(100)[a]	(100)[a]	97
Annema[317]	2005	100	cN2-3	Sys	36	71	90	86	85
Wallace[322]	2004	69	cN0	Sys	36	61	(100)[a]	(100)[a]	82
LeBlanc[321]	2005	67	cN0	Sel	33	45	(100)[a]	(100)[a]	79
Wallace[296]	2008	138	cN2-3	Sys	30	69	(100)[a]	(100)[a]	88
Szlubowski[308]	2010	120	cN0	Sel	22	50	99	93	87
Fernandez-Esparrach[314]	2006	47	cN0	Sys	21	50	(100)[a]	(100)[a]	88
Median: prevalence > 80		% sys	50%			**96**			**90**
Median: prevalence 60-79		% sys	40%			**92**			**82**
Median: prevalence 40-59		% sys	71%			**88**			**88**
Median: prevalence 20-39		% sys	71%			**61**			**87**
Median: cN1-3		% sys	47%			**92**			**89**
Median: cN0-1		% sys	50%			**50**			**85**
Summary: median		**2,443**			**58**	**89**	**(100)[a]**	**(100)[a]**	**86**

Chest. 2013;143(5_suppl):e211S-e250S.
doi:10.1378/chest.12-2355

Author	Reference standard	Test order	Patients, n	Prevalence N2/N3, %	EBUS		EUS		EBUS + EUS (95 %CI)	
					Sensitivity (95 %CI)	NPV (95 %CI)	Sensitivity (95 %CI)	NPV (95 %CI)	Sensitivity (95 %CI)	NPV (95 %CI)
Vilmann 2005 [32]	■ Surgery: – Pulmonary resection with lymph node exploration ■ Clinical follow-up	EUS – EBUS	28	71 %	0.85 (0.62 – 0.97)	0.72 (0.39 – 0.94)	0.80 (0.56 – 0.94)	0.67 (0.35 – 0.90)	1.00 (0.83 – 1.00)	1.00 (0.63 – 1.00)
Wallace 2008 [31]	■ Surgery: – Pulmonary resection with mediastinal exploration – Mediastinoscopy – Thoracoscopy ■ Clinical follow-up	EBUS – EUS	138	30 %	0.69 (0.53 – 0.82)	0.88 (0.80 – 0.93)	0.69 (0.53 – 0.82)	0.88 (0.80 – 0.93)	0.93 (0.81 – 0.99)	0.97 (0.91 – 0.99)
Annema 2010 [18]	■ Surgery: – Pulmonary resection with node dissection	EUS – EBUS	123	54 %	–	–	–	–	0.85 (0.74 – 0.92)	0.85 (0.74 – 0.93)
Herth 2010 [34]	■ Surgery: – Thoracoscopy – Pulmonary resection with node dissection ■ Clinical follow-up	EBUS – EUS-B	139	52 %	0.92 (0.83 – 0.97)	0.92 (0.83 – 0.97)	0.89 (0.79 – 0.95)	0.89 (0.80 – 0.95)	0.96 (0.88 – 0.99)	0.96 (0.88 – 0.99)
Ohnishi 2011 [33]	■ Surgery: – Pulmonary resection with nodal exploration	EBUS – EUS	110	28 %	–	–	–	–	0.84 (0.71 – 0.97)	0.94 (0.89 – 0.99)
Kang (1) 2014 [35]	■ Surgery: – Pulmonary resection with node dissection – Video-assisted thoracic surgery	EBUS – EUS-B	74	46 %	–	–	–	–	0.84 (0.66 – 0.95)	0.94 (0.87 – 0.98)
Kang (2) 2014 [35]	■ Surgery: – Pulmonary resection with node dissection – Video-assisted thoracic surgery	EUS-B – EBUS	74	34 %	0.82 (0.65 – 0.93)	0.87 (0.74 – 0.95)	–	–	0.85 (0.69 – 0.95)	0.89 (0.76 – 0.96)

Vilmann Peter et al. Endoscopy 2015; 47: 545–559

Περιορισμοί EBUS TBNA

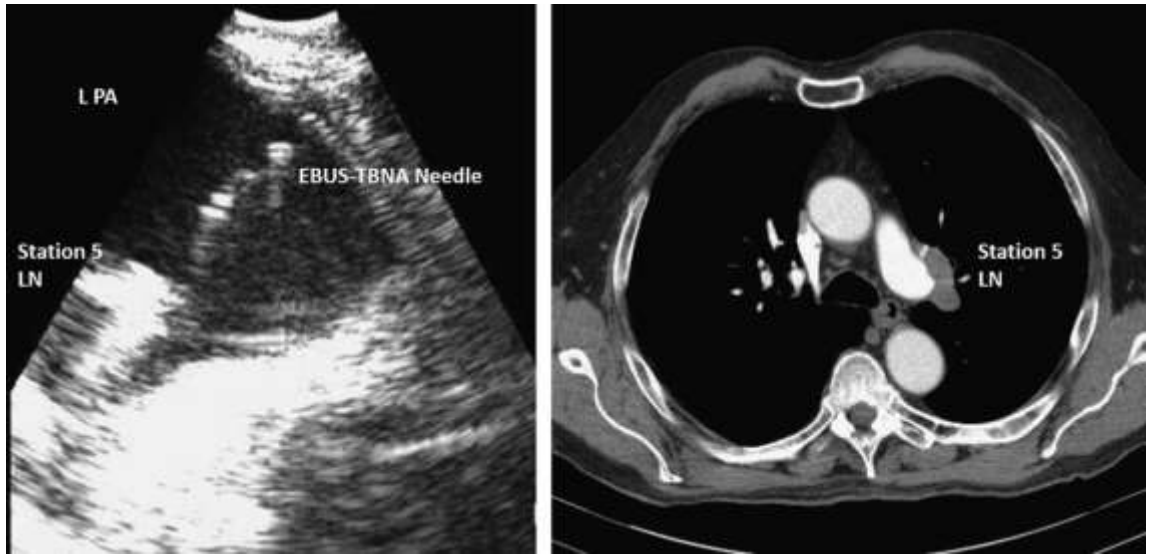
- Οι λεμφαδενικοί σταθμοί 5,6 δεν προσεγγίζονται από το linear EBUS

- Stations 5 and 6 can be well visualized by EUS but can rarely be sampled without traversing the pulmonary artery/aorta.

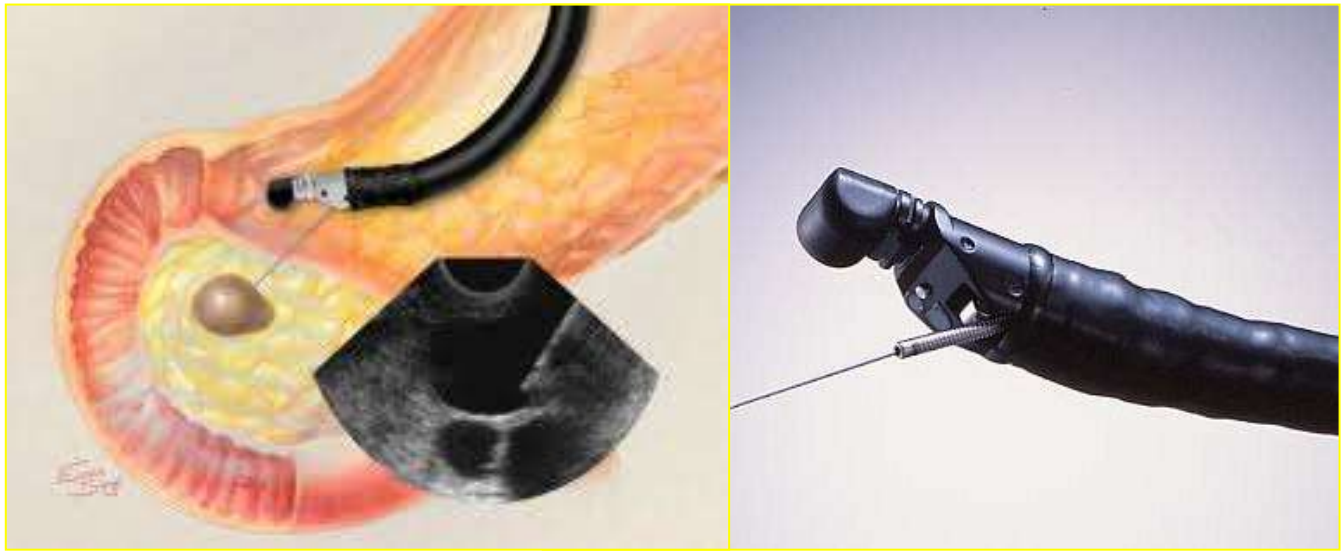
- Surgical staging by video-assisted thoracic surgery(VATS) is the method of choice for nodes in stations 5 and 6.

