Endobronchial Ultrasound Guided Transbronchial Needle Aspiration (EBUS-TBNA)

; Technical Aspect

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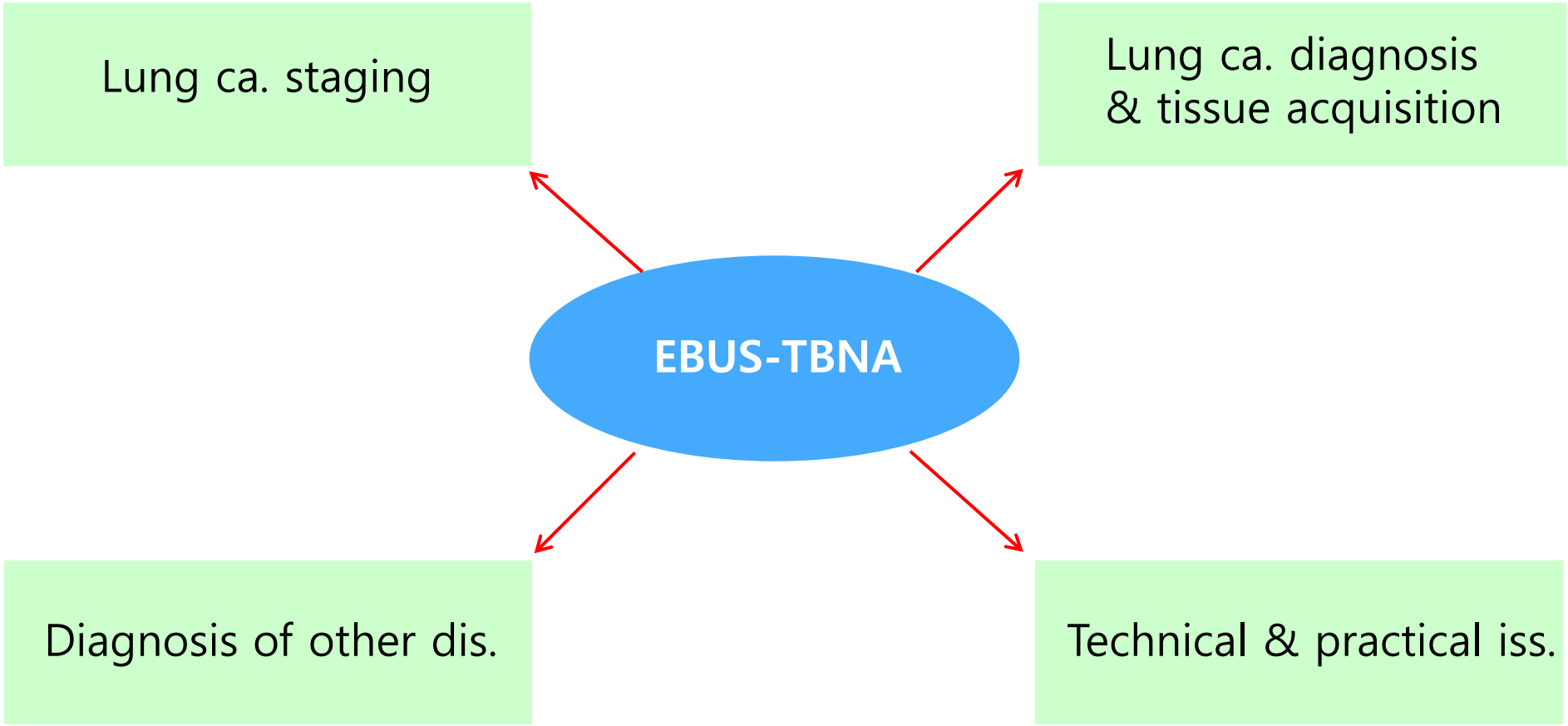
Increasing Use of EBUS-TBNA

- First Report; 2003
- About 300 articles on Pubmed
- EBUS-TBNA ; available at 31 hospitals

EBUS available institutes in Korea

2005	2006	2007	2008	2009	2010	2011	2012
1 (NCC)	1	2	4	12	21	22	31

Researches on EBUS-TBNA



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3. Manipulation of the needle
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6. Number of aspirations
7. Needle size & forceps
8. Sample preparation & use of ROSE
9. Complications
10. Learning curve

Conscious Sedation vs. General Anesthesia

Tolerable procedure under sedation

Costy, easy to perform

Some difficulties in the high trachea

Sedation, NCC

- Fentanyl 50μg first
  Midazolam 2mg ; add 1mg by observing sedation feature

  → add fentanly 12.5μg, midazolam 1mg
  if needed

Patient Satisfaction to EBUS-TBNA under Sedation

Midazolam/fentanyl or propofol, 41 pts

Symptom	Likert Scale of Symptom Severity (*n* and % who reported this symptom severity)		
	None	Small Amount	Substantial Amount
Anesthetic throat spray	30 (73)	9 (22)	2 (5)
Discomfort during scope insertion	32 (78)	8 (20)	1 (2)
Dyspnea	33 (80)		
Cough	12 (29)		
Throat pain	30 (73)		
Chest pain	37 (90)	4 (10)	0 (0)

EBUS-TBNA = endobronchial ultrasound-guided transbronchial needle aspiration

Willing to return ; 98%

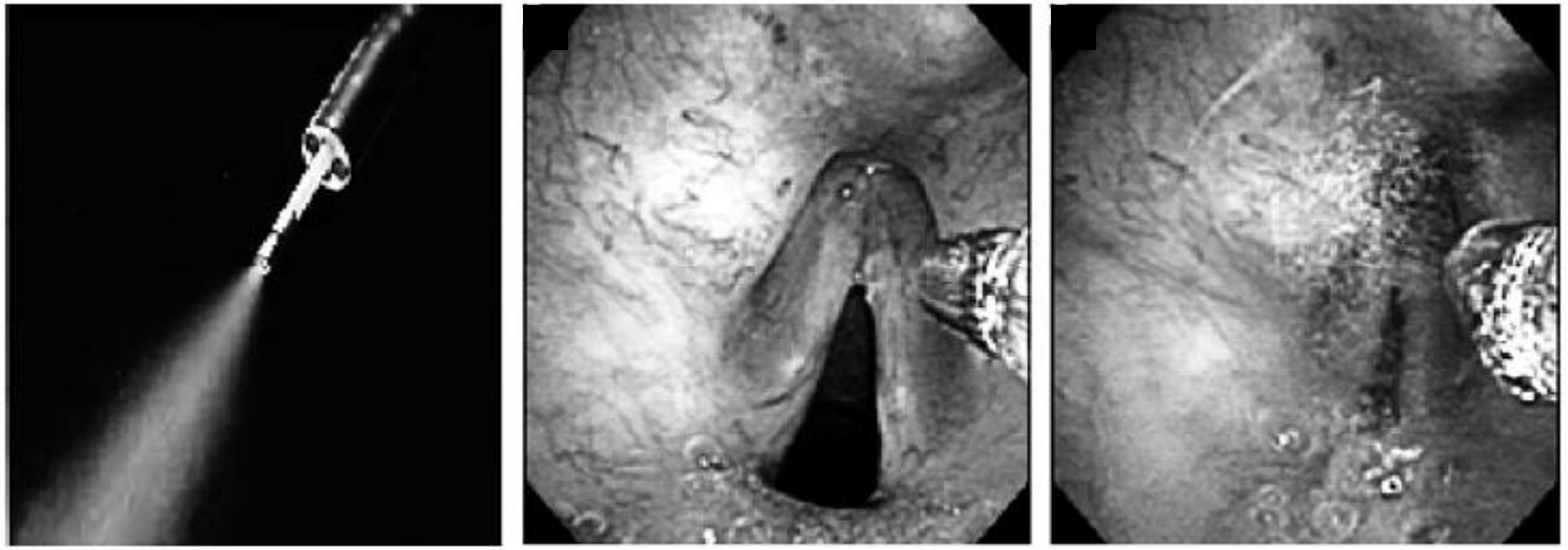
Steinfort et al. Respir Care 2010;55(6):702–706

Local Anesthesia with Lidocaine, NCC protocol

- 4% lidocaine 5ml

→ 1% lidocaine spray as you go technique with conventional bronchoscopy

Local Anesthesia Technique



40 pts EBUS-TBNA, Reduced number of cough (P< 0.004)
Increased number of aspirations (p=0.008)

