EBUS Guided Mediastinal Lymph node Sampling

The Future of Lymph node Sampling

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Objectives

- Endobronchial Ultrasound in Lung Cancer Diagnosis
- EBUS scopes
- EBUS in the Era od Molecular Testing and NGS
- Future of Lymph node Sampling

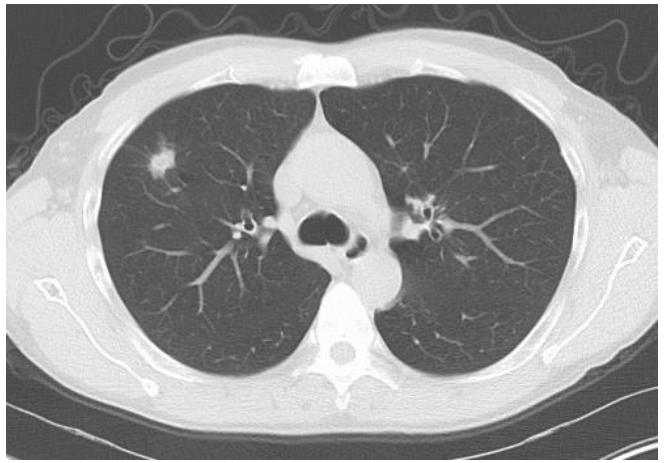
EBUS Development - Historical Aspects

"Everything we see hides another thing; we always want to see what is hidden by what we see. There is an interest in that which is hidden and which the visible doesn't show us"

Rene Magritte [quoted in Sylvester: Magritte, the Silence of the World. Huston, Menil Foundation, 1992, p 24]

The Need to Develop Endobronchial Ultrasound

- 1980 - CT was the standard for Pre-operative staging
- Primary Tumors and Metastasis - ✓
- Lymph nodes and Airway Involvement - ⊗
- The view of Bronchoscopist in the airways was limited

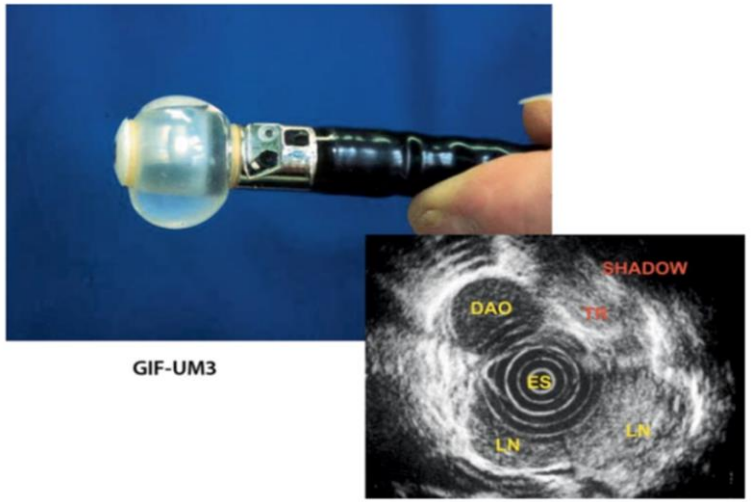


✓ **Discoloration**
✓ **Displacement**
✓ **Destruction**

- Demand for a new pre-operative staging modality

How EBUS was in the air

- Ultrasound in Medicine - 1970
- Late 80s – Transesophageal Ultrasound and RP EBUS
- The GI EUS – GIF -UM 3 -1989
- **Mediastinum - still in question !**

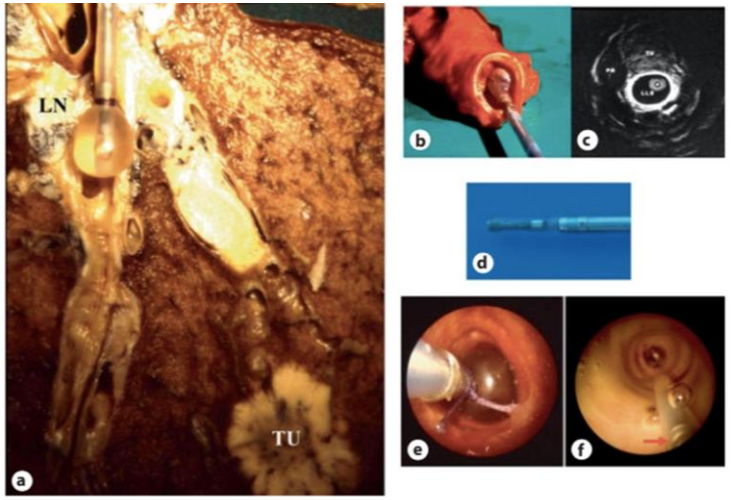


- Large size of the GI scopes
- Access to all lymph node stations

This led to transfer of application to endobronchial space

EBUS Development (1990-1994)

- UM 1-W/ Olympus
- Market 1990
- GI application - small ducts
- 7.5 MHz, 360 degree / OD - 3.4
- Rigid Bronchoscopy application



❖Thomas Hurther - Aachen

❖Miniature probe - blood vessels

❖Boston sc sonocath probes

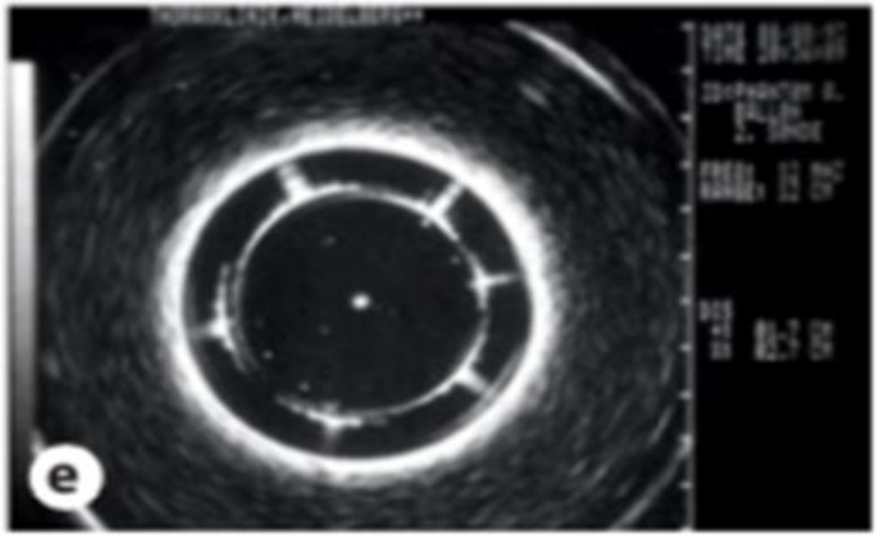
❖First to publish - First Pioneer 1992 paper / 100 patients' data