•Οι σταθμοί 8,9 προσεγγίζονται με το **EUS-FNA- υπερηχογαστροσκόπιο**).

TVNA, transvascular needle aspiration



Journal of Bronchology & Interventional ulmonology22(4):306-311, October 2015.



Vilmann Peter et al. Endoscopy 2015; 47: 545–559

Μέση ευαισθησία και ειδικότητα από κέντρα τα οποία πραγματοποίησαν έλεγχο με EBUS TBNA και EUS FNA

FIGURE 16. [Section 4.3.2.5] Real-time EBUS-TBNA and EUS-NA of the mediastinum in patients with lung cancer.

First Author	Year	No.	Stage	Thoro	Prev	Sens	Spec[a]	PPV[a]	NPV
Vilmann[353]	2005	31	cN0-3	sys	65	100	(100)[a]	(100)[a]	100
Annema[228]	2010	123	cN1-3	sys	54	82	(100)[a]	(100)[a]	80
Herth[307]	2010	139	cN1-3	sel	52	96	(100)[a]	(100)[a]	96
Ohnishi[352]	2011	110	cN0-3	sys	35	72	(100)[a]	(100)[a]	87
Hwangbo[335]	2010	150	cN2-3	sys	31	91	(100)[a]	(100)[a]	96
Wallace[296]	2008	138	cN2-3	sys	30	93	(100)[a]	(100)[a]	97
Szlubowski[308]	2010	120	cN0	sel	22	68	98	91	91
Median: prevalence 40-65						**96**			**96**
Median: prevalence 20-39						**82**			**94**
Summary: median		**811**			**33**	**91**	**(100)[a]**	**(100)[a]**	**96**

Chest. 2013;143(5_suppl):e211S-e250S. doi:10.1378/chest.12-2355

Author	Reference standard	Test order	Patients, n	Prevalence N2/N3, %	EBUS		EUS		EBUS + EUS (95 %CI)	
					Sensitivity (95 %CI)	NPV (95 %CI)	Sensitivity (95 %CI)	NPV (95 %CI)	Sensitivity (95 %CI)	NPV (95 %CI)
Vilmann 2005 [32]	■ Surgery: – Pulmonary resection with lymph node exploration ■ Clinical follow-up	EUS – EBUS	28	71 %	0.85 (0.62 – 0.97)	0.72 (0.39 – 0.94)	0.80 (0.56 – 0.94)	0.67 (0.35 – 0.90)	1.00 (0.83 – 1.00)	1.00 (0.63 – 1.00)
Wallace 2008 [31]	■ Surgery: – Pulmonary resection with mediastinal exploration – Mediastinoscopy – Thoracoscopy ■ Clinical follow-up	EBUS – EUS	138	30 %	0.69 (0.53 – 0.82)	0.88 (0.80 – 0.93)	0.69 (0.53 – 0.82)	0.88 (0.80 – 0.93)	0.93 (0.81 – 0.99)	0.97 (0.91 – 0.99)
Annema 2010 [18]	■ Surgery: – Pulmonary resection with node dissection	EUS – EBUS	123	54 %	–	–	–	–	0.85 (0.74 – 0.92)	0.85 (0.74 – 0.93)
Herth 2010 [34]	■ Surgery: – Thoracoscopy – Pulmonary resection with node dissection ■ Clinical follow-up	EBUS – EUS-B	139	52 %	0.92 (0.83 – 0.97)	0.92 (0.83 – 0.97)	0.89 (0.79 – 0.95)	0.89 (0.80 – 0.95)	0.96 (0.88 – 0.99)	0.96 (0.88 – 0.99)
Ohnishi 2011 [33]	■ Surgery: – Pulmonary resection with nodal exploration	EBUS – EUS	110	28 %	–	–	–	–	0.84 (0.71 – 0.97)	0.94 (0.89 – 0.99)
Kang (1) 2014 [35]	■ Surgery: – Pulmonary resection with node dissection – Video-assisted thoracic surgery	EBUS – EUS-B	74	46 %	–	–	–	–	0.84 (0.66 – 0.95)	0.94 (0.87 – 0.98)
Kang (2) 2014 [35]	■ Surgery: – Pulmonary resection with node dissection – Video-assisted thoracic surgery	EUS-B – EBUS	74	34 %	0.82 (0.65 – 0.93)	0.87 (0.74 – 0.95)	–	–	0.85 (0.69 – 0.95)	0.89 (0.76 – 0.96)

Vilmann Peter et al. Endoscopy 2015; 47: 545–559

Συνδυαστική προσπέλαση μεσοθωρακίου από το EBUS βρογχοσκόπιο μέσω οισοφάγου και τραχείας

Combined Endoscopic-Endobronchial Ultrasound-Guided Fine-Needle Aspiration of Mediastinal Lymph Nodes Through a Single Bronchoscope in 150 Patients With Suspected Lung Cancer

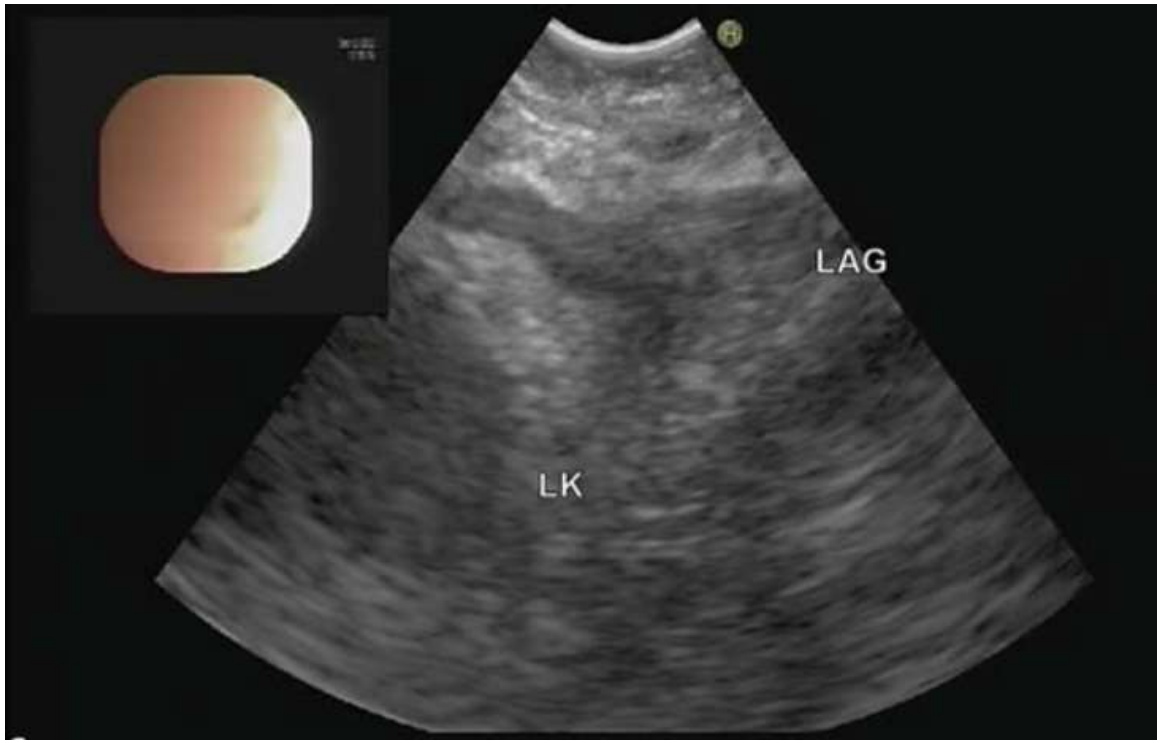
Felix J. F. Herth, Mark Krasnik, Nicolas Kahn, Ralf Eberhardt and Armin Ernst

Chest 2010;138;790-794; Prepublished online February 12, 2010;
DOI 10.1378/chest.09-2149

The combined approach had a sensitivity of 96% and a negative predictive value of 95%, values higher than either approach alone. No complications occurred.
Conclusions: The two procedures can easily be performed with a dedicated linear endobronchial ultrasound bronchoscope in one setting and by one operator. They are complementary and provide better diagnostic accuracy than either one alone. The combination may be able to replace more invasive methods as a primary staging method for patients with lung cancer.

