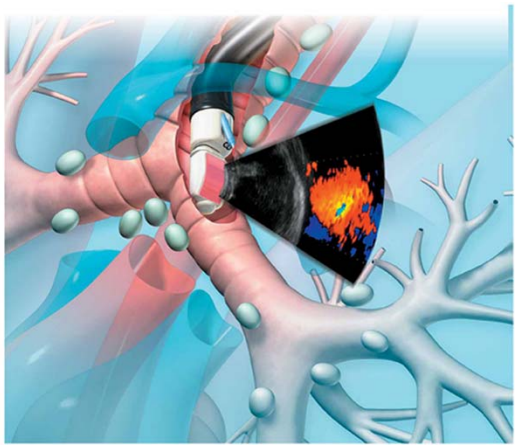
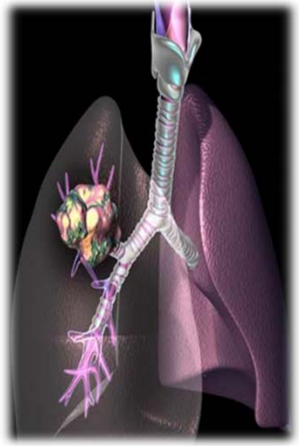
The Various Methods to Biopsy the Lung





PROF SHITRIT DAVID

HEAD, PULMONARY DEPARTMENT

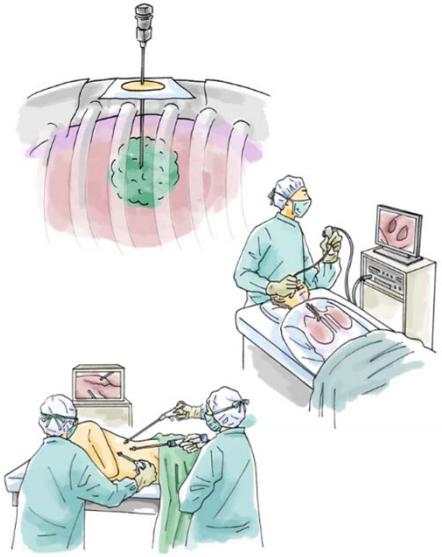
MEIR MEDICAL CENTER, ISRAEL

Conflict of Interest

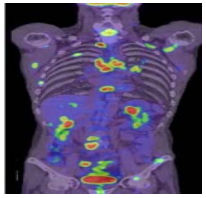
This presentation is supported by AstraZeneca

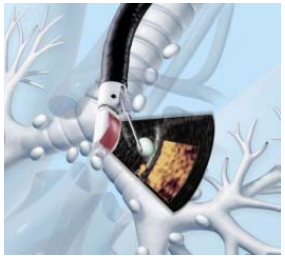
Two main steps before treatment

Tissue Diagnosis



Staging



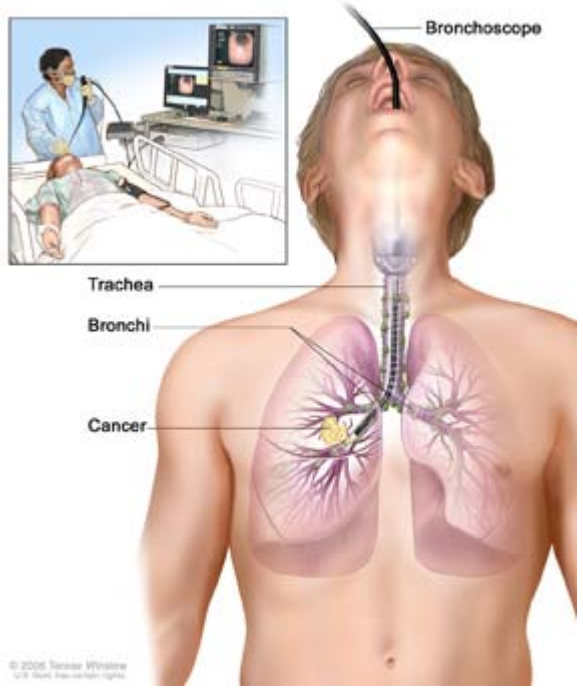


Bronchoscopy

Easy to perform as an outpatient procedure

Moderate Sedation

Risk of complications is minimal



Bronchoscopy: modalities

- BAL
- Brushing
- Cytology
- Biopsy
  - Endobronchial (EBB)
  - Transbronchial (TBB)
  - Cryobiopsy

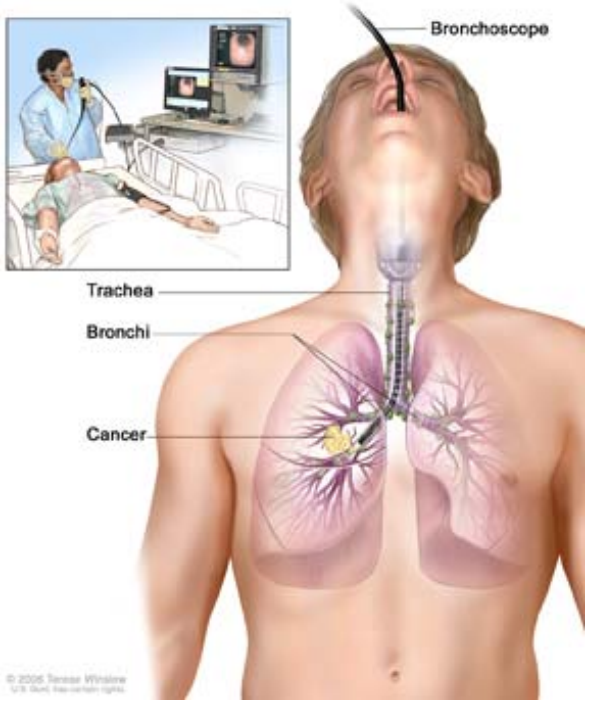
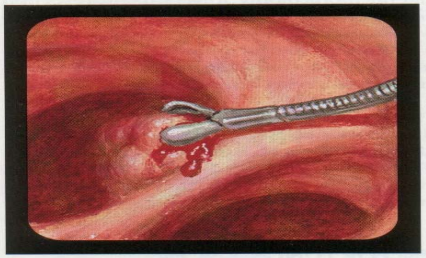


Plate 6

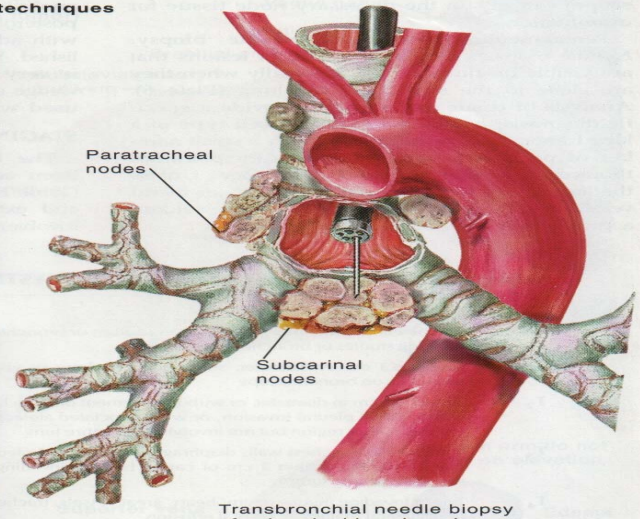
Bronchoscopy and Needle Biopsy

Bronchoscopic diagnostic and staging techniques



Bronchoscopic biopsy of lesion in left lower lobe

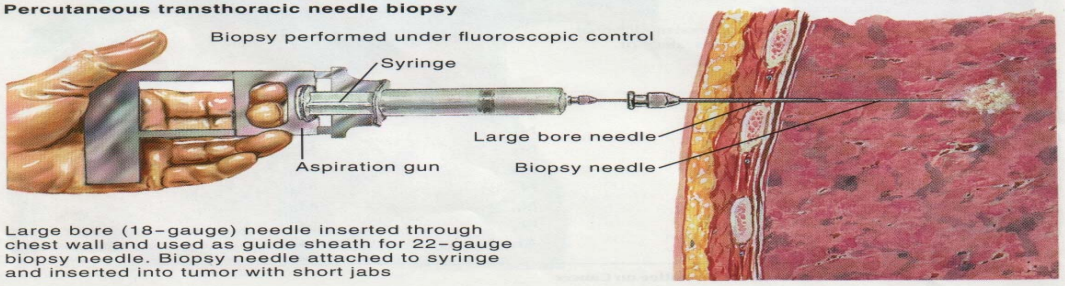
Brush cytologic investigation of lesion obstructing bronchus



Transbronchial needle biopsy of subcarinal lymph node

F. Netter M.D.
© CIBA-GEIGY

Percutaneous transthoracic needle biopsy



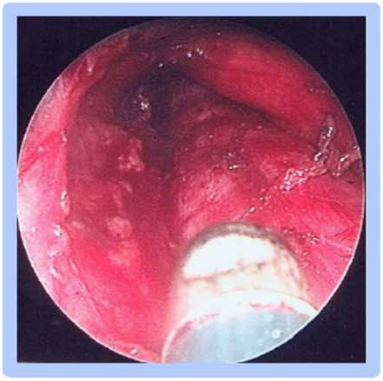
Large bore (18-gauge) needle inserted through chest wall and used as guide sheath for 22-gauge biopsy needle. Biopsy needle attached to syringe and inserted into tumor with short jabs

Pleural effusion

- Pleural aspiration
- Pleural biopsy
  US/CT Guided
  Thoracoscopy
  (with or
without pleurodesis)