a


b

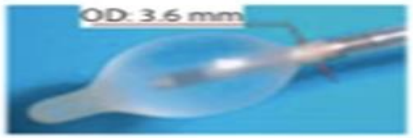

c


d


e

EBUS Development (1994 -1999) - Radial Probes

a



b

UM-2R/3R
Balloon sheath
XMH-246R

c

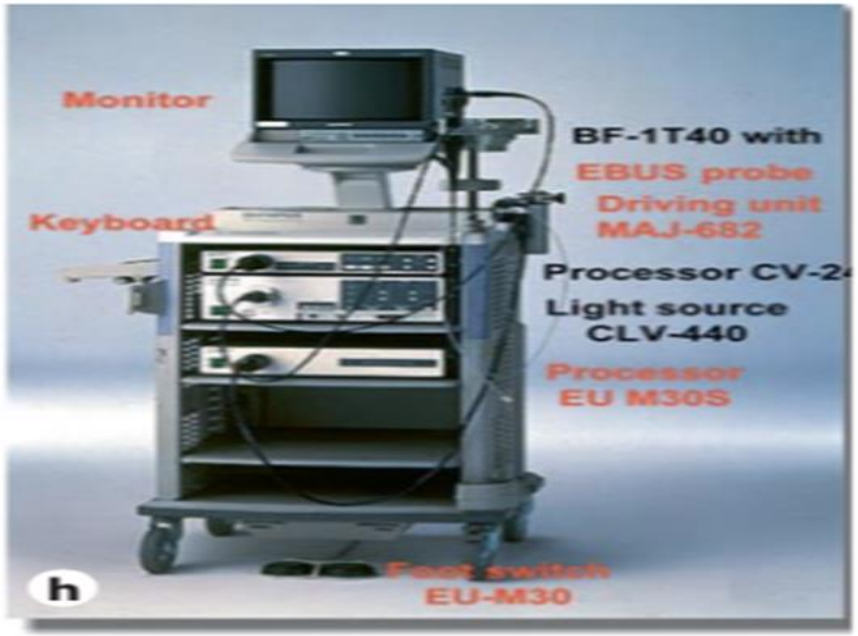
XUM-B20-26R

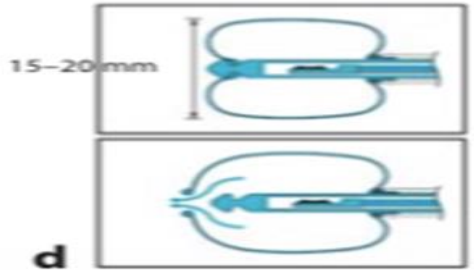
f

UM-S20/20R
Guide sheath

UM-3RDT

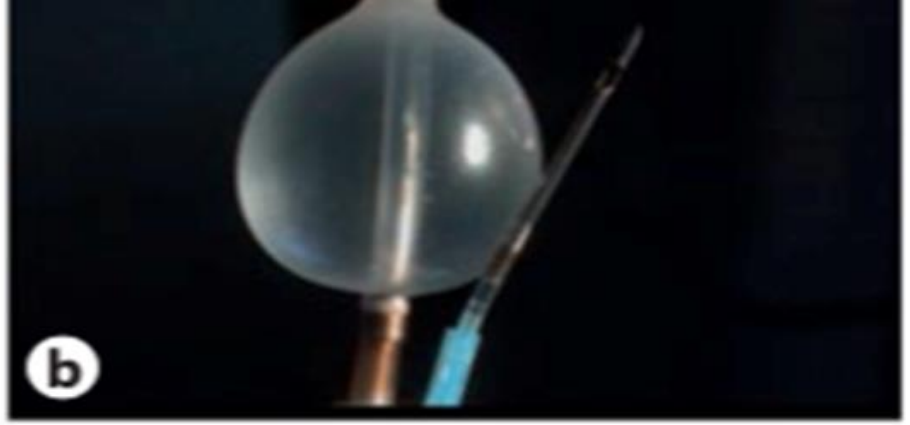
g

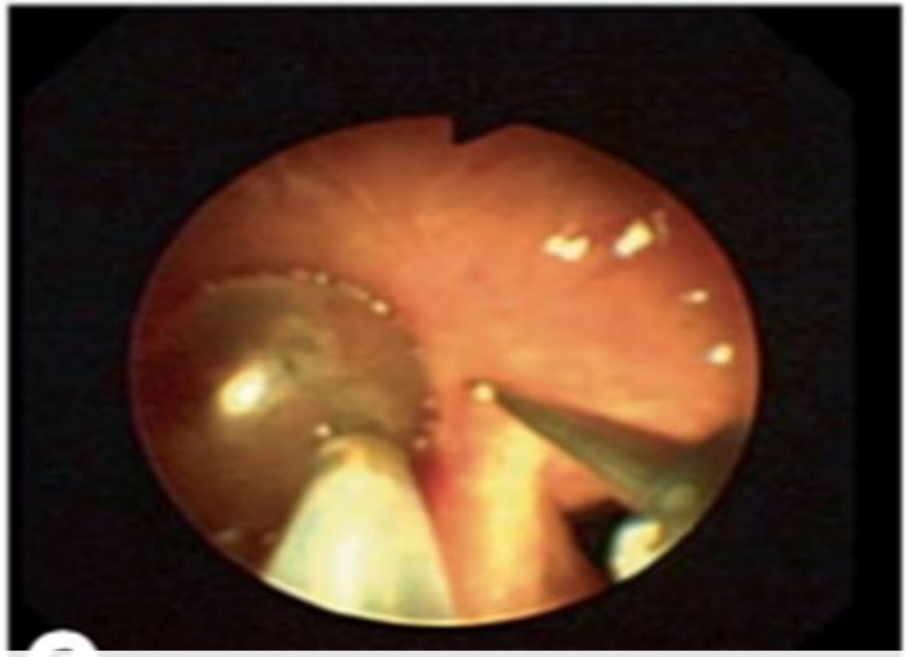




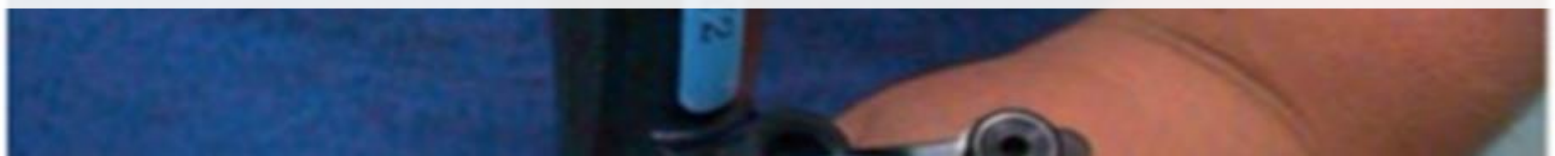
UM-2R/UM-3R
Balloon sheath
UM-BS20-26R

d



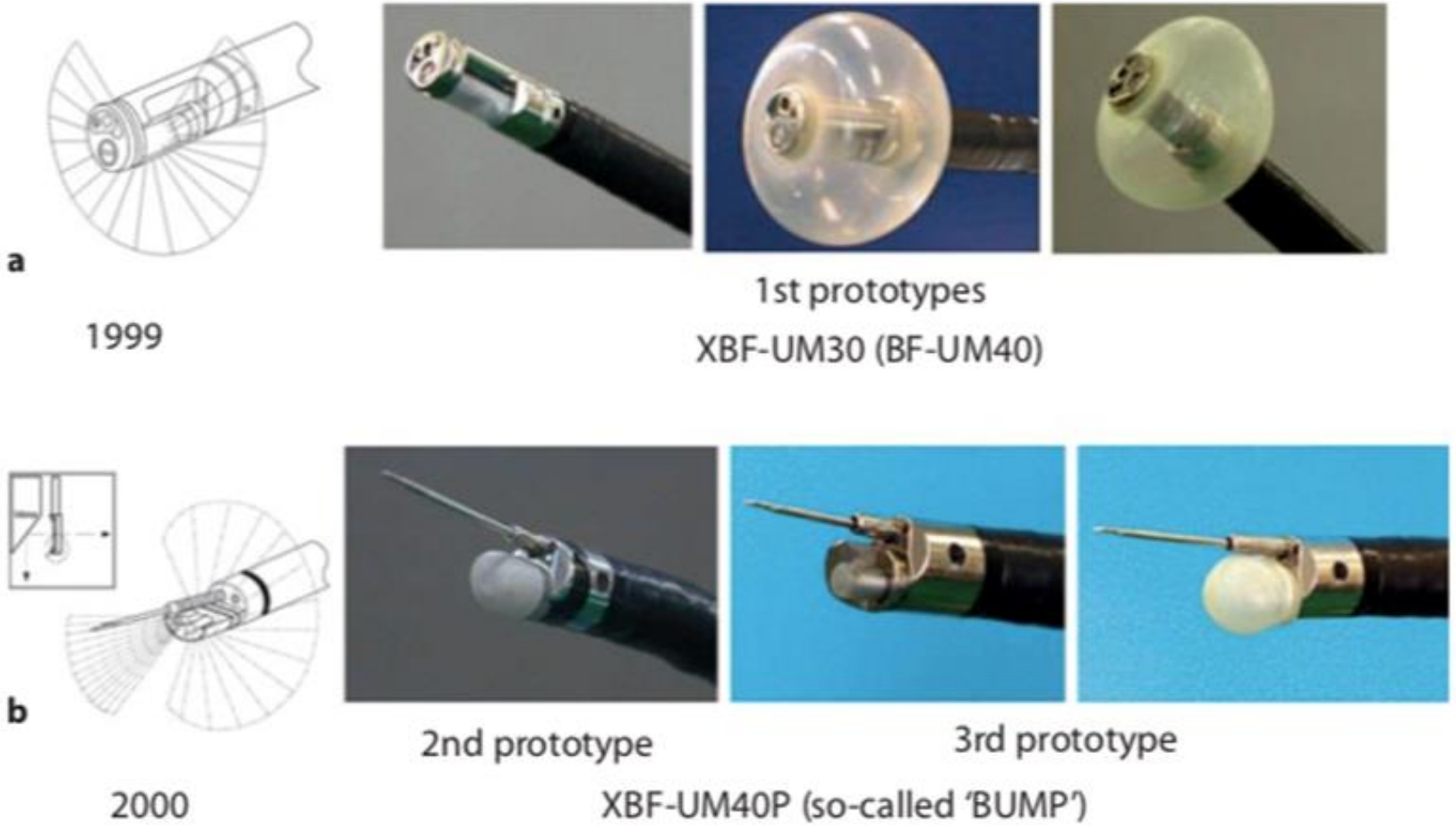


M.Krasnik - request for integrated EBUS Scope



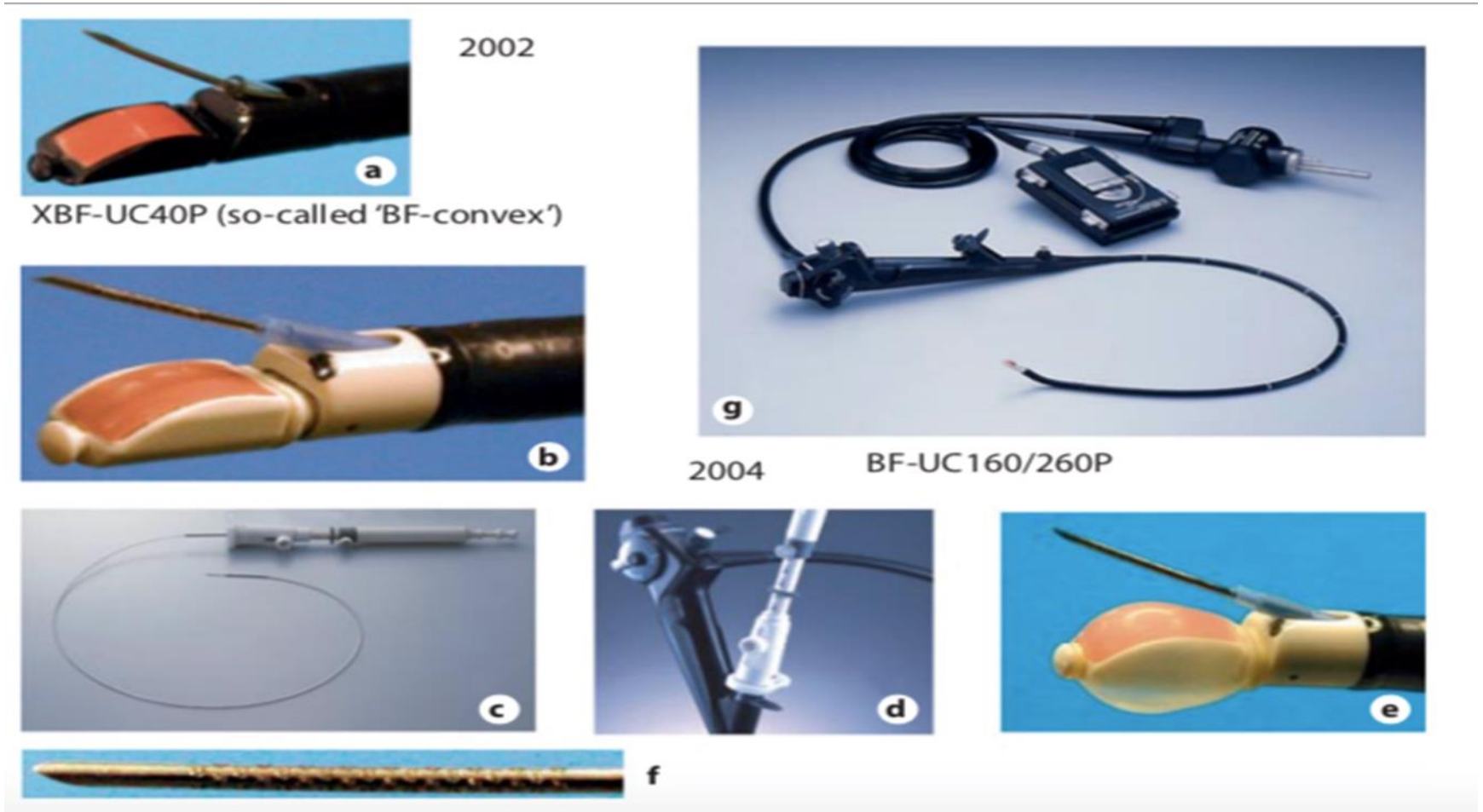
EBUS Development (1999) - Prototype EBUS Scopes

- 1999 - First prototype - BUMP - XBF-UM30P



EBUS Development (2002) - Prototype EBUS Scopes

- 2002 - BF Convex



LUNG CANCER

Preliminary experience with a new method of endoscopic transbronchial real time ultrasound guided biopsy for diagnosis of mediastinal and hilar lesions

M Krasnik, P Vilmann, S S Larsen, G K Jacobsen

Thorax 2003;**58**:1083–1086

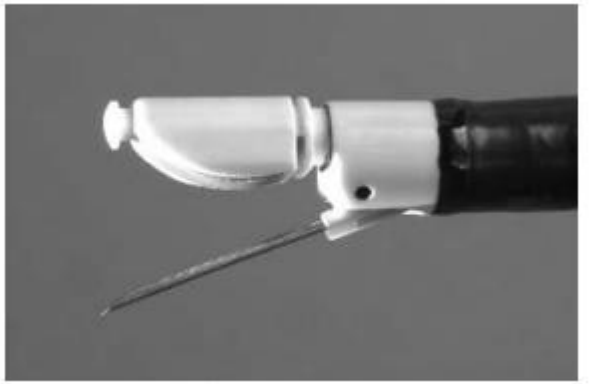


Table 1 Demographic data of 11 patients describing the clinical problem, location of lesions targeted by EBUS-FNA, and treatment

Patient	Location of lesion targeted	Cytology results	Treatment
Unknown hilar lesion, suspicion of recurrent renal cancer	10L	Clear cell carcinoma	Chemotherapy
Unknown mediastinal mass	10L	Squamous cell carcinoma	Explorative surgery (inoperable oesophageal cancer)
Right sided lung cancer	10R	NSCLC	Chemotherapy
Right sided lung cancer	10R 4L	Benign NSCLC	Chemotherapy
Recurrent lung cancer	10L	NSCLC	Chemotherapy
Unknown right sided mediastinal lesion	4R	Carcinoma	Pneumonectomy
Right sided lung cancer	10R 4R	NSCLC NSCLC	Chemotherapy
Unknown mediastinal lesion	10L	Benign	Mastectomy
Right sided lung cancer	10L 4R	SCLC SCLC	Chemotherapy
Cava superior syndrome (unknown nature)	2R	Adenocarcinoma	Chemotherapy
Left sided lung cancer	1 7	Carcinoma Carcinoma	Chemotherapy

- 11 patients
- 15 Lesions
- 13 Malignant
- 02 Benign
- No complications

Recommendations (2007)

Invasive Mediastinal Staging of Lung Cancer

ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition)

Detterbeck Frank C., MD, FCCP • Jantz Michael A., MD, FCCP • Wallace Michael, MD, FCCP • Vansteenkiste Johan, MD, PhD • Silvestri Gerard A., MD, FCCP

DOI: https://doi.org/10.1378/chest.07-1362

Conclusions

In patients with extensive mediastinal infiltration, invasive staging is not needed. In patients with discrete node enlargement, staging by CT or positron emission tomography (PET) scanning is not sufficiently accurate. The sensitivity of various techniques is similar in this setting, although the false-negative (FN) rate of needle techniques is higher than that for mediastinoscopy. In patients with a stage II or a central tumor, invasive staging of the mediastinal nodes is necessary. Mediastinoscopy is generally preferable because of the higher FN rates of needle techniques in the setting of normal-sized lymph nodes. Patients with a peripheral clinical stage I NSCLC do not usually need invasive confirmation of mediastinal nodes unless a PET scan finding is positive in the nodes. The staging of patients with left upper lobe tumors should include an assessment of the aortopulmonary window lymph nodes.

Recommendations (2013)

CHEST Supplement

DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

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

Conclusions: Since the last iteration of the staging guidelines, PET scanning has assumed a more prominent role both in its use prior to surgery and when evaluating for metastatic disease. Minimally invasive needle techniques to stage the mediastinum have become increasingly accepted and are the tests of first choice to confirm mediastinal disease in accessible lymph node stations. If negative, these needle techniques should be followed by surgical biopsy. All abnormal scans should be confirmed by tissue biopsy (by whatever method is available) to ensure accurate staging. Evidence suggests that more complete staging improves patient outcomes.

CHEST 2013; 143(5)(Suppl):e211S–e250S

EBUS Scopes

- BF-UC 180 F
- BF-UC 190 F with 20 forward oblique view
- Processors : EU-ME1, EU-ME2, EU-ME3

- Angle of view - 35° **Forward oblique / 20 ° Forward oblique**
- Scan Direction **- Longitudinal**
- Insertion Tube Diameter **- 6.2mm / OD 6.9 mm**
- Instrument Channel Diameter - **2.2mm**
- Angulation Up/down - **120/90**

EBUS Scopes

- **EB-1970UK, EB19-J10U**
- Hitachi ultrasound systems with thoracic probes

- Angle of view - **45° Forward oblique**
- Scan Direction **- Longitudinal**
- Insertion Tube Diameter **– 6.3mm**
- Instrument Channel Diameter – **2/2.2mm**
- Angulation Up/down – **120/90**

EBUS Scopes

- **EB-530US**
- SU-8000 ultrasound processor

- Angle of view - **10° Forward oblique**
- Scan Direction **- Longitudinal**
- Insertion Tube Diameter **– 6.3mm**
- Instrument Channel Diameter – **2mm**
- Angulation Up/down – **130/90**

Established EBUS Scopes

	Diameter (mm)	Working channel (mm)	Working length (mm)	Field of view	Depth penetration (mm)	Frequency (MHz)	Scan modus	Comment
EB19-J10U Video EBUS-scope (Pentax)	7.3	2.2	600	100°/45° Oblique optic	2-50	5.0-13.0	Electronic 75° curved linear array	Compatible with Hitachi Hi-Vision Scanner
BF-UC190F Video-EBUS-scope (Olympus)	6.6	2.2	600	80°/20° Oblique optic	2-50	5.0-12.0	Electronic 65° curved linear array	Compatible with EU-ME2, Hitachi Aloka ProSound F75
EB-530US Video-EBUS-scope (Fujifilm)	6.7	2.0	610	120°/10° Oblique optic	3-100	5.0-12.0	Electronic 60° curved	Compatible with SU-1-S/H

Endobronchial Ultrasound - Clinical Applications

- **Lymph node staging of Lung Cancer**
  - Pre-operative staging
  - Post-operative evaluation
  - Restaging