Hans et al. Respirology (2011) 16, 102–106

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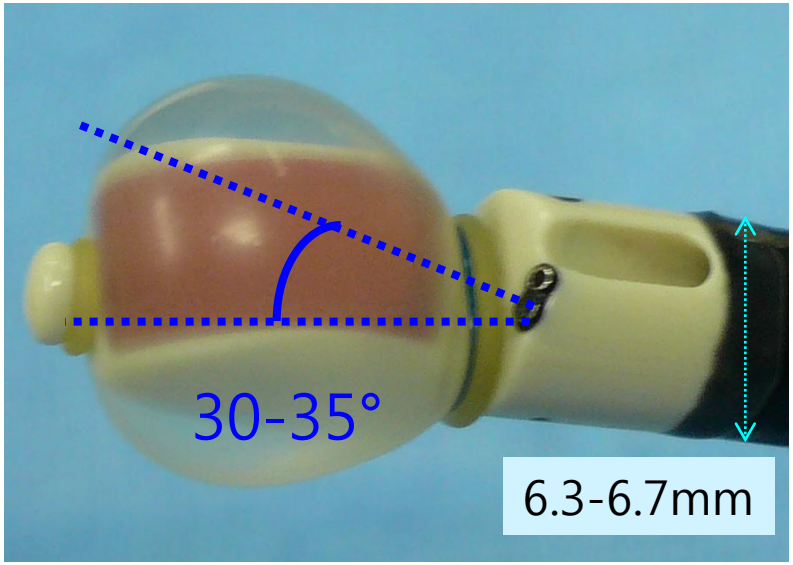
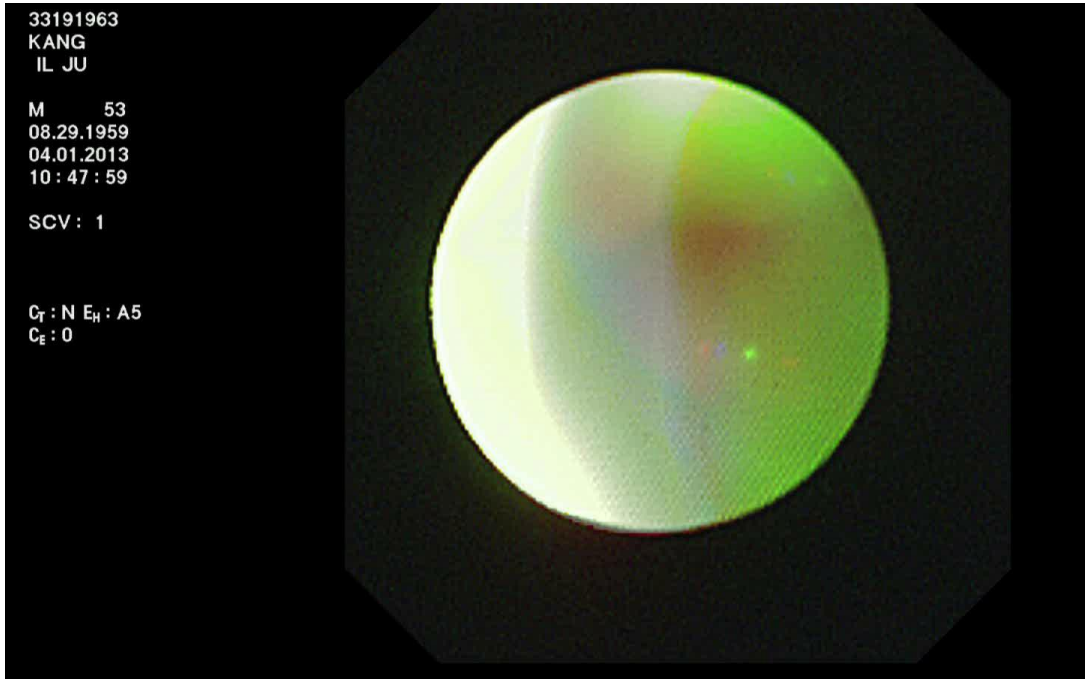
EBUS-TBNA bronchoscope

