27.30 NOV '25

CONGRESSO
SPP
SOCIEDADE PORTUGUESA DE PNEUMOLOGIA
1º CONGRESSO IBERO-AMERICANO DE PNEUMOLOGIA

Novas Indicações para EBUS/EUS

Sessão Intervenção Pulmonar: Ferramentas Avançadas em Ação

Helder Novais e Bastos

hnovaisbastos@med.up.pt

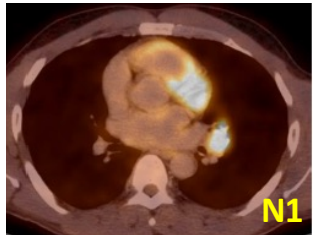
TIVOLI MARINA HOTEL
ALGARVE - PORTUGAL

SPP SOCIEDADE PORTUGUESA DE PNEUMOLOGIA

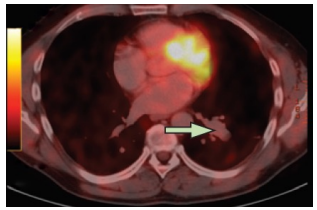
Agenda

- Indications for lung cancer staging
- EBUS/EUS vs surgical staging
- 9th Edition of TNM staging system
- T4 assessment through E(B)US
- M1 staging through EUS/EUS-B
- E(B)US used for primary tumor diagnosis
- Improving the yield through cryo-EBUS

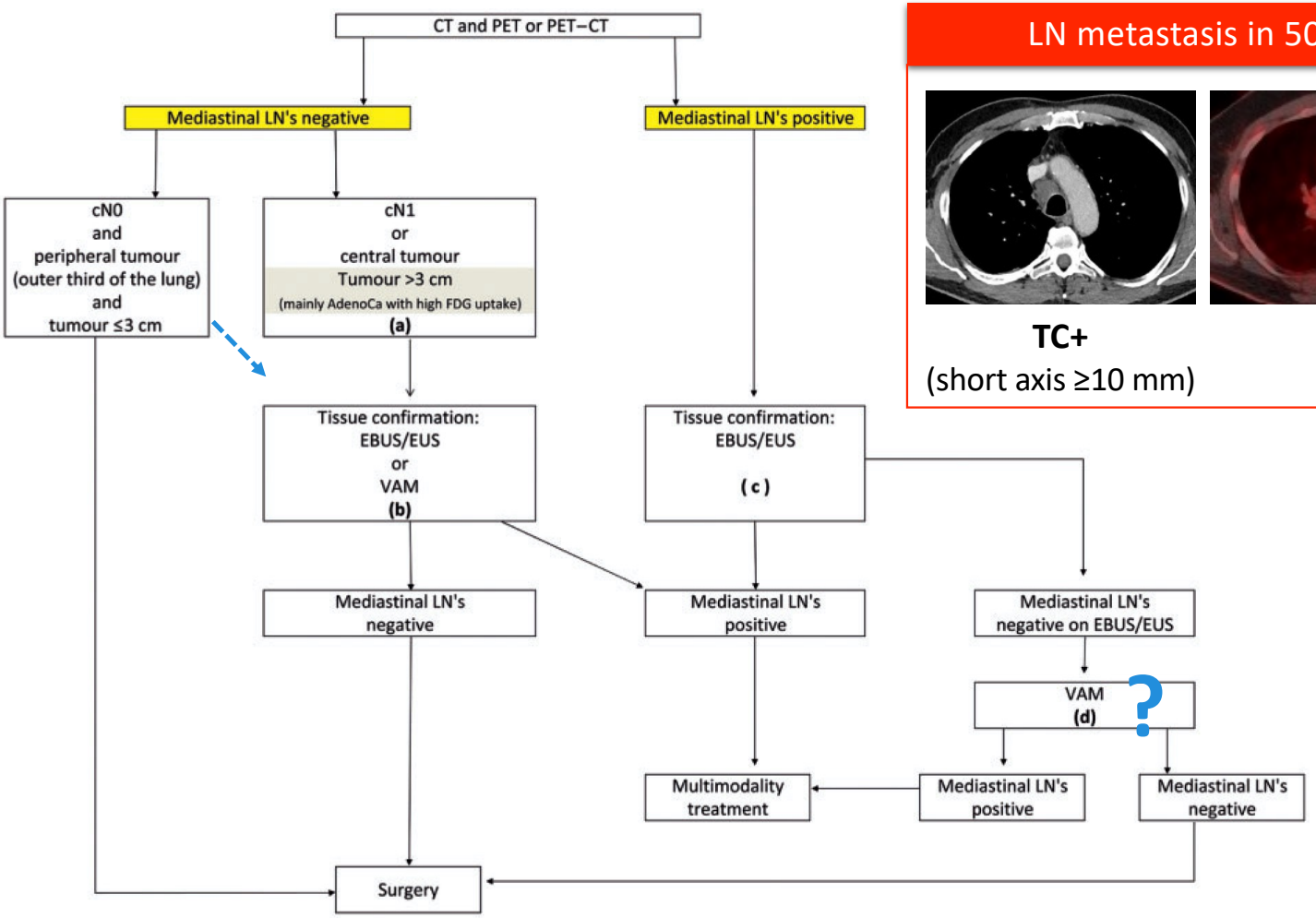
LN metastasis (N2/N3) in 6-30%



T >3 cm
T central

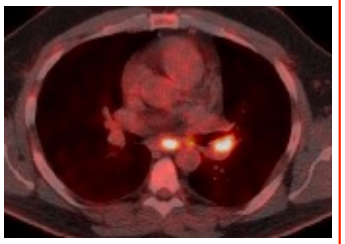


PET (-)



LN metastasis in 50-80%

TC+
(short axis ≥10 mm)

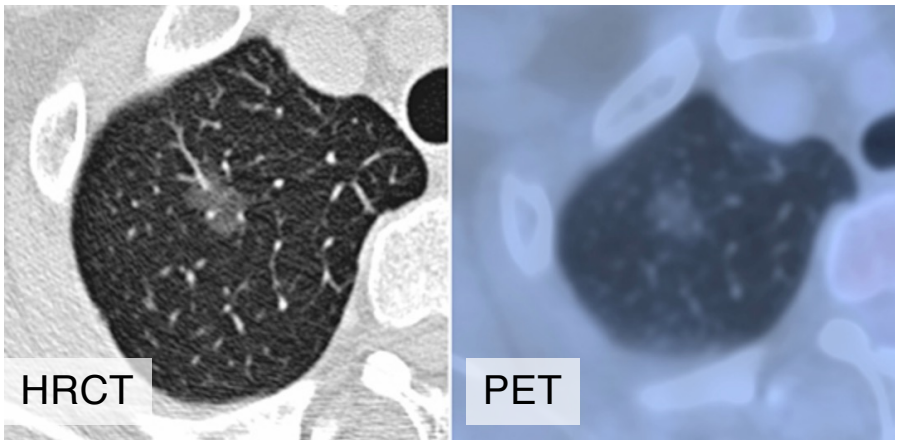


PET+

(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

De Leyn et al. European Journal of Cardio-Thoracic Surgery (2014);45:787–798

Let's talk about PET negative nodules



GUIDELINES AND CONSENSUS STATEMENTS

American Association for Bronchology and Interventional Pulmonology (AABIP) Evidence-Based Guidelines on Bronchoscopic Diagnosis and Staging of Lung Cancer

Recommendation

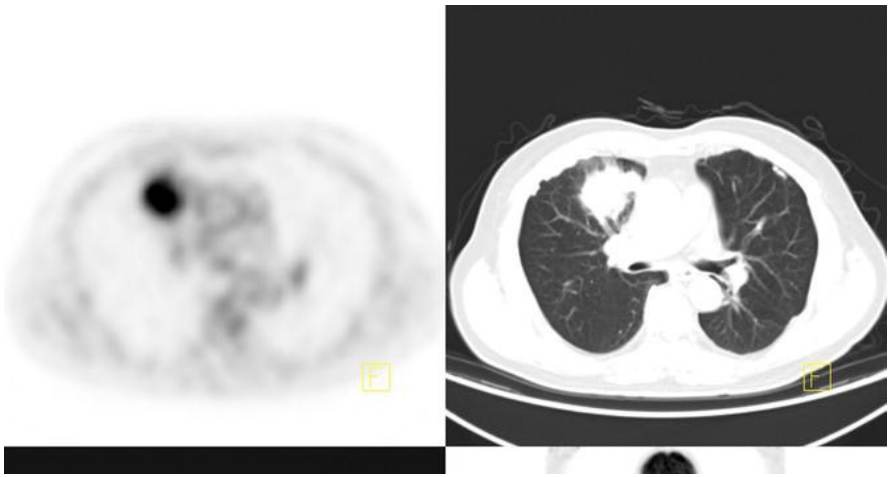
Do not routinely offer invasive mediastinal staging for patients with pure GGNs and a radiographically normal mediastinum by CT and PET scan.