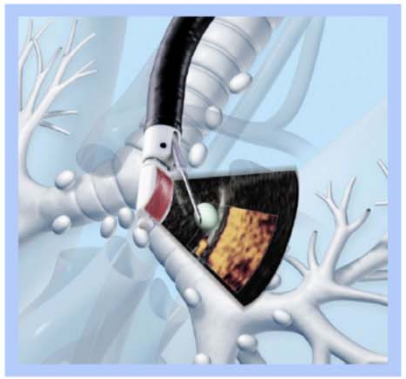
Invasive Mediastinal Staging

- Mediastinoscopy
- Anterior Mediastinotomy

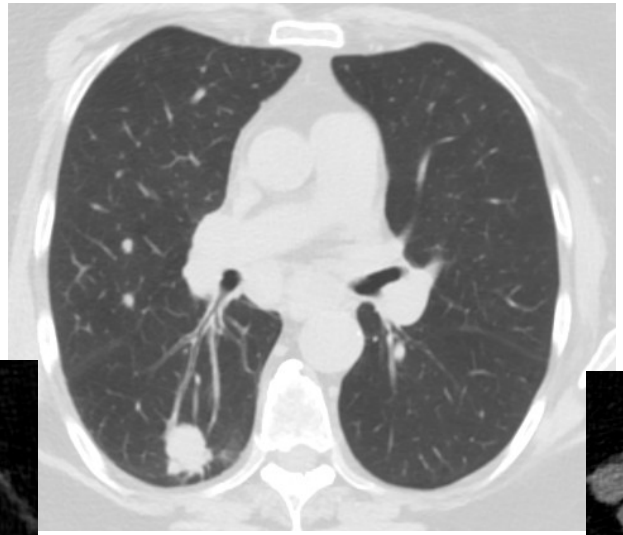


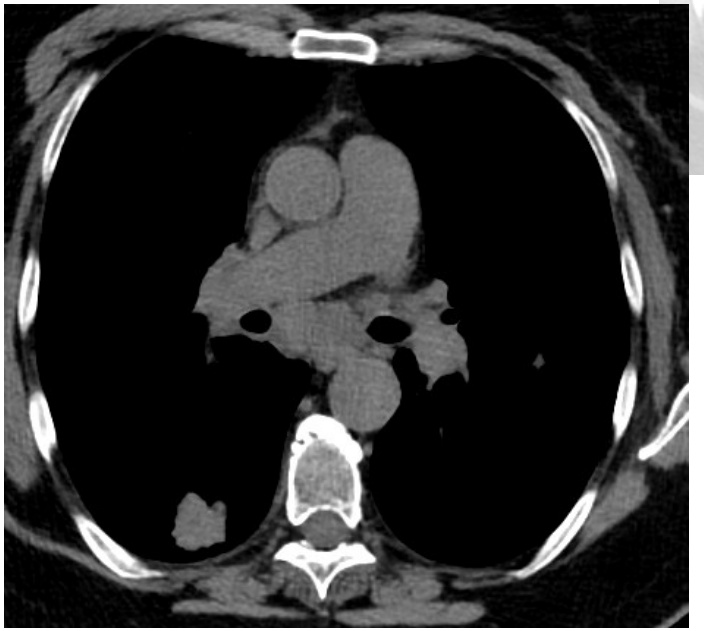
Minimally Invasive Mediastinal Staging

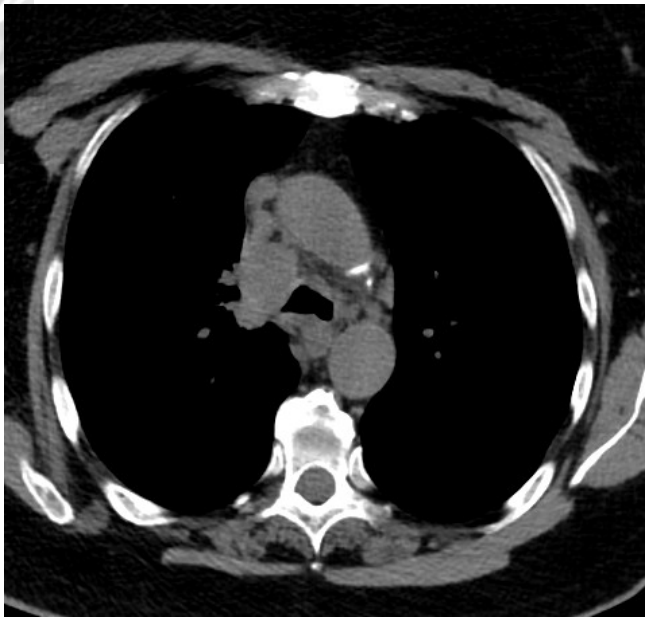
- Endobronchial Ultrasound
  EBUS



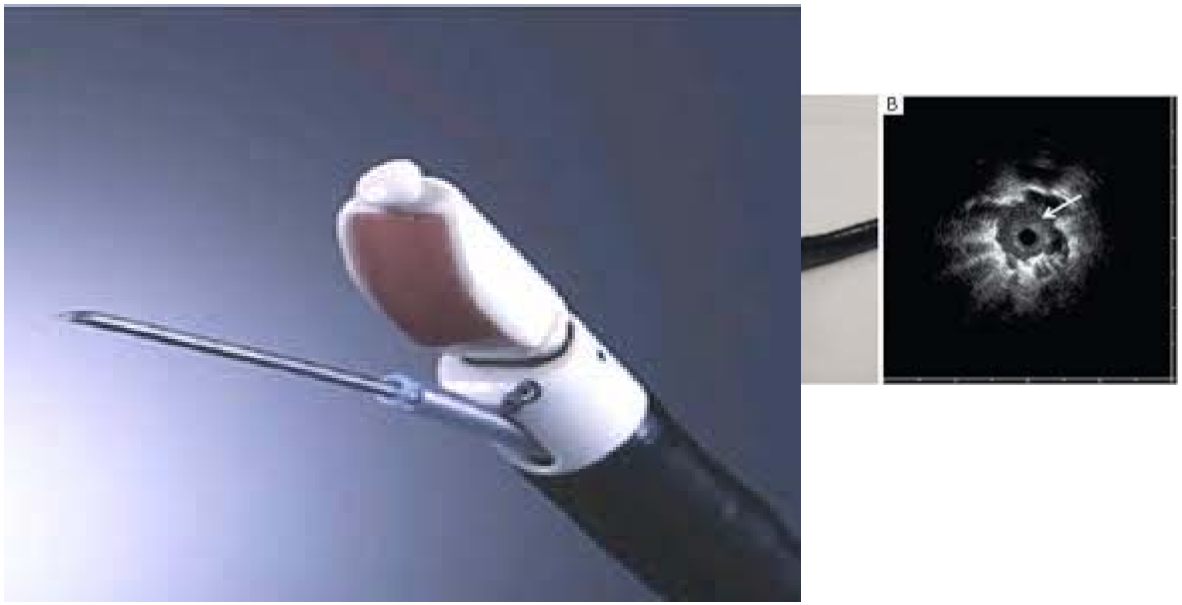
- Endoscopic Ultrasound
  EUS



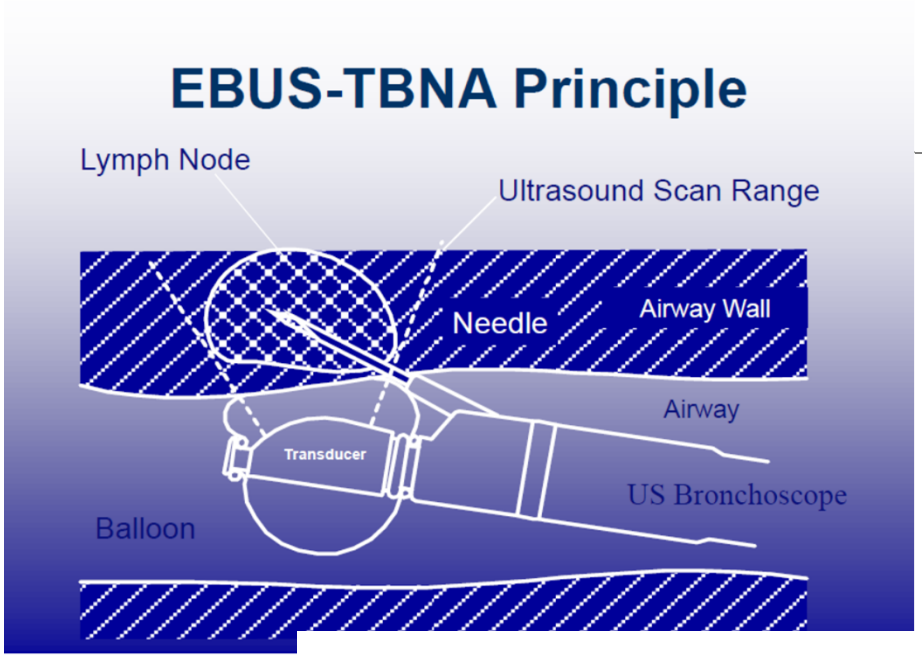


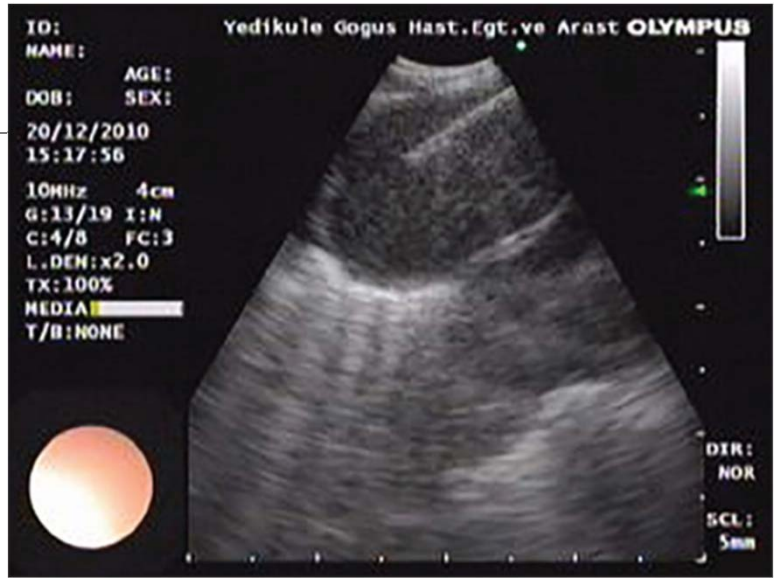


EBUS – Endobronchial Ultrasound Linear (Convex) and Radial



What is the EBUS?