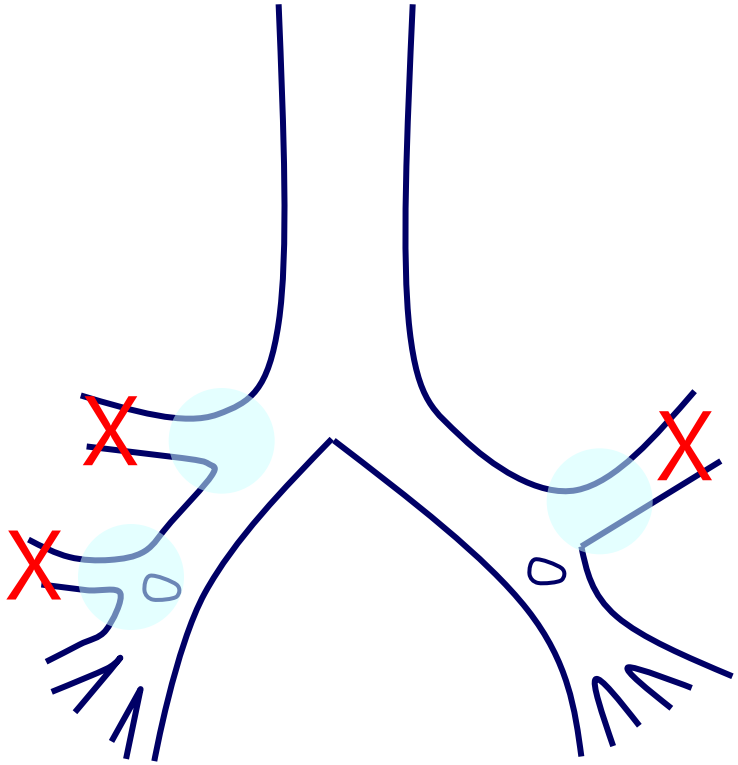




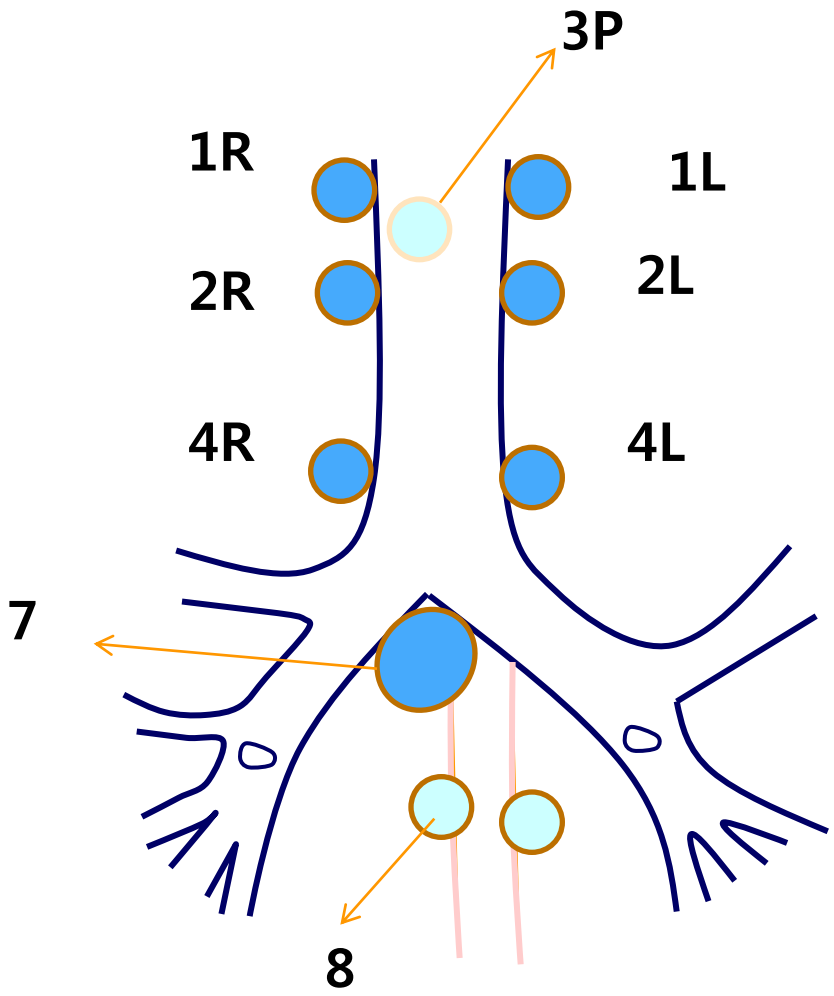
EBUS-TBNA bronchoscope; Flexibility

Without needle

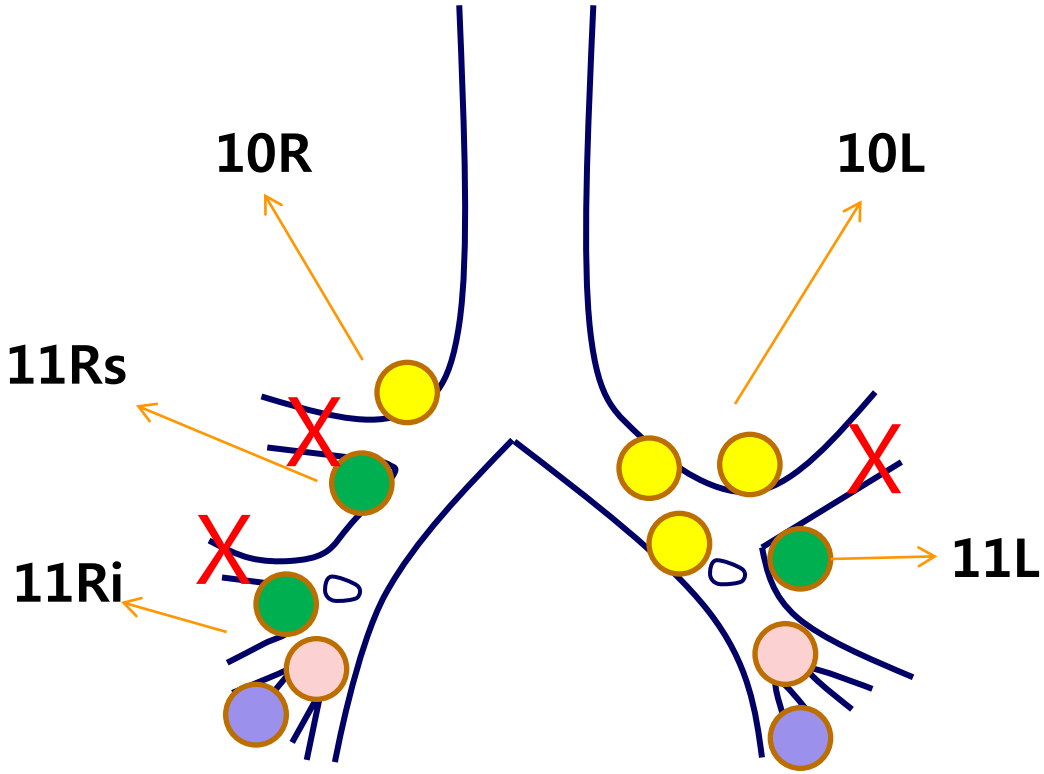
With needle



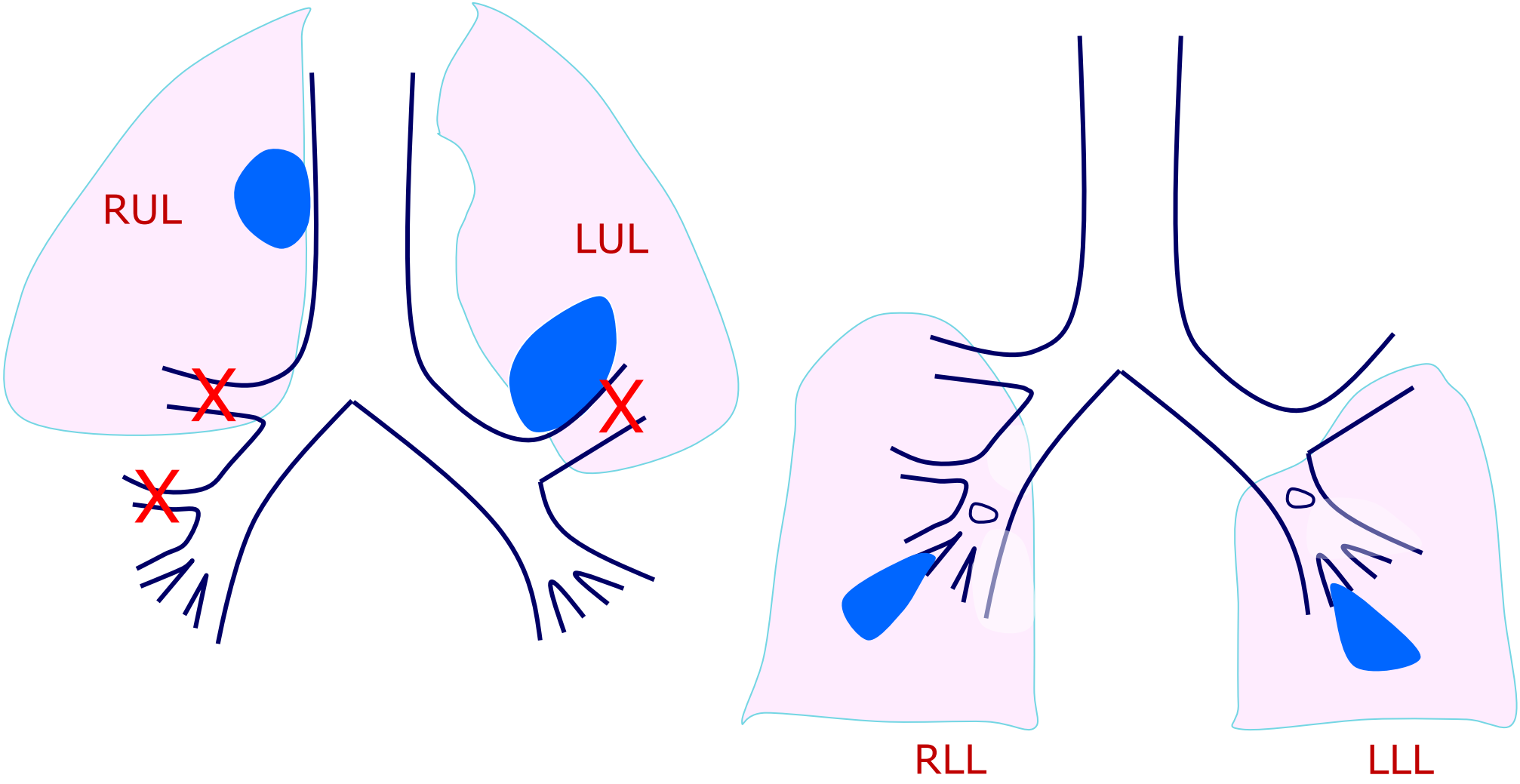
EBUS-TBNA Bronchoscope; Accessibility to Nodes



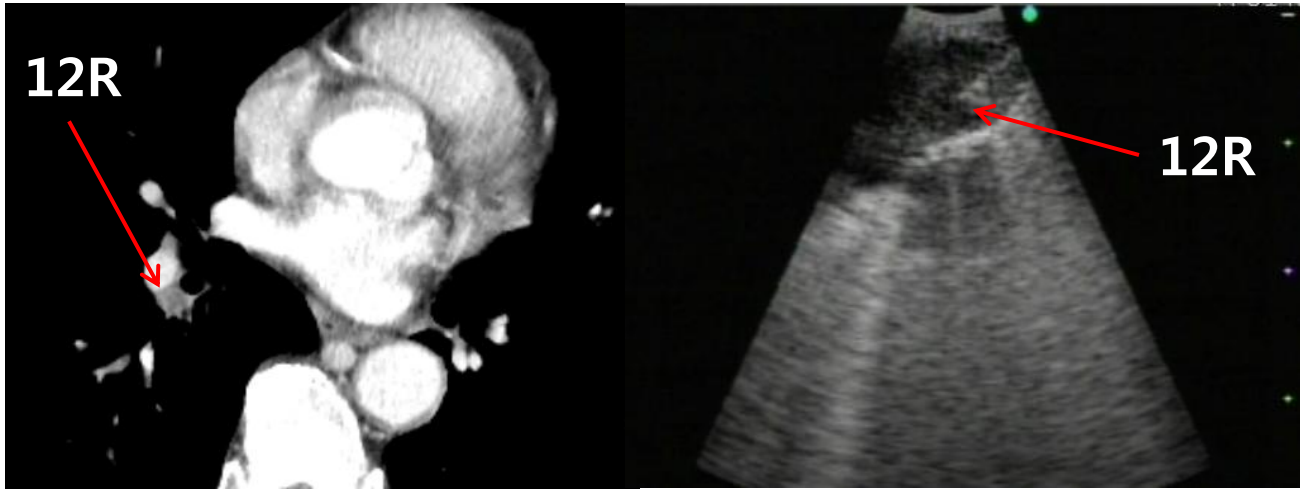
EBUS-TBNA bronchoscope; Accessibility to Nodes

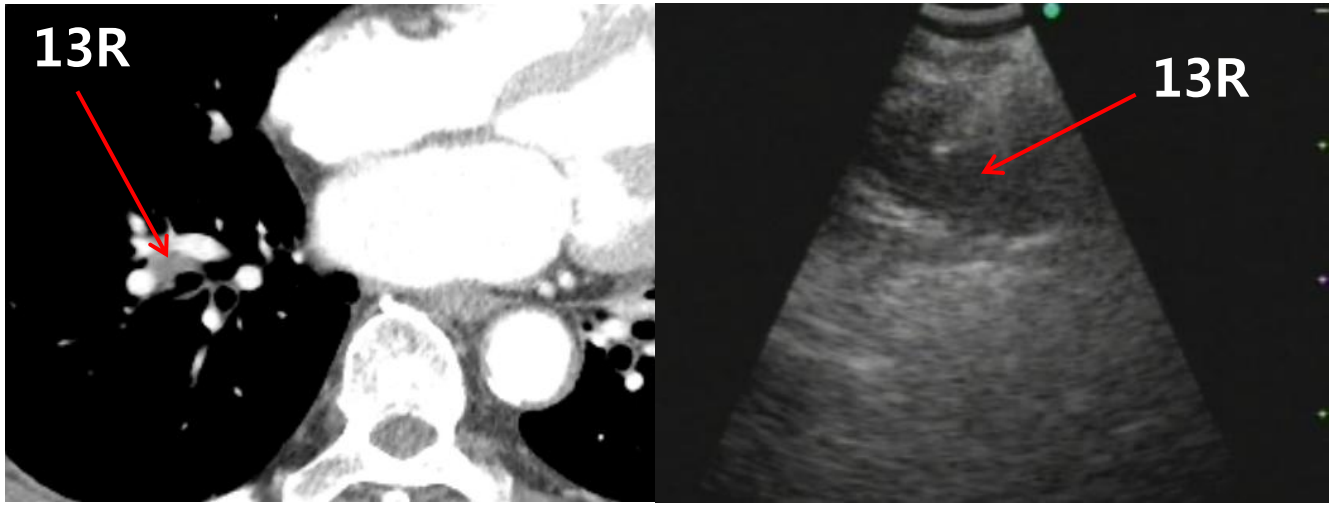


EBUS-TBNA bronchoscope; Accessibility to Lung Lesions

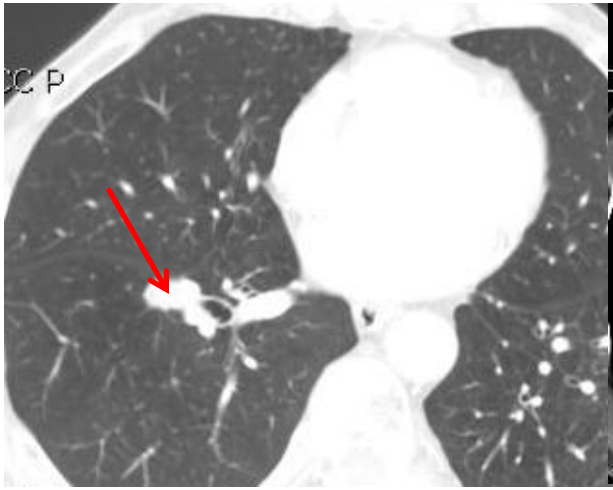


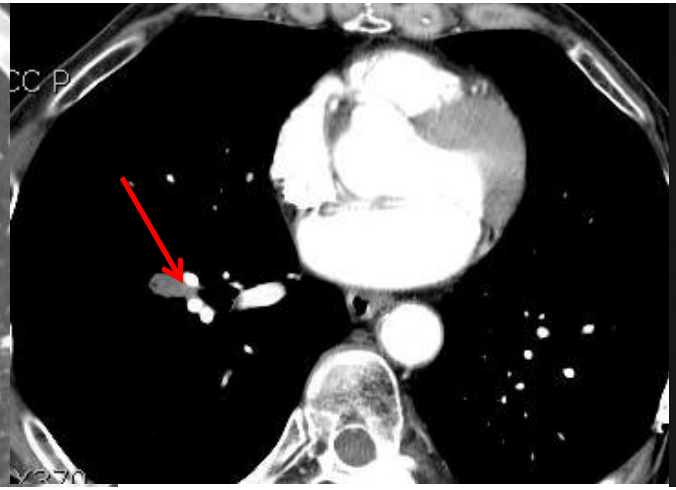
Lobar or Segmental LNs in the Lower Lobes by EBUS-TBNA