CHEST 2010; 138(4):790–794

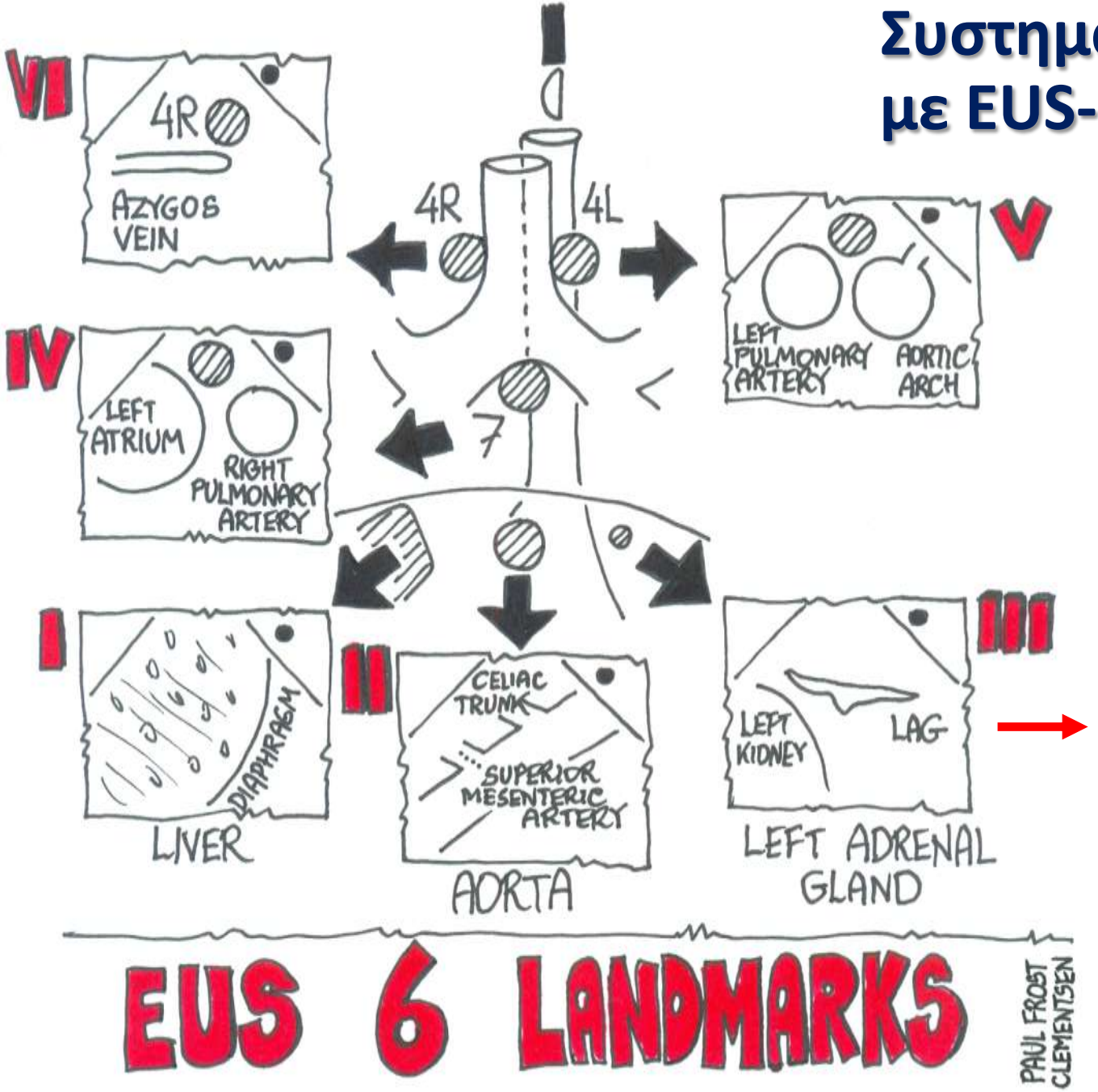
Left Adrenal Gland Analysis in Lung Cancer Patients Using the Endobronchial Ultrasound Scope: A Feasibility Trial



- Retrospective analysis 143 patients, EBUS and EUS-B, LAG with identification of LAG
- LAG was detected in 85% of patients
- Punctured only in 9 patients, but puncture was successful
- Length of scope is not a limiting factor

Crombag L et al Respiration 2016;91:235-240

Συστηματική προσέγγιση σταθμών με EUS-B



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)

ESGE ERS EUROPEAN RESPIRATORY SOCIETY every breath counts

- In patients with a left adrenal gland suspected for distant metastasis **we suggest performance of endoscopic ultrasound fine needle aspiration (EUS-FNA)** (Recommendation grade C), while **the use of EUS-B with a transgastric approach is at present experimental** (Recommendation grade D).

- 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).

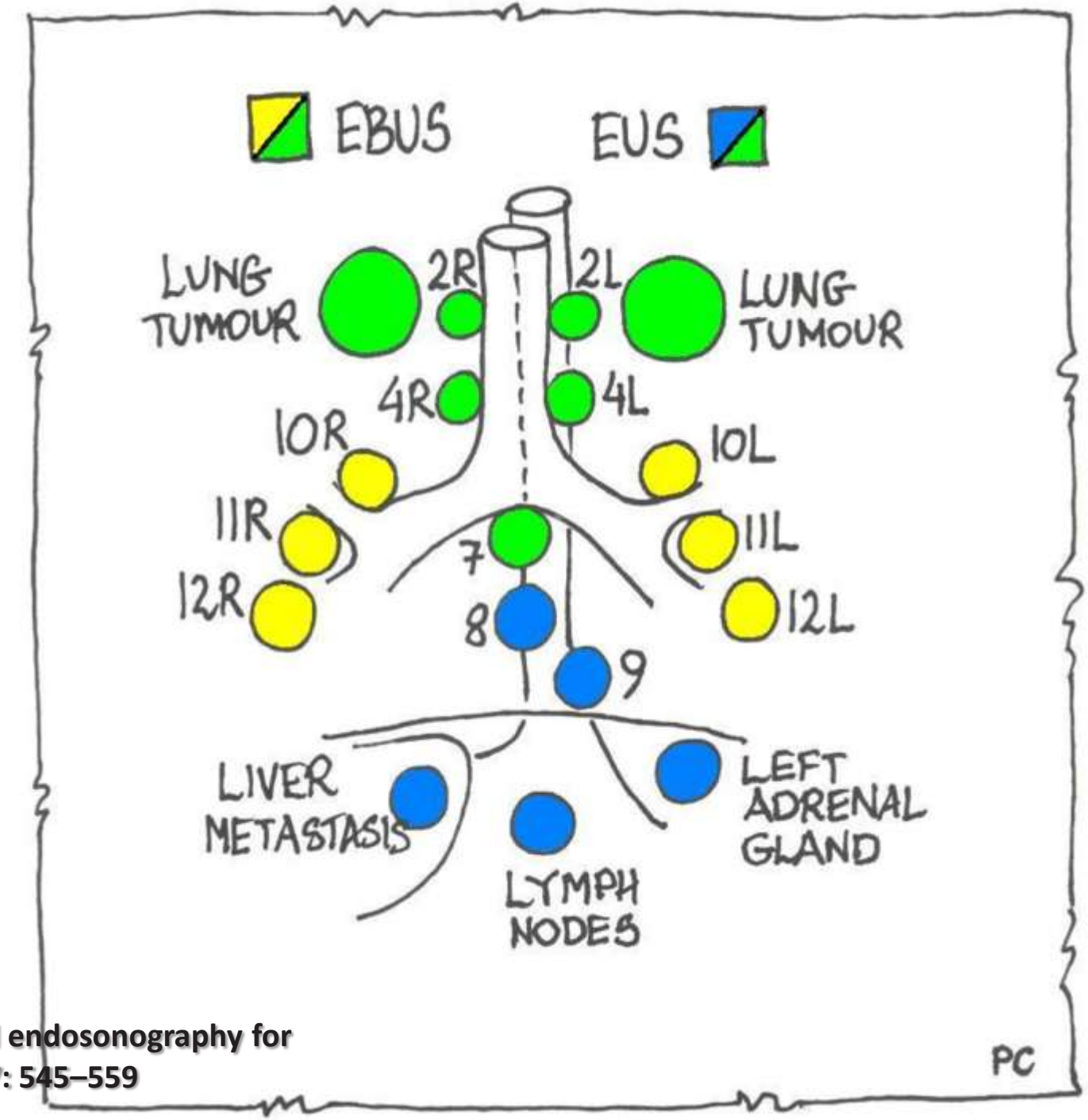
Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