EBUS-TBNA Principle
Lymph Node
Ultrasound Scan Range
Needle
Airway Wall
Airway
Transducer
US Bronchoscope
Balloon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AGE:
DOB:
SEX:
20/12/2010
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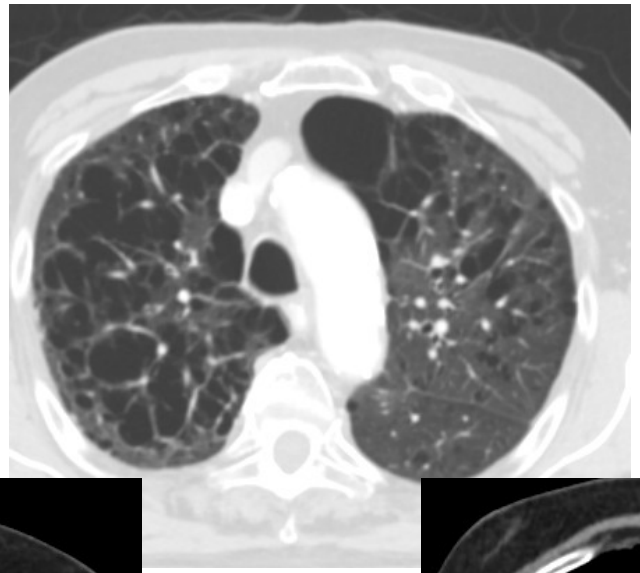
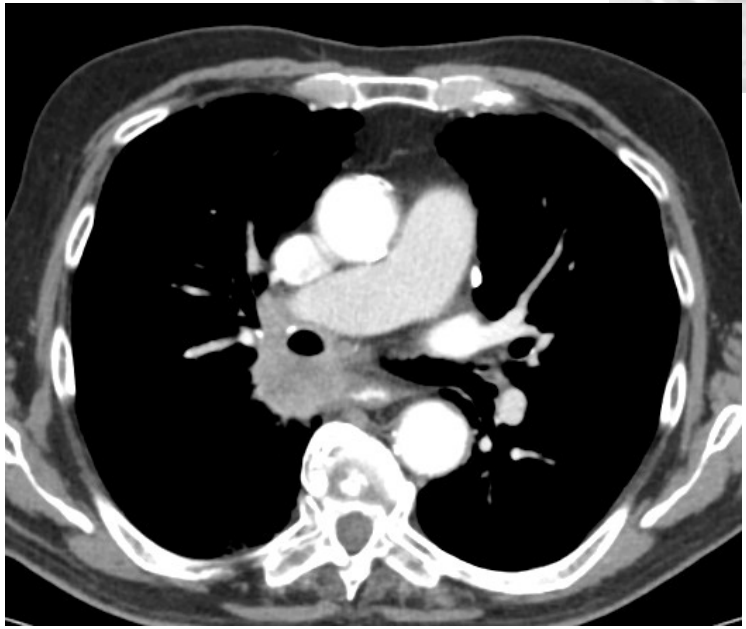
10MHz 4cm
G:13/19 I:N
C:4/8 FC:3
L.DEN:x2.0
TX:100%
MEDIA
T/B:NONE
Yedikule Gogus Hast.Egt.ve Arast
OLYMPUS
DIR:
NOR
SCL:
5mm

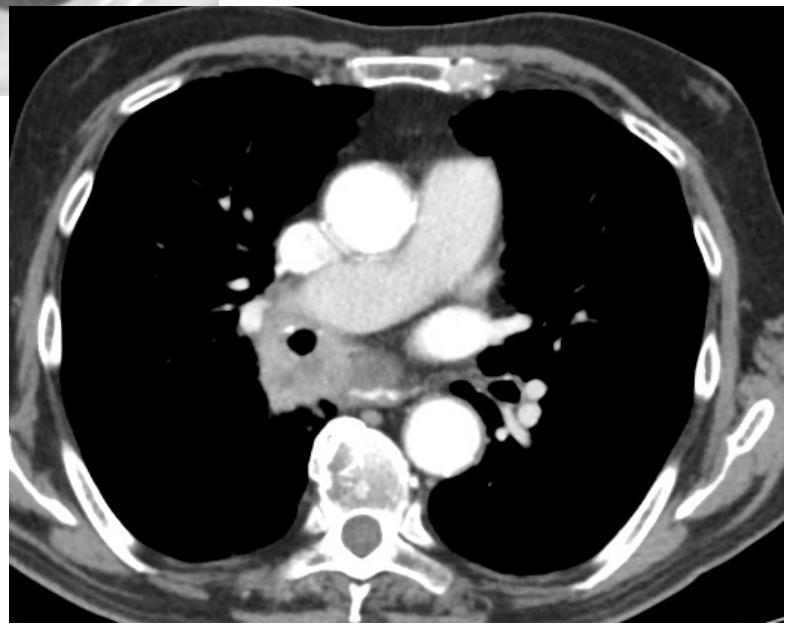
Medi-Globe

EBUS

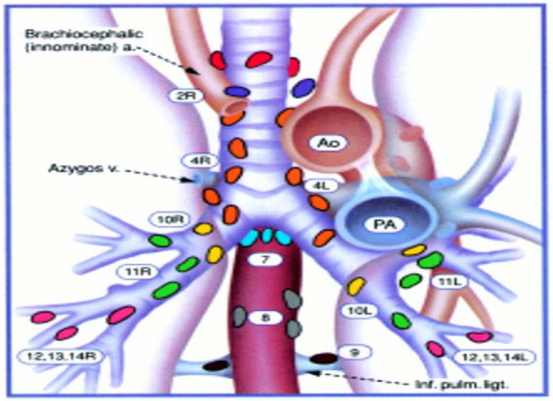
Bronchoscopy suite

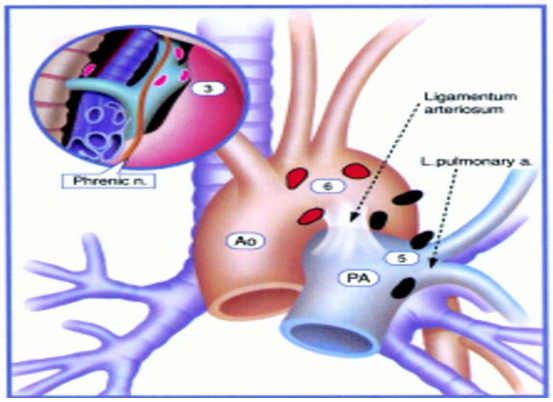






Lymph nodes stations for EBUS





Superior mediastinal nodes

- 1 Highest mediastinal
- 2 Upper paratracheal
- 3 Prevascular and retrotracheal
- 4 Lower paratracheal (including azygos nodes)

N2 = single digit, ipsilateral
N3 = single digit, contralateral or supraclavicular

Aortic nodes

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

Inferior mediastinal nodes

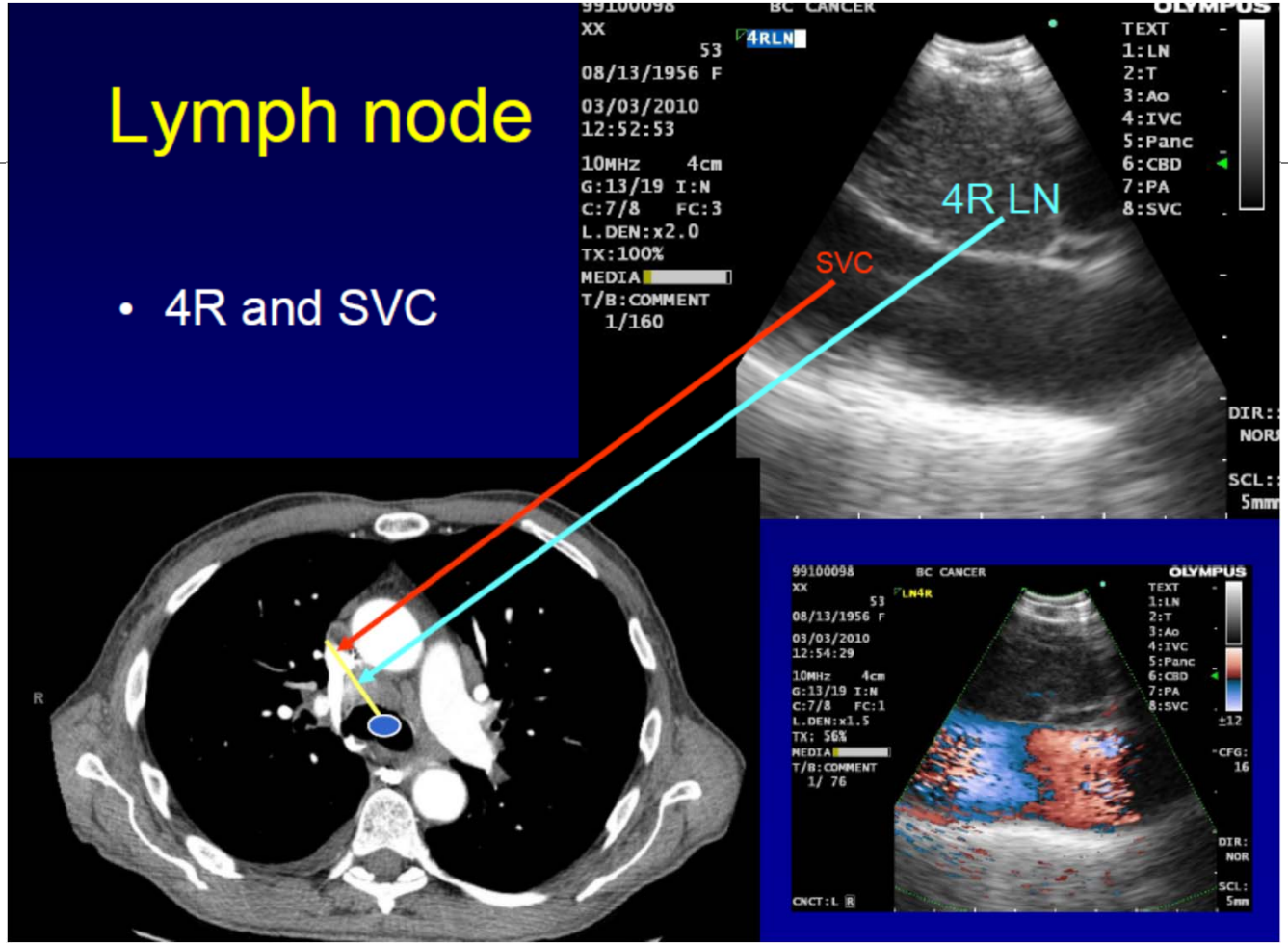
- 7 Subcarinal
- 8 Para-oesophageal (below carina)
- 9 Pulmonary ligament