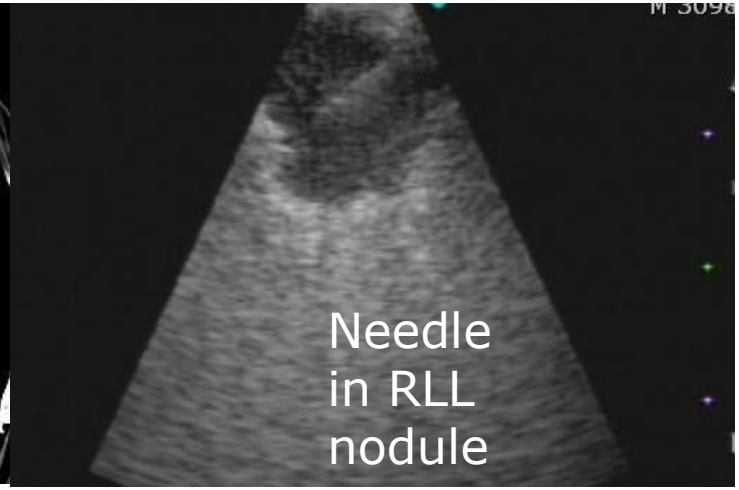


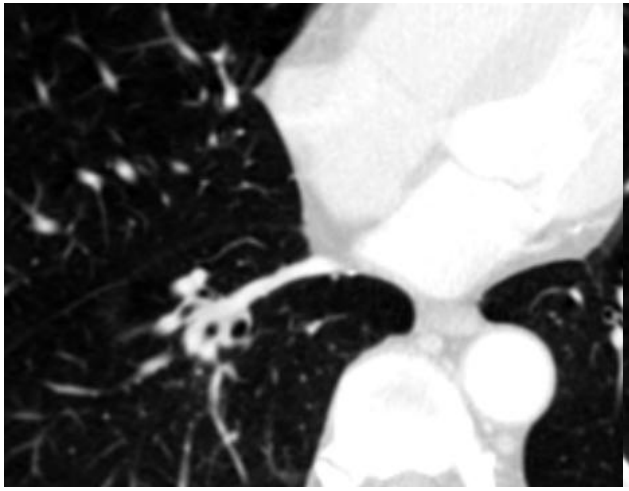


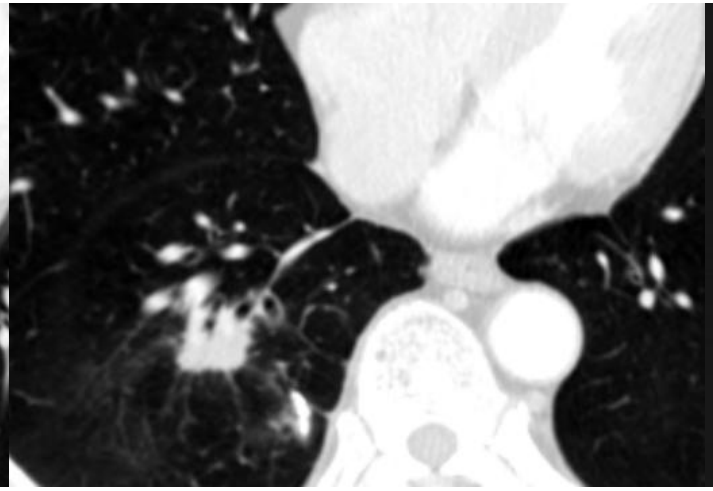
Nodule adjacent to the bronchus, RLL

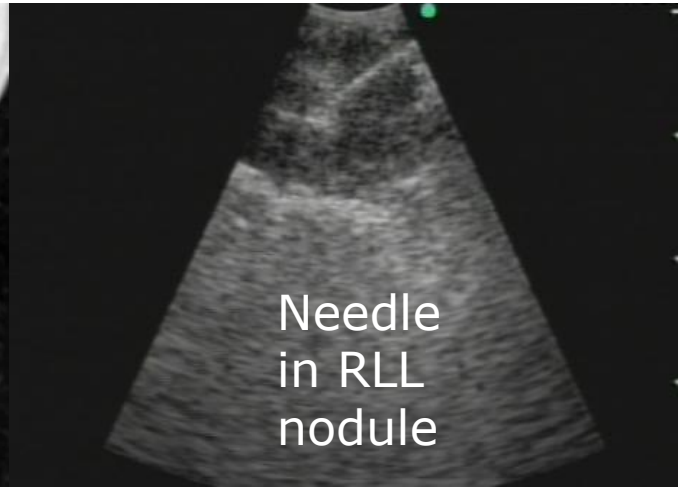












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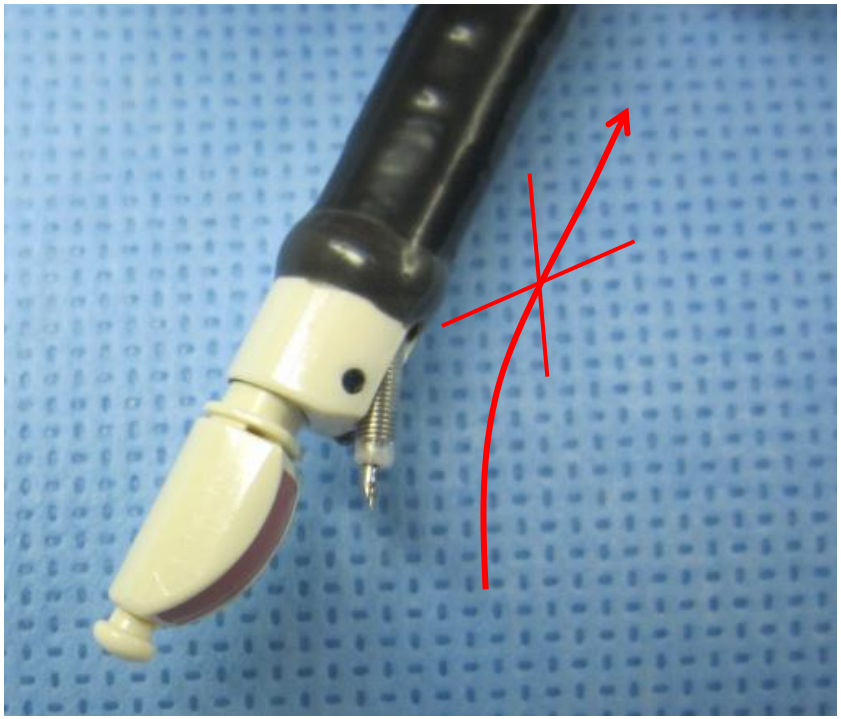
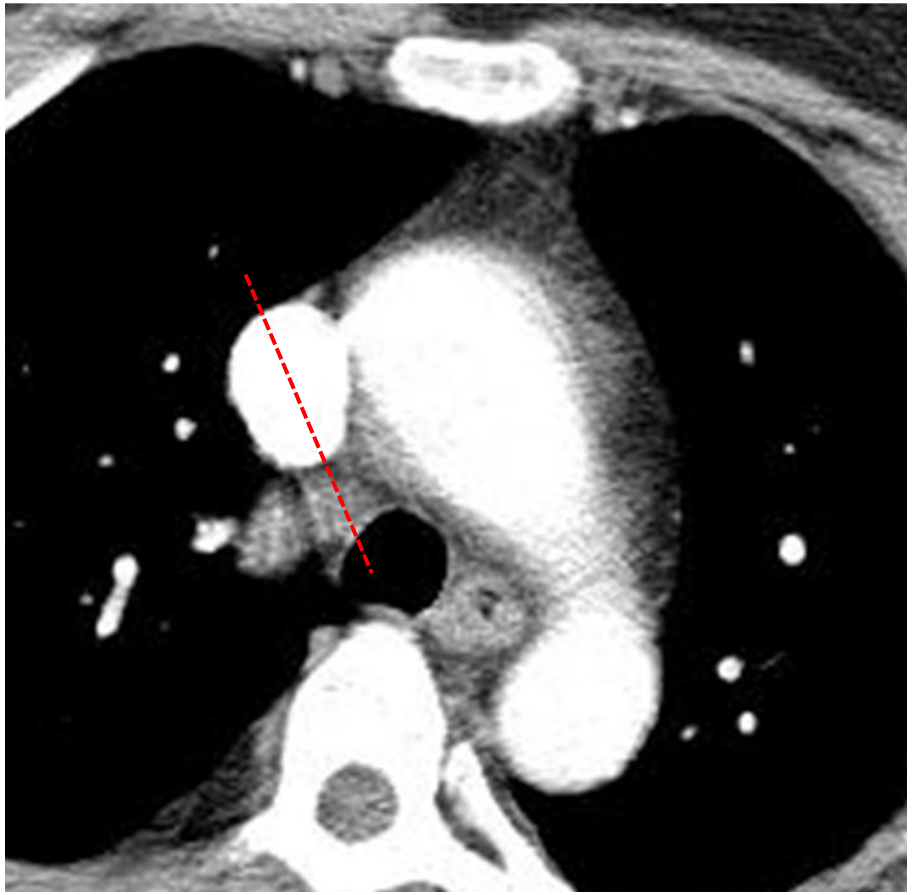
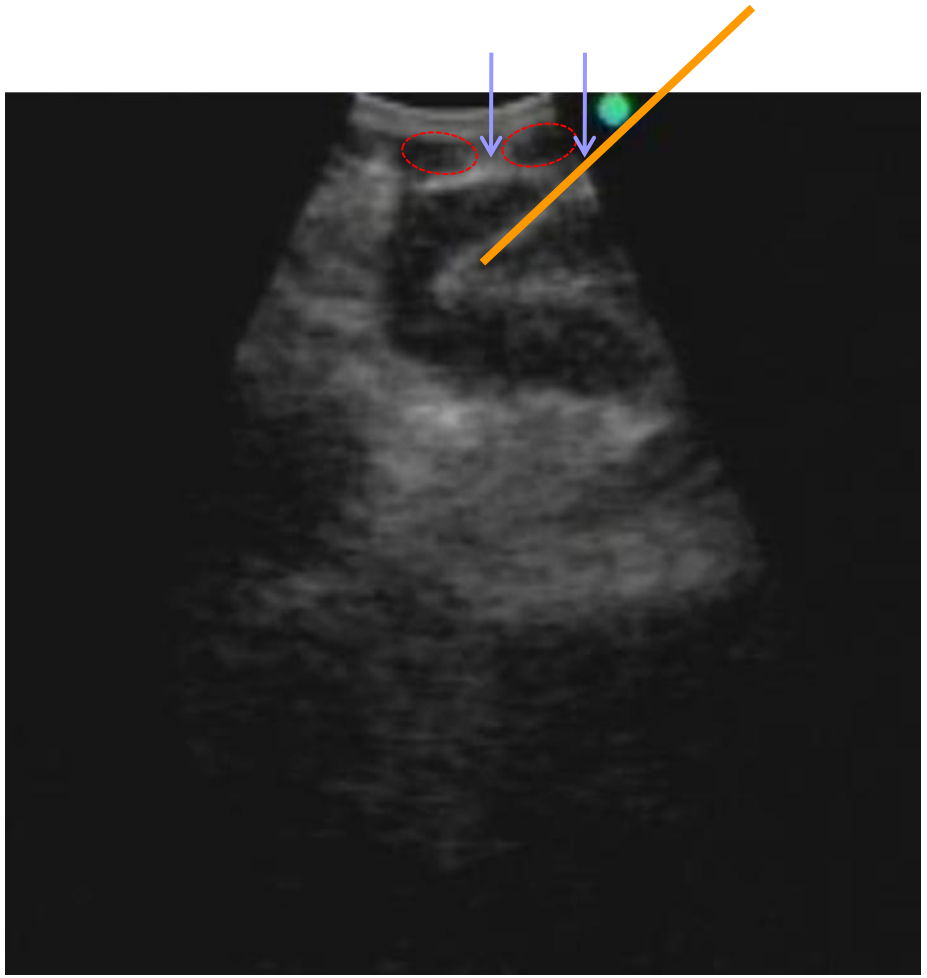
To Avoid Damages of Bronchoscope