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)

ESGE ERS EUROPEAN RESPIRATORY SOCIETY every breath counts

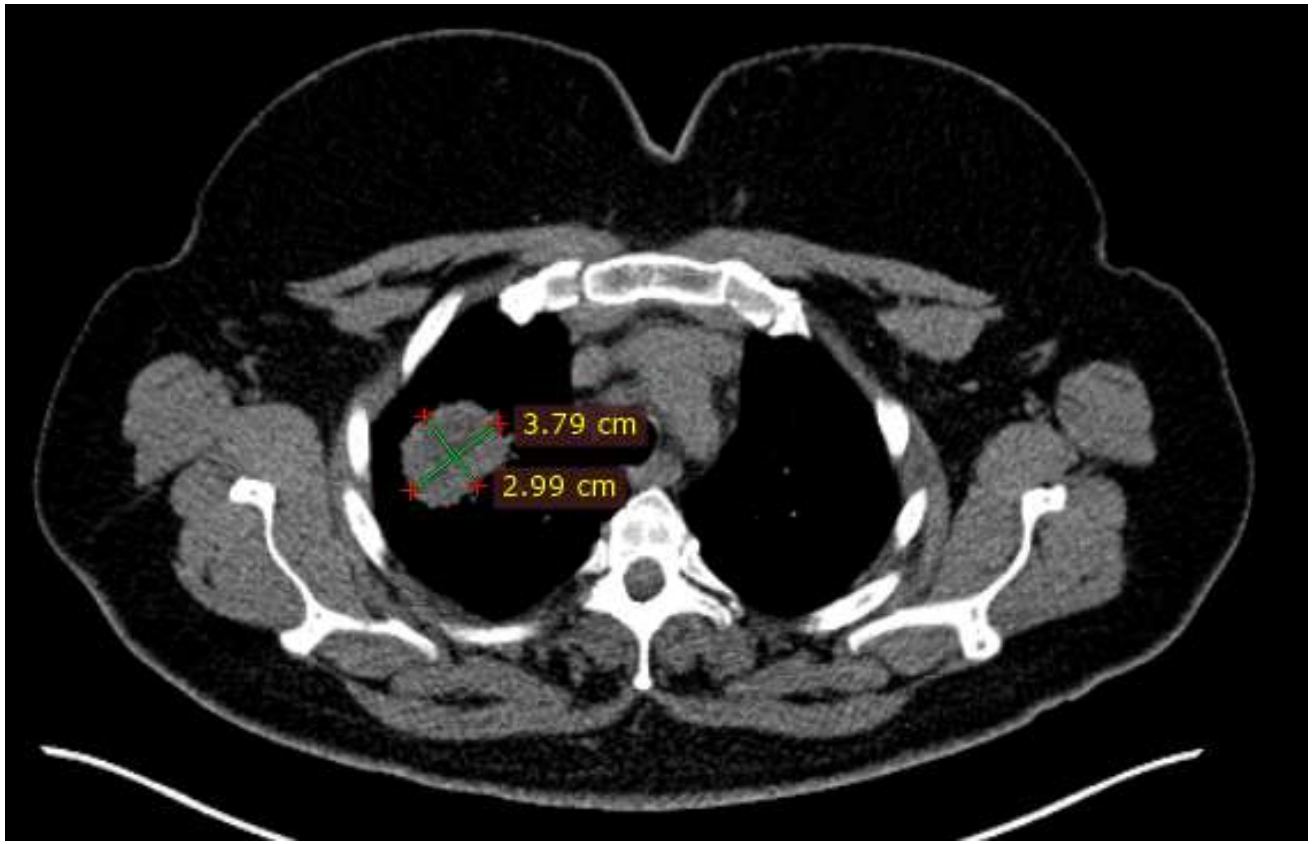
- The combination of endobronchial ultrasound with real-time guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic (esophageal) ultrasound with fine needle aspiration,with use of a gastrointestinal (EUS-FNA) or EBUS (EUS-B-FNA) scope, is preferred over either test alone (Recommendation grade C).