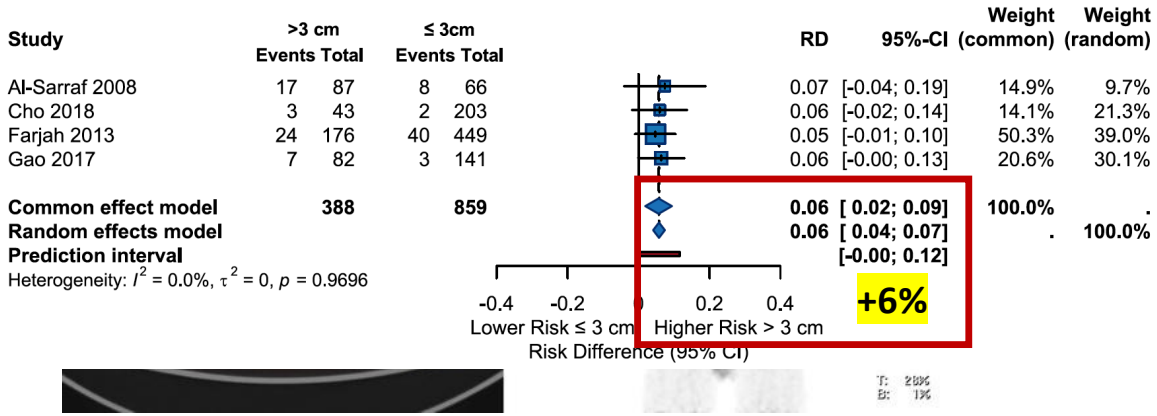
- Most GGNs represent preinvasive or minimally invasive adenocarcinomas with an indolent course and favorable prognosis
- Even large (>3 cm) GGO-dominant lesions remain node-negative until the solid portion exceeds 50%
  - **0-1%** lymph node (LN) metastases in pure ground-glass nodules or part-solid nodules with low consolidation-to-tumor ratio (CTR ≤0.5)
  - **~1.6-8%** LN metastases in part-solid nodules with higher when consolidation-to-tumor ratio >0.5

Invasive staging can likely be omitted for pure ground-glass nodules or those with a small solid component (CTR ≤ 0.5)

Miller et al. J Bronchol Intervent Pulmonol 2025;32:e1034

Large tumors (T >3 cm) should undergo invasive mediastinal staging





GUIDELINES AND CONSENSUS STATEMENTS

American Association for Bronchology and Interventional Pulmonology (AABIP) Evidence-Based Guidelines on Bronchoscopic Diagnosis and Staging of Lung Cancer

Recommendation

Clinicians should recognize a primary tumor size > 3 cm as a significant risk factor for occult mediastinal metastasis and consider invasive nodal staging in patients with peripheral tumors and a radiographically normal hilum and mediastinum.

- Unsuspected N2 prevalence ranged from ~3% to 19%
- Additional risk factors further heighten concern for nodal involvement: suspicious N1 uptake and central tumor location

Miller et al. J Bronchol Intervent Pulmonol 2025;32:e1034

Occult N2 in small tumors T<3 cm

Tumor Diameter	N1	N2
≤10 mm	0	**3.3%**
10-20 mm	15.3%	**15.3%**

Bao et al. J Thorac Dis 2014

Tumor Diameter	N1	N2
≤10 mm	25%	0
10-20 mm	6.5%	**5.7%**
>20 mm	4.2%	**5.6%**

Roy et al. Ann Am Thorac Soc 2020

Tumor Diameter	N1	N2	N3
≤10 mm	13%	6%	0
10-20 mm	9.5%	**9.5%**	**1.2%**
>20 mm	14%	**8%**	**4%**

DuComb E, et al. CHEST 2020

Variables	OR (95% CI)	P-value
Size 1-2 cm (≤1 cm)	4.3 (1.3-14.4)	0.019
Non-upper lobe (vs upper lobe)	2.6 (1.2-5.5)	0.015
CEA ≥5 ng/mL (vs <5)	1.1 (1.0-1.2)	0.004
Micropapillary adenocarcinoma	4.0 (1.5-11.0)	0.006

Bao et al. J Thorac Dis 2014

Location (third)	N1	N2
Inner	19%	0%
Middle	4.8%	**7.1%**
Outer	6.1%	**5.4%**

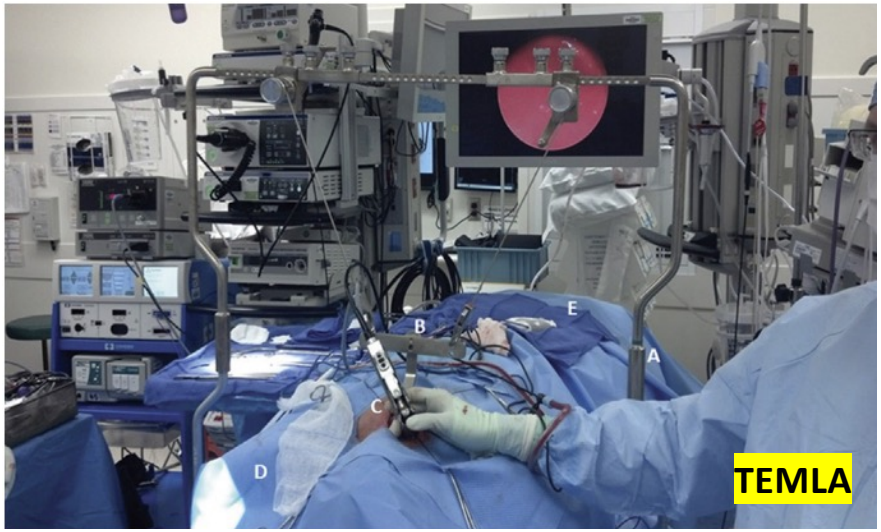
Roy et al. Ann Am Thorac Soc 2020

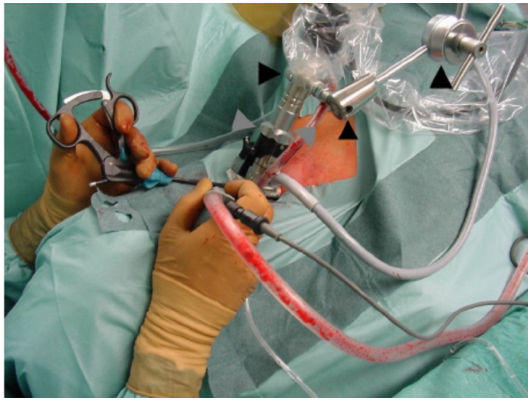
- Based on PET/CT, the prevalence of occult N2 disease increased significantly when:
  - SUVmax of the primary tumor ≥ 4
  - SUVmax of mediastinal lymph node ≥ 2.5

Liao et al. BMC Medical Imaging 2023

Occult N2/N3 in 5-13% of cT1N0M0

What is the current role of surgical mediastinoscopy





Potential advantages: provides treatment (lymphadenectomy); some nodal stations are only accessible by surgical methods

Disadvantages: safety; longer operative time; costs; technically more demanding (vs EBUS)

Yendamuri et al. Ann Thorac Surg 2017 | Martínez et al. Video-assist Thorac Surg 2023 | Hürtgen et al. GMS Thoracic Surgical Science 2005 | Kuzdzał J et al. Eur J of Cardio-thoracic Surgery 2005

What is the current role of surgical mediastinoscopy

Complications	Morbidity	Sensitivity
• Laryngeal recurrent nerve palsy (++surgery)	0-13%	75-95%
		70-92%
• Infection		99%
• Bleeding		100%
• Respiratory failure		94%
• Arrythmia	0-1%	80-90%
• Pneumothorax	0-2%	80-90%

Bradley et al. Breathe 2025| Bugalho et al. Pulmonology 2018 | Kuzdzał J et al. Eur J of Cardio-thoracic Surgery 2005

TABLE 1 Mediastinal node accessibility by clinical staging technique

Surgical procedure	2R	2L	3	4R	4L	5	6	7	8	9	10R	10L	11R	11L
Cervical mediastinoscopy	+	+	–	+	+	–	–	+	–	–	+	–	–	–
Extended mediastinoscopy	+	+	–	+	+	+	+	+	–	–	–	–	–	–
Left VATS	–	–	–	–	+/–	+	+	+	+	+	–	+	–	+
Right VATS	+	–	+	+	–	–	–	+	+	+	+	–	+	–
VAMLA	+	+	–	+	+	–	–	+	+	–	–	–	–	–
TEMLA	+	+	+	+	+	+	+	+	+	+	+	+	–	–
EBUS	+	+	+	+	+	–	–	+	–	–	+	+	+	+
EUS/EUS-(B)	+	+	+	+	+	+	+	+	+	+	–	–	–	–

+: accessible; –: not accessible. VATS: video-assisted thoracoscopic surgery; VAMLA: video-assisted mediastinoscopic lymphadenectomy; TEMLA: transcervical extended mediastinal lymphadenectomy; EBUS: endobronchial ultrasound; EUS: endoscopic ultrasound; EUS-(B): EUS with an EBUS scope.

ASTER trial

Annema et al. JAMA 2010

Sensitivity higher for EBUS/EUS (85% vs 79% with VAM)

Sensitivity increase 9% (+4% metastatic LN detected)

Fewer unnecessary thoracotomies

MEDIASTrial

Bousema et al. J Clin Oncol 2023

E(B)US → Resection : Unforeseen N2 rate **8.8%**

E(B)US → VAM → Resection : Unforeseen N2 rate **7.7%**

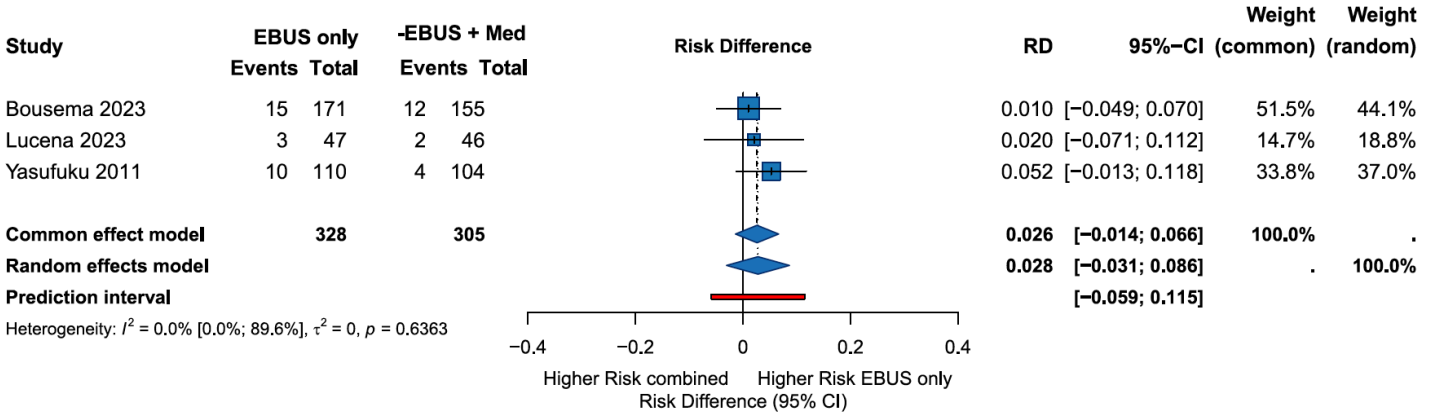
Combined approach [E(B)US + VAM] has a NNT 12.5