N1 nodes

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Lymph node

- 4R and SVC



Indications for EBUS in lung cancer

- Diagnosis of lung cancer
- Staging of lung cancer
- Re-staging after neoadjuvant therapy
- Recurrence of lung cancer
- To obtain more specimen for molecular testing
- To diagnose lung metastasis from other known primary cancer

What should be the first modality for LN Staging?

- The ACCP Guidelines for Lung Cancer recommended EBUS as first-line approached for invasive mediastinal staging of NSCLC.

Why EBUS and not ~~Mediastinoscopy?~~

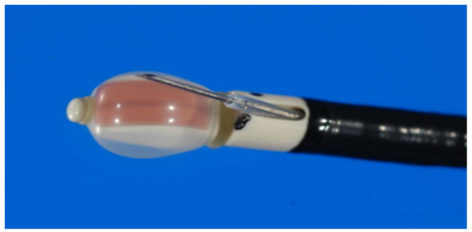
Surgery!

Complication rate 1-2.6%

Mortality 0.08%

Very difficult after the first procedure.

No option to reach hillar adenopathy (10,11,12 stations).



What is the benefit of EBUS?

Minimally invasive

Outpatient procedure

Same benefit in elderly (above 75 yrs old) patients.

ROSE-Rapid Onsite Evaluation

The EBUS is indicated in every case of unexplained mediastinal lymphadenopathy.

Diagnosis and staging of lung cancer

EBUS-TBNA Systematic Review and Meta-analysis

- 10 studies (n=817)
- **Sensitivity = 0.88** (95%CI, 0.79-0.94), **Specificity = 1.00** (95%CI, 0.92-1.00)

Table 1 Study characteristics

Paper	Eligible patients (n)	Patient population	Inclusion criteria
Okamoto (2002)[18]	37	Suspected lung cancer	ND
Yasufuku (2005)[15]	108	Known/suspected lung cancer	CT mediastinal lymph nodes >1 cm on short axis
Rintoul (2005)[16]	20	Known/suspected lung cancer	CT mediastinal lymph nodes >1 cm on short axis
Yasufuku (2006)[17]	102	Known/suspected lung cancer	Stage I–IIIa
Plat (2006)[10]	33	Suspected lung cancer	PET positive mediastinal lymph nodes
Pierard (2006)[19]	51	Suspected lung cancer	PET positive mediastinal lymph nodes
Herth (2006)[13]	100	Known NSCLC	CT mediastinal lymph nodes <1 cm on short axis
Yasufuku (2007)[12]	45	Known/suspected lung cancer	Operable disease
Skwarski (2007)[14]	300	Known/suspected lung cancer	ND
Annema (2007)[11]	21	Known NSCLC	ND

ND, not described; NSCLC, non-small cell lung cancer; PET, positron emission tomography.

Adams et al. Thorax; 2009; 64: 757-62

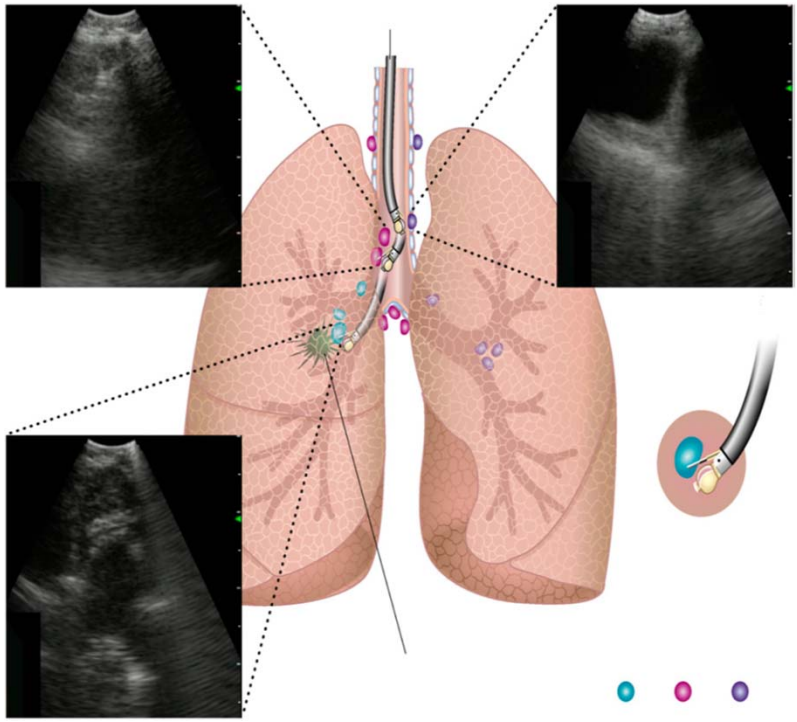
EBUS vs. MED

TABLE 1. Diagnostic Yield of EBUS-TBNA and Mediastinoscopy in the Evaluation of Mediastinal Lymph Nodes

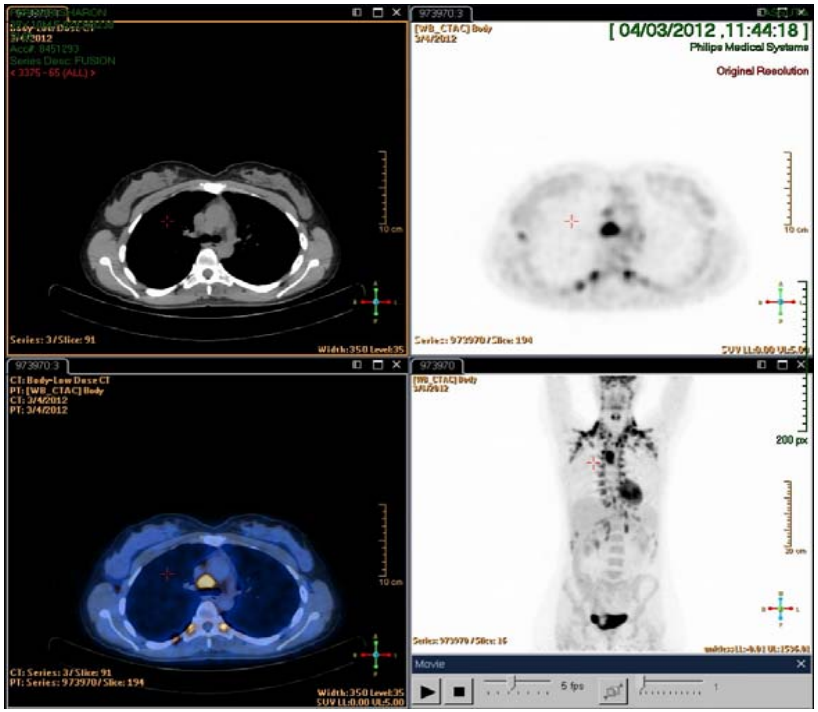
	Lymph Node Size in mm: Mean ± SD (Range)	EBUS Yield (%)	Mediastinoscopy Yield (%)	p^a
All lymph nodes	15 ± 2.6 (10–21)	109/120 (91)	94/120 (78)	0.007
Lymph node station				
2 all	16 ± 3.1 (10–21)	24/25 (96)	22/25 (88)	0.30
2 right	18 ± 1.6 (14–20)	12/13 (92)	11/13 (85)	0.99
2 left	14 ± 3.6 (10–21)	12/12 (100)	11/12 (92)	0.99
4 all	15 ± 2.6 (10–19)	45/54 (83)	40/54 (74)	0.24
4 right	15 ± 2.6 (10–19)	29/34 (85)	24/34 (71)	0.14
4 left	15 ± 2.6 (10–19)	16/20 (80)	16/20 (80)	0.99
7	15 ± 2.4 (10–19)	40/41 (98)	32/41 (78)	0.007
Pathology				
Malignant	16 ± 2.7 (10–21)	64/74 (86)	49/74 (66)	0.004
Benign	15 ± 2.5 (10–21)	45/46 (98)	45/46 (98)	0.99