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

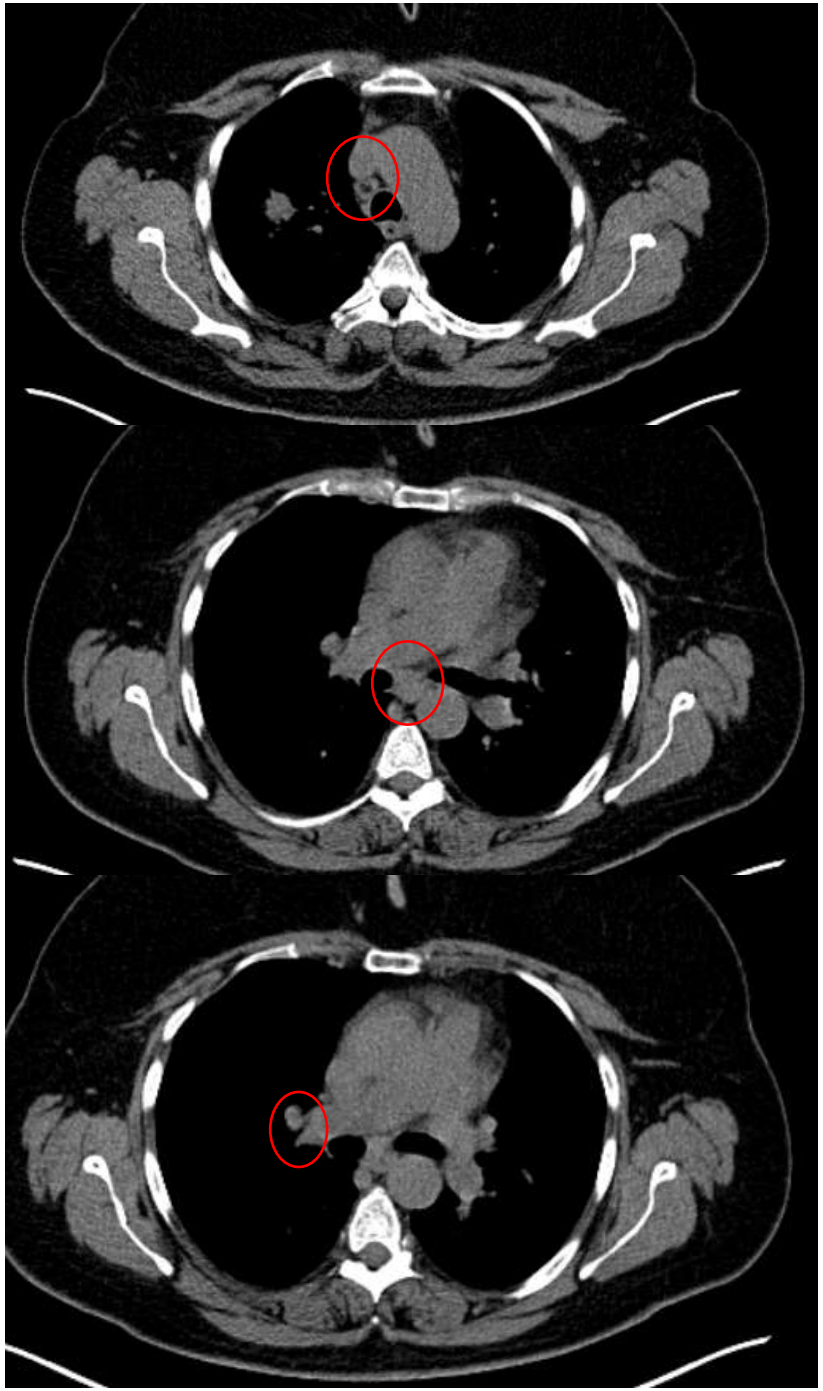


Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

Γυναίκα, 52 ετων, πρώην καπνίστρια με ξηρό βήχα



Εξεργασία δεξιού άνω λοβού- T2a



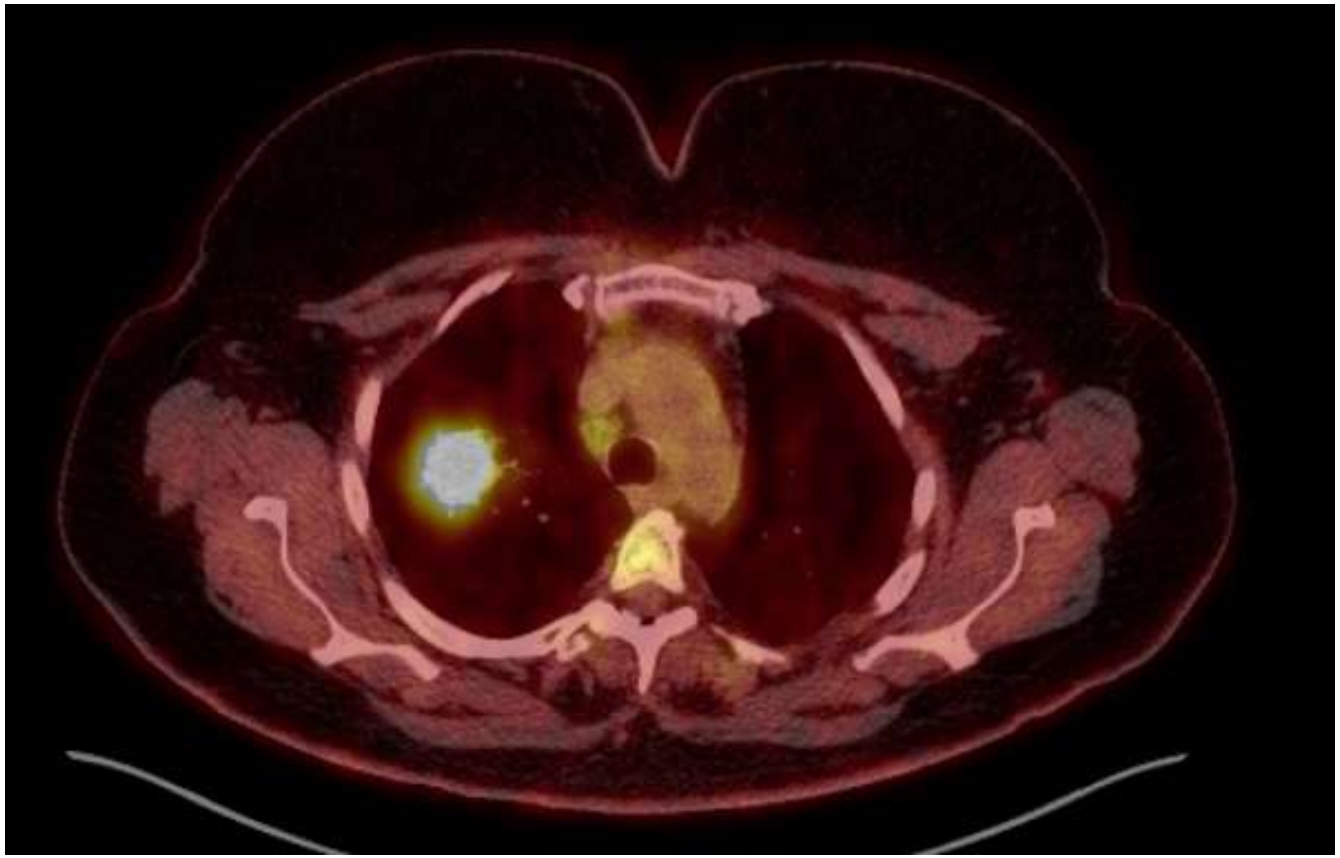
4R

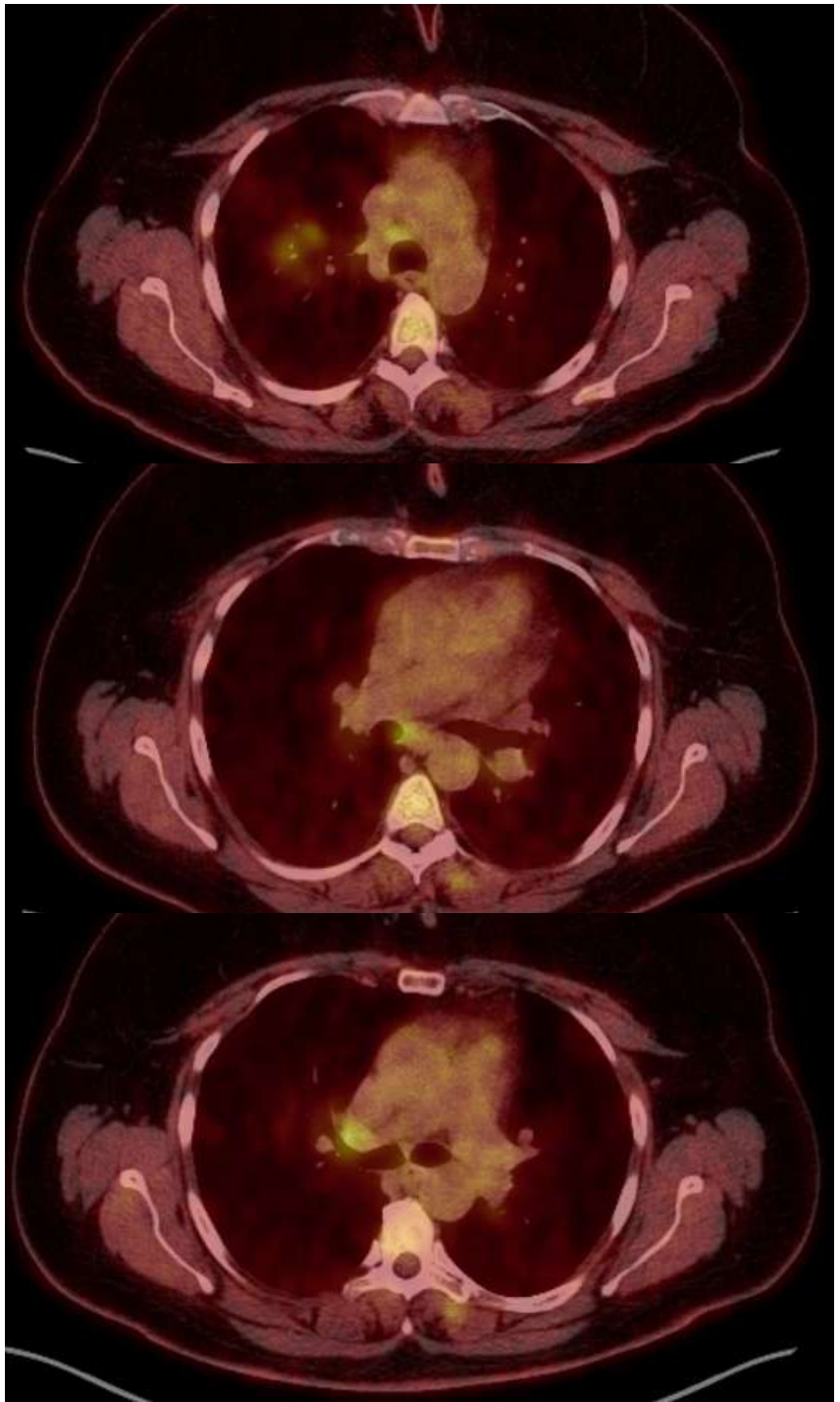
7

10R

N?

PET CT υψηλή πρόσληψη στη βλάβη, αλλά και σε λεμφαδένες 4R, 7 και 10R





4R

7

10R

ΠΟΙΟ ΈΙΝΑΙ ΤΟ ΕΠΟΜΕΝΟ ΒΗΜΑ?

11L - 4 mm PET CT (-) όχι παρ.