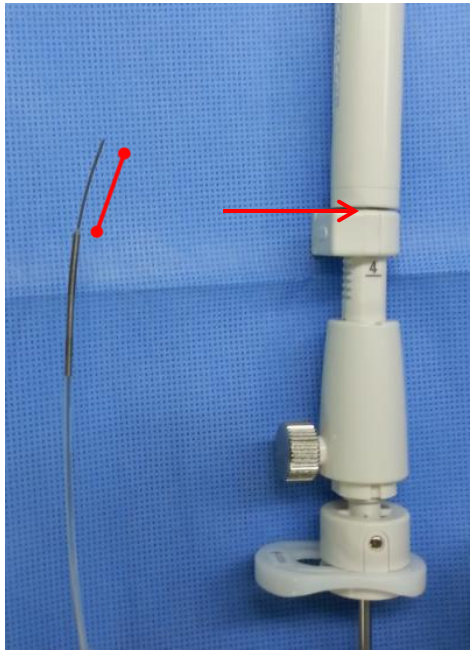


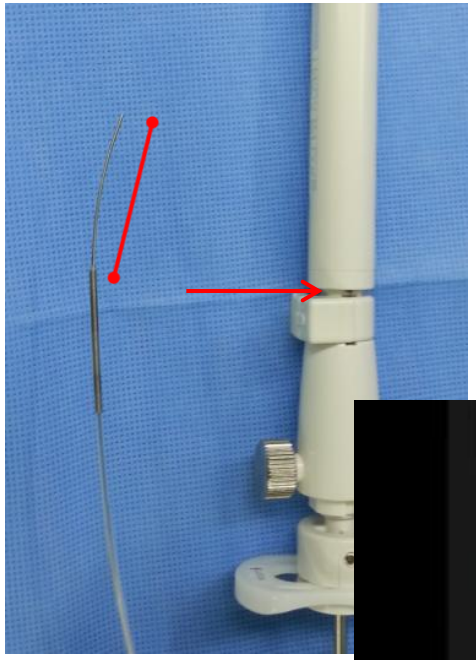
Insertion of Needle to Inter-cartilaginous Space



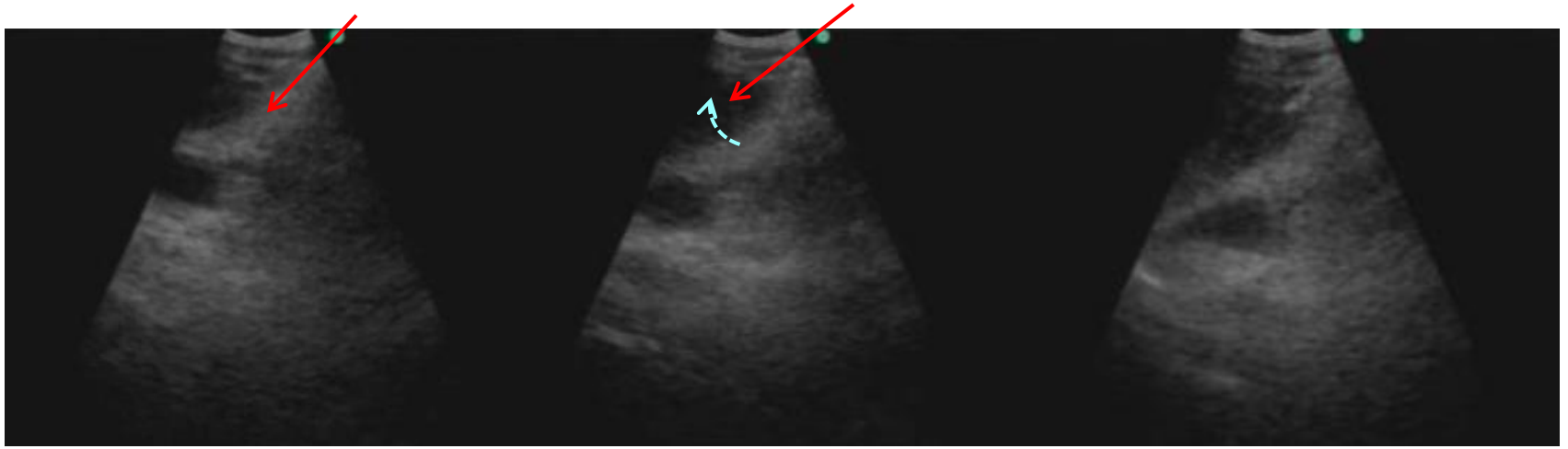


Insertion of the Needle





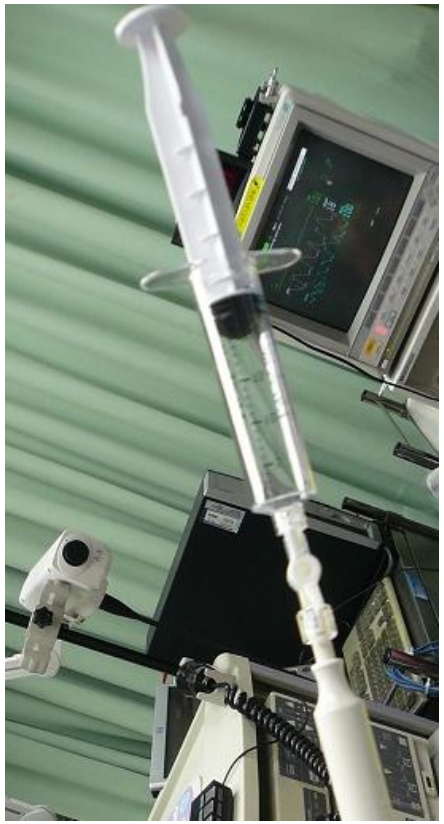
Difficult Targeting



Needle Movement

Back & forth movement & changing direction

Negative Pressure



Without (-) pressure

Negative Pressure Aspiration during EBUS-TBNA

115 pts, 192 LNs (>5mm), random allocation of (-) pressure ; 1st, 3rd or 2nd, 4th

	Aspiration(+)	Aspiration (-)	Concordance rate
Adequacy	88%	88%	83.9%
Diagnostic yield	36%	34%	95.8%