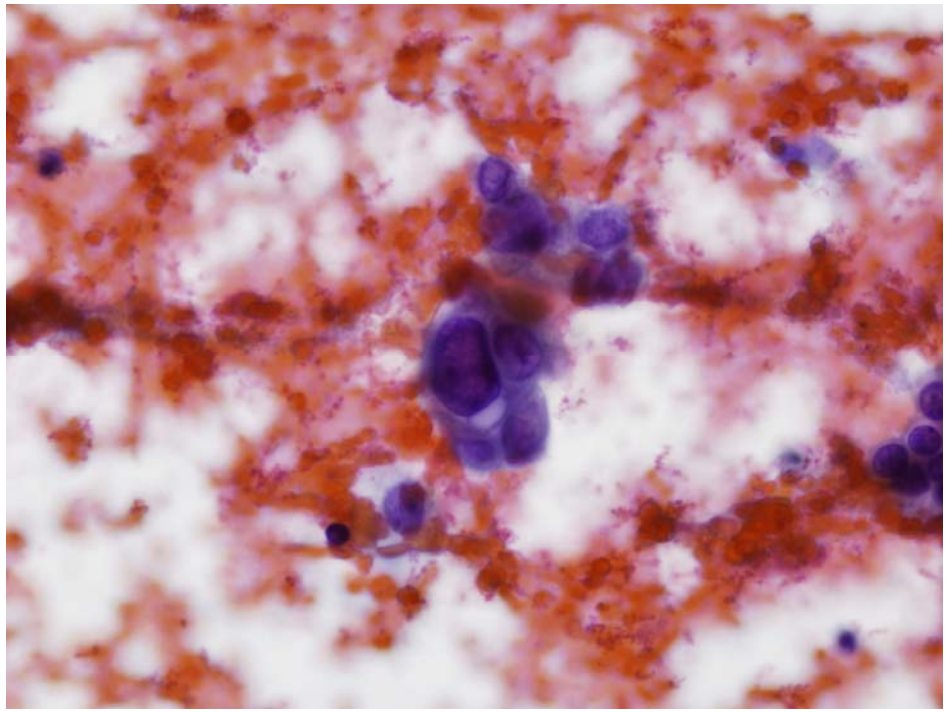
Ernst et al, J Thorac Oncol 2008; 3: 577

How to do the Staging examination?



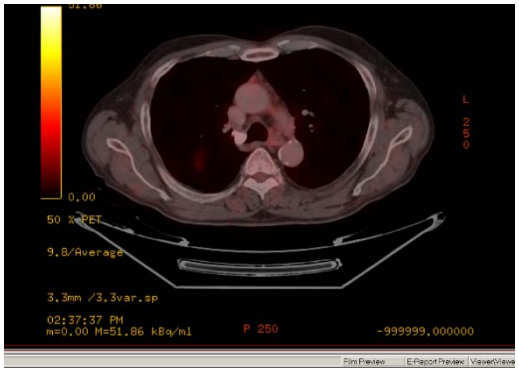
Case 1: Adenocarcinoma (Lung)





Case 2: CT

Case 2: PET


0.00
50 % PET
9.8/Average
3.3mm /3.3var.sp
02:37:37 PM
m=0.00 M=51.86 kBq/ml
P 250
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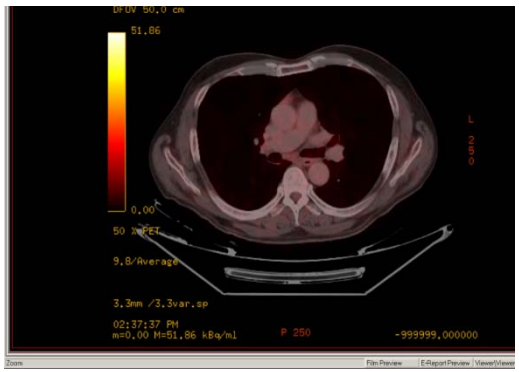
51.86
0.00
50 % PET
9.8/Average
3.3mm /3.3var.sp
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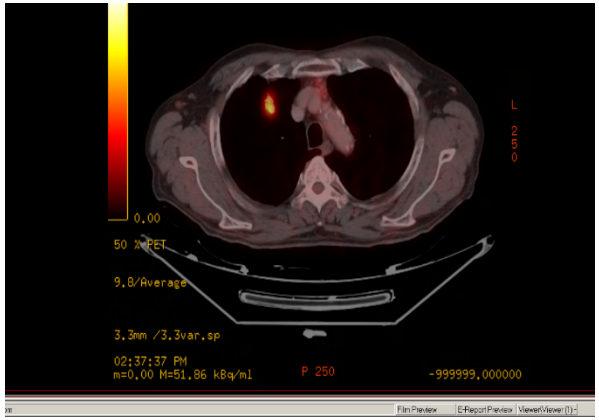
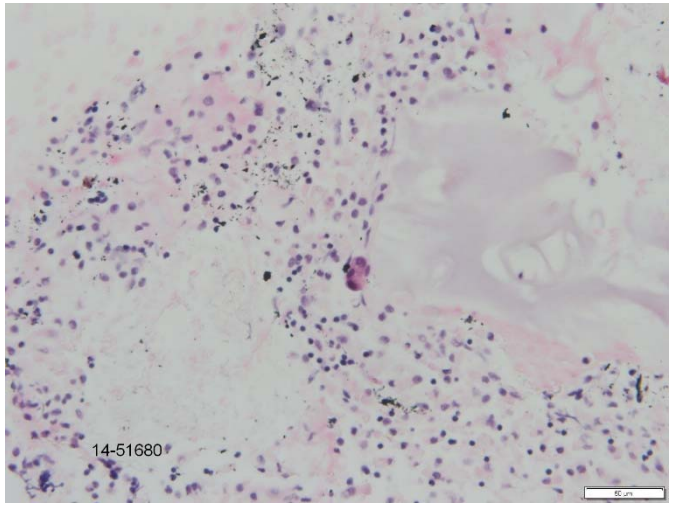
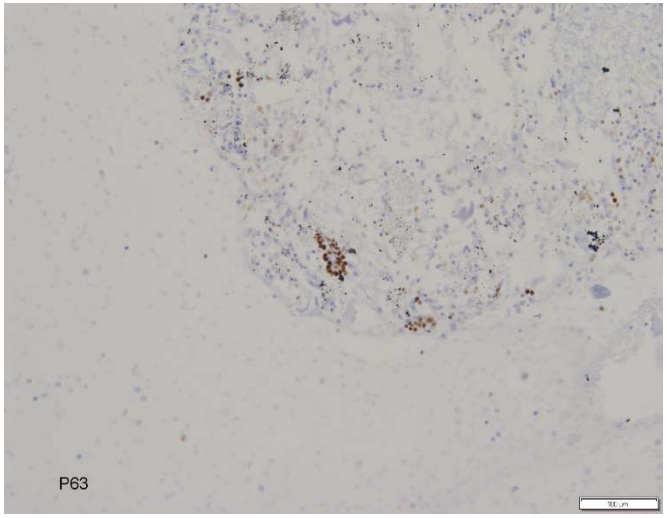

0.00
50 % PET
9.8/Average
3.3mm /3.3var.sp
02:37:37 PM
m=0.00 M=51.86 kBq/ml
P 250
-999999.000000

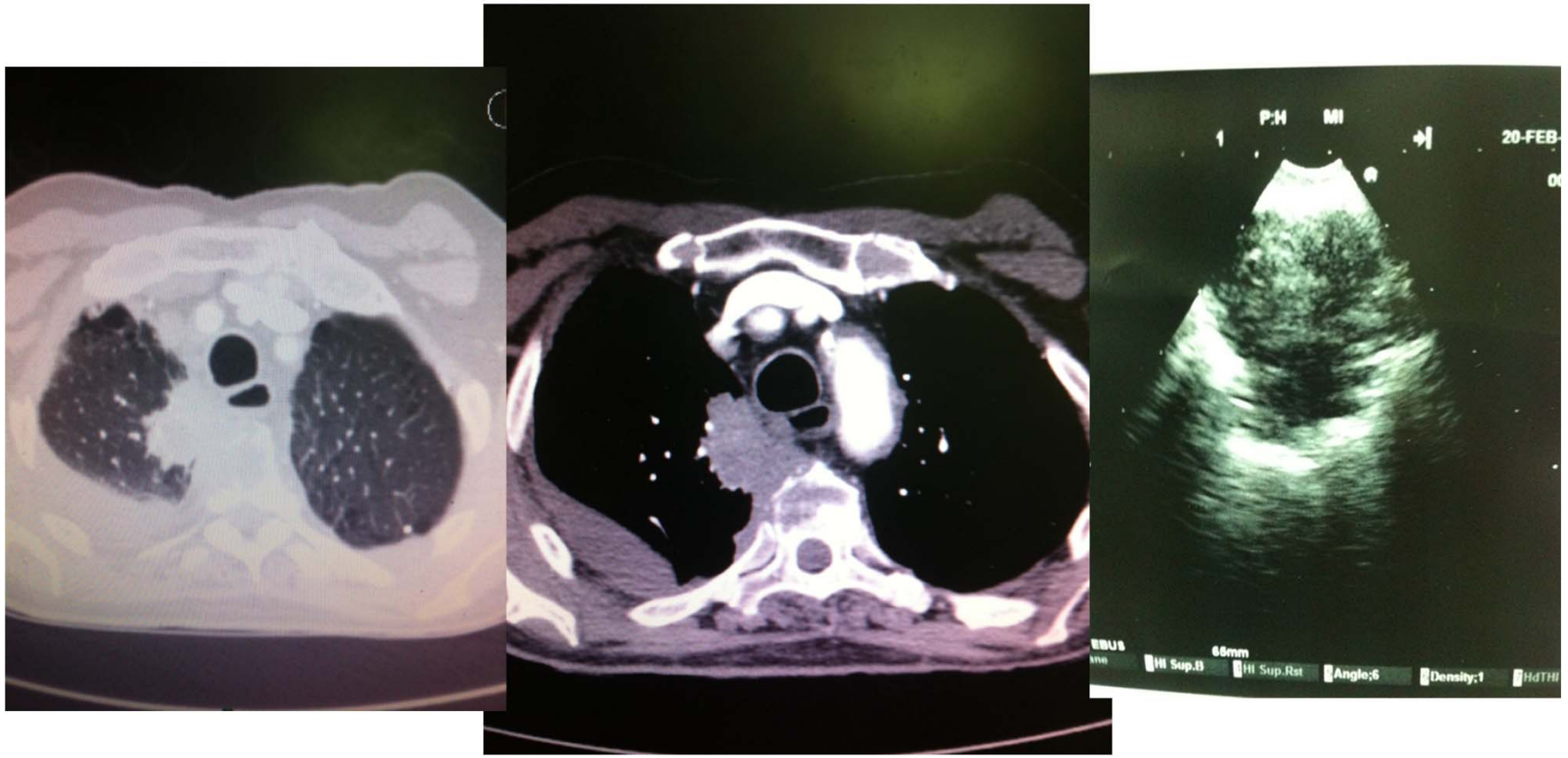
Case 2: EBUS- Lymph node station 5

A few atypical cells (positive for 5/6 and p63 immunostains) present in a background of lymphocytes and reactive respiratory cells (CK 7 positive), **consistent with metastasis of squamous cell carcinoma**.