N3

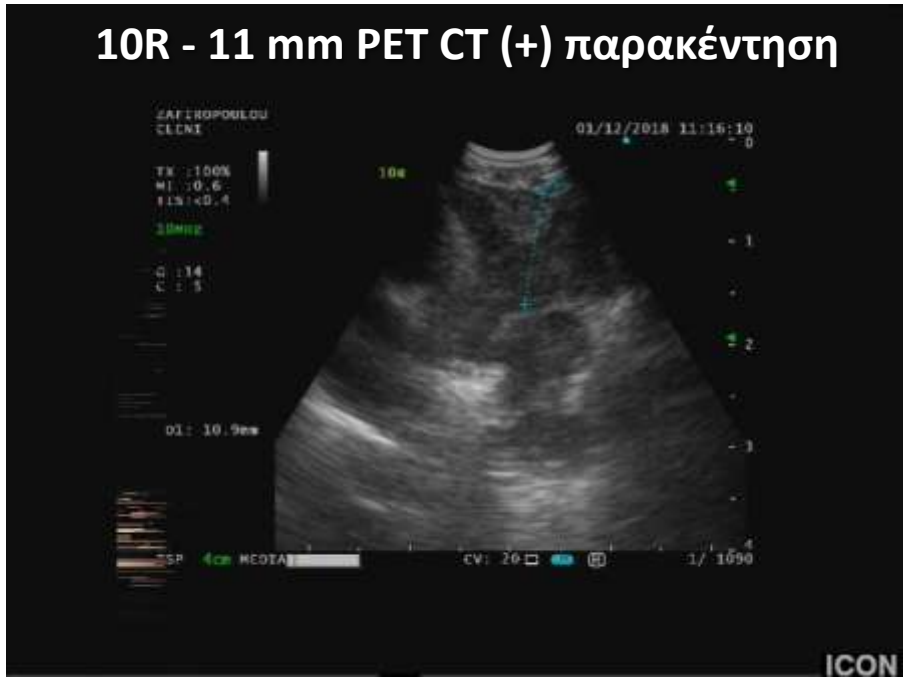
7 - 9 mm PET CT (+) παρακέντηση

N2

4R - 5 mm PET CT (+) παρακέντηση

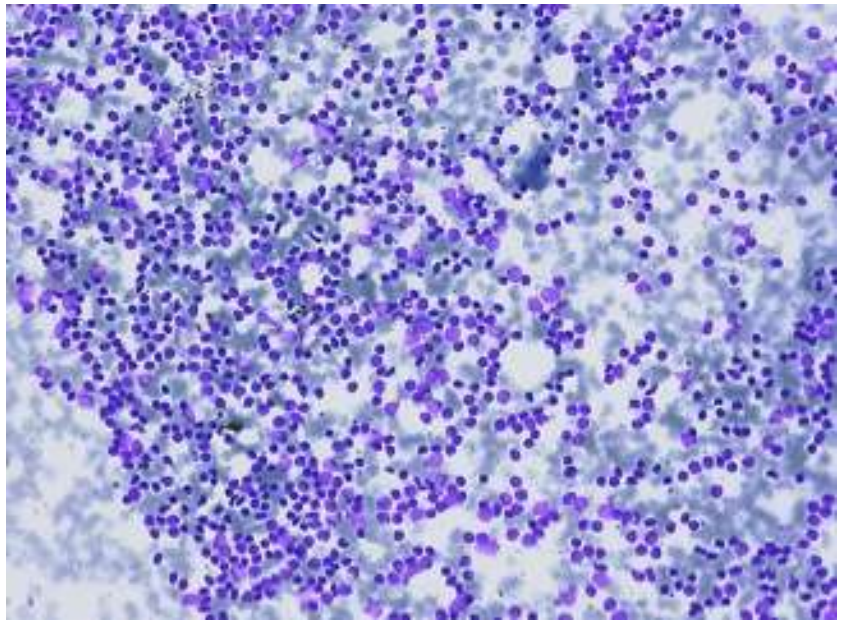
N2

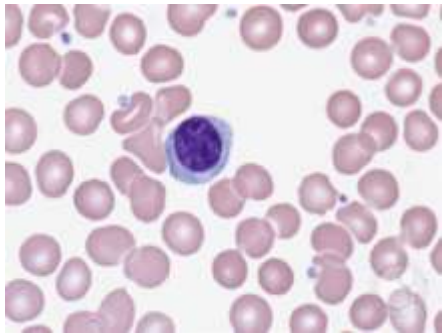
10R - 11 mm PET CT (+) παρακέντηση

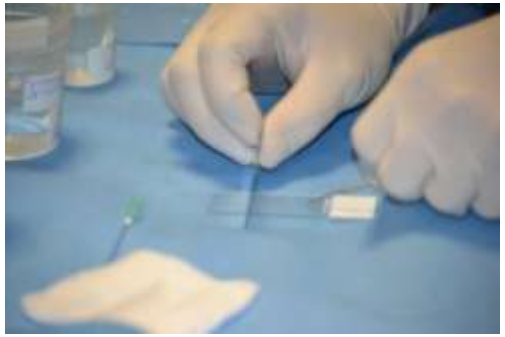


N1

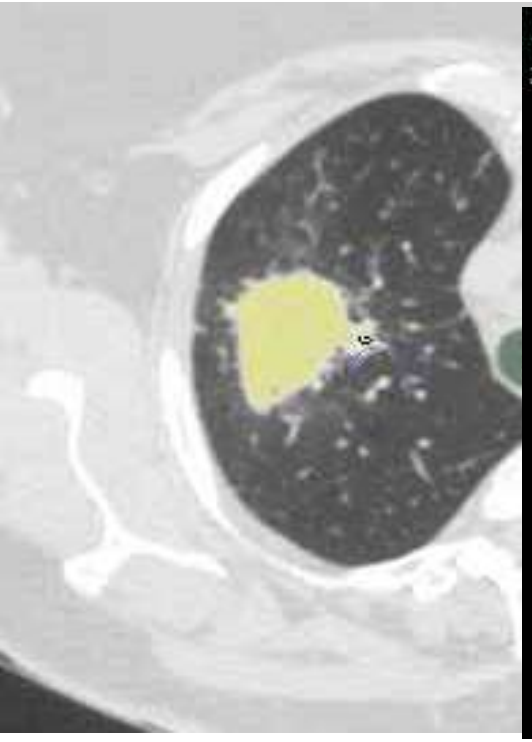
RAPID ON SITE EVALUATION (ROSE)