- **Diagnosis of centrally located intra-pulmonary pathologies**

- **Mediastinal and Hilar adenopathy - Benign and Malignant**
  - Sarcoidosis (overall yield of 90-92%)
  - Lymphoma (sensitivity 57-91%)

Endobronchial Ultrasound - Anesthesia

Outpatient

LA with conscious sedation

LMA /IGEL #4

ET Tubes - 8 and above

TIVA + LMA

GA vs Moderate sedation for EBUS TBNA - RCT

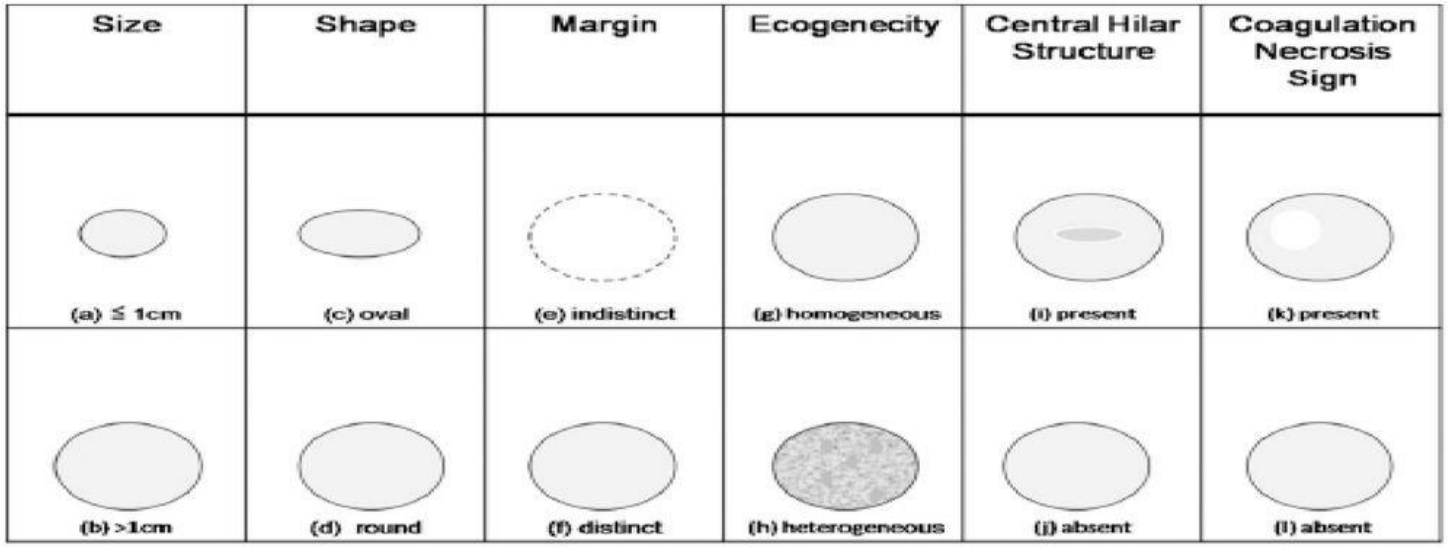
	General Anethesia (n=75)	Moderate Sedation (n=74)	P value
LNs sampled/pt	3.2±1.9	2.8±1.5	0.199
Dx Yield	70.7%	68.9%	0.816
Sensitivity	98.2%	98.1%	0.979
Completion Rate	100%	93.3%	0.028
Major Complication	0	0	
Minor Complication	5.3%	29.6%	< 0.001

Roberto F Casal et.al.Am J Respir Crit Care Med. 2015 Apr 1;191(7):796-803.

Standard EBUS Image Classification

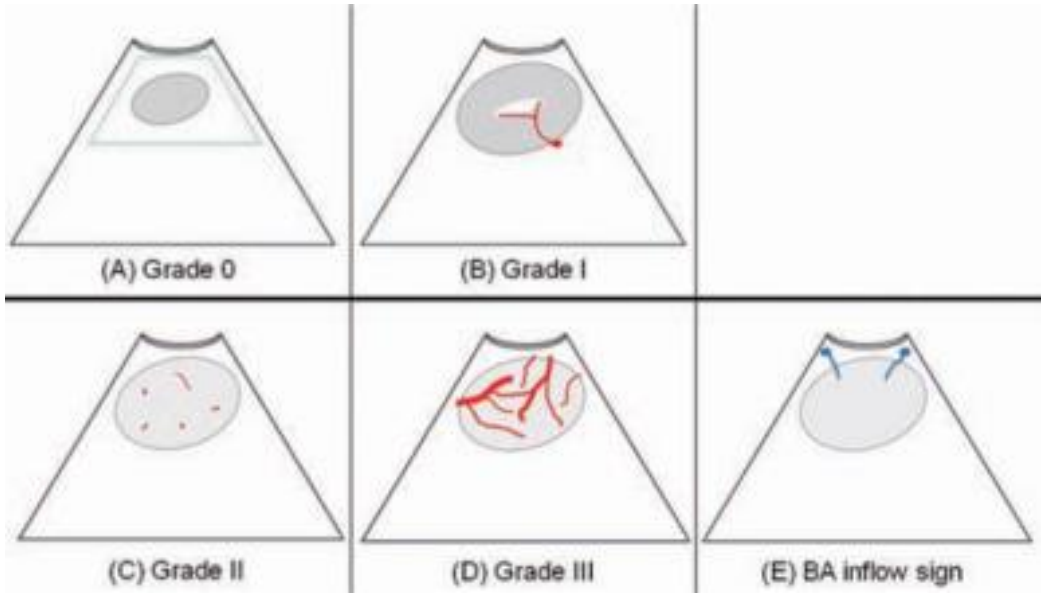
Malignant Predictors

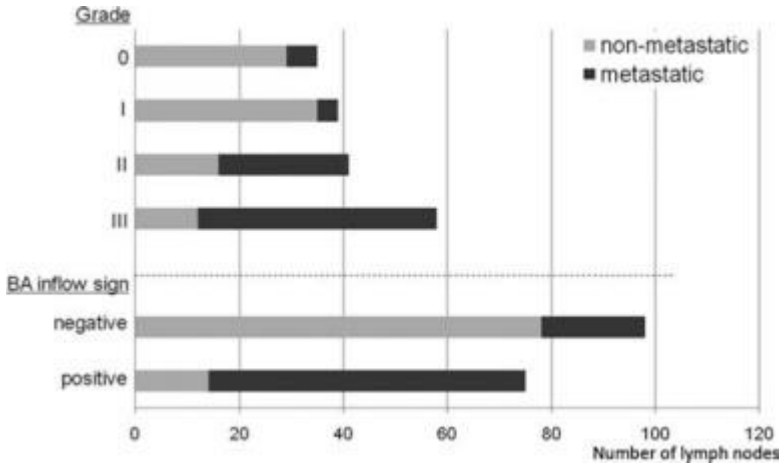
- ✓ Size > 1cm
- ✓ Round Shape
- ✓ Distinct Margins
- ✓ Heterogenous Echo signal
- ✓ Absence of CHS
- ✓ High color power doppler index
- ✓ Absent CNS

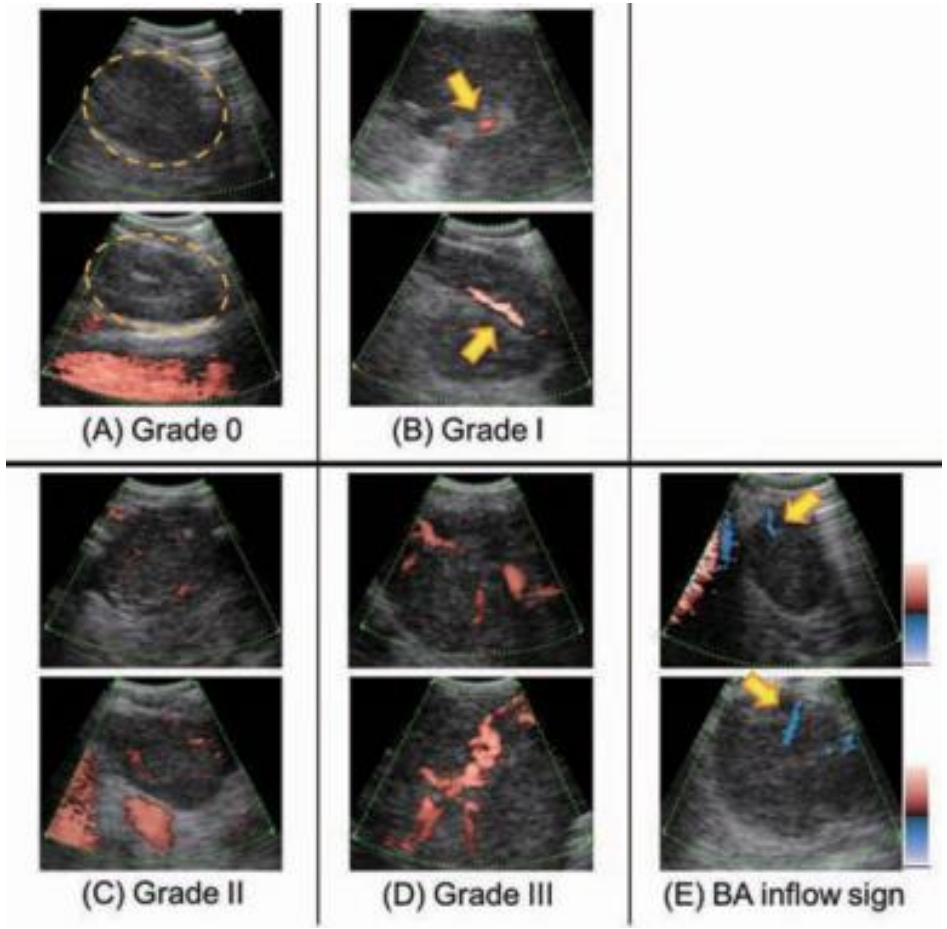


Morphologic Category	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnosis Accuracy
Size: > 10 mm	77.9	75.8	55.9	89.7	76.4
Shape: round	88.0	75.8	59.0	94.1	79.3
Margin: distinct	94.4	54.3	45.5	96.0	65.7
Echogenicity: heterogeneous	77.3	86.6	69.5	90.6	83.9
Central hilar structure: absence	89.7	53.5	43.3	92.9	63.8
Coagulation necrosis sign: presence	69.4	92.6	78.9	88.4	86.0