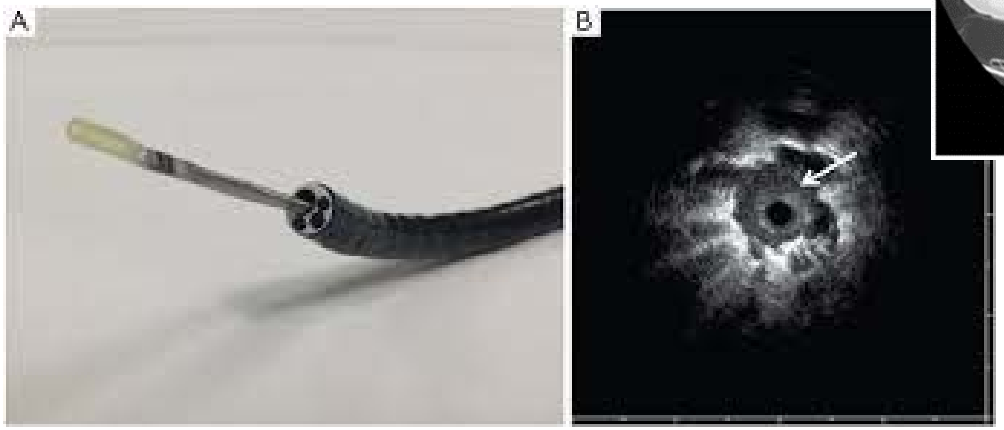


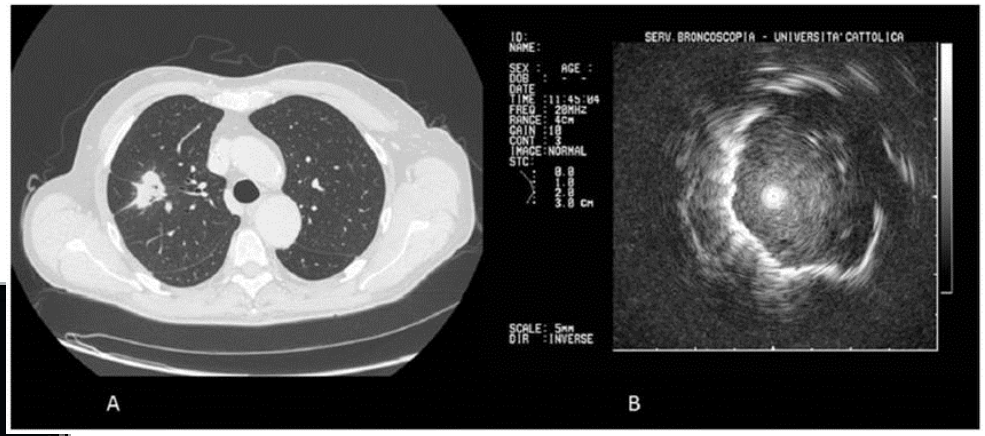


EBUS GUIDED FNA OF CENTRAL PARATRACHEAL LESIONS



Radial US


A
B


ID:
NAME:
SEX : AGE :
DOB : - -
DATE
TIME : 11:43:44
FREQ : 20MHz
RANGE: 4cm
GAIN : 18
CONT : 2
IMAGE:NORMAL
STC:
0.0
1.0
2.0
3.0 cm
SCALE: 5mm
DIR : INVERSE
SERV. BRONCOSCOPIA - UNIVERSITA' CATTOLICA
A
B

How many aspirations?

Table 2—*Cumulative Diagnostic Values of EBUS-TBNA Shown by the Number of Aspirations

Variables	Aspirations, No. 1	2	3	4
Sensitivity	69.8 (30/43)	83.7 (36/43)	95.3 (41/43)	95.3 (41/43)
Specificity	100 (83/83)	100 (83/83)	100 (83/83)	100 (83/83)
PPV	100 (30/30)	100 (36/36)	100 (41/41)	100 (41/41)
NPV	86.5 (83/96)	92.2 (83/90)	97.6 (83/85)	97.6 (83/85)
Accuracy	89.7 (113/126)	94.4 (119/126)	98.4 (124/126)	98.4 (124/126)

*Data are presented as % (No./total). We considered inadequate samples as negative results.

- "Pass" or "Aspiration": the needle is inserted in the LN, agitated several times, and removed
- Yield plateaus after 3 passes

Lee HS *et al.* CHEST 2008; 134:368–374

FNA technique: Hitting the node

- Allways send to **cell block**
- Estimation of 50-100 cells in every aspiration
- The 19 and the 21-gauge needle resulted in better preservation of histologic structure.
- The needle has to move inside the node.
- Sample the node from capsule to capsule.
- Sample different areas of the node .

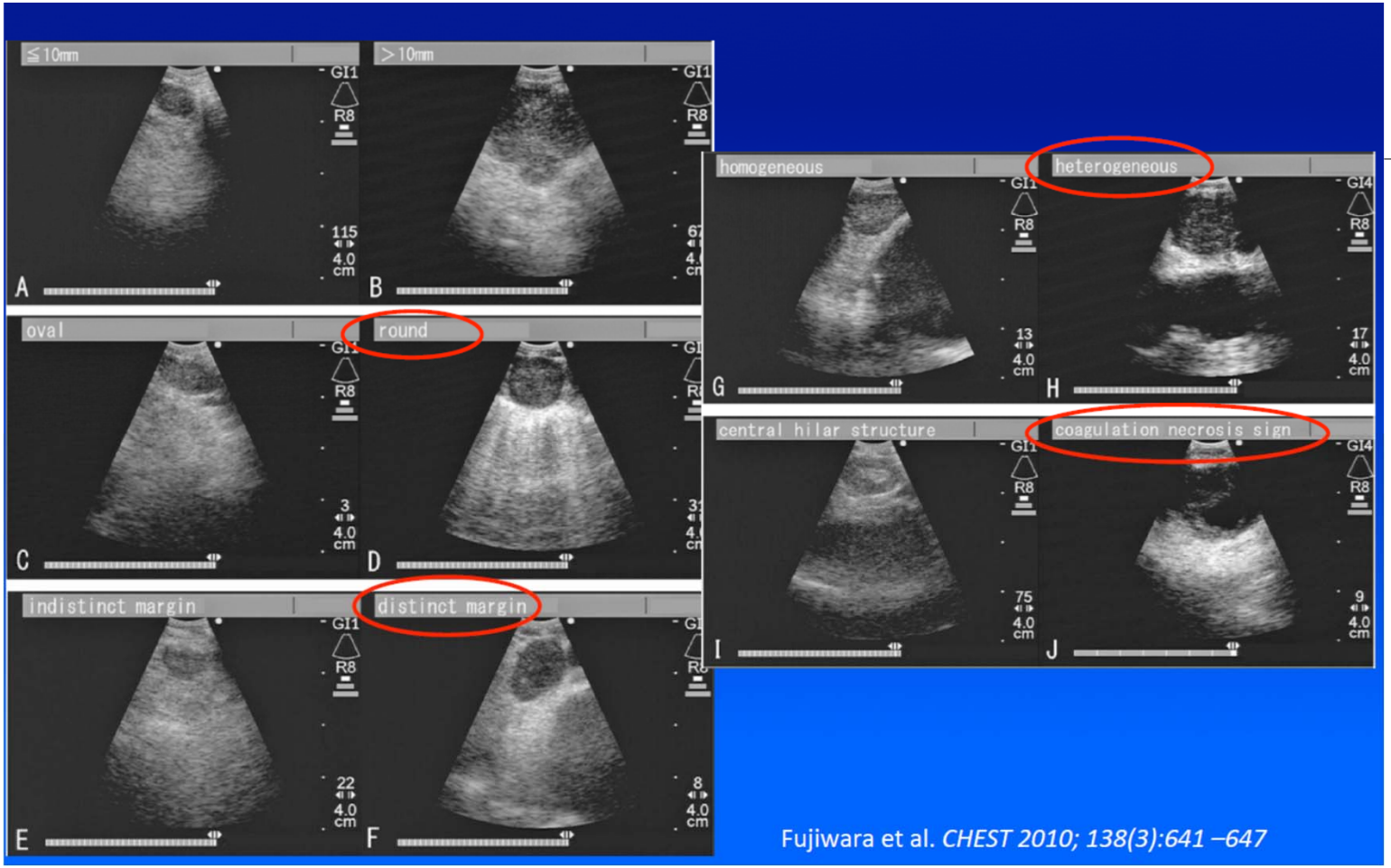
Lee H, Chest 2008; 134: 368-374

The typical features of benign nodes

- Oval shape
- Size <1 cm
- Indistinct margin
- Presence of a central hilar structure
- Relatively high echogenicity
- Homogenous echogenicity.