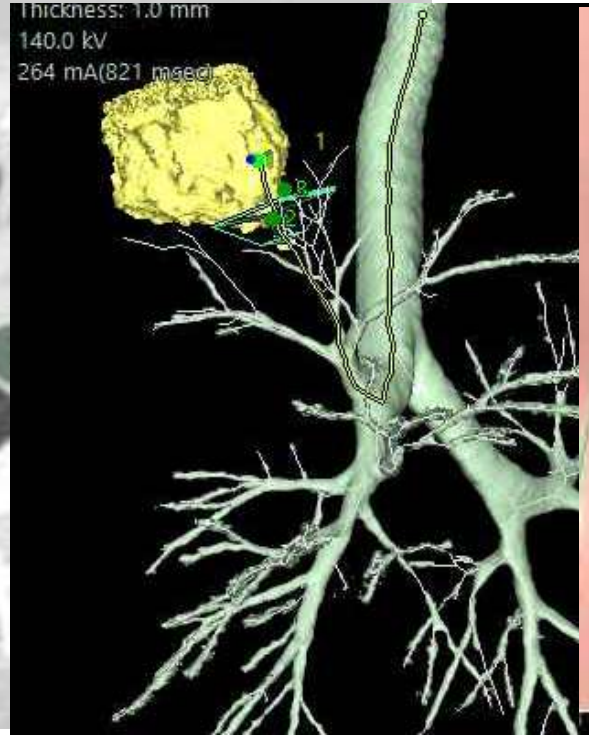


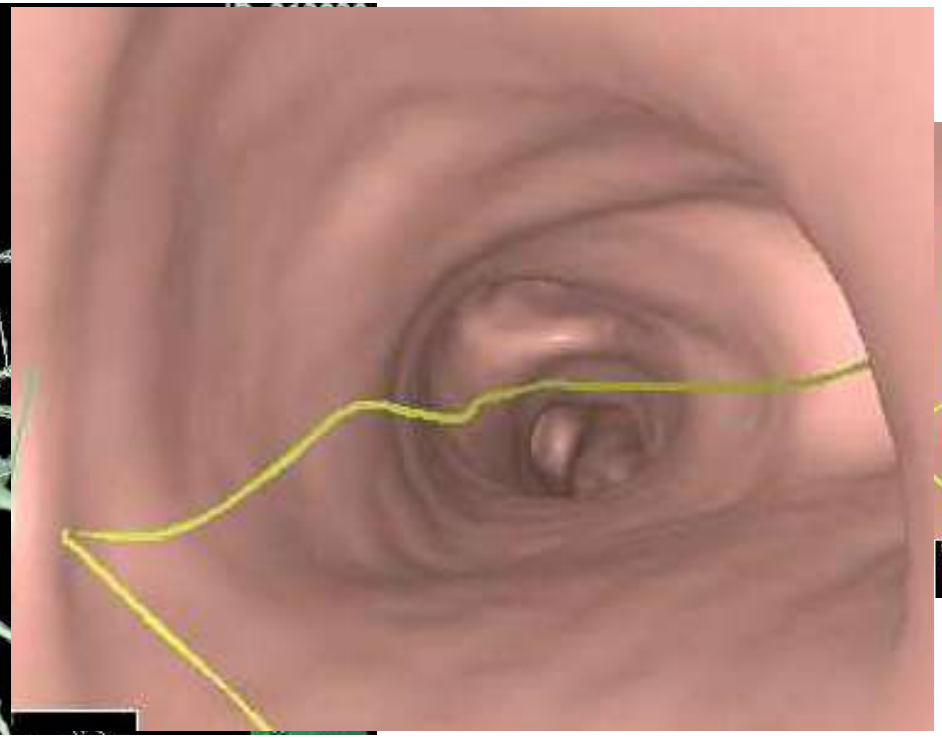


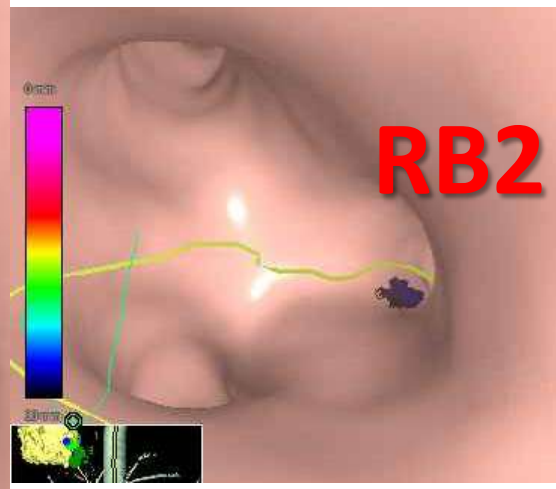


Virtual Bronchoscopy- χαρτογράφηση των βρόγχων με το σύστημα synapse®

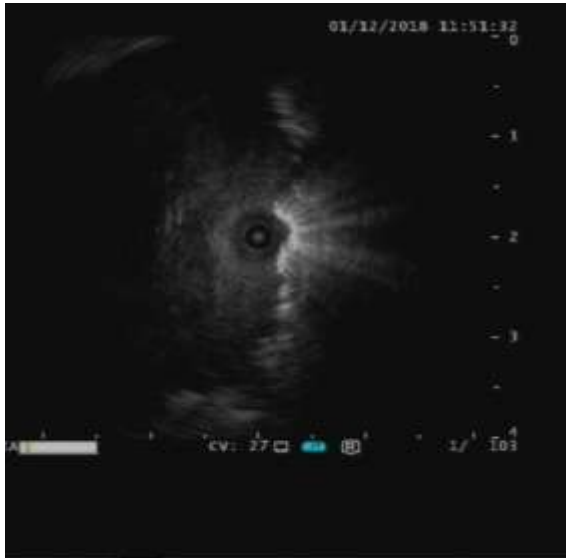


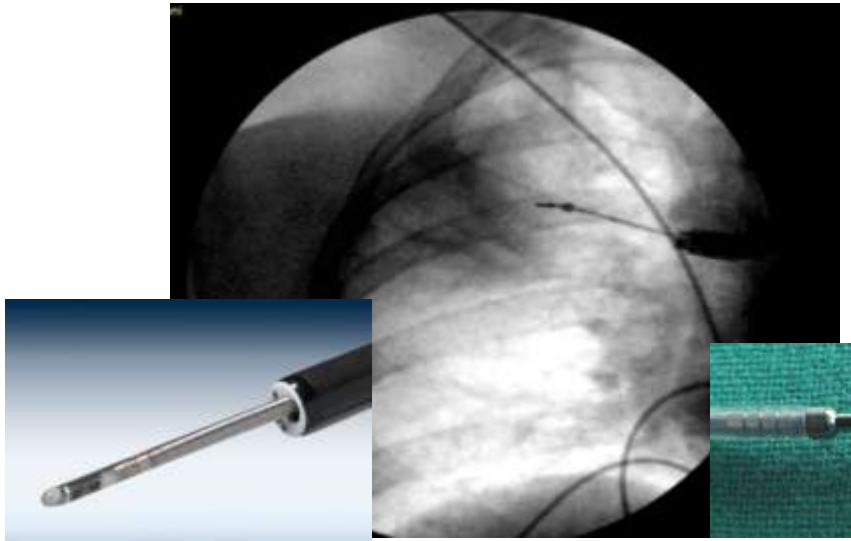






Συνδυασμός εύκαμπτης βρογχοσκόπησης- radial EBUS- ακτινοσκόπησης – βελόνας 22G - ΑΔΕΝΟΚΑΡΚΙΝΩΜΑ





Επανασταδιοποίηση με EBUS-EUS-b?

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)

ESGE ERS EUROPEAN RESPIRATORY SOCIETY every breath counts

- 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).

Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

Endobronchial Ultrasound With Transbronchial Needle Aspiration for Restaging the Mediastinum in Lung Cancer

- 124 ασθενείς (IIIA) επανασταδιοποίηση με EBUS TBNA
- CT: 58(47%) stable, 66(53%) downstaged
- EBUS: Persistent 89(72%) nodal metastasis
- **From 35 patients in whom no metastases were assessed by EBUS TBNA 28 had residual N2 disease**
- **Negative predictive value: 20%**

Table 2. Outcomes for Restaging EBUS-TBNA According to Tumor Response After Chemotherapy As Assessed by RECIST Criteria

	Tumor Response Outcome (%)	
Criteria	Partial Response (n = 66)	Stable Disease (n = 58)
Sensitivity	77	75
Specificity	100	100
PPV	100	100
NPV	22	18
Accuracy	79	76

Abbreviations: EBUS-TBNA, endobronchial ultrasound–guided transbronchial needle aspiration; RECIST, Response Evaluation Criteria in Solid Tumors Group; PPV, positive predictive value; NPV, negative predictive value.

Λόγω της χαμηλής αρνητικής προγνωστικής αξίας προτείνεται μεσοθωρακοσκόπηση για επιβεβαίωση των αρνητικών EBUS TBNA

Herth et al J Clin Oncol 2008; 26:3346-3350

Ανάλυση μεταλλάξεων με EBUS TBNA

Adequacy of Samples Obtained by EBUS-TBNA for Molecular Analysis in Patients with Non-Small Cell Lung Cancer: Systematic Review and Meta-Analysis

Gonzalo Labarca [1,2,3], Erik Folch[3,4], Michael Jantz[3,5], Hiren J. Mehta[3,5], Adnan Majid[3,6], Sebastian Fernandez-Bussy[3,7]

Table 6. Summary of findings: Molecular analysis from NSCLC using samples obtained by EBUS-TBNA.

Outcomes	Explanation, measure effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
EGFR (overall)	Samples achieved by EBUS-TBNA are 94.8% (93% to 96.4) adequate for EGFR analysis	2497 (28 observational studies)	⊕◯◯◯[1,2,3] VERY LOW
EGFR (Asia)	Samples achieved by EBUS-TBNA is Asia are 98.9% (98.1% to 99.7%) adequate for EGFR analysis	626 (8 observational studies)	⊕⊕◯◯[1,3] LOW
ALK (overall)	Samples achieved by EBUS-TBNA are 94.9% (89.4% to 98.8) adequate for ALK analysis	607 (10 observational studies)	⊕◯◯◯[1,2,3] VERY LOW