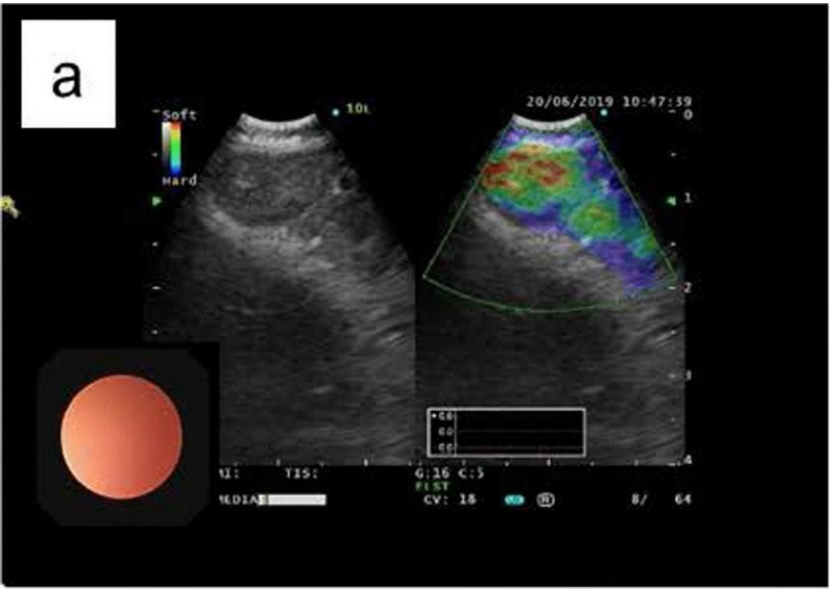
EBUS Imaging - Vascular Patterns

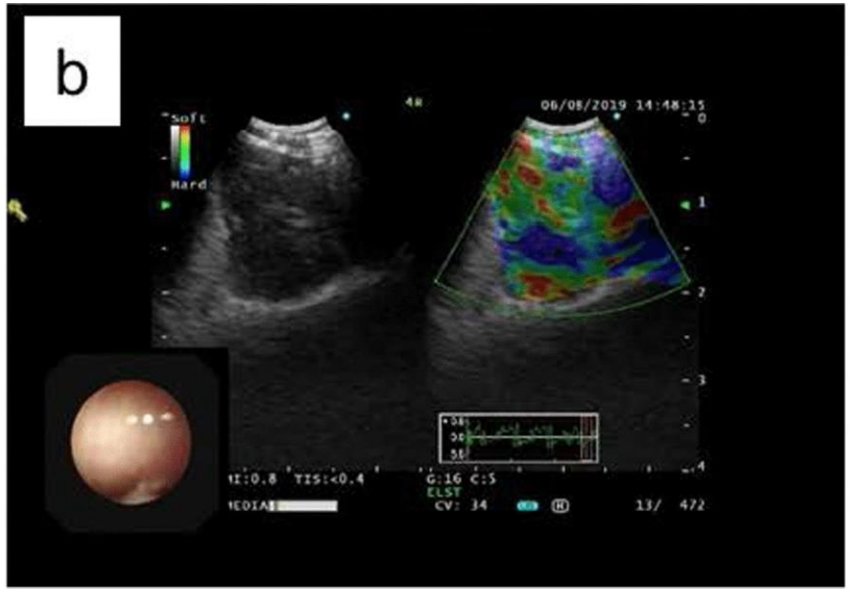


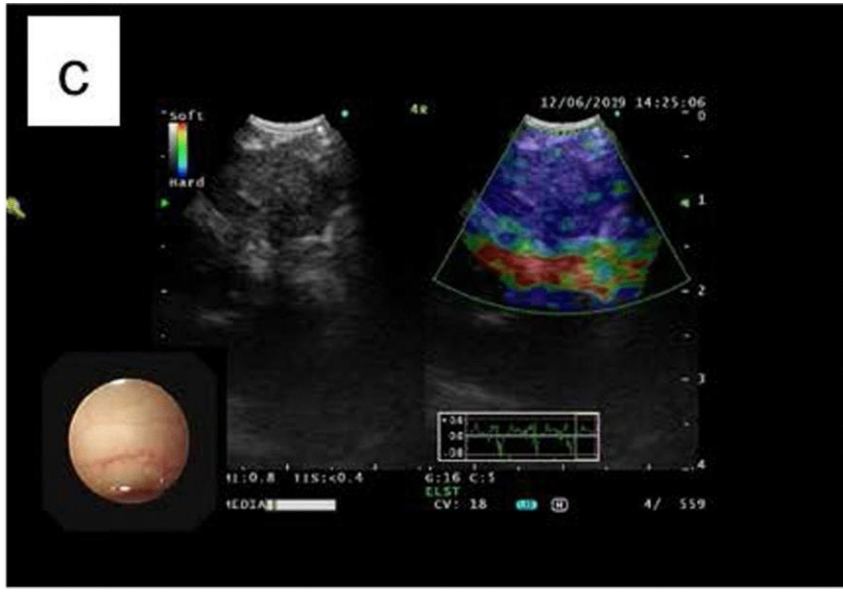




EBUS Imaging - Elastography







Group	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	−LR	AUC	Youden index
EBUS elastography	90.65	57.63	71.60	84.00	2.14	0.16	0.776	0.4827
ROSE	95.73	79.05	87.70	92.20	4.57	0.05	0.875	0.7478
Combination Group	85.84	92.65	95.10	79.70	11.67	0.15	0.940	0.7849

Combination of ROSE + Elastography

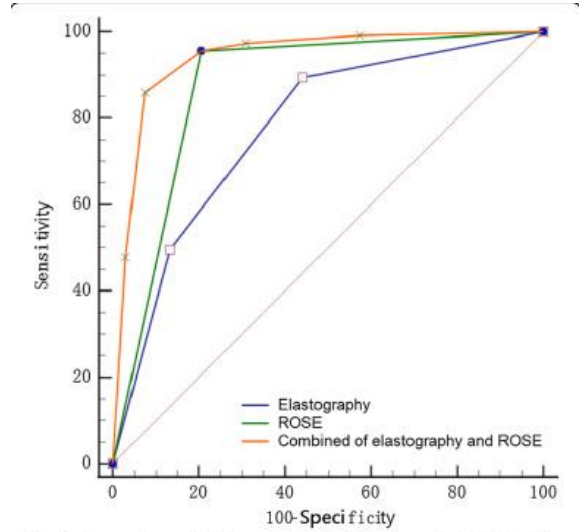


Fig. 3 Comparison of ROC curves of EBUS elastography, ROSE and combined EBUS elastography and ROSE groups

EBUS - Procedural Aspects

Beginners

- Forward Oblique view
- Reaching 4R , 10R and 4L
- Bronchoscopy image
- Use of second bronchoscope
- Financial implications

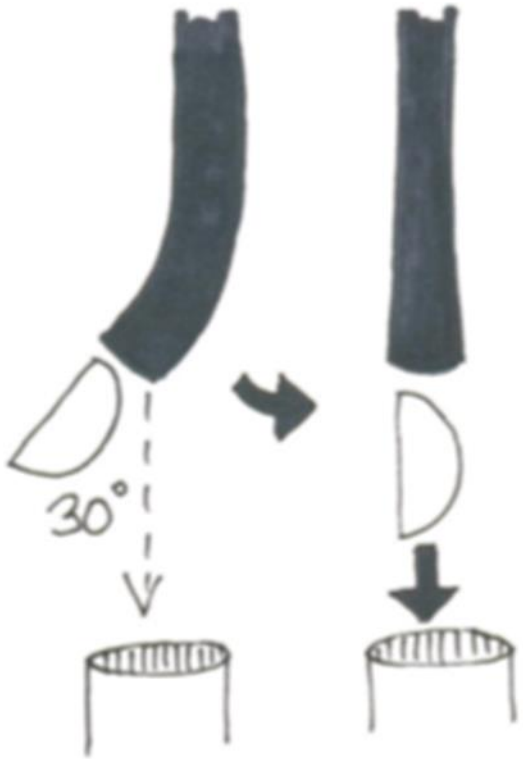
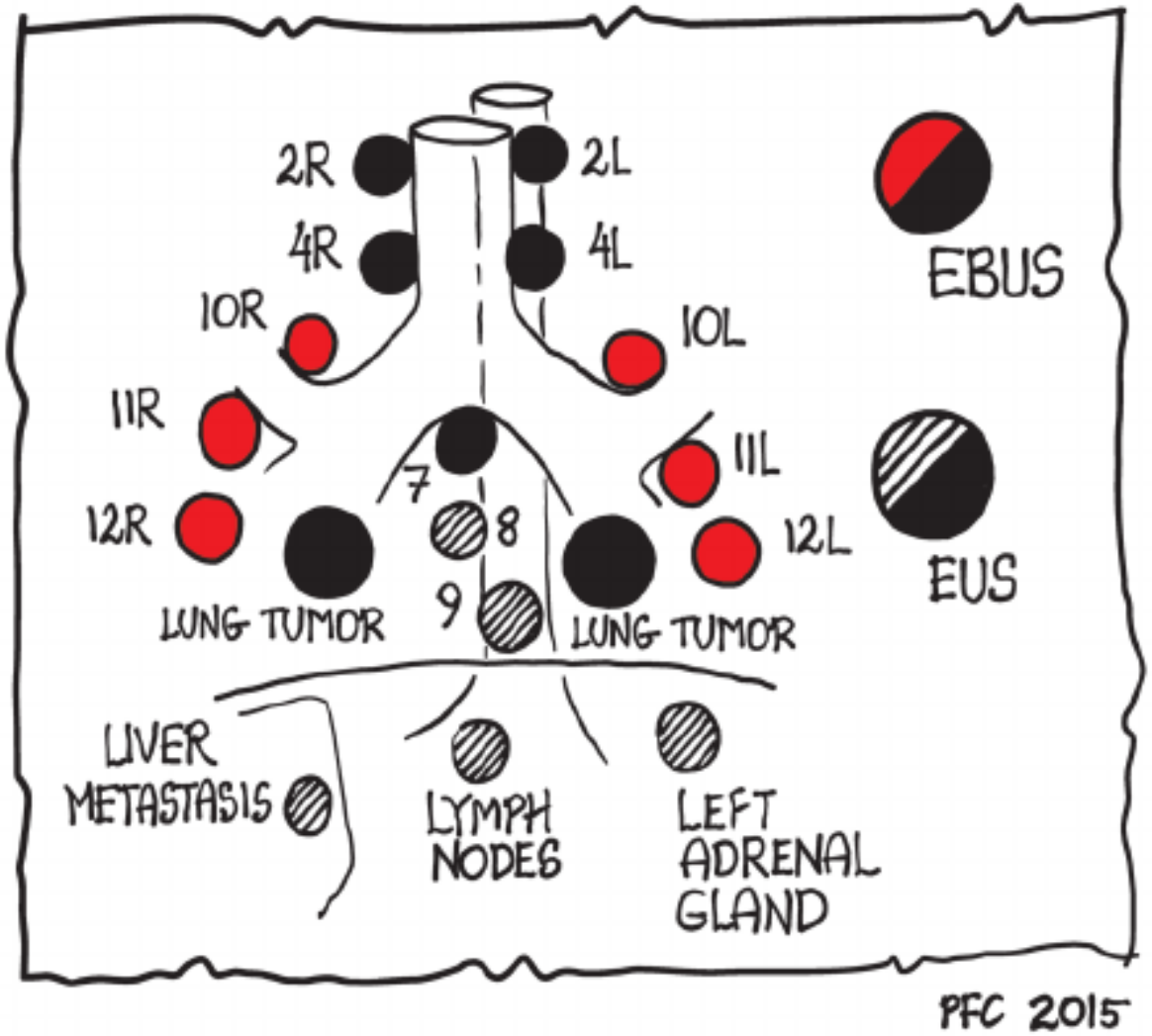
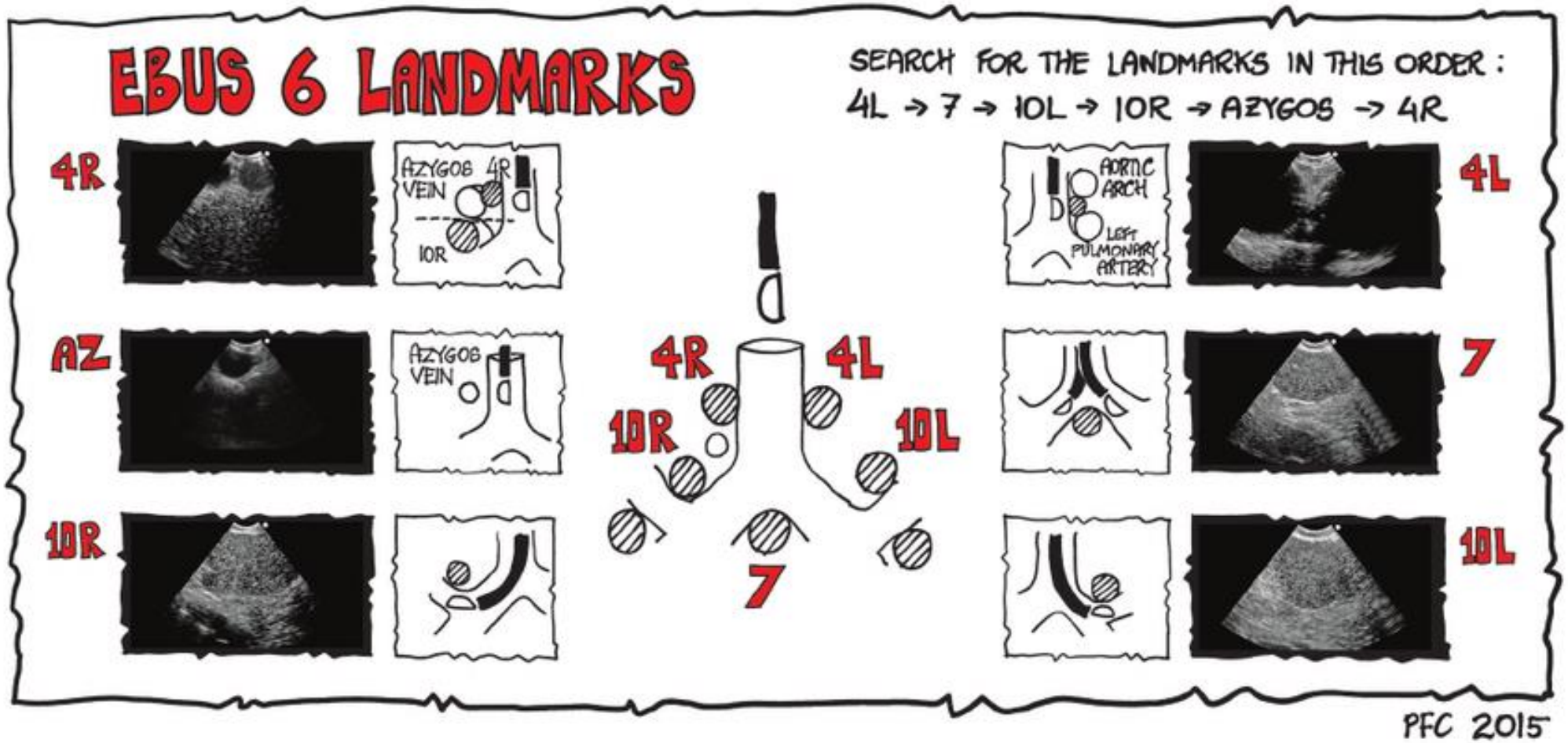


Figure 8.4(a)