What is the current role of surgical mediastinoscopy

GUIDELINES AND CONSENSUS STATEMENTS

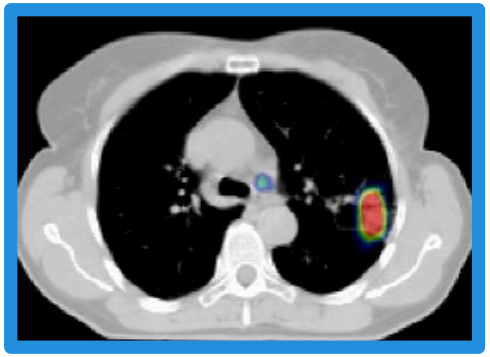
American Association for Bronchology and Interventional Pulmonology (AABIP) Evidence-Based Guidelines on Bronchoscopic Diagnosis and Staging of Lung Cancer

Recommendation 6: Evidence-Based (Meta-analysis) Do not routinely offer preoperative surgical mediastinoscopy to patients with a negative CP-EBUS-guided mediastinal staging examination who have risk factors for occult N2/N3 disease but no overt radiographic involvement.[38–40]



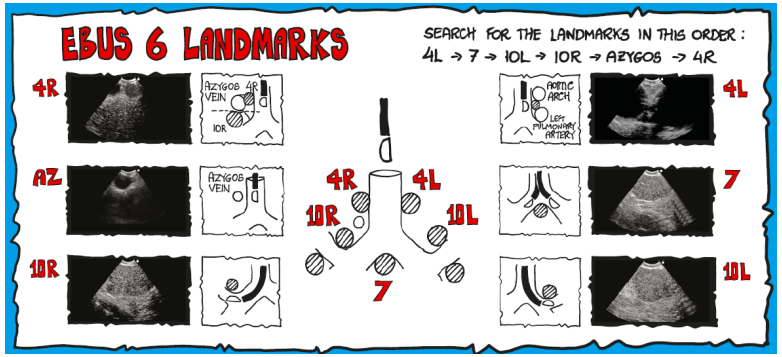
There was no statistically significant difference in missed N2/N3 disease between EBUS alone and a combined strategy EBUS+Mediastinoscopy (P=0.18)

Miller et al. J Bronchol Intervent Pulmonol 2025



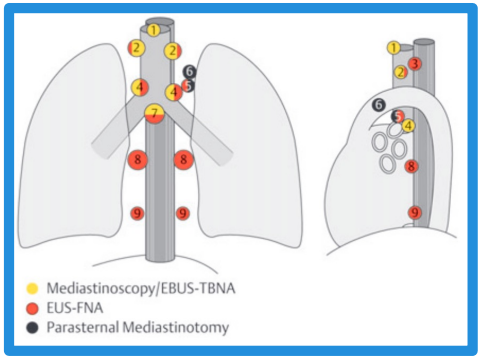
Targeted EBUS

- EBUS to nodal target lesion(s) defined based on PET+ or ≥10 mm
- **Sensitivity 79%**
- **VPN 85%**



Systematic EBUS

- Systematic inspection 4L→10/11L→7→10/11R→azygos→4R
- TBNA on suspicious LN based on features found in EBUS, PET or TC
- Routine biopsy of 4R, 4L e 7 (if ≥8 mm)
- <u>Detects 5-15% more occult N2/N3</u>
- **Sensitivity 83%**
- **VPN 88%**



Systematic EBUS + EUS-B

- Systematic inspection Aorta with celiac trunk→ left adrenal gland →7→4L→4R (if visible)
- Routine biopsy of suspicious 4L and 7, even if already sampled through EBUS
- **Sensitivity 87%**
- **VPN 91%**
- **NNT 25**

Crombag et al. Eur Respir J 2019 (SCORE study) | Korevaar et al. Lancet Respir Med 2016 | Miller et al. J Bronchol Intervent Pulmonol 2025

Triple negative

[Thoracic Oncology Original Research]

CHEST

Endobronchial Ultrasound Staging of Operable Non-small Cell Lung Cancer

Do Triple-Normal Lymph Nodes Require Routine Biopsy?

Check for updates

Danielle A. Hylton, MSc; Biniam Kidane, MSc; Jonathan Spicer, PhD; Simon Turner, MEd; Isabella Churchill, MSc; Kerrie Sullivan, MSc; Christian J. Finley, MPH; Yaron Shargall, MD; John Agzarian, MPH; Andrew J. E. Seely, PhD; Kazuhiro Yasufuku, PhD; and Waël C. Hanna, MBA; on behalf of the Canadian Association of Thoracic Surgery Research Group

CHEST 2021; 159(6):2470-2476

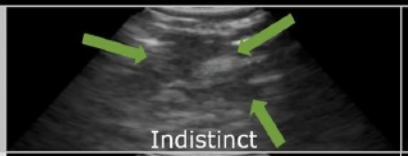
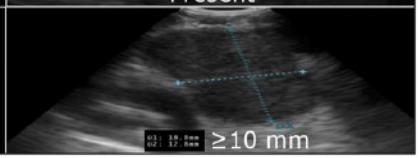
"Triple Normal":
cN0 on CT (using 10mm)
PET negative
CLNS < 2

Malignant status

5.6% **(n = 8/143)**

NPV of 93.1%
(95% CI, 85.6%-97.4%)

Canada Lymph Node Score

Ultrasonographic Features	Benign Features (0 points)	Malignant Features (1 point)
Margins	 Indistinct	 Well-Defined
Central Hilar Structure	 Present	 Absent
Central Necrosis	 Absent	 Present
Small Axis Diameter	 <10 mm	 ≥10 mm

Scores: 0-1 = Low chance of malignancy | 2-4 = High chance of malignancy

- Lymph nodes with ultrasonographic short axis <5 mm are usually benign
- Most trials have defined biopsy threshold at 8 mm

The impact of 9th Edition of TNM staging system

8th Ed TNM Categories

8th Ed TNM Categories

T/M	Label	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a Inv	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 Inv	IIB	IIIA	IIIB	IIIC
	T3 Same Lobe Nod	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 Inv	IIIA	IIIA	IIIB	IIIC
	T4 Ipsi Nod	IIIA	IIIA	IIIB	IIIC
M1	M1a Pl Dissem	IVA	IVA	IVA	IVA
	M1a Contr Nod	IVA	IVA	IVA	IVA
	M1b Single Les	IVA	IVA	IVA	IVA
	M1c Mult Les	IVB	IVB	IVB	IVB

Proposed 9th Ed TNM Categories

Proposed 9th Ed TNM Categories

T/M	Description	N0	N1	N2		N3
				N2a	**N2b**	
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ≤3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 >5 to ≤7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Same lobe tumor nodule	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral tumor nodule	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Pleural / pericardial dissemination	IVA	IVA	IVA	IVA	IVA
	M1a Contralateral tumor nodule	IVA	IVA	IVA	IVA	IVA
	M1b Single extrathoracic lesion	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple lesions, 1 organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple lesions, >1 organ system	IVB	IVB	IVB	IVB	IVB

Downgrade:

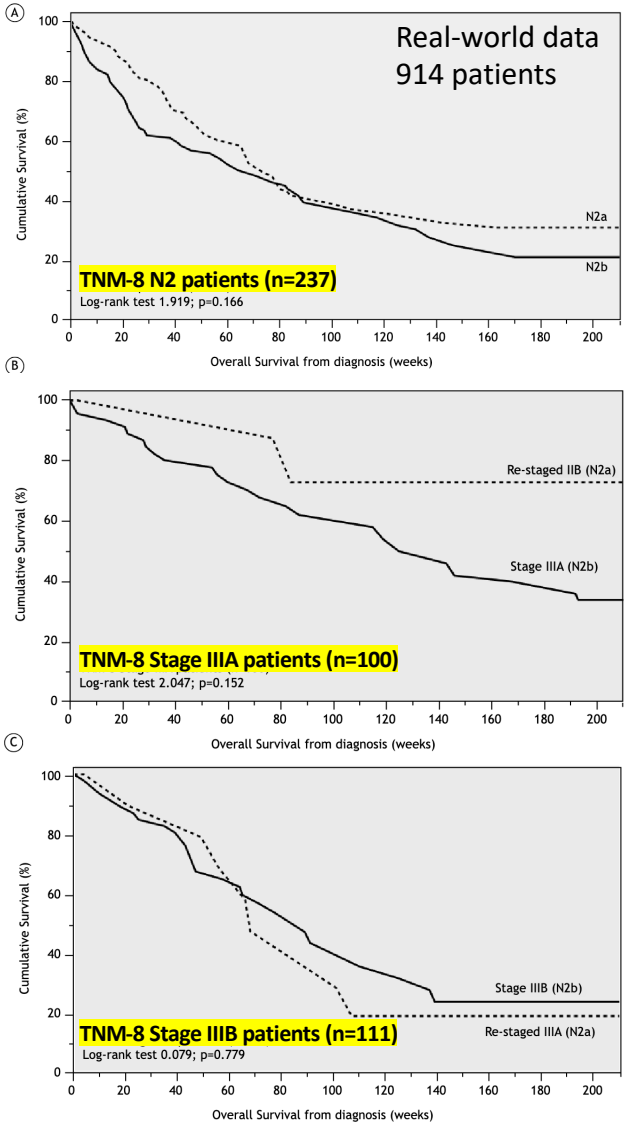
- T1 tumours with N1
- T1 tumours with single-station N2 involvement
- T3 tumours with single-station N2 involvement

Upgrade:

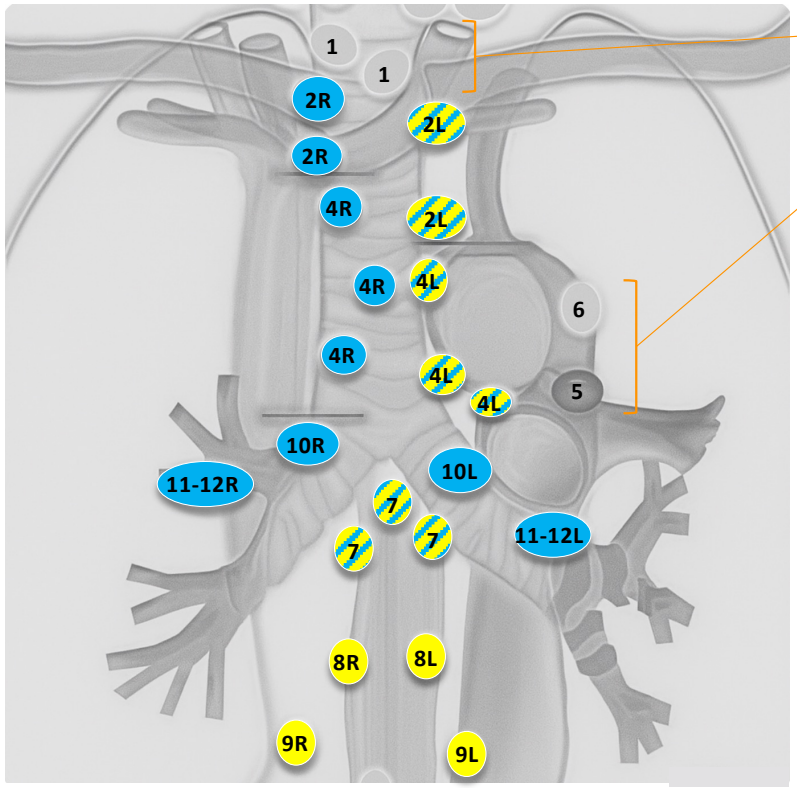
- T2 tumours with multiple-station N2 involvement

Bastos HN. Thorac 2025;2(1):6-11

Ferreira PM et al. J Bras Pneumol. 2025;51(3):e20250022



A multimodal approach in mediastinal lung cancer staging



Ultrasound-guided LN biopsy

Low cervical, supraclavicular and sternal notch LN (1)

Surgery / Percutaneous biopsy

Prevascular (3a), subaortic (5) and para-/pre-aortic (6)

EBUS (endobronchial route)

Paratracheal (2L/2R, 4L/4R), subcarinal (7), hilar (10L/10R) and inter-lobar (11L/12L)

EBUS/EUS

Left paratracheal (2L, 4L), retrotracheal (3P) and subcarinal (7)

EUS (esophageal route)

Paraesophageal (8L/8R) and pulmonary ligament (9L/9R)

Controversies

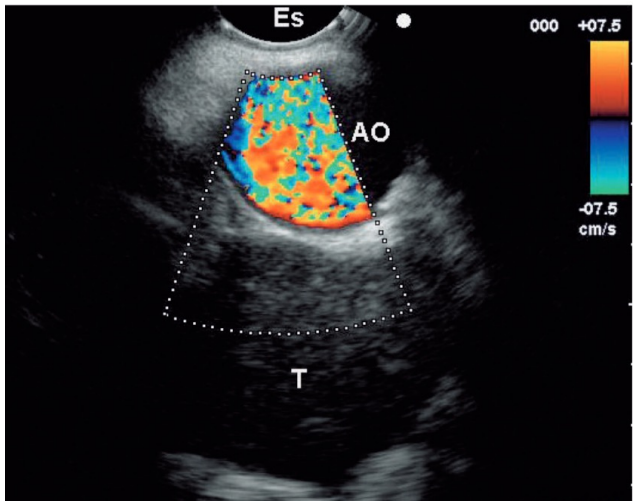
New role for ROSE?

Controversial impact on treatment decision:
With the new perioperative systemic treatment regimens, the main question is whether the patient is resectable?

Bastos HN. Thorac 2025;2(1):6-11 | Dietrich et al. J Thorac Dis 2015;7(9):e311-325

T4 assessment through E(B)US

- Lesion detected by EUS (n=426)
- Resection n=74
- Pathological T4 n=19 (26%)
  - Vascular invasion n=8
  - Mediastinum invasion n=8
  - Both n=1
  - Vertebral body invasion n=1



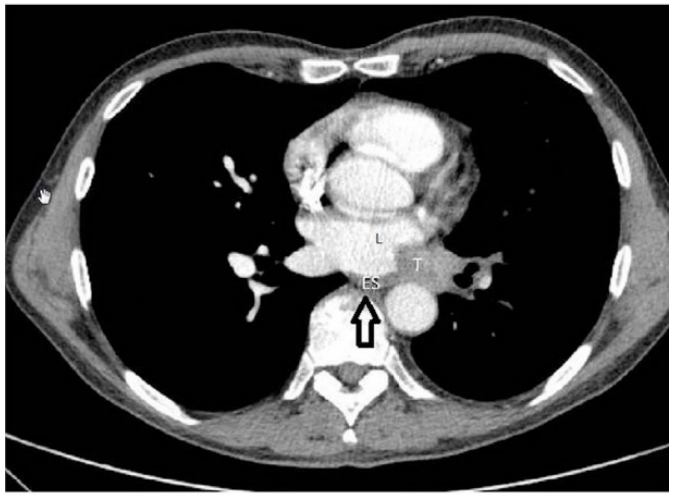
Annema & Rabe. Endoscopy 2006

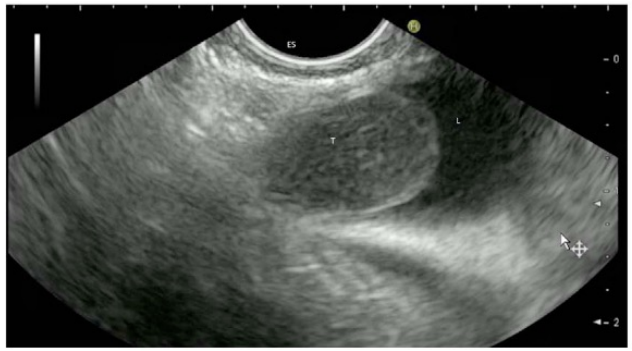
	EUS (n=74)	CT (n=66)	EUS + CT (n=34)
Sensitivity	42%	76%	83%
Specificity	95%	61%	100%
PPV	73%	41%	100%
NPV	83%	88%	97%