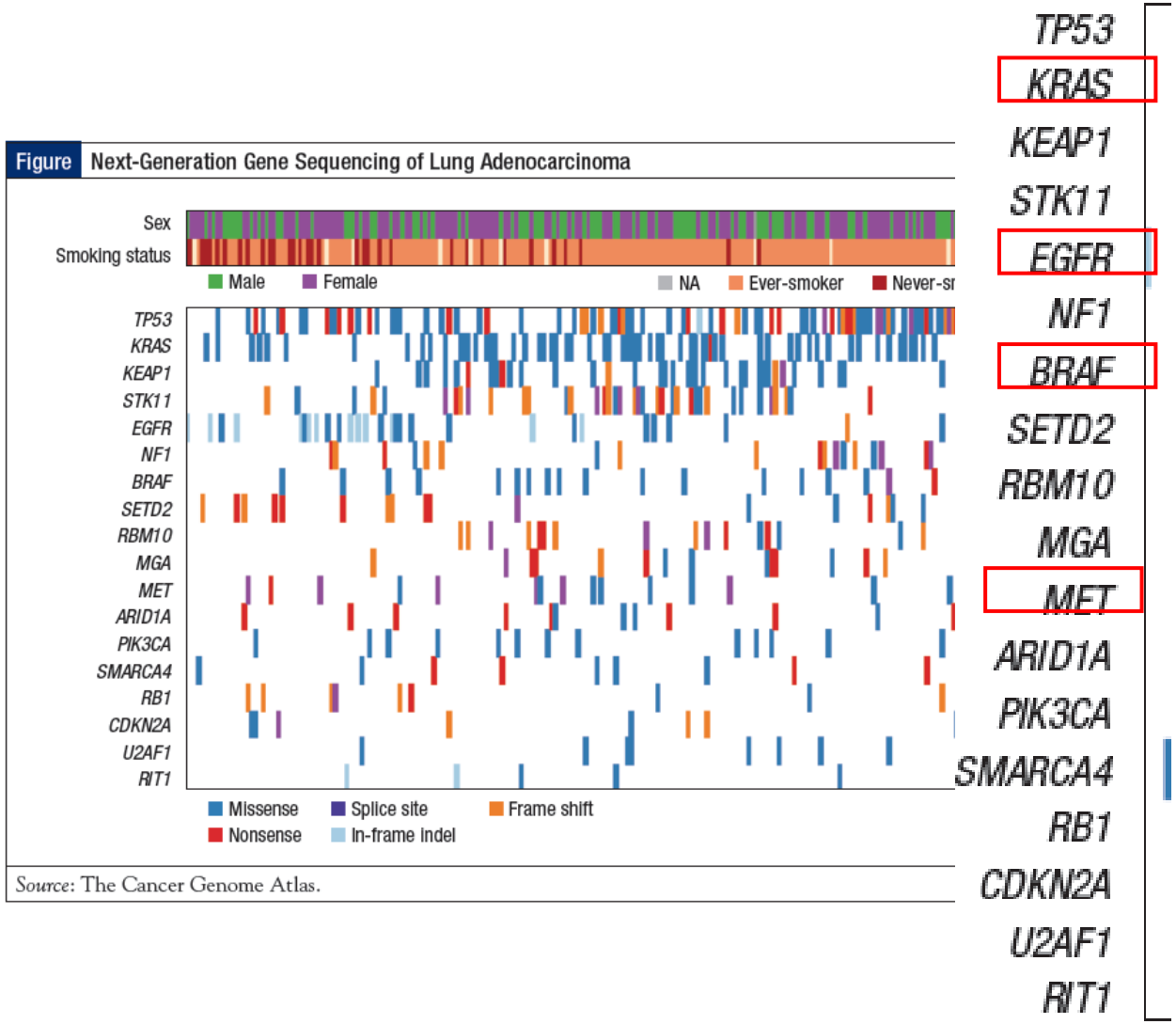
1: Risk of bias; 2: Imprecision; 3: Indirectness.

Conclusion: EBUS-TBNA has a high yield for molecular analysis of both EGFR and ALK mutations.

Ann Am Thorac Soc. 2018 Oct;15(10):1205-1216.

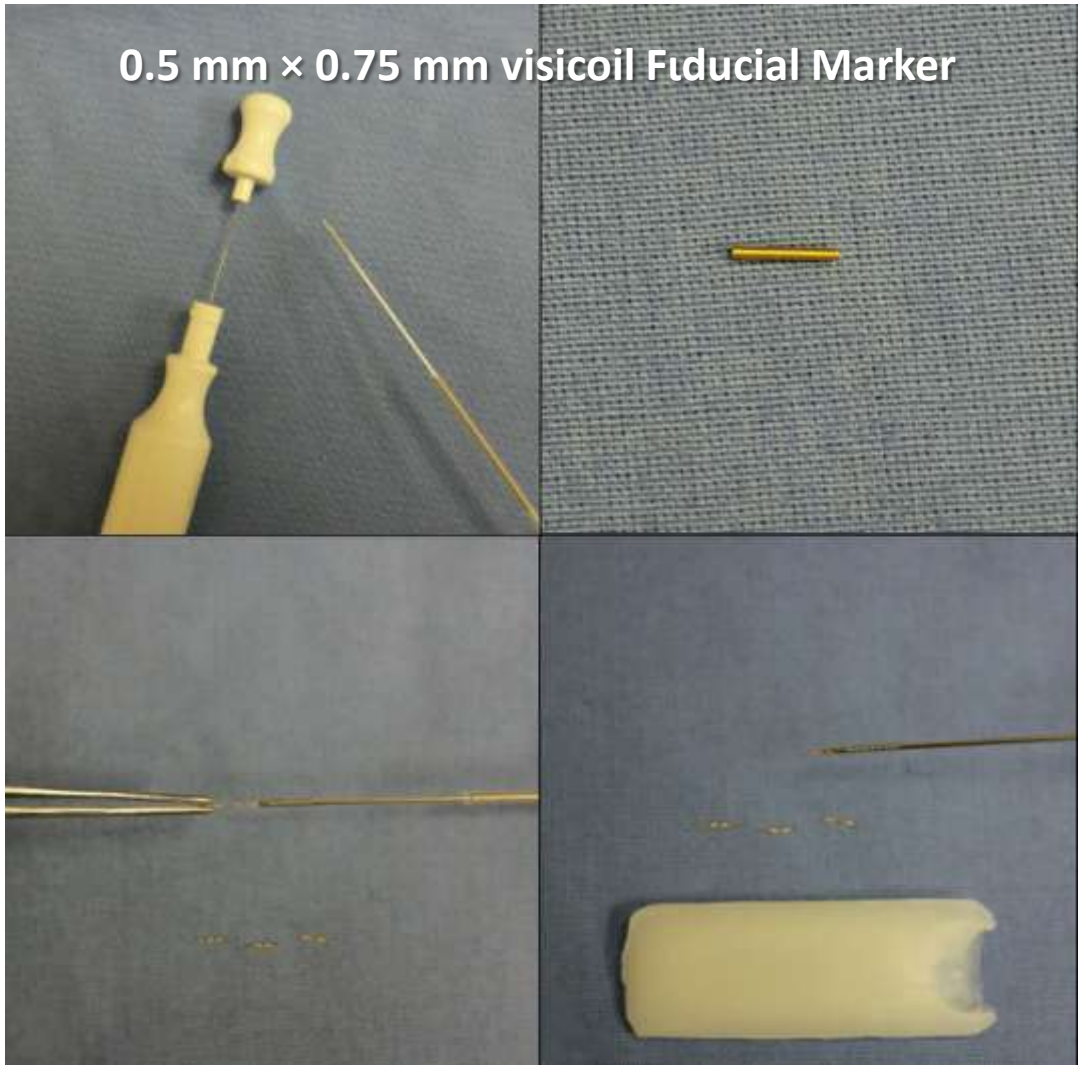
Linear EBUS needle aspiration for massively parallel next-generation sequencing in thoracic cancer patients.

- Next-generation sequencing (NGS) allows for the identification of a growing number of therapeutic and prognostic molecular targets.
- 784 EBUS-TBNA procedures performed
- MSK-IMPACT was requested for 115 malignant samples and was successful for 99 (86.1%), identifying an average of 12.7 mutations at a mean coverage depth of 806X.
- NGS was performed on paraffin-embedded cell blocks in 93 cases (93.9%) and on cell-free DNA in needle rinse fluid in 6 cases.
- The success rate of the assay improved significantly from the first third of cases (76.3%), to 92.3% for the final one-third of cases ($p < 0.05$).
- **EBUS-TBNA reliably provided adequate tissue for hybrid capture NGS**



Lung Cancer. 2018 May;119:85-90. doi: 10.1016/j.lungcan.2018.03.003. Epub 2018 Mar 7.

Fiducial marker placement for stereotactic body radiation therapy via convex probe endobronchial ultrasound: a case series and review of literature



J Thorac Dis 2018;10(3):1972-1983

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)

ESGE ERS EUROPEAN RESPIRATORY SOCIETY every breath counts

- 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).

Vilmann Peter et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer… Endoscopy 2015; 47: 545–559

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