EBUS - Procedural Aspects

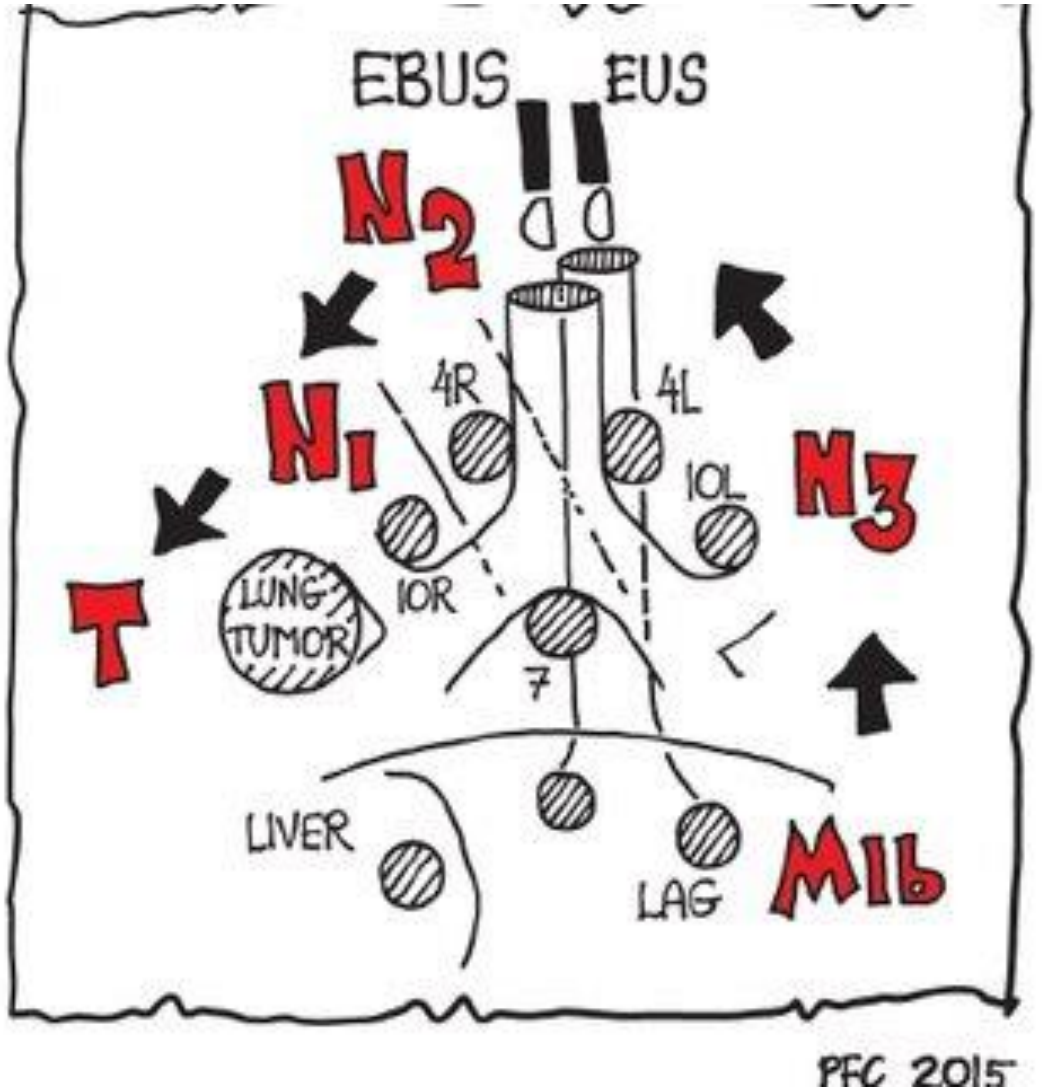


EBUS - Procedural Aspects

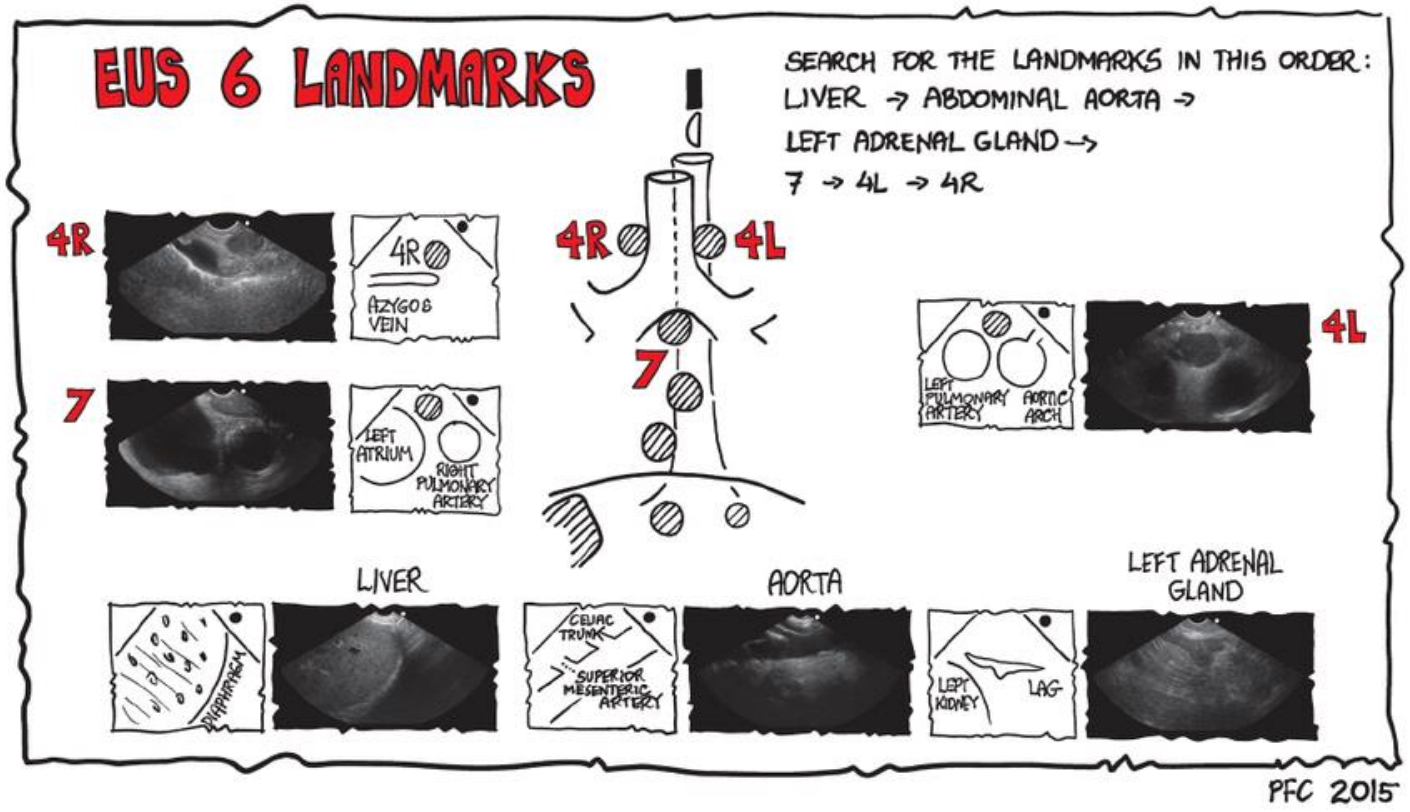


EBUS - Procedural Aspects - Sampling Order

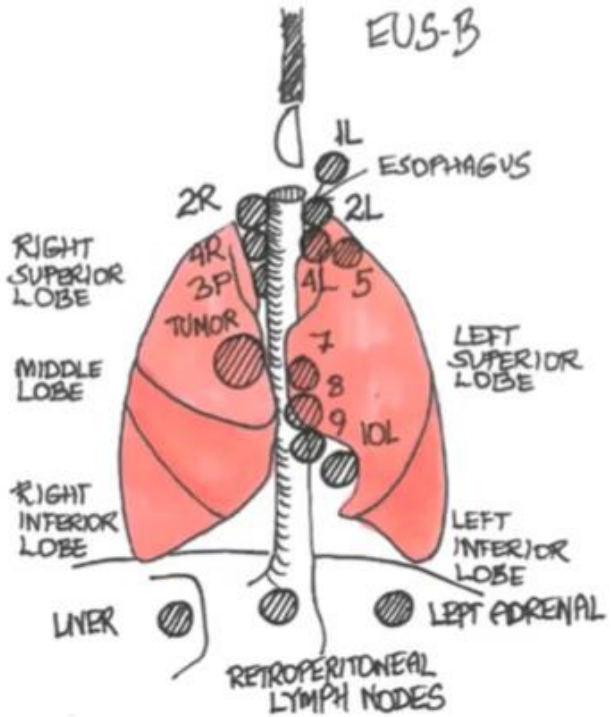
M1b – N3 – N2 – N1



EBUS - Procedural Aspects



EUS-B-FNA in lung cancer work up



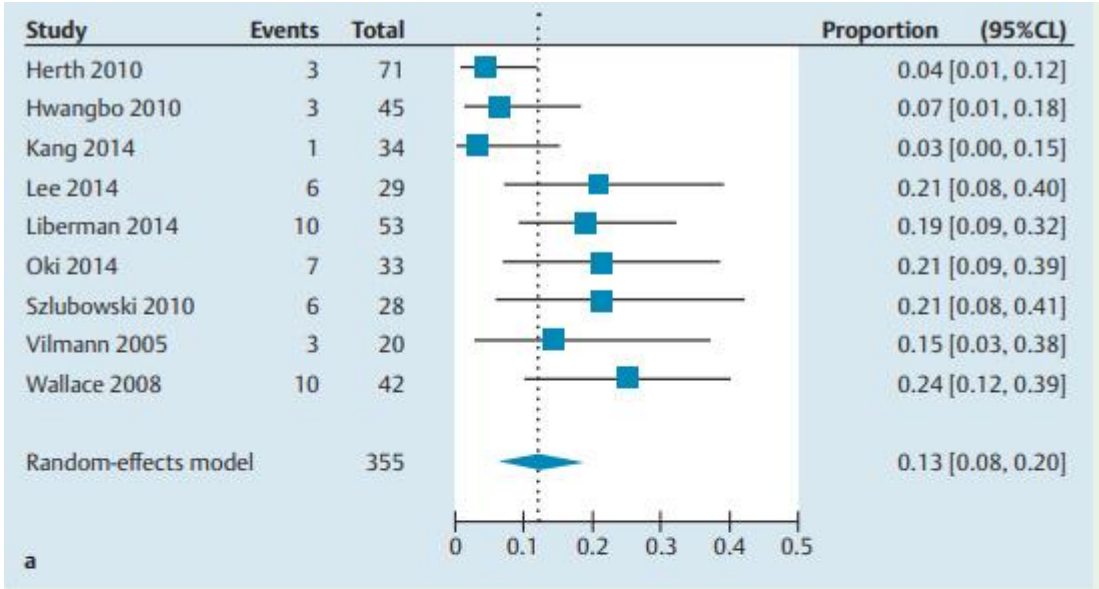
EBUS - Procedural Aspects

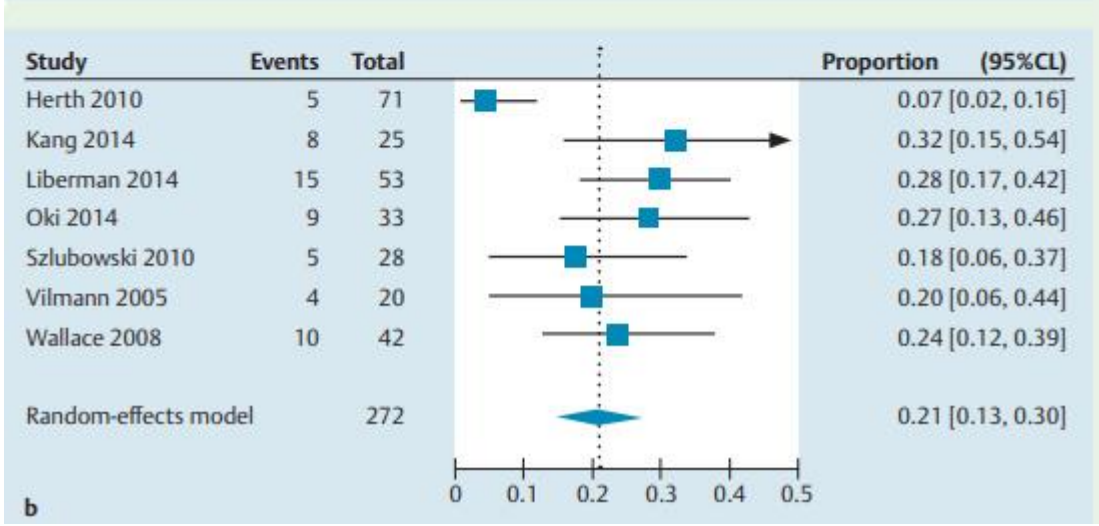
Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer: European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS)