Common features of malignant nodes

- Round shape
- Size >1 cm
- Distinct margin
- Absence of the central hilum
- Eccentric cortical thickening
- Relatively low echogenicity
- Heterogeneous echogenicity
- Presence of necrosis
- Increased vascularity in lymph nodes


≦10mm
>10mm
A
B
oval
round
C
D
indistinct margin
distinct margin
E
F
homogeneous
heterogeneous
G
H
central hilar structure
coagulation necrosis sign
I
J
Fujiwara et al. CHEST 2010; 138(3):641 –647

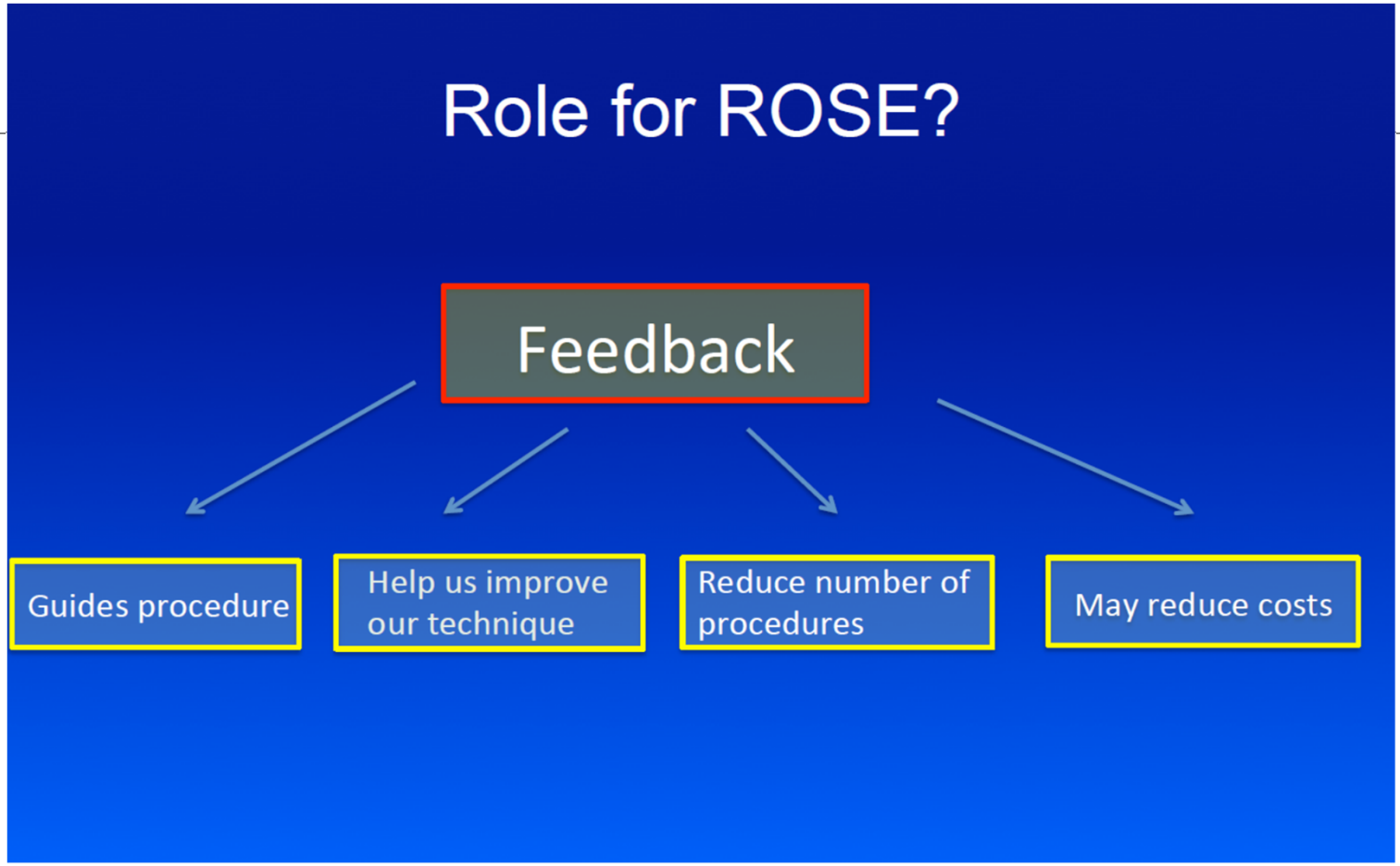
Rapid On Site Evaluation

With or without ROSE?

Reference	Study design	Population	Intervention	Comparator	Primary objective (endpoint)	Outcome	Quality metric indicator
Trisolini [47] 2011	Prospective, experimental RCT	Enlarged mediastinal or hilar LN (n = 168)	TBNA + ROSE (n = 83)	TBNA (n = 85)	Diagnostic yield; secondary: biopsy sites	Yield: 78 vs. 75% (NS); adequate sample 78 vs. 87% (NS); number of TBB (IQR) 1 vs. 2 ($p < 0.001$); complication rate 6 vs. 20% ($p < 0.05$)	Good
Yarmus [48] 2011	Prospective, experimental RCT	Enlarged mediastinal or hilar LN (n = 68)	TBNA + ROSE (n = 34)	TBNA (n = 34)	Diagnostic yield; secondary: number of needle passes and procedure time	Yield: 55 vs. 53% (NS); adequate sample 94 vs. 88% (NS); number of needle passes 4 vs. 4 (NS); number of TBB (NS); procedure duration time and amount of sedatives needed (NS); complication rate not reported; study was powered to detect differences in yield >30%	Fair
Oki [49] 2013	Prospective, experimental RCT	Enlarged mediastinal or hilar LN + (suspected) lung cancer (n = 120)	EBUS + ROSE (n = 55)	EBUS (n = 53)	Number of additional procedures	Additional procedures 11 vs. 57% ($p < 0.001$); number of aspirations 2.2 vs. 3.1 ($p < 0.001$; in non-ROSE group predetermined to 3); procedure time 22.3 vs. 22.1 min (NS); sensitivity 88 vs. 86% (NS); accuracy 89 vs. 89% (NS)	Good

- No good quality data (RCT) on EBUS +/-ROSE, mostly for standard TBNA +/- ROSE

Role for ROSE?



A.In experienced hands, mediastinal staging could be performed under moderate sedation without decreasing diagnostic yield

ORIGINAL ARTICLE

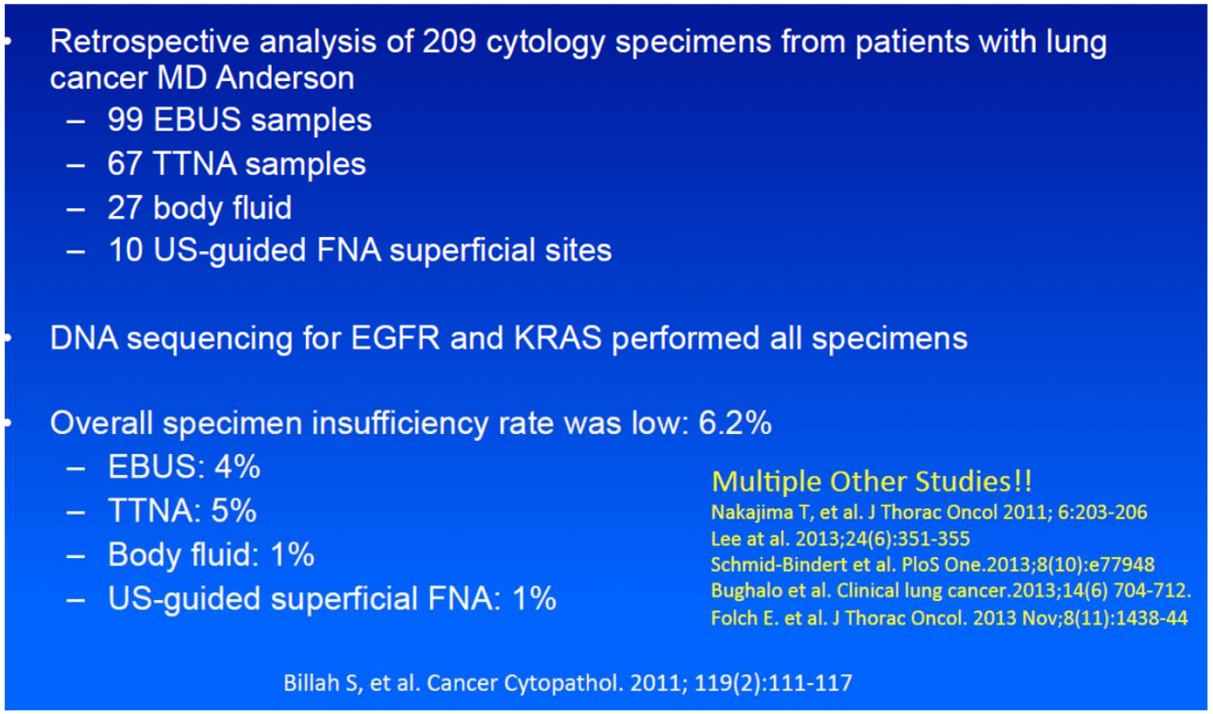
Randomized Trial of Endobronchial Ultrasound–guided Transbronchial Needle Aspiration under General Anesthesia versus Moderate Sedation

Roberto F. Casal[1,2], Donald R. Lazarus[1], Kristine Kuhl[3], Graciela Nogueras-González[4], Sarah Perusich[2], Linda K. Green[1,5], David E. Ost[6], Mona Sarkiss[7], Carlos A. Jimenez[6], Georgie A. Eapen[6], Rodolfo C. Morice[6], Lorraine Cornwell[1,8], Sheila Austria[9], Amir Sharafkanneh[1,2], Rolando E. Rumbaut[1,2], Horiana Grosu[6], and Farrah Kheradmand[1,2]

- RCT, EBUS under MS vs. GA (1:1 randomization)
- Adults referred for EBUS-TBNA of hilar/mediastinal LN or masses
- Cytologist blinded to randomization
- 1ry Outcome: Diagnostic yield
- 2ry Outcomes: sensitivity, sample adequacy, procedure time, procedure completion rates, complication rates, escalation of care, tolerance

Am J Respir Crit Care Med Vol 191, Iss 7, pp 796–803, Apr 1, 2015

EBUS also for Molecular Testing?