Kuijvenhoven et al. Lung Cancer 2017

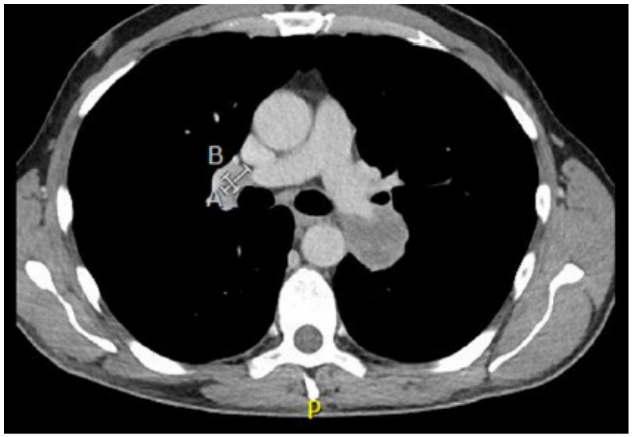
T4 assessment through E(B)US

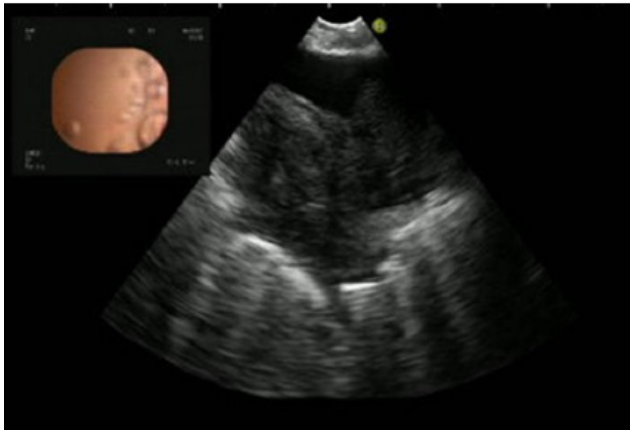
Left atrium invasion



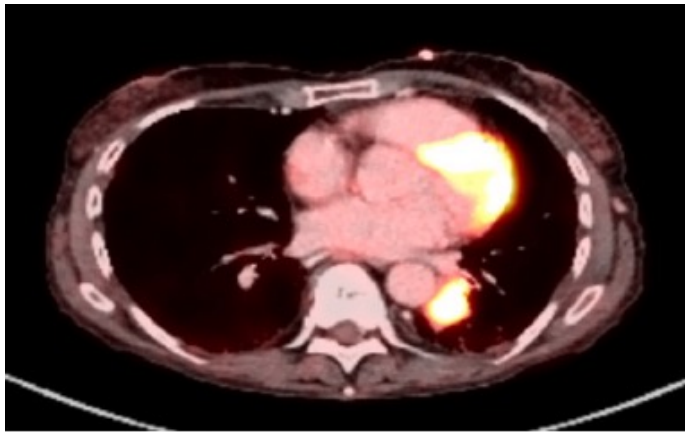


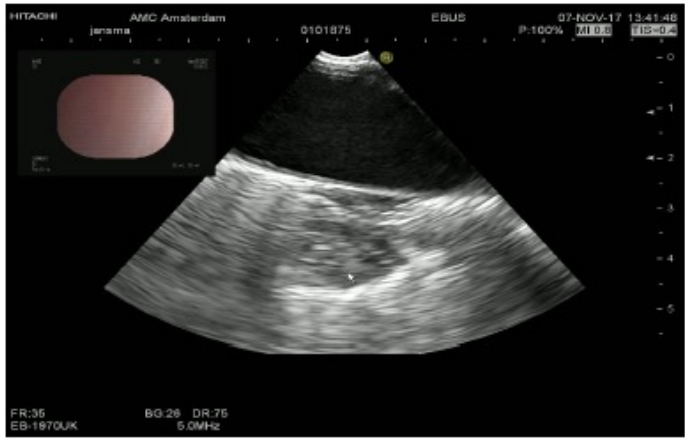
Left pulmonary artery invasion





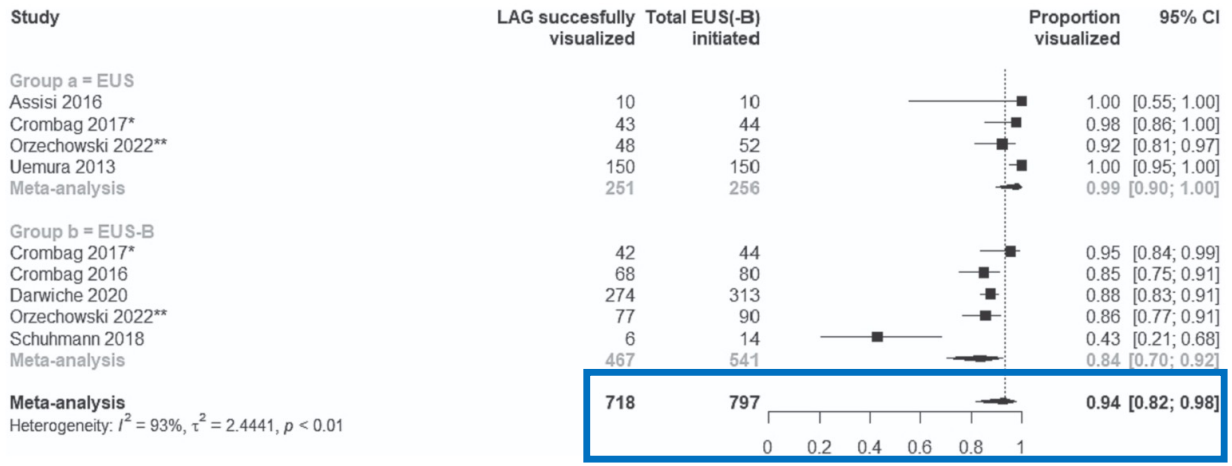
Aorta non-invaded

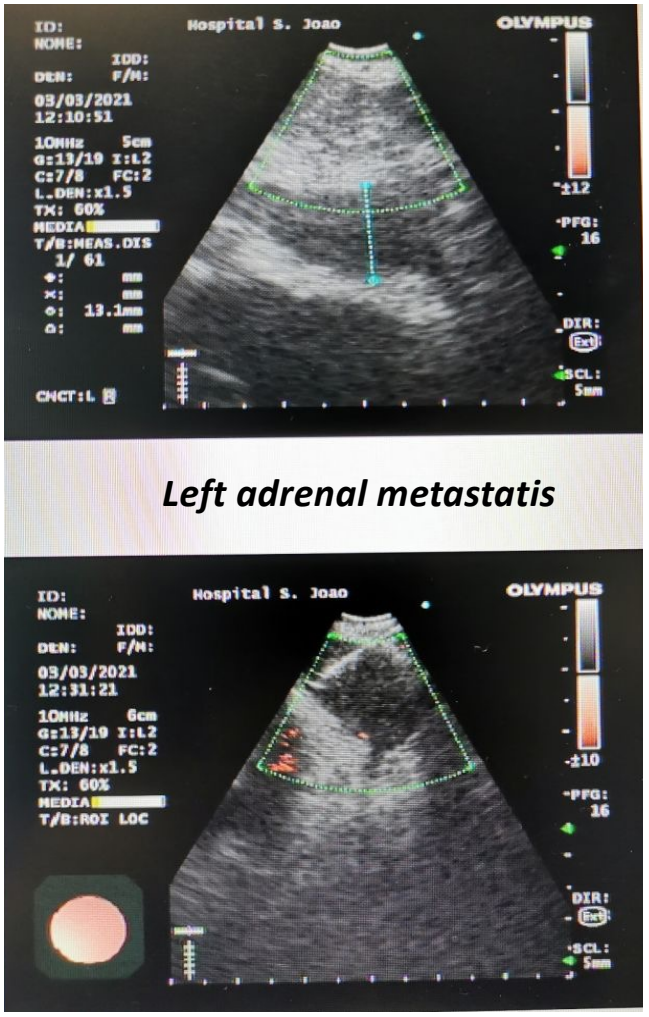




M1 staging through EUS/EUS-B

- Left adrenal gland **detection rate 43-100%** (n=797)

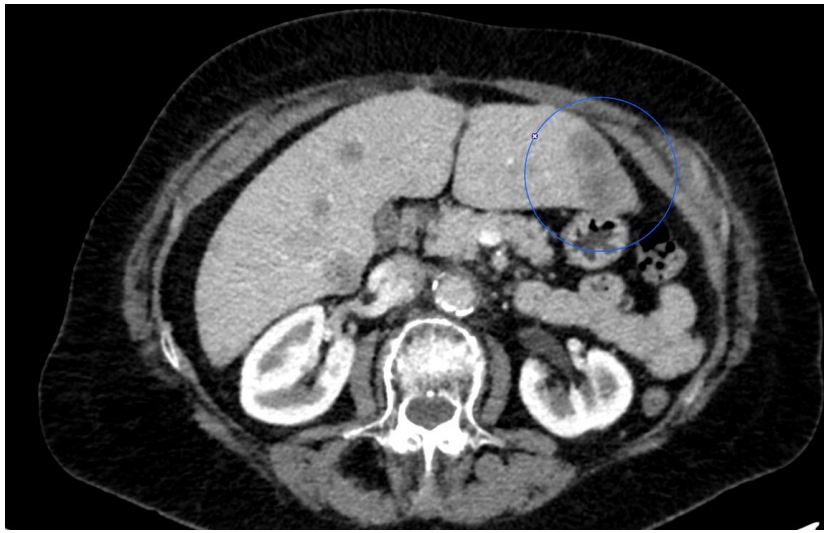


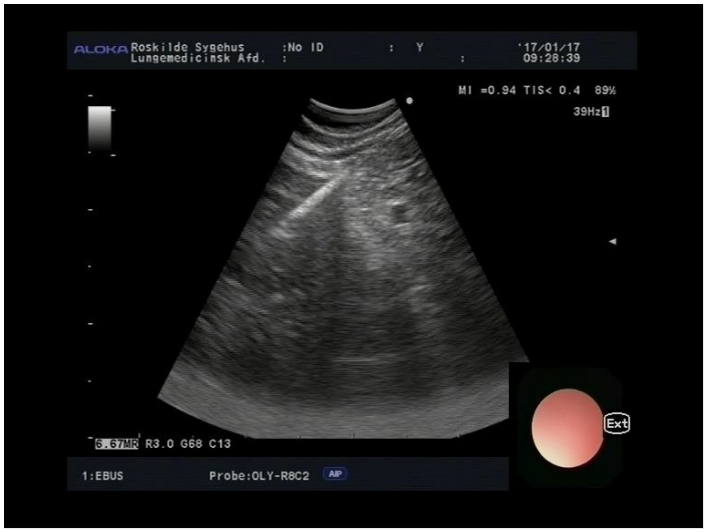


- Average **ability to sample 1.00** (95% CI 0.99–1.00) (n=366)
- Average **ability to obtain adequate material 0.96** (95% CI 0.93–0.98) (n=1266)
- Average **malignancy detection rate** 0.42 (95% CI 0.34–0.49)

Moretti et al. Lung Cancer 2023

M1 staging through EUS/EUS-B



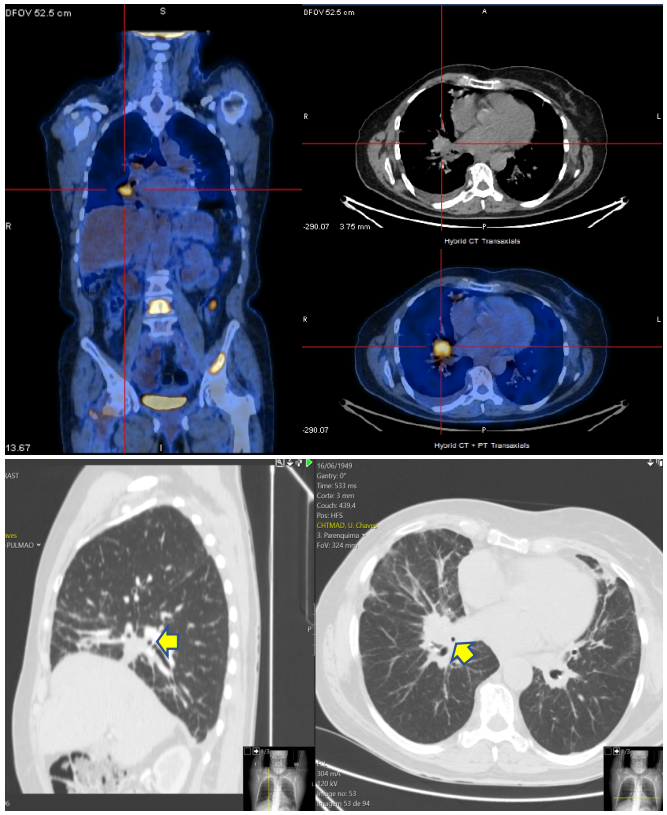


Fally et al. Respiration 2016

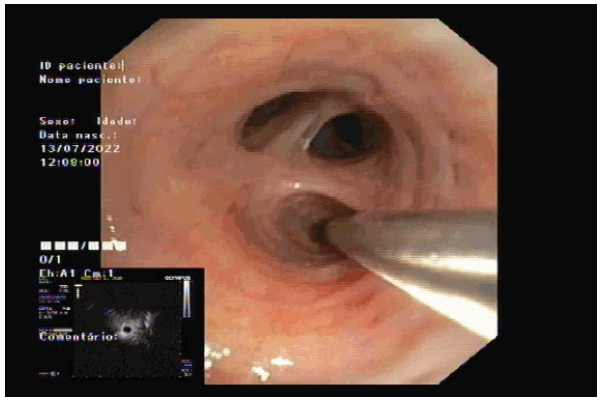
Biopsy of liver metastasis

E(B)US used for primary tumor diagnosis

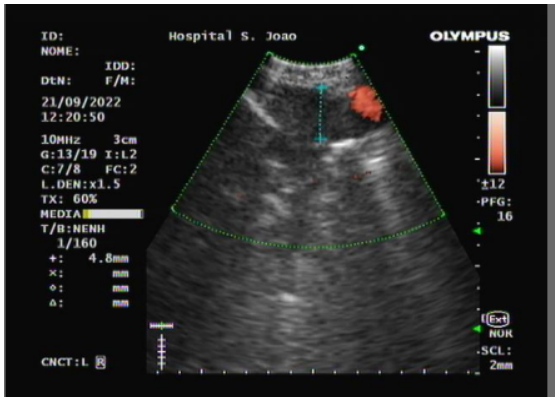
Female 72 year, non-smoker, previous history of breast cancer