ESGE

ERS EUROPEAN RESPIRATORY SOCIETY every breath counts

EBUS + EUS b - Complimentary





EBUS - Procedural Aspects

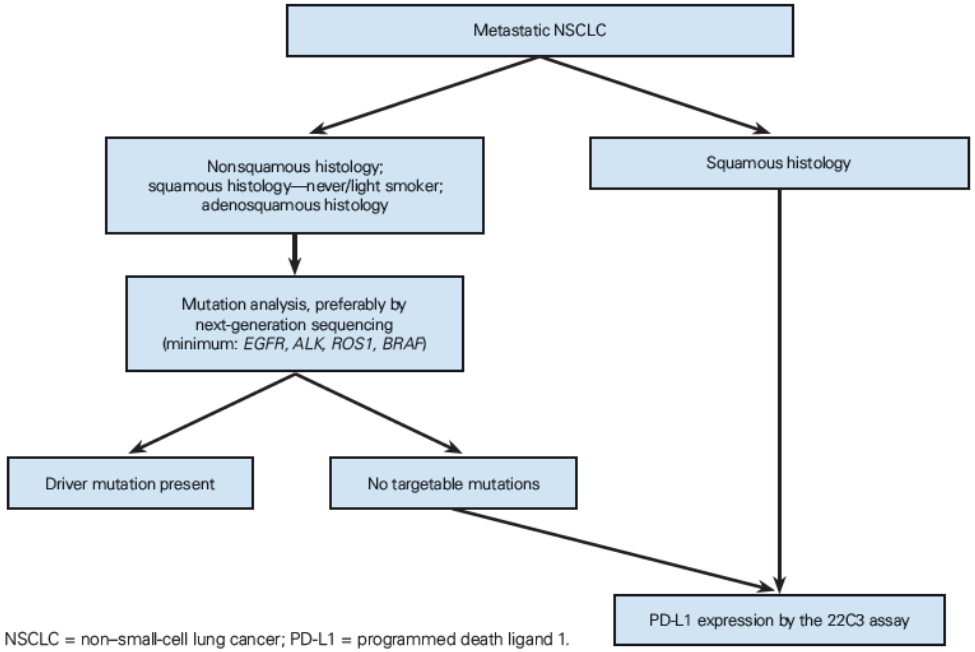
First Author	Year	No.	Prev	Sens	Spec	PPV	NPV
Changlai[185]	2001	127	64	88	83	90	79
Marom[98]	1999	79	56	73	94	85	88
Bury[155]	1996	30	53	88	86	88	86
Vansteenkiste[158]	1998	56	50	86	43	60	75
Sazon[192]	1996	32	50	100	100	100	100
Nosotti[84]	2008	413	48	97	97	97	97
Fritscher-Ravens[170]	2003	33	48	75	88	86	79
Wahl[195]	1994	23	48	82	75	75	82
Tatsumi[186]	2000	21	48	80	82	80	82
Guhlmann[193]	1997	32	47	87	100	100	89
Verhagen[26]	2004	56	46	58	90	83	71
Vansteenkiste[251]	1998	68	41	93	95	93	95
Vesselle[184]	2002	118	36	81	96	92	90
Turkmen[138]	2007	59	36	76	79	67	86
Zimny[182]	2003	33	36	83	81	71	89
Liewold[187]	2000	78	35	93	78	69	95
Scott[183]	1996	27	33	100	100	100	100
Magnani[188]	1999	28	32	67	84	67	84
Pieterman[80]	2000	102	31	91	86	74	95
Yen[127]	2008	96	31	73	92	81	88
Chin[194]	1995	30	30	78	81	64	89
Demura[176]	2003	50	30	87	63	50	92
Steinert[191]	1997	47	28	92	97	92	97
Melek[175]	2008	170	28	75	68	48	87
Kieman[138]	2002	88	28	88	86	71	95
Halpern[177]	2005	36	28	50	77	45	80
Pozo-Rodriguez[74]	2005	132	27	81	76	56	91
Dunagan[146]	2001	81	26	52	88	61	84
Reed[78]	2003	302	25	61	84	56	87
Bernasconi[178]	2006	51	25	54	76	44	83
Roberts[180]	2000	100	24	88	91	75	96
Gonzalez-Stawinski[190]	2003	202	23	66	78	48	88
Bury[152]	1997	64	22	86	100	100	96
Takamochi[132]	2005	71	21	40	88	46	84
Saunders[148]	1999	84	20	71	97	86	93
Kernstine[183]	2002	237	19	82	82	51	95
Kelly[134]	2004	69	19	62	98	(89)[a]	92
Nomori[133]	2004	80	18	86	97	(86)[a]	97
Lee[90]	2007	210	17	61	94	(69)[a]	92
Ebihara[131]	2006	205	15	74	90	(58)[a]	95
Poncelet[162]	2001	61	15	67	85	(43)[a]	94
Von Haag[140]	2002	52	12	67	91	(50)[a]	95
Yamamoto[174]	2008	34	9	33	84	(17)[a]	93
Konishi[181]	2003	54	9	80	92	(50)[a]	98
Farrell[12]	2000	84	5	100	93	(40)[a]	100
Median: prevalence > 30				**85**	**87**	**84**	**88**
Median: prevalence 21-30				**77**	**83**	**56**	**89**
Median: prevalence ≤ 20				**71**	**92**	**51**	**95**
Summary: median		**4,105**	**28**	**80**	**88**	**75**	**91**

First Author	Year	No.	Stage	Thoro	Prev	Sens	Spec[a]	PPV[a]	NPV
TM									
Hammoud[235]	1999	1,369	cN0-3	Sel	36	85	(100)[a]	(100)[a]	92
Lemaire[230]	2006	1,362	cN0-3	Sys	29	86	(100)[a]	(100)[a]	95
Coughlin[243]	1985	1,259	cN0-3	Sel	29	92	(100)[a]	(100)[a]	97
Luke[242, b]	1986	1,000	cN0-2	Sel	39	85	(100)[a]	(100)[a]	91
De Leyn[238]	1996	500	cN0-2	Sys	39	76	(100)[a]	(100)[a]	87
Anraku[227]	2010	352	cN0-3	Sys	37	92	(100)[a]	(100)[a]	
Page[241, b]	1987	345	cN0-2	Sel	48	73	(100)[a]	(100)[a]	
Dillemans[239]	1994	331	cN0-3	Sys	41	72	(100)[a]	(100)[a]	
Brion[244]	1985	153	cN0-2	Sel	35	67	(100)[a]	(100)[a]	
Fibla[231]	2006	142	cN0-3	Sel	42	67	(100)[a]	(100)[a]	
Jolly[160]	1991	136	cN0-2	Sel	54	92	(100)[a]	(100)[a]	
Ratto[125]	1990	123	cN0-2	Sel	33	88	(100)[a]	(100)[a]	
Ebner[236, b]	1999	116	cN0-2	Sys	50	81	(100)[a]	(100)[a]	
Annema[228]	2010	110	cN0-3	Sel	46	80	(100)[a]	(100)[a]	
Gdeedo[153]	1997	100	cN0-3	Sys	32	78	(100)[a]	(100)[a]	
Riordain[240]	1991	74	cN0-2	Sel	50	81	(100)[a]	(100)[a]	
Aaby[156]	1995	57	cN0-3	Sys	44	84	(100)[a]	(100)[a]	
Block[226]	2010	54	cN0-3	Sel	44	88	(100)[a]	(100)[a]	
Kim[224]	2011	750	cN0	Sys	15	44	(100)[a]	(100)[a]	
Choi[233]	2003	291	cN0	Sys	15	44	(100)[a]	(100)[a]	
Meyers[229]	2006	169	cN0	Sel	8	38	(100)[a]	(100)[a]	
Cerfolio[232]	2006	153	cN0-1	Sys	14	32	(100)[a]	(100)[a]	
Deneffe[245]	1983	124	cN0	Sel	31	68	(100)[a]	(100)[a]	
Park[225]	2010	78	cN0	Sys	8	50	(100)[a]	(100)[a]	
Gurses[234]	2002	67	cN0	Sys	15	40	(100)[a]	(100)[a]	
Leschber[222]	2008	52	cN0	Sys	19	…	(100)[a]	…	
Median: cN0-3			***cN0-3***	*39% sys*	**40**	**83**			
Median: cN0			***cN0***	*75% sys*	**16**	**47**			
Median: sys			*46% cN0*	***sys***	27	**74**			
Median: sel			*17% cN0*	***sel***	39	**81**			
Summary TM: median		**9267**			**33**	**78**	**(100)[a]**	**(100)[a]**	
VAM									
Venissac[255]	2003	154	cN2-3	Sys	71	97	(100)[a]	(100)[a]	
Kimura[250]	2007	209	cN0-3	Sel	31	78	(100)[a]	(100)[a]	
Lardinois[246]	2003	195	cN0-3	Sys	34	87	(100)[a]	(100)[a]	
Kimura[135]	2003	125	cN0-3	Sys	36	85	(100)[a]	(100)[a]	
Sayar[249]	2011	104	cN0-2	Sel	29	90	(100)[a]	(100)[a]	
Anraku[227]	2010	89	cN0-3	Sys	22	95	(100)[a]	(100)[a]	
Leschber[222]	2008	119	cN0	Sys	17	…	(100)[a]	…	
Summary VAM: median		**995**			**31**	**89**	**(100)[a]**	**(100)[a]**	
LA									
Zielinski[364]	2007	256	cN0-2	Compl	31	94	(100)[a]	(100)[a]	97
Witte[365]	2006	130	cN0-2	Compl	…	94	(100)[a]	(100)[a]	99
Summary LA: median		**386**		**compl**	**31**	**94**	**(100)[a]**	**(100)[a]**	**98**
Summary ALL: median		**10,648**			**34**	**81**	**(100)[a]**	**(100)[a]**	**91**

Study	Year	No.	Stage	Thoro	Prev	Sens	Spec[a]	PPV[a]	NPV
Fielding[341]	2009	68	cN1-3	Sel	87	95	(100)[a]	(100)[a]	(67)[b]
Steinfort[334]	2011	117	cN1-3	Sys	80	97	(100)[a]	(100)[a]	87
Cetinkaya[332]	2011	52	cN2-3	Sys	80	95	(100)[a]	(100)[a]	83
Rintoul[344]	2009	109	cN1-3	Sys	77	91	(100)[a]	(100)[a]	60
Gilbert[339]	2009	67	cN1-3	Sel	70	93	(100)[a]	(100)[a]	83
Yasufuku[349]	2005	108	cN1-3	Sys	69	95	(100)[a]	(100)[a]	90
Yasafuku[350]	2004	70	cN1-3	Sys	67	96	(100)[a]	(100)[a]	92
Szlubowski[343]	2009	226	cN0-3	Sys	64	89	(100)[a]	(100)[a]	84
Ye[333]	2011	101	cN1-3	Sel	63	95	(100)[a]	(100)[a]	93
Cerfolio[336]	2010	92	cN2	Sys	63	57	(100)[a]	(100)[a]	79
Lee BE[329]	2012	73	cN0-3	Sys	62	95	(100)[a]	(100)[a]	94
Bauwens[345]	2008	106	cN1-3	Sys	58	95	(100)[a]	(100)[a]	91
Sun[337]	2010	49	cN1-3	Sys	53	85	96	96	85
Herth[307]	2010	139	cN1-3	Sel	52	91	(100)[a]	(100)[a]	92
Memoli[331]	2011	100	cN1-3	Sys	47	87	(100)[a]	(100)[a]	89
Omark Petersen[340]	2009	151	cN2-3	Lim	43	85	(100)[a]	(100)[a]	89
Yasufuku[330]	2011	153	cN0-3	Sys	35	81	(100)[a]	(100)[a]	91
Hwangbo[335]	2010	150	cN2-3	Sys	31	84	(100)[a]	(100)[a]	93
Wallace[296]	2008	138	cN2-3	Sys	30	69	(100)[a]	(100)[a]	88
Lee HS[346]	2008	102	cN2-3	Sys	30	94	(100)[a]	(100)[a]	97
Hwangbo[342]	2009	117	cN2-3	Sys	26	90	(100)[a]	(100)[a]	97
Yasufuku[348]	2006	102	cN1-3	Sys	25	92	(100)[a]	(100)[a]	97
Szlubowski[343]	2010	120	cN0	Sel	22	46	99	93	86
Herth[211]	2006	100	cN0	Sys	21	92	(100)[a]	(100)[a]	96
Nakajima[338]	2010	49	cN1-3	Sys	18	67	(100)[a]	(100)[a,c]	93
Herth[210]	2008	97	cN0	Sys	10	89	(100)[a]	(100)[a,c]	99
Median: Prevalence ≥ 80						**96**			**83**
Median: Prevalence 60-79						**91**			**83**
Median: Prevalence 40-59						**87**			**89**
Median: Prevalence 20-39						**87**			**95**
Median: Prevalence < 20						**78**			**96**
Median: cN1-3						**91**			**89**
Median: cN0						**89**			**96**
Summary: median		**2,756**			**58**	**89**	**(100)[a]**	**(100)[a]**	**91**

EBUS in the Era of Molecular analysis and NGS

Figure. Molecular Diagnosis of NSCLC: A Suggested Approach



NSCLC = non–small-cell lung cancer; PD-L1 = programmed death ligand 1.

Table 1. Common Molecular Abnormalities in Lung Adenocarcinoma

Molecular Abnormality	Frequency	Possible Management Options
KRAS	25%	No targeted agent[a]
EGFR	23%	Erlotinib, afatinib, gefitinib, osimertinib
ALK	6%	Alectinib, ceritinib, crizotinib
TP53	4%	No targeted agent[a]
BRAF	3%	Dabrafenib/trametinib
PIK3CA	3%	No targeted agent[a]
MET	2%	Crizotinib
ROS1	1.5%	Crizotinib, ceritinib
HER2	1%	Ado-trastuzumab emtansine
RET	1%	Cabozantinib, vandetanib
MEK1	0.4%	No targeted agent[a]
NRAS	0.2%	No targeted agent[a]
β-catenin	0.2%	No targeted agent[a]
IDH1	0.1%	No targeted agent[a]
No identified abnormality	33%	No targeted agent[a]

[a]These patients may be candidates for pembrolizumab if their tumors exhibit high programmed death ligand 1 expression.

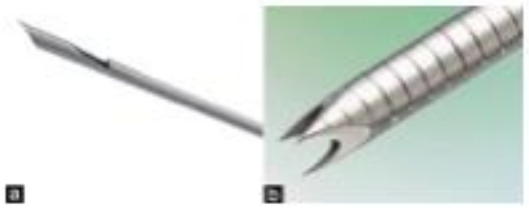
EBUS in the Era of Molecular analysis and NGS

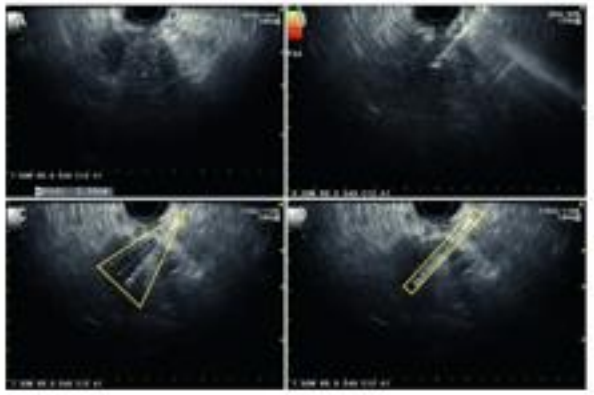
- Molecular classification - essential part of routine lung cancer care
- Growing number of targetable molecular alterations
- 30% of the patients diagnosed with NSCLC, tumor cellularity is < 40%
- In approximately 23% of patients, the tissue is not adequate for molecular analyses due to the difficulty of reaching tumor sites with non-invasive methods
- Moreover, in some cases, tumor necrotic cells decrease cellular density, resulting in low-quality sequencing.