The Efficacy of EBUS-Guided Transbronchial Needle Aspiration for Molecular Testing in Lung Adenocarcinoma

(Ann Thorac Surg 2013;96:1196–202)

Table 3. Molecular Analysis of Tested Samples

Sample Type	No. of Samples Tested	Positive (%)	Negative (%)	Insufficient (%)	Sufficient for Testing
EGFR	51	5 (10%)	41 (80%)	5 (10%)	46 (90%)
ALK	43	5 (12%)	34 (79%)	4 (9%)	39 (91%)
Kras	40	10 (25%)	20 (50%)	10 (25%)	30 (75%)

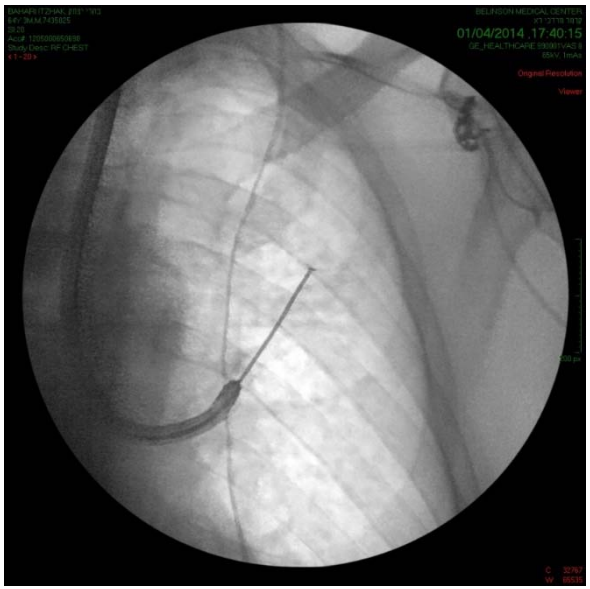
Numbers in parentheses represent proportion in total number of samples tested.

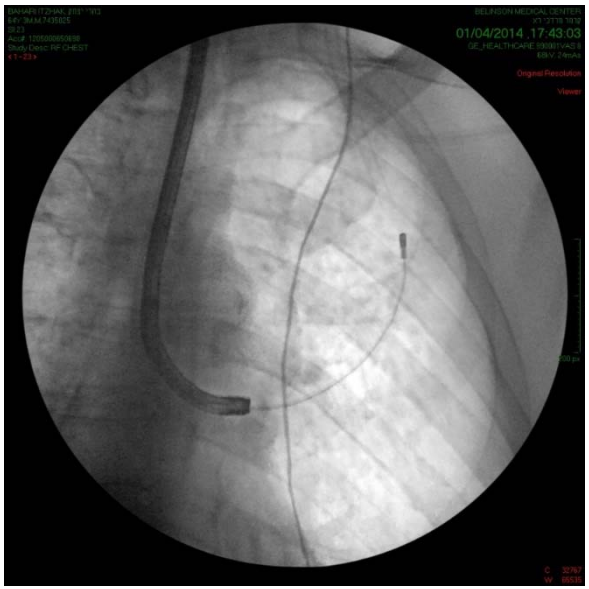
ALK = anaplastic lymphoma; EGFR = epidermal growth factor receptor; Kras = Kirsten rat sarcoma.

Who many procedure for Training and Competency?

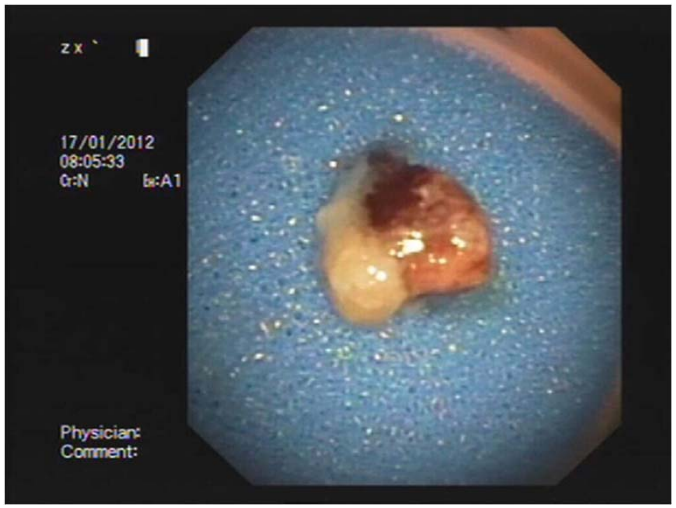
- The European Respiratory Society/American Thoracic Society statement on interventional pulmonology recommends completion of 40 supervised procedures for achievement of initial competency in EBUS.

Cryobiopsy





קריוביופסיה מול ביופסיה רגילה



כללית מעל 100 שנה
הכי טובה למשפחה

מרכז רפואי מאיר
מסונף לפקולטה לרפואה, אוניברסיטת תל אביב

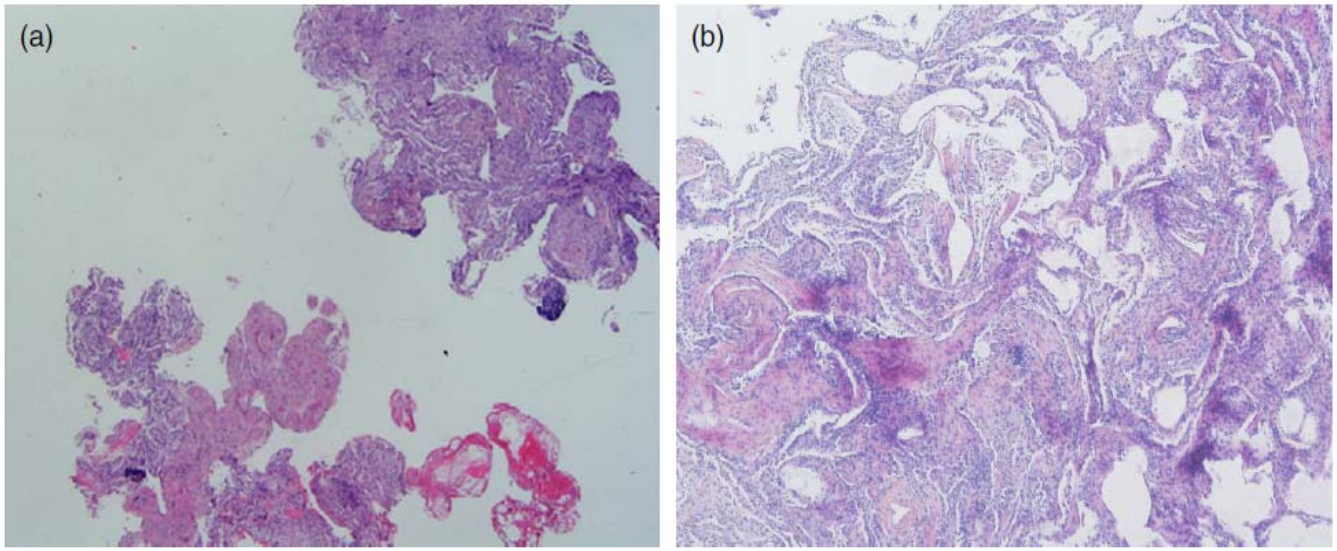
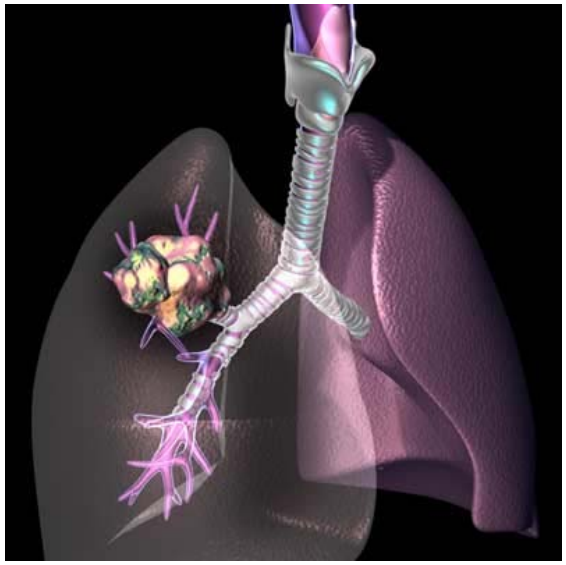


Figure 2 Histological sample of (a) forceps-transbronchial biopsies (TBB) (×4 magnification) showing mainly peribronchial alveolar tissue with interstitial infiltration but no signs of rejection versus (b) cryo-TBB (×4 magnification) composed of alveolar tissue with abundant alveoli and blood vessels with peri-vascular infiltration by lymphocytes indicating acute cellular rejection A1.

Meir MC experience: 2018

- 587 EBUS procedures.
- 37% from all bronchoscopies.
- 85% of all EBUS performed under moderate sedation.
- 40% of the EBUS for diagnosis and staging of lung cancer.
- 40% only for staging of lung cancer.
- 15% for obtaining more specimen for molecular testing.
- 5% for other indications including lung metastasis LN.

Thank you!