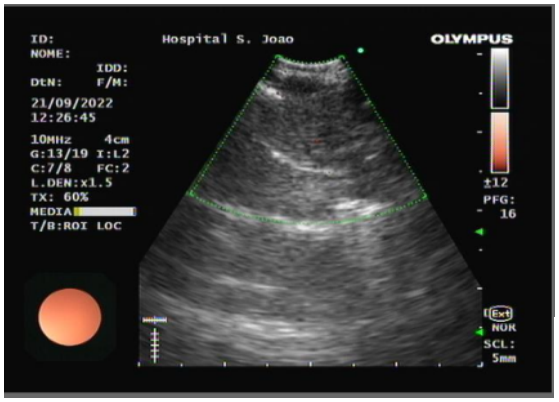


rEBUS (RML)



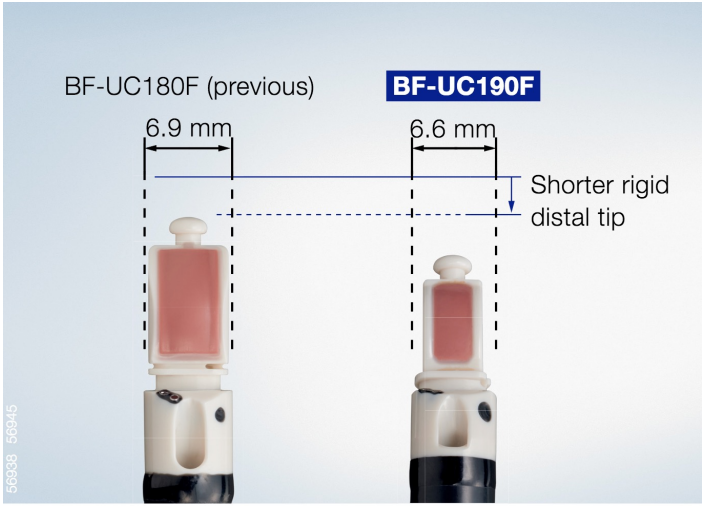
EBUS (RLL)





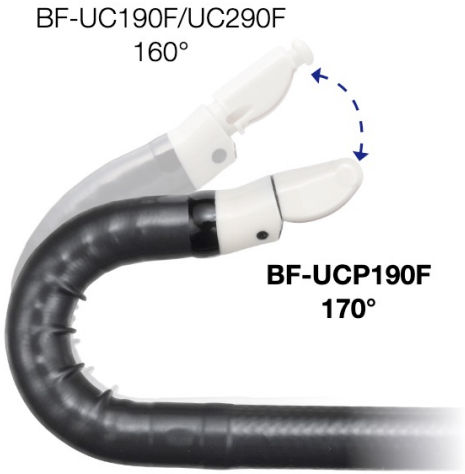
SÃO JOÃO HOSPITAL

EBUS scopes are getting slimmer

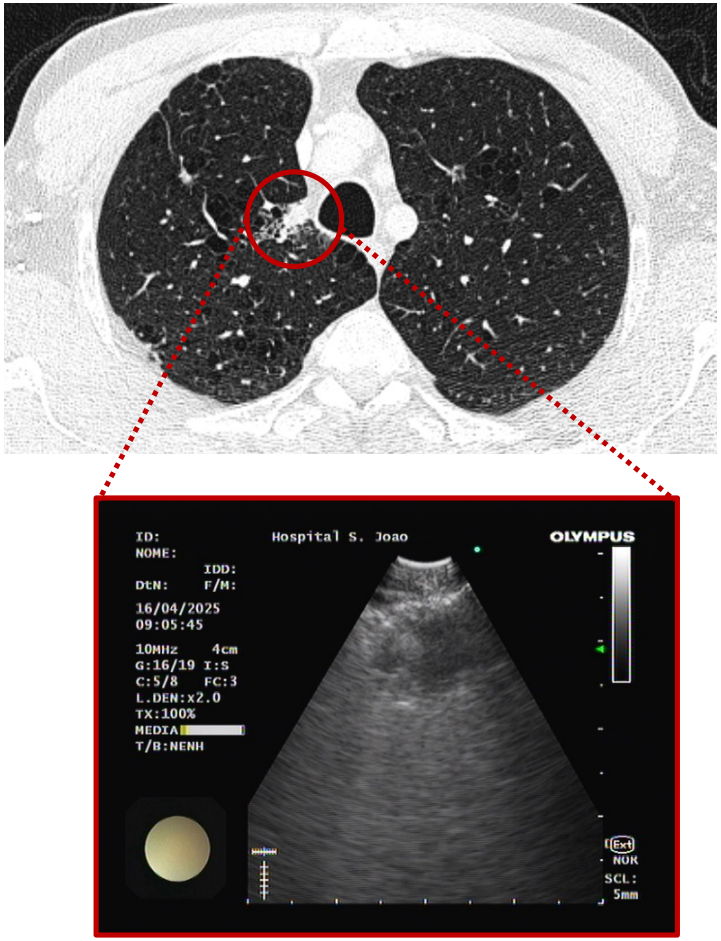


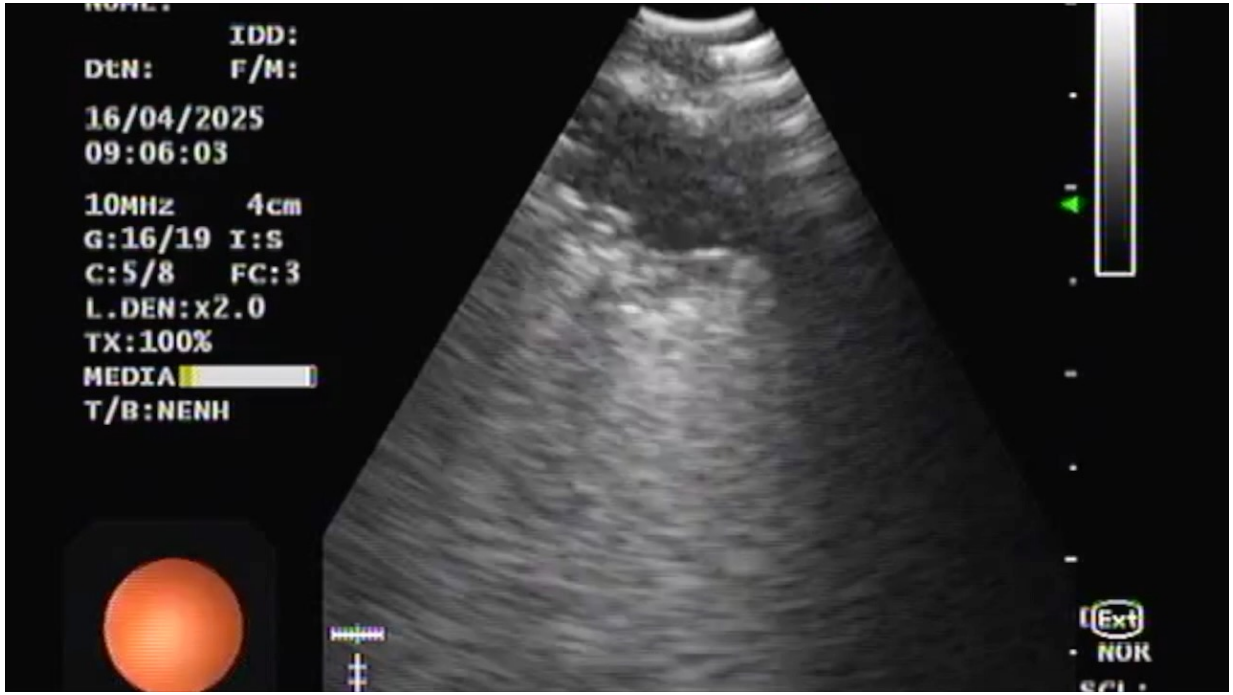
BF-UC190F/UC290F
6.6 mm

BF-UCP190F
5.9 mm



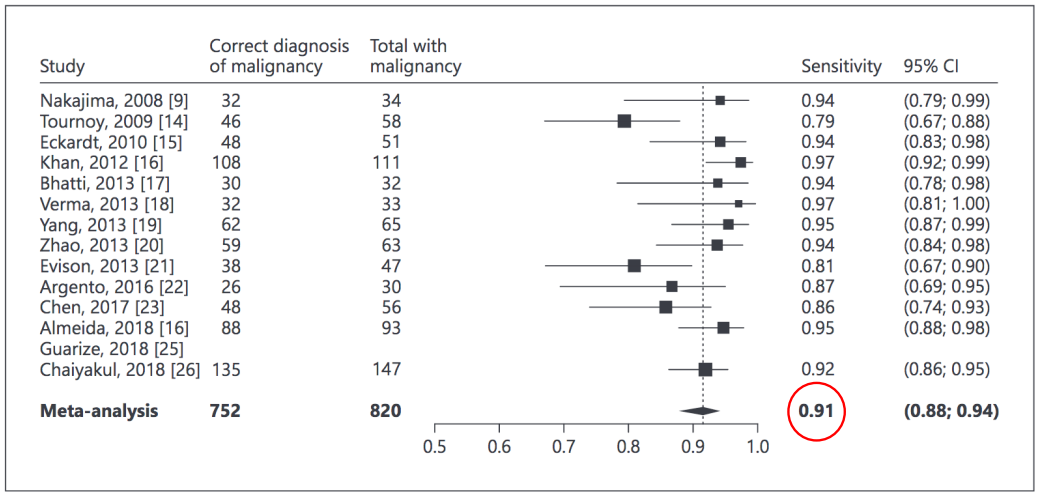
Ultrasound-guided biopsy of lung tumour... from the inside.