EBUS in the Era of Molecular analysis and NGS

EBUS - Techniques

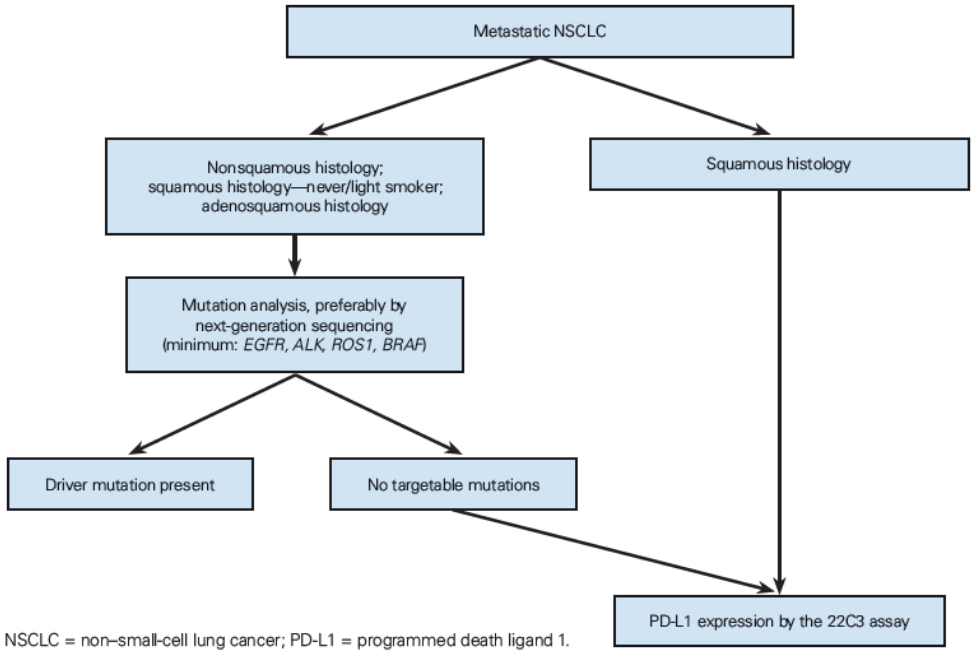
- Size - 19G / 25G
  Shape - Procore/Acquire
- Slow Pull
- Fanning
- IFB





The need for new Techniques of Tissue Acquisition

Figure. Molecular Diagnosis of NSCLC: A Suggested Approach



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No identified abnormality	33%	No targeted agent[a]

[a]These patients may be candidates for pembrolizumab if their tumors exhibit high programmed death ligand 1 expression.

EBUS in the Era of Molecular analysis and NGS

IntraNodal Forceps Biopsy

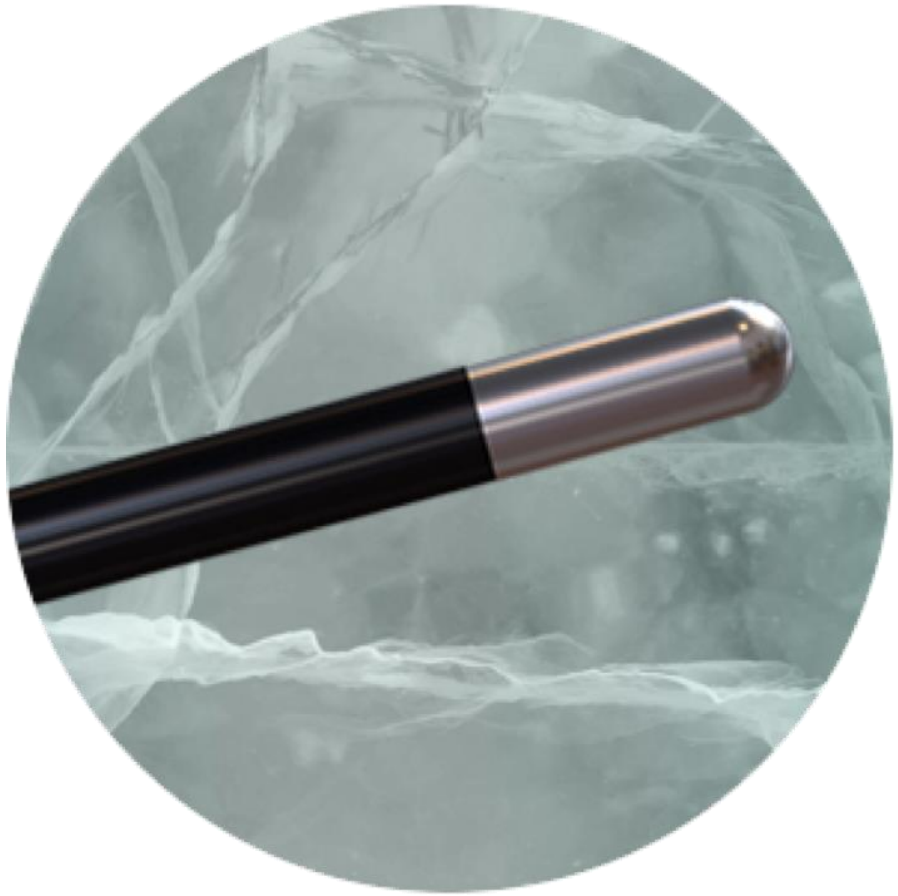
Herth FJ, Morgan RK, Eberhardt R, Ernst A: EBUS-guided miniforceps biopsy in the biopsy of subcarinal masses in pts with low likelihood of NSCLC. Ann Thorac Surg 2008; 85: 1874–1878

EBUS in the Era of Molecular analysis and NGS

IntraNodal Forceps Biopsy

Modality	Diagnostic yield	Numbers	Significance
EBUS-TBNA	81%	60/74	p=0.09
EBUS-MFB	91%	67/74	
TBNA+MFB	97%	72/74	p<0.001

Chrissian A, Misselhorn D, Chen A: Endobronchial-ultrasound guided miniforceps biopsy of mediastinal and hilar lesions. Ann Thorac Surg 2011; 92: 284–288

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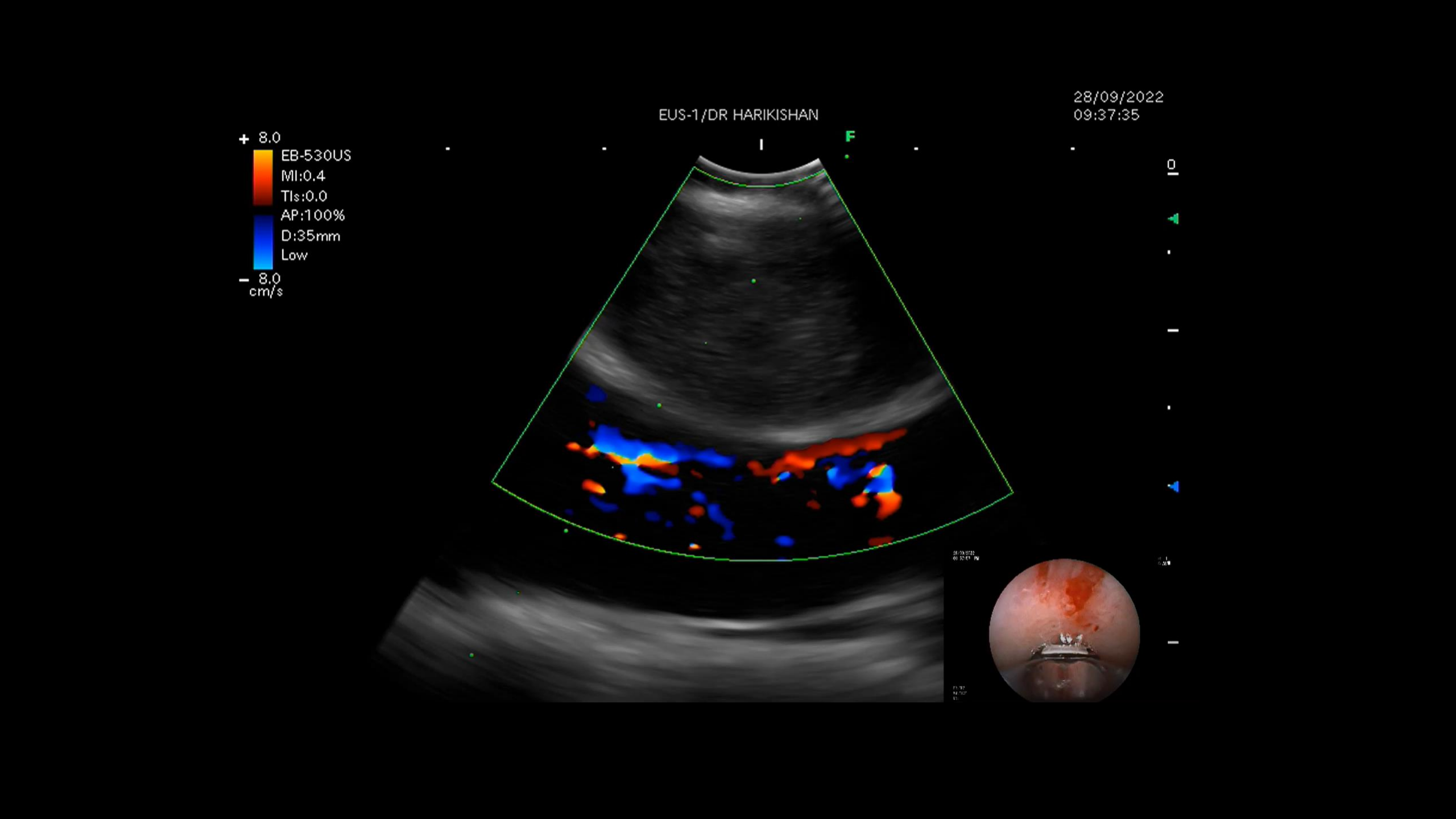
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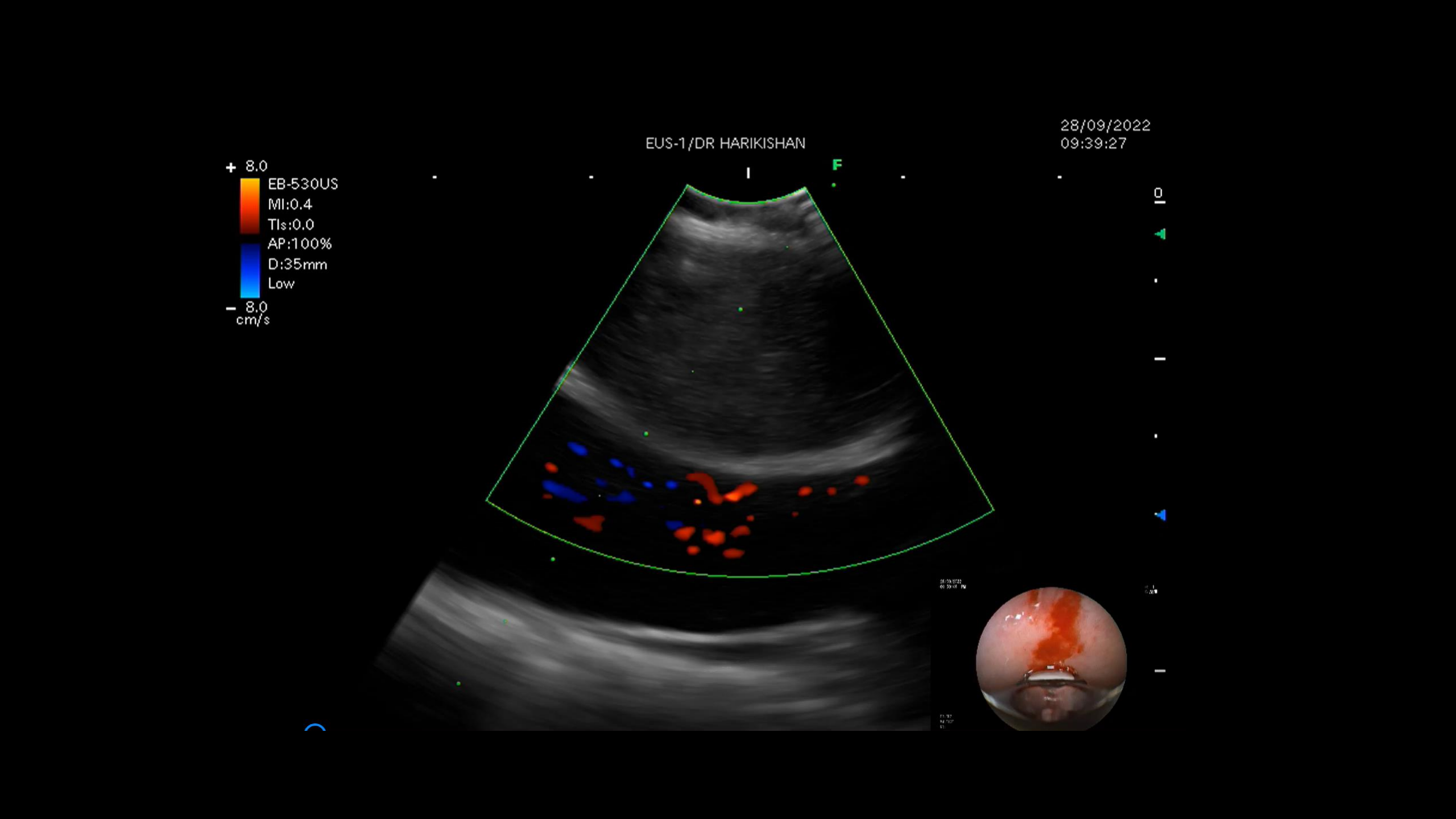
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Official Case Reports Journal of the Asian Pacific Society of Respirology

Respirology Case Reports

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APSR

Endobronchial ultrasound-guided transbronchial cryo-nodal biopsy: a novel approach for mediastinal lymph node sampling

Hari Kishan Gonuguntla[1], Milap Shah[2], Nitesh Gupta[3], Sumita Agrawal[4], Venerino Poletti[5] & Gustavo Cumbo Nacheli[6]

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[2]Department of Laboratory Medicine, Yashoda Hospital, Hyderabad, India.
[3]Department of Pulmonary, Critical Care and Sleep Medicine, VMMC and Safdarjung Hospital, New Delhi, India.
[4]Department of Pulmonary, Critical Care and Sleep Medicine, Medipulse Hospital, Jodhpur, India.
[5]Department of Diseases of the Thorax, Ospedale GB Morgagni, Forli, Italy.
[6]Division of Bronchoscopy and Interventional Pulmonology, Pulmonary and Critical Care Division, Spectrum Health Medical Group, Grand Rapids, MI, USA.