Casal et al Chest 2012; 142(3) :568-573

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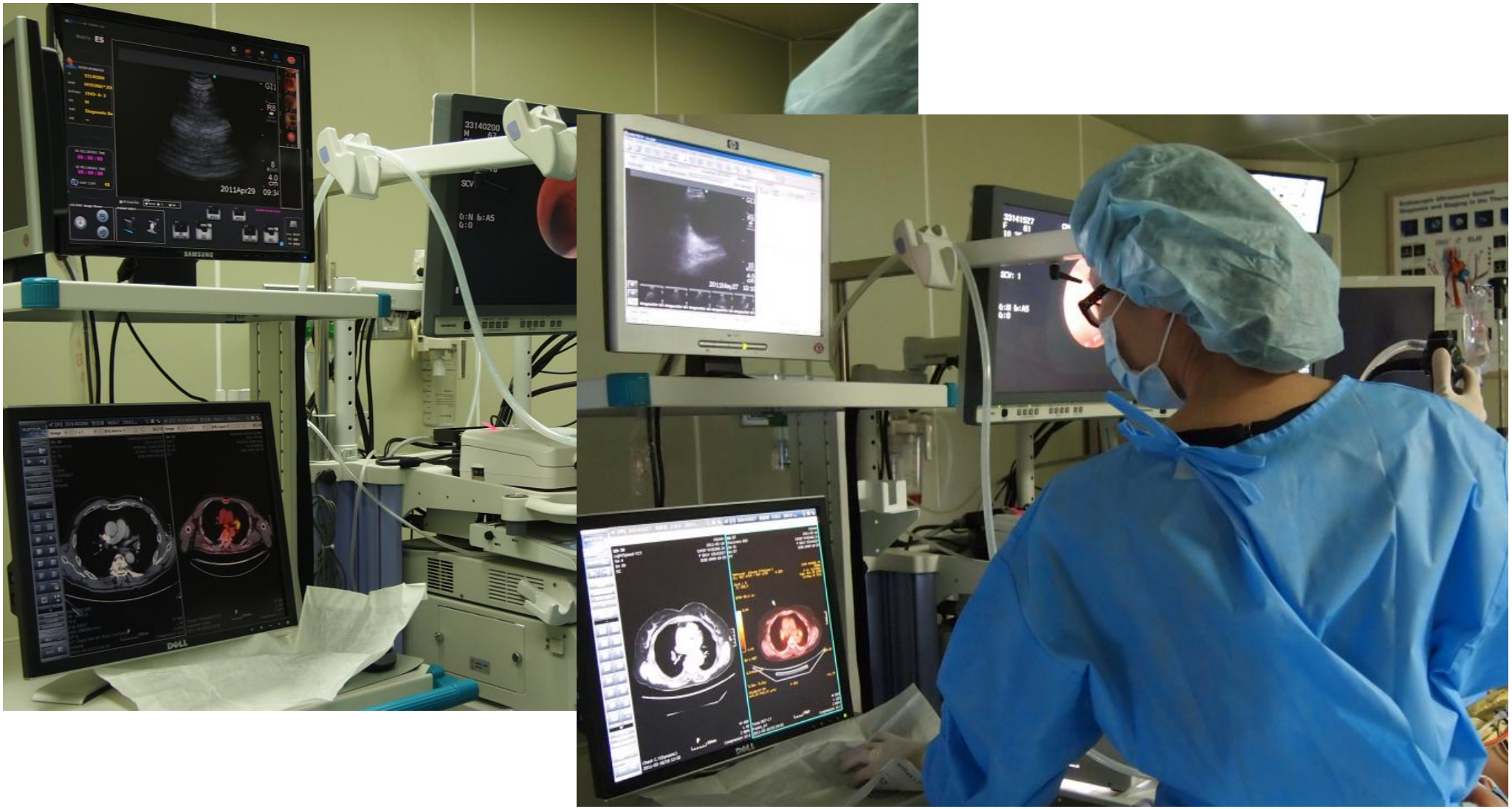
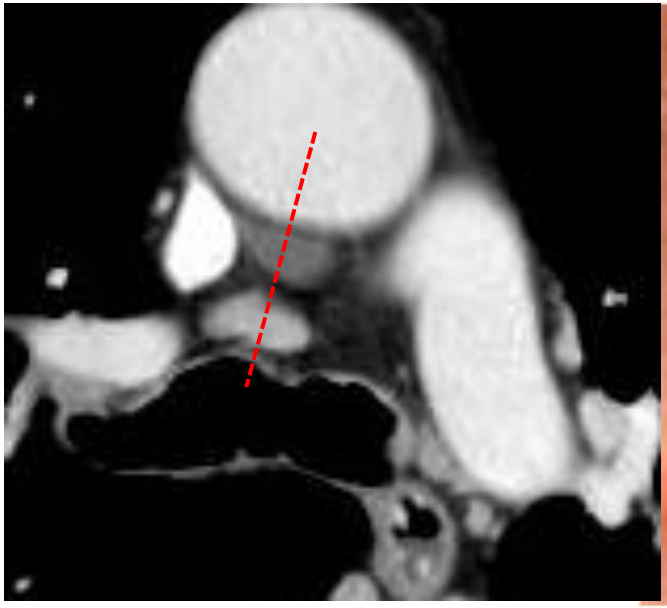
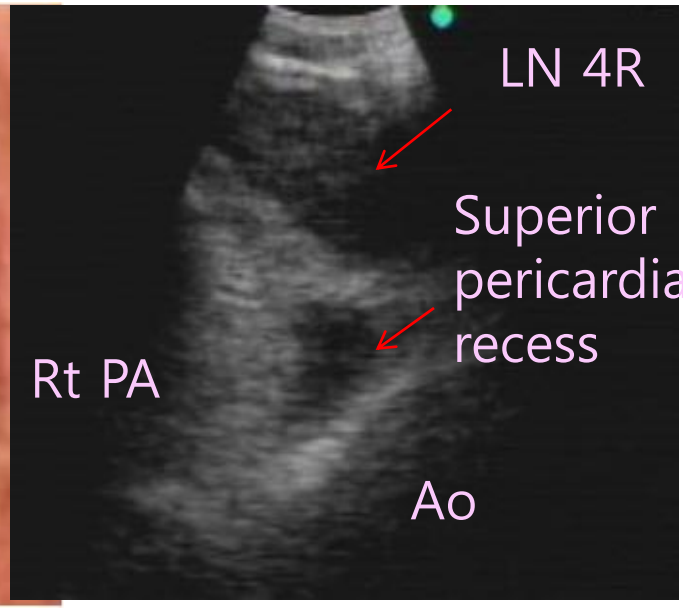
Matching of CT(and/or PET) with EBUS



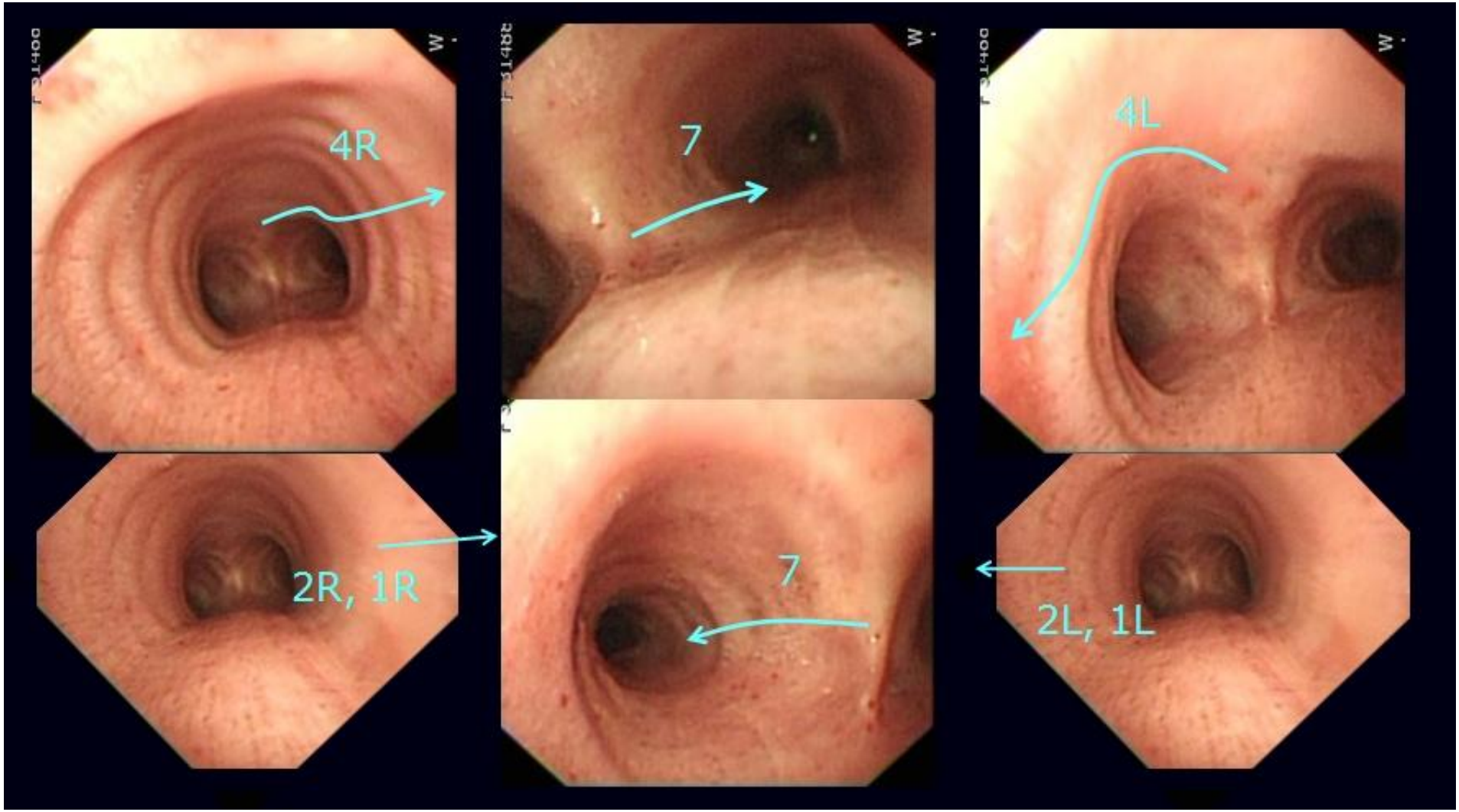
Searching for the Target

2D CT Images→ 3D mental reconstruction → EBUS Image

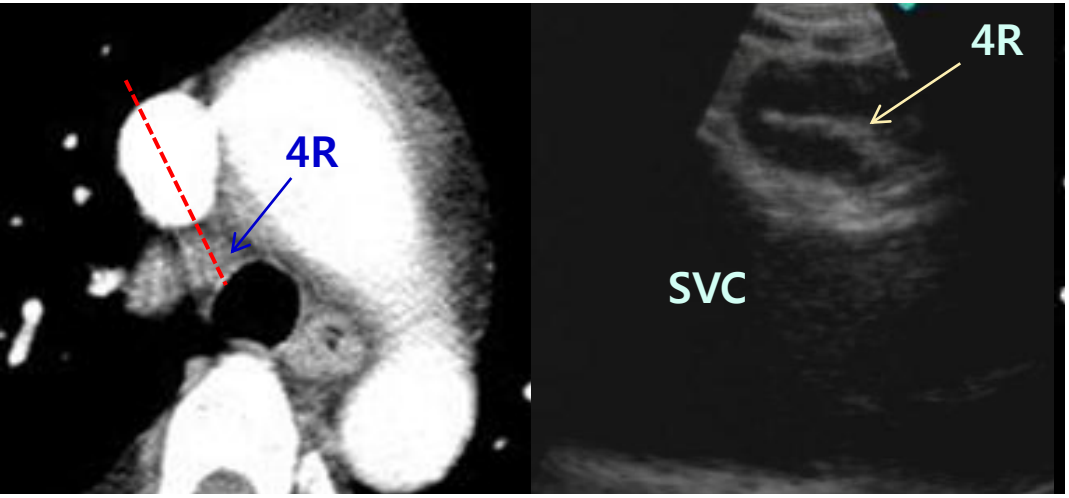


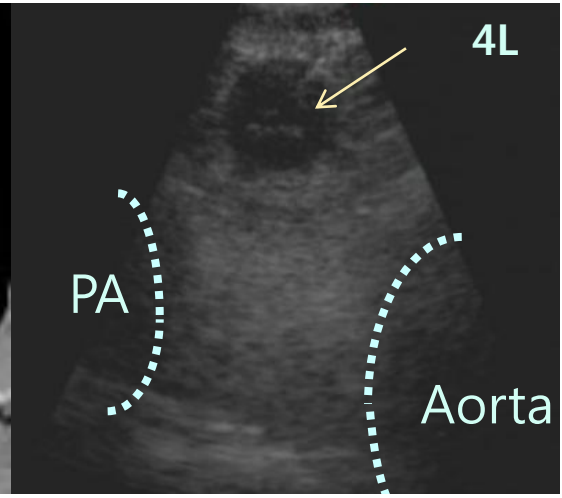


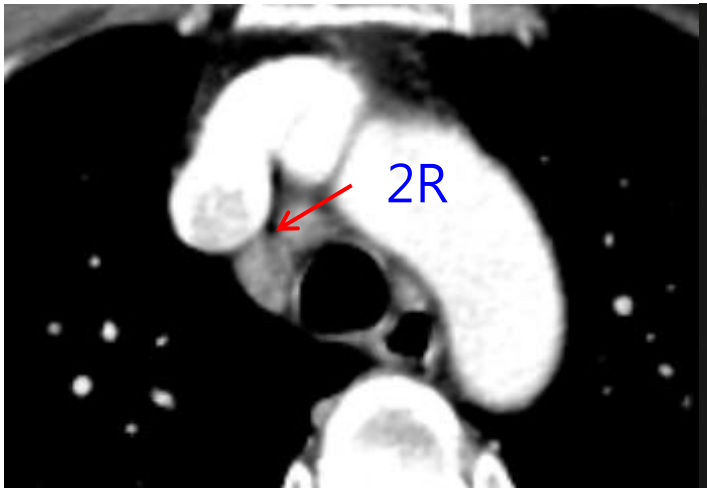
Systematic Mediastinal Lymph Nodes Visualization During EBUS-TBNA for Lung Cancer Staging

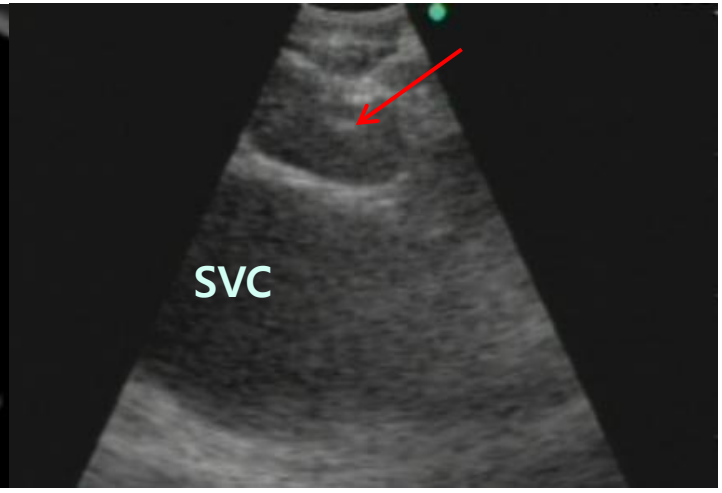


Some Landmarks









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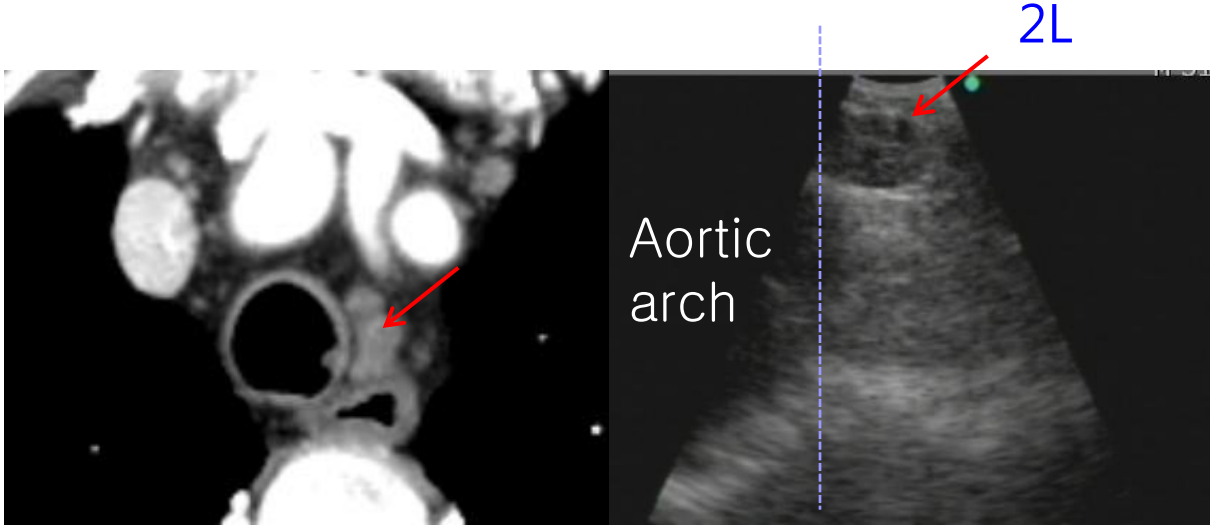

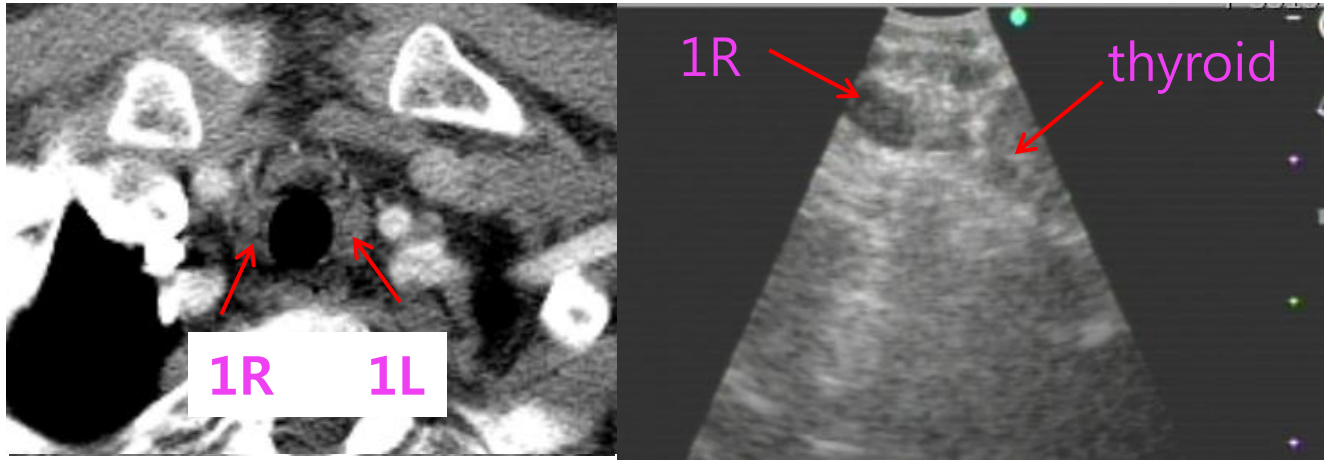

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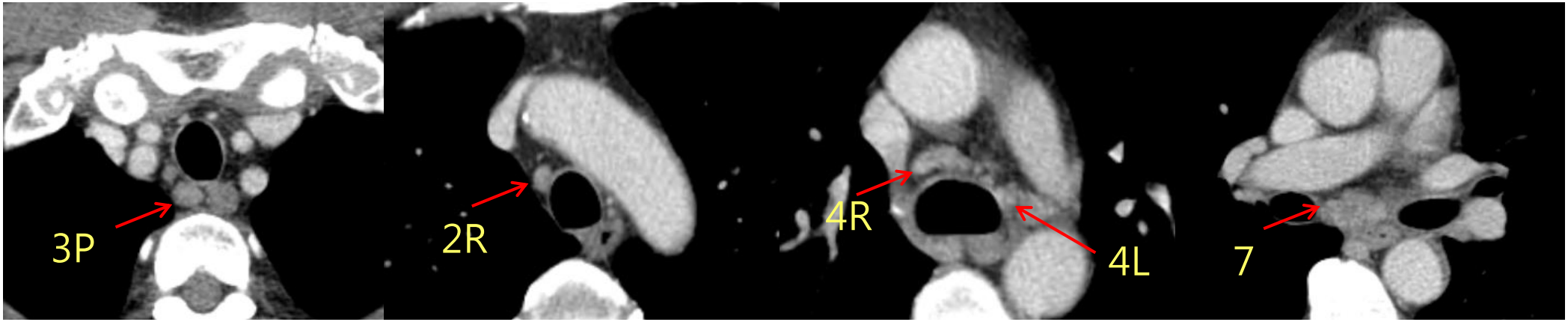
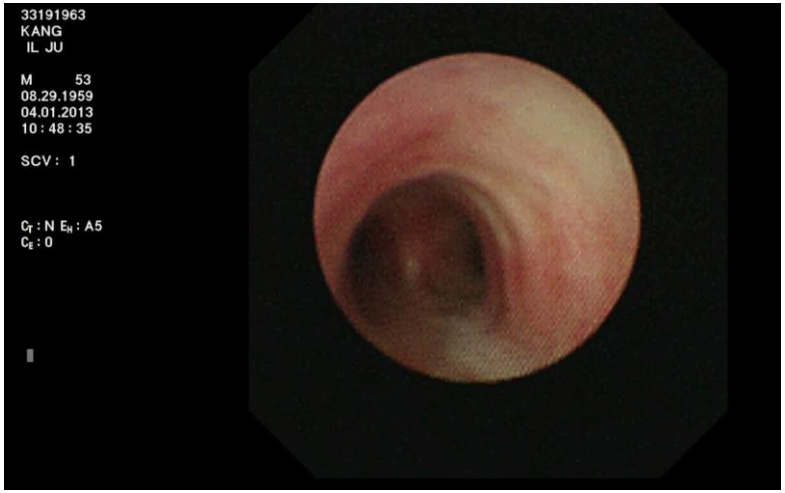
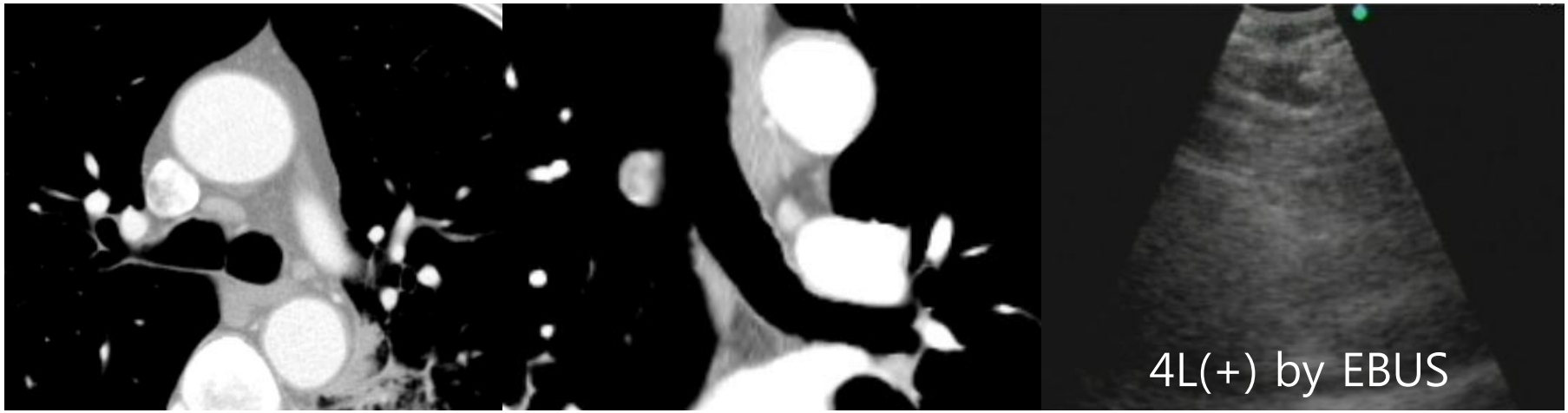




IASLC LN Classification ; Ambiguous Locations **Station 4L & 10L**



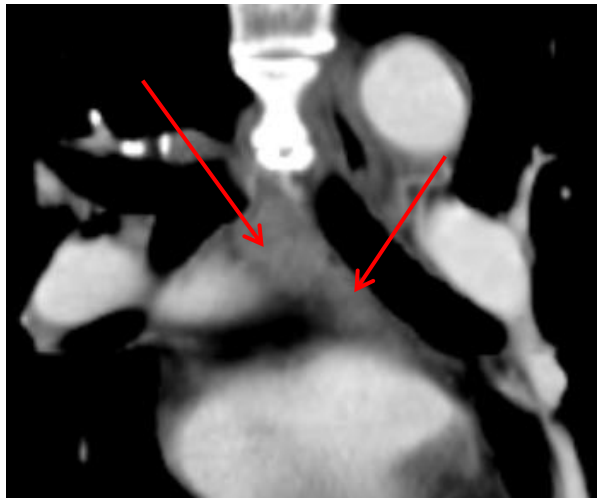
Surgery ; N1 10L - 4mm metastasis

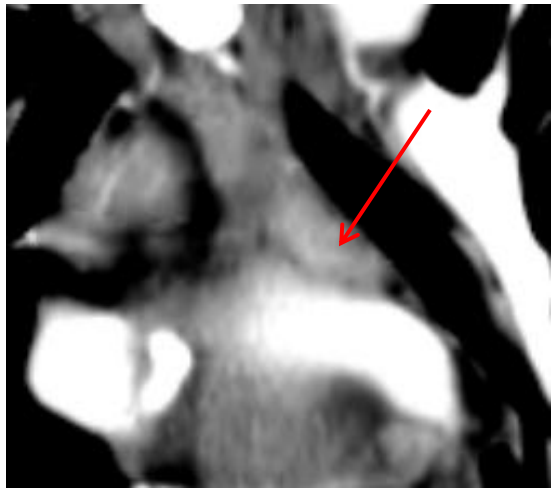
IASLC LN Classification ; Ambiguous Locations **Station 7 & 10L**

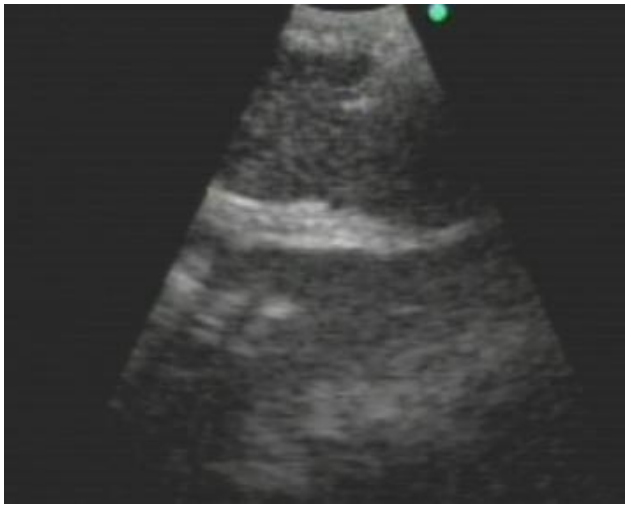
LN7, flat

LN7, flat

LN10Lor LN7

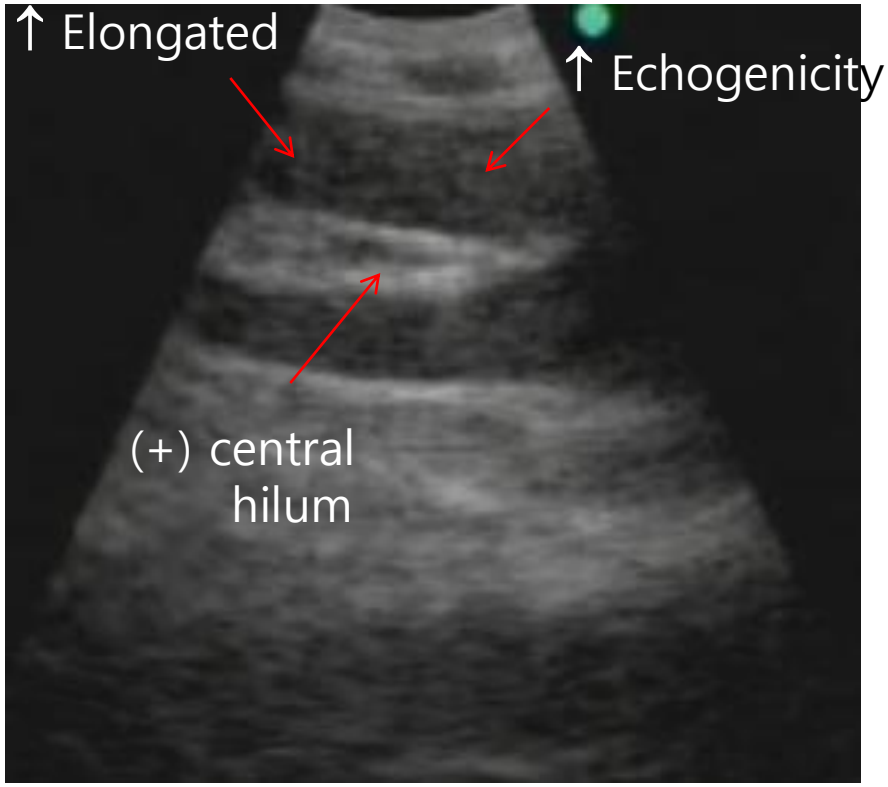


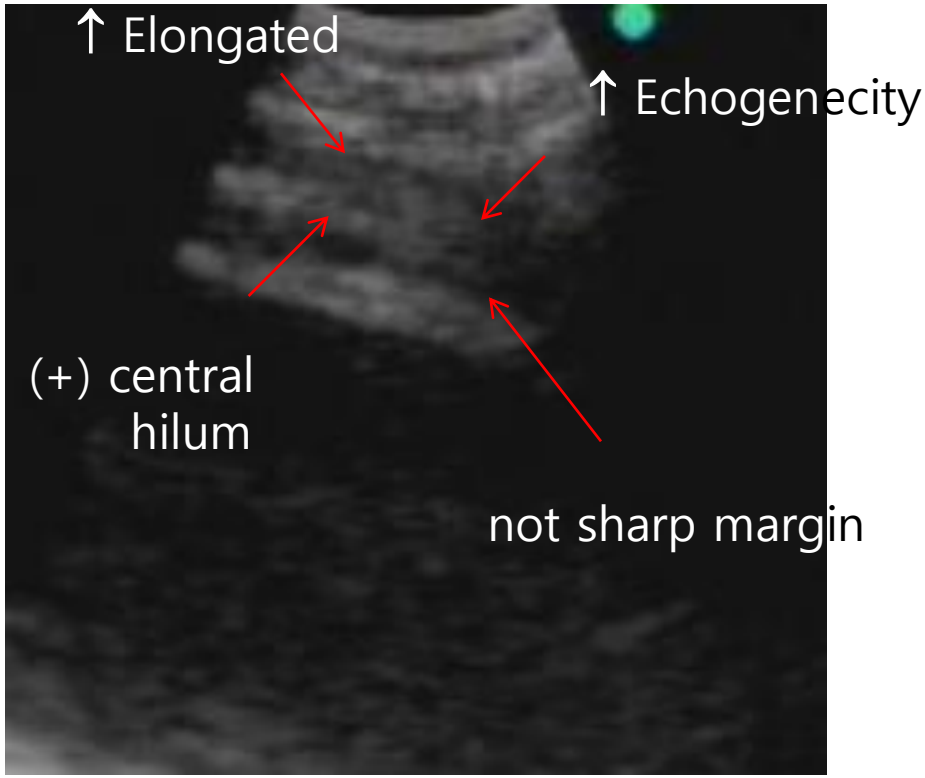




Understanding of EBUS Images