Lung Adenocarcinoma

Sensitivity of EBUS-TBNA to diagnose central tumors

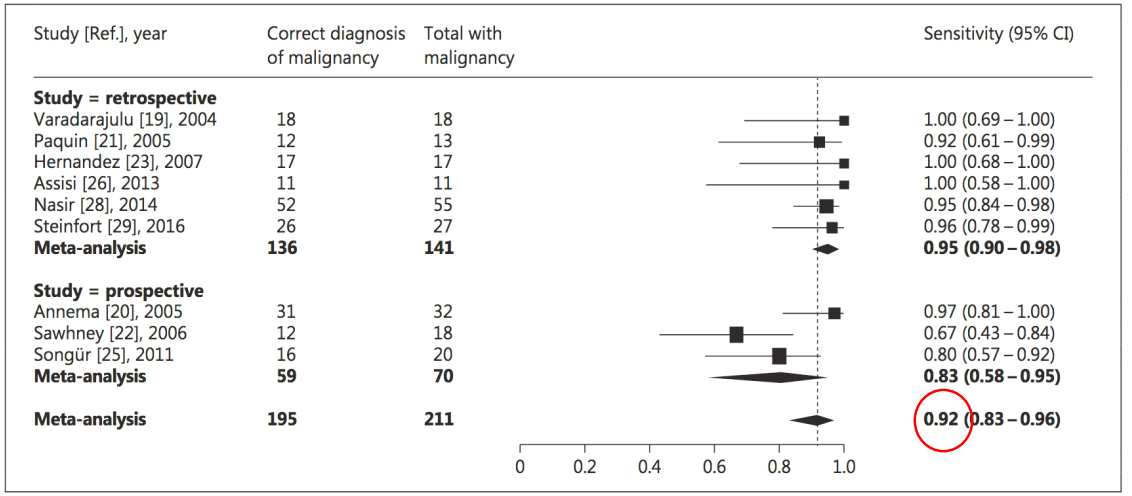


Study	Correct diagnosis of malignancy	Total with malignancy	Sensitivity	95% CI
Nakajima, 2008 [9]	32	34	0.94	(0.79; 0.99)
Tournoy, 2009 [14]	46	58	0.79	(0.67; 0.88)
Eckardt, 2010 [15]	48	51	0.94	(0.83; 0.98)
Khan, 2012 [16]	108	111	0.97	(0.92; 0.99)
Bhatti, 2013 [17]	30	32	0.94	(0.78; 0.98)
Verma, 2013 [18]	32	33	0.97	(0.81; 1.00)
Yang, 2013 [19]	62	65	0.95	(0.87; 0.99)
Zhao, 2013 [20]	59	63	0.94	(0.84; 0.98)
Evison, 2013 [21]	38	47	0.81	(0.67; 0.90)
Argento, 2016 [22]	26	30	0.87	(0.69; 0.95)
Chen, 2017 [23]	48	56	0.86	(0.74; 0.93)
Almeida, 2018 [16]	88	93	0.95	(0.88; 0.98)
Guarize, 2018 [25]				
Chaiyakul, 2018 [26]	135	147	0.92	(0.86; 0.95)
Meta-analysis	**752**	**820**	**0.91**	**(0.88; 0.94)**

Fig. 3. Sensitivity of EBUS-TBNA for diagnosing malignant centrally located intrapulmonary tumors.

Kuijvenhoven et al. Respiration 2020

Sensitivity of EUS-FNA to diagnose central tumors adjacent to the esophagus

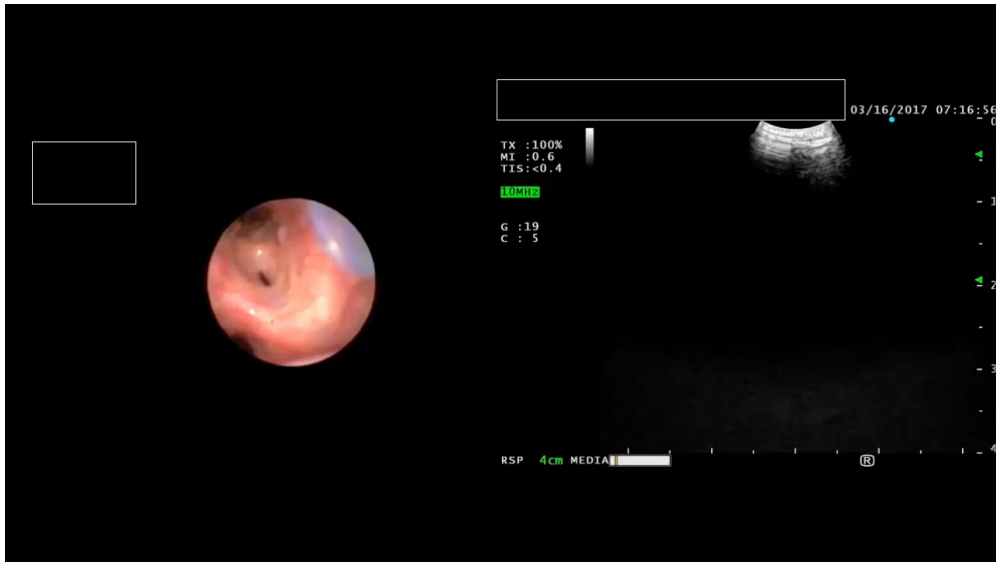


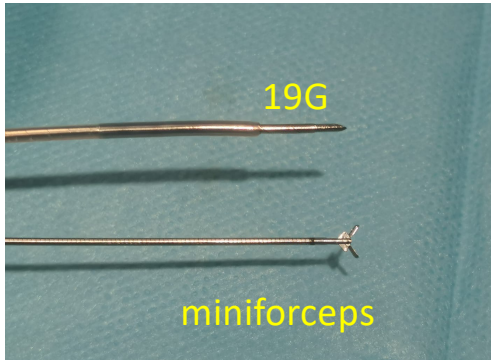
Study [Ref.], year	Correct diagnosis of malignancy	Total with malignancy	Sensitivity (95% CI)
Study = retrospective			
Varadarajulu [19], 2004	18	18	1.00 (0.69 – 1.00)
Paquin [21], 2005	12	13	0.92 (0.61 – 0.99)
Hernandez [23], 2007	17	17	1.00 (0.68 – 1.00)
Assisi [26], 2013	11	11	1.00 (0.58 – 1.00)
Nasir [28], 2014	52	55	0.95 (0.84 – 0.98)
Steinfort [29], 2016	26	27	0.96 (0.78 – 0.99)
Meta-analysis	**136**	**141**	**0.95 (0.90 – 0.98)**
Study = prospective			
Annema [20], 2005	31	32	0.97 (0.81 – 1.00)
Sawhney [22], 2006	12	18	0.67 (0.43 – 0.84)
Songür [25], 2011	16	20	0.80 (0.57 – 0.92)
Meta-analysis	**59**	**70**	**0.83 (0.58 – 0.95)**
Meta-analysis	**195**	**211**	**0.92 (0.83 – 0.96)**

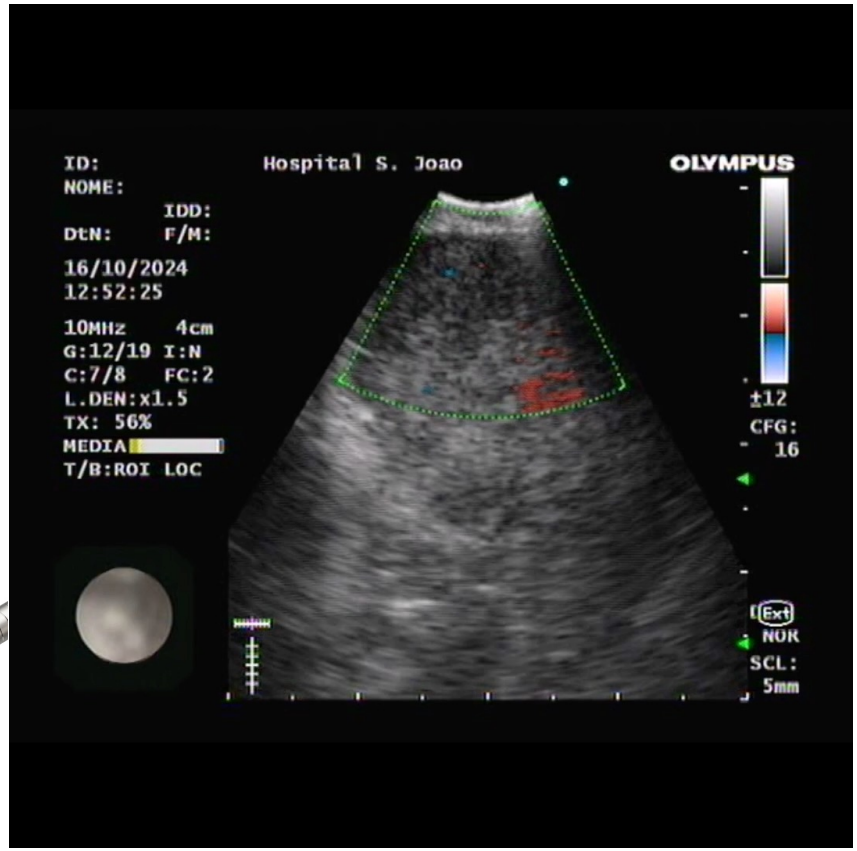
Fig. 4. Sensitivity of EUS-FNA for diagnosing malignant intrapulmonary tumors located near or adjacent to the esophagus. The difference in sensitivity between retrospective and prospective studies was not statistically significant ($p = 0.06$).