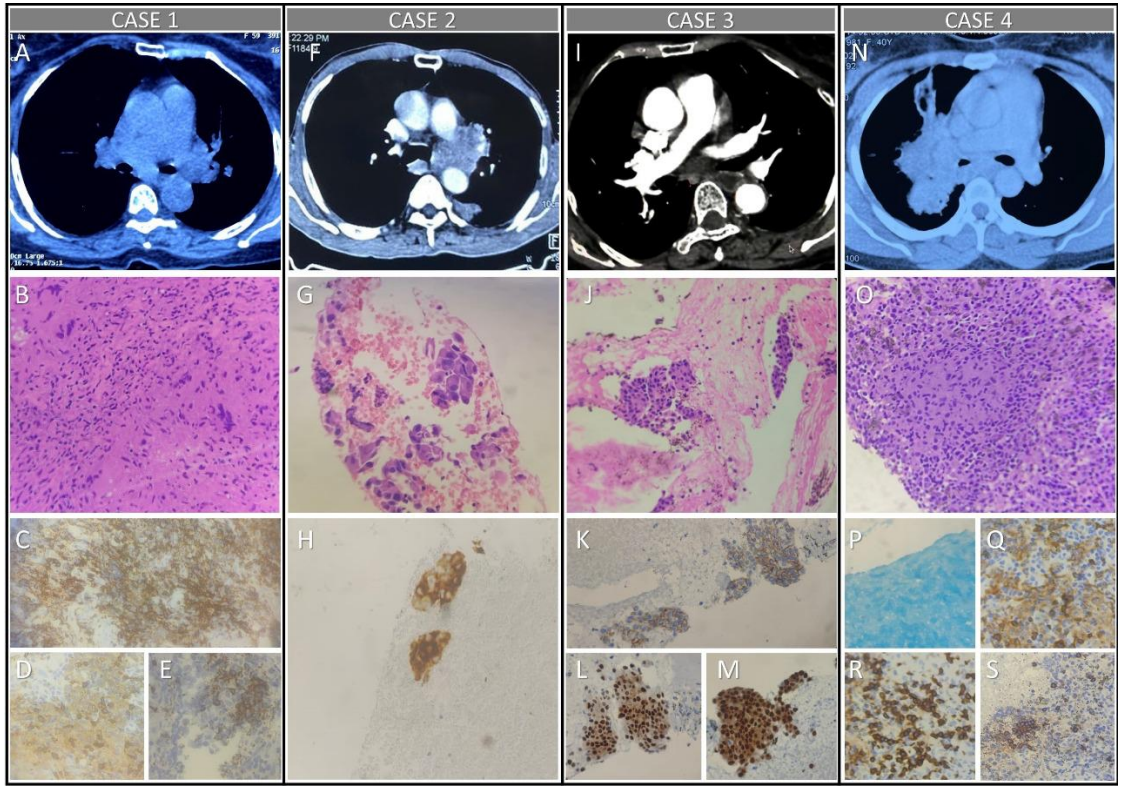
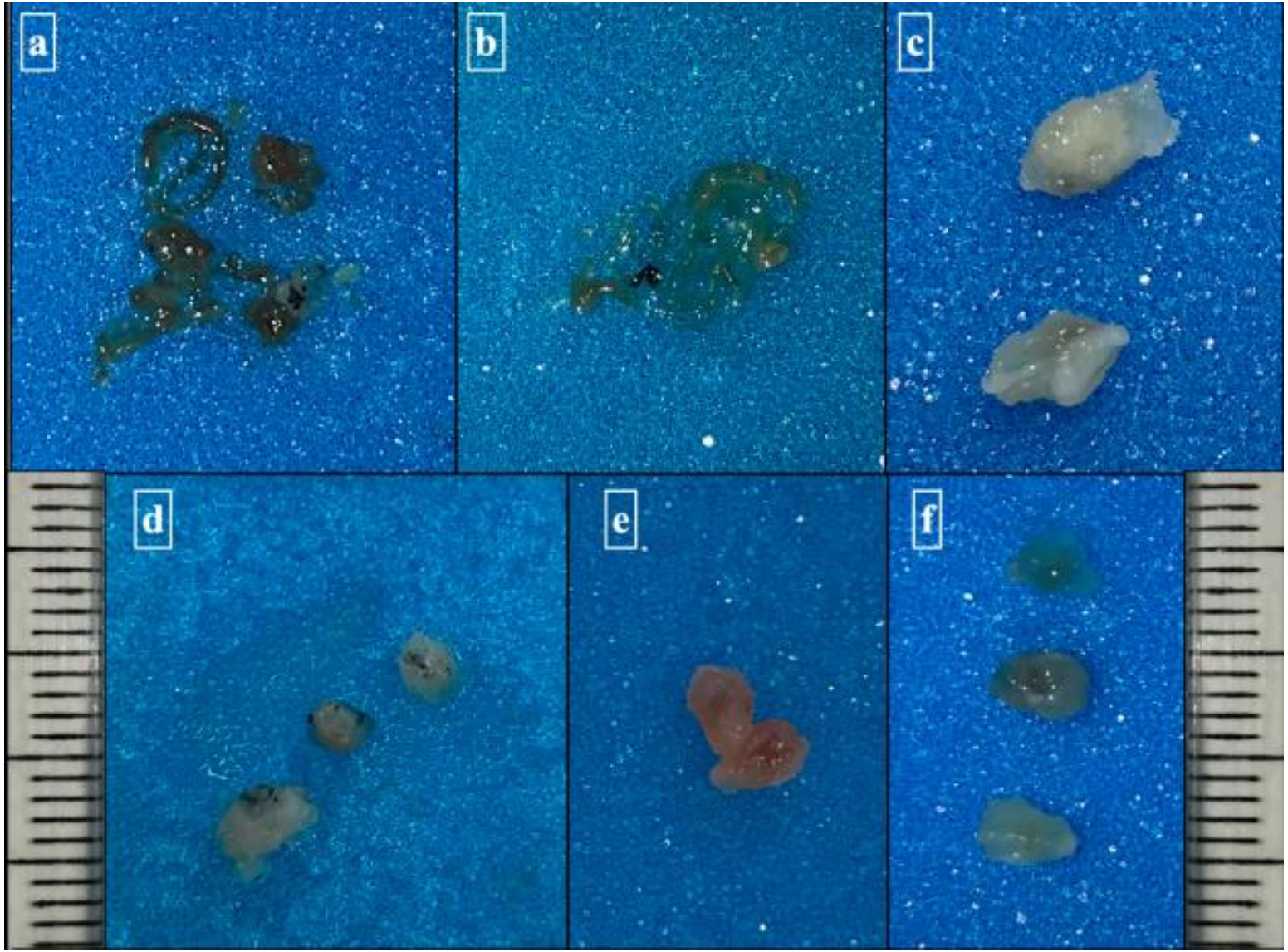


Figure 1: Case 1 – (A) Non-contrast CT thorax showing sub-carninal and hilar nodes, (B) Non caseating epithelioid granuloma with giant cells and fibrosis. H&E 40x, CD4 cells (C) are is more evident than CD 8 cells (D) while few B lymphocytes are highlighted with CD 20 (E); Case 2 – (F) Contrast CT thorax showing left hilar mass with paratracheal lymphnodes, (G) Adenocarcinoma cells,H&E ,10x (H) with positivity for ROS1(D4D6) , 10x; Case 3 – (I) Contrast CT showing left interlobar node, (J) Metastatic Carcinoma from breast,H&E,10x, Tumour cells are positive for Her2 (K) ,ER (L) and GATA3 (M); Case 4 – (N) Non-contrast CT showing right para-hilar lesion with sub-carinal lymphnode, (O) Necrotising Granuloma,H&E,40x (P) Ziehl-Neelsen stain highlights few pink rod shaped bacilli (red arrow), CD8 cells (Q) are more evident than CD 4 cells (R) while few B lymphocytes are highlighted with CD 20 (S)

EBUS in the Era of Molecular analysis and NGS



EBUS - Mediastinal Cryobiopsy

No needle Technique

Dr. Hari Kishan Gonuguntla MD.DM

EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: a randomised trial

Jing Zhang, Jie-Ru Guo, Zan-Sheng Huang, Wan-Lei Fu, Xian-Li Wu, Na Wu, Wolfgang M. Kuebler, Felix J.F. Herth, Ye Fan

European Respiratory Journal 2021 58: 2100055; **DOI:** 10.1183/13993003.00055-2021

Results

Definitive Diagnosis - 181/197 patients (93.3%)
152 patients - Both TBNA and cryobiopsy - yield diagnosis

26 additional cases where TBNA failed - Cryobiospy established the diagnosis

6 - NSCLC
6- Lymphoma
1 - Seminoma
8 - Tuberculosis
5 - Sarcoidosis

Conversely - 3 NSCLC patients - diagnosis was established only by TBNA

Overall diagnostic yield for TBNA - 79.9% and for Cryo 91.8%

Sub group analysis - no difference in diagnostic yield in common lung cancer (94.1% for TBNA vs 95.6% for cryobiopsy)

The diagnostic yield of mediastinal cryobiopsy was significantly higher in Uncommon tumors (91.7% versus 25.0%)

Benign lesions - 80.9% versus 53.2%

Table 2. Variability in Transbronchial Mediastinal Cryobiopsy technique

First author	Year	Anesthesia	Airway	Targeted LN	Needle size / passes	ROSE	Cryo size	Track creation	# MCB pass	Freezing time
Zhang(28)	2021	CS	transoral	2R/L to 12R/L	?G x 4	no	1.1	EC knife	3	7
Fan(29)	2023	CS	transoral	2R/L to 13R/L	22G x 4	no	1.1	EC knife	1	7
Ariza-Prota(30)	2023	CS	transoral	7, 4R mostly	22G x 3-5	no	1.1	TBNA	3	4
Gershman(31)	2022	CS/DS	LMA	7, 4L	19G x 3	no	1.1 / 1.7	TBNA/Nd YAG/ track dilation	2-4	3-4
Oikonomidou(50)	2022	CS/DS	LMA/ETT+ jet vent	N/A	19/21/22G x 4	no	1.1	TBNA + 19G sheath	2	3
Maturu(32)	2023	GA	LMA	7,4R,11L,11R	19G	yes	1.1	TBNA	4-7	5-6
Gonuguntla (37)	2021	GA	LMA	7, 11L	19/21/22	yes	1.1	TBNA	1-2	3
Ariza-Prota (45)	2022	CS	transoral	7,11R	22G x 4	yes	1.1	TBNA	3	3
Genova(33)	2022	DS	?	7, 10R	19G x 3	no	1.1	TBNA	2	4
Salcedo-Lobera(51)	2022	CS	transoral	7, retrotrach mass	22G x 3	no	1.1	TBNA	1-2	8
Zhang(27)	2020	CS	transoral	10L	22G x 4	no	1.1	EC knife	2	15
Huang(36)	2021	CS	transoral+ esophageal	paraaortic LN	21G x 4	no	1.1	air inflation + EC knife	2	7
Ishiguro(52)	2022	N/A	?	esophageal mass	22G x 3	no	?	TBNA	2	?
Kho(38)	2022	TIVA	RB	7	22G x 4	yes	1.1	TBNA	2	7
Tamburrini(34)	2022	GA	RB	7	21G	no	1.1	TBNA+forceps	2	4
Zhang(35)	2022	CS	transoral	7	21G x 4	no	1.1	TBNA+sheath	1	7
Hetze(53)l	2023	?	transoral	4L	(?)G x 4	yes	1.1	EC knife	several	7
Schwick (41)	2023	GA	ETT	7	19G x 2-3	no	1.1	TBNA + sheath	1	5-7
Takemura(54)	2023	?	?	11s	25G x 3	no	1.7	TBNA	4	?
Zhang(55)	2023	CS	transoral	11L	21G x 4	no	1.1	EC knife	1	7

LMA, laryngeal mask airway; ETT, endotracheal tube; RB, rigid bronchoscopy, LN, lymph node, G, gauge; EC, electrocautery; Nd YAG, neodymium-doped yttrium aluminum garnet

Courtesy - Arthur Oliver Romero

Take Home Message

- EBUS - Diagnostic procedure of choice in Lung Cancer Staging
- EBUS + EUSb – Complete Mediastinal Staging
- In the Era of Molecular Analysis - More tissue acquisition
- Mediastinal Cryo biopsy - safe and feasible
- Mediastinal Cryobiopsy - Improves the Diagnostic yield in all pathologies
- Training aspects - Simulator Training is essential

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