Korevaar et al. Respiration. 2017

Novel strategies to increase diagnostic yield







CryoEBUS

Endobronchial Ultrasound-Guided Transbronchial Mediastinal Cryobiopsy versus Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for Mediastinal Disorders: A Meta-Analysis

Respiration 2024;103:359–367
DOI: 10.1159/000538609

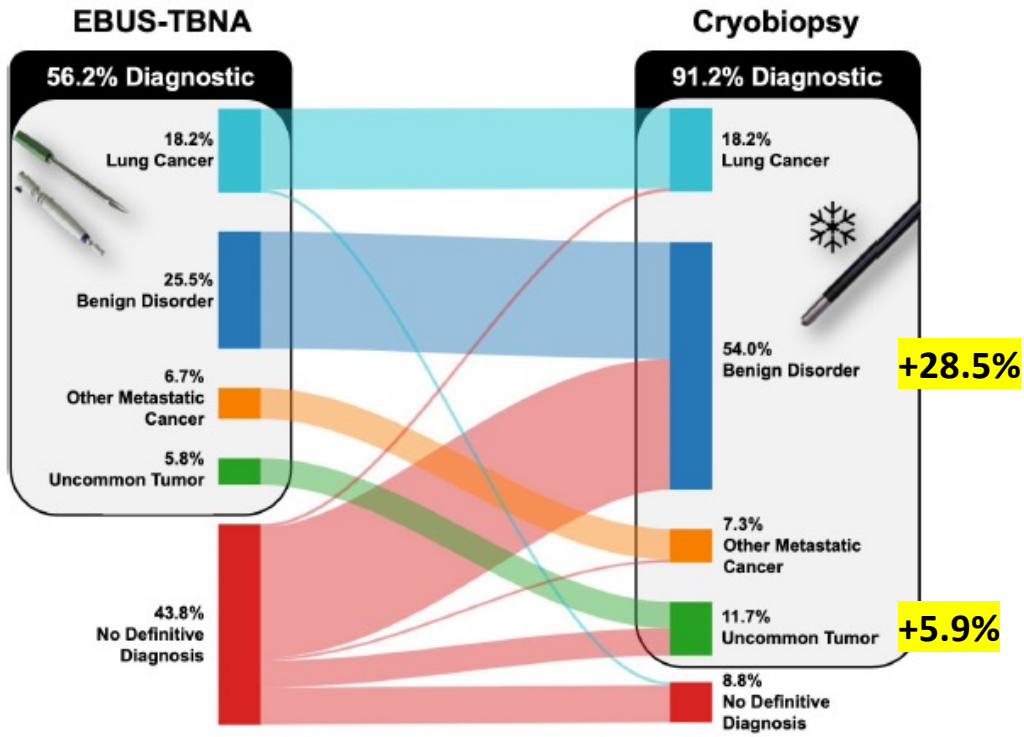
Zhenming Zhang Shengping Li Yu Bao

Department of Endoscopy Center, Sichuan Clinical Research Center for Cancer, Sichuan Cancer Hospital and Institute, Sichuan Cancer Center, Affiliated Cancer Hospital of University of Electronic Science and Technology of China, Chengdu, China

N=538, 10 studies
2-4 needle passes (19-22G)
1-4 cryobiopsies (3-7 s cooling time)

	EBUS-TBNA	CryoEBUS
Diagnostic yield	77.1%	89.6%
Lung cancer	93%	95%
Lymphoma	27.3%	86.4%
Benign disorders	60%	87.6%
Complications*		
Pneumothorax		0.7%
Pneumomediastinum		0.4%
Mediastinitis		0
Bleeding		1%

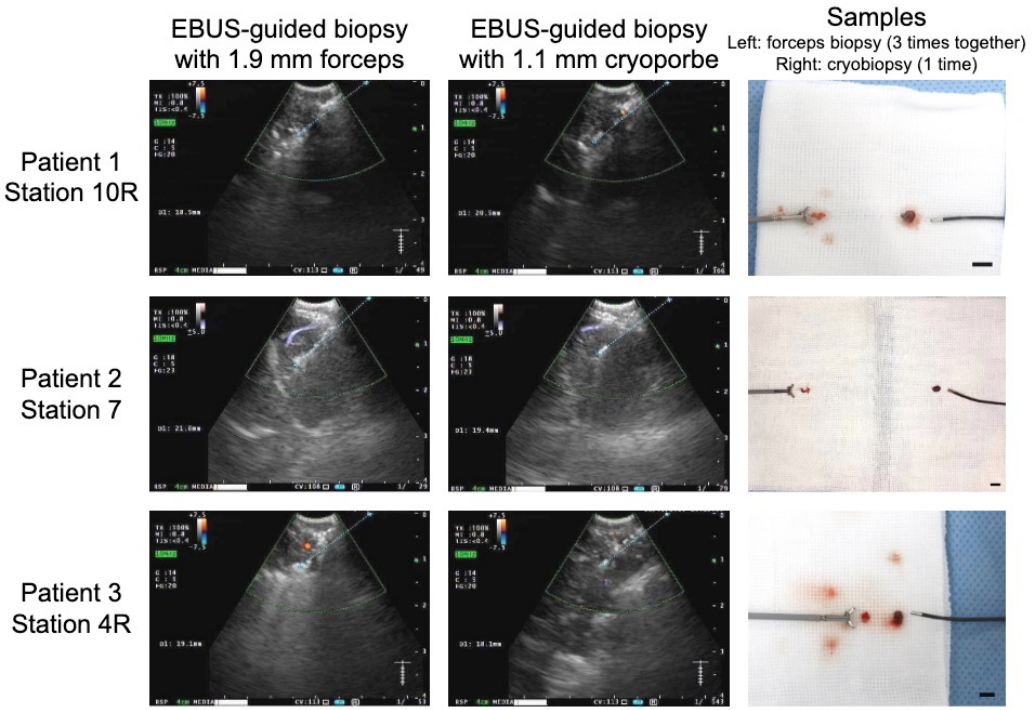
*More common in studies using needle-knife for incision



N=137

Mangold MS, et al. BMJ Open Respir Res 2024

CryoEBUS vs forceps



Cheng et al. Pulmonology 30(2024)466 474

Technical details

- N=155
- Randomized comparative trial
- Topical anesthesia (2% lidocaine), moderate sedation (midazolam+fentanyl), supplemental oxygen
- Electric needle knife creates airway incision
- Olympus ViziShot 21 or 22G needle
- 3 Forceps biopsies
- Cryobiopsy 7s freezing-time, in-block removal

	EBUS-TBNA	TBNA + CrioEBUS	TBNA + Forceps
Diagnostic yield (DY), overall	76.6%	91.6%***	85.7%*
DY, lung cancer Adequacy for molecular testing	96.3% 80.7%	98.8% 89.5%	98.8% 100%
DY, metastatic carcinoma or uncommon tumor	46.2%	92.3%***	81%**
DY, benign	59.6%	78.7%*	66%
Sample size (mean)		8.1 mm^2***	2.1 mm^2
Duration of EBUS (mean)		21.6 min	22.4 min
Procedural time (mean)		1.7 min***	3.3 min

*P<0.05, **P<0.01, ***P<0.001

Take home messages

- Invasive staging can likely be omitted for pure ground-glass nodules or those with a small solid component (CTR ≤ 0.5)
- Large tumors (T >3 cm) have +6% of N2/N3 (when compared to T<3 cm)
- But... Occult N2/N3 in 5-13% of cT1N0M0
- Preoperative surgical mediastinoscopy is not routinely recommended (NNT 12.5)
- Systematic EBUS detects 5-15% more occult N2/N3 (compared to targeted approach)
- Systematic EBUS + EUS-B increase sensitivity (but... NNT 25)
- E(B)US complement the T4 and M1 assessment/staging
- E(B)US may be crucial to diagnose central primary tumors
- Cryo-EBUS improves diagnostic yield in benign disorders, lymphoma and uncommon tumors

TIVOLI MARINA HOTEL
ALGARVE – PORTUGAL

27.30
NOV
'25

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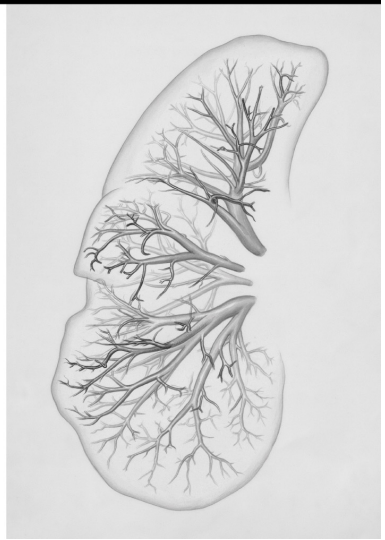
3 de novembro a
31 de dezembro de 2025

DOCENTE RESPONSÁVEL
Hélder Novais Bastos

DESTINATÁRIOS
Médicos internos de formação específica e especialistas em Pneumologia.

DATA E HORÁRIOS
7, 14 e 21 de fevereiro (9h00 às 13h00 – online)
26 de fevereiro (8h30 às 17h00 – presencial)
27 de fevereiro (9h00 às 13h30 – presencial)

VALOR
990 €



MAIS INFORMAÇÕES
fmuponline.med.up.pt
fmuponline@med.up.pt
+351 220 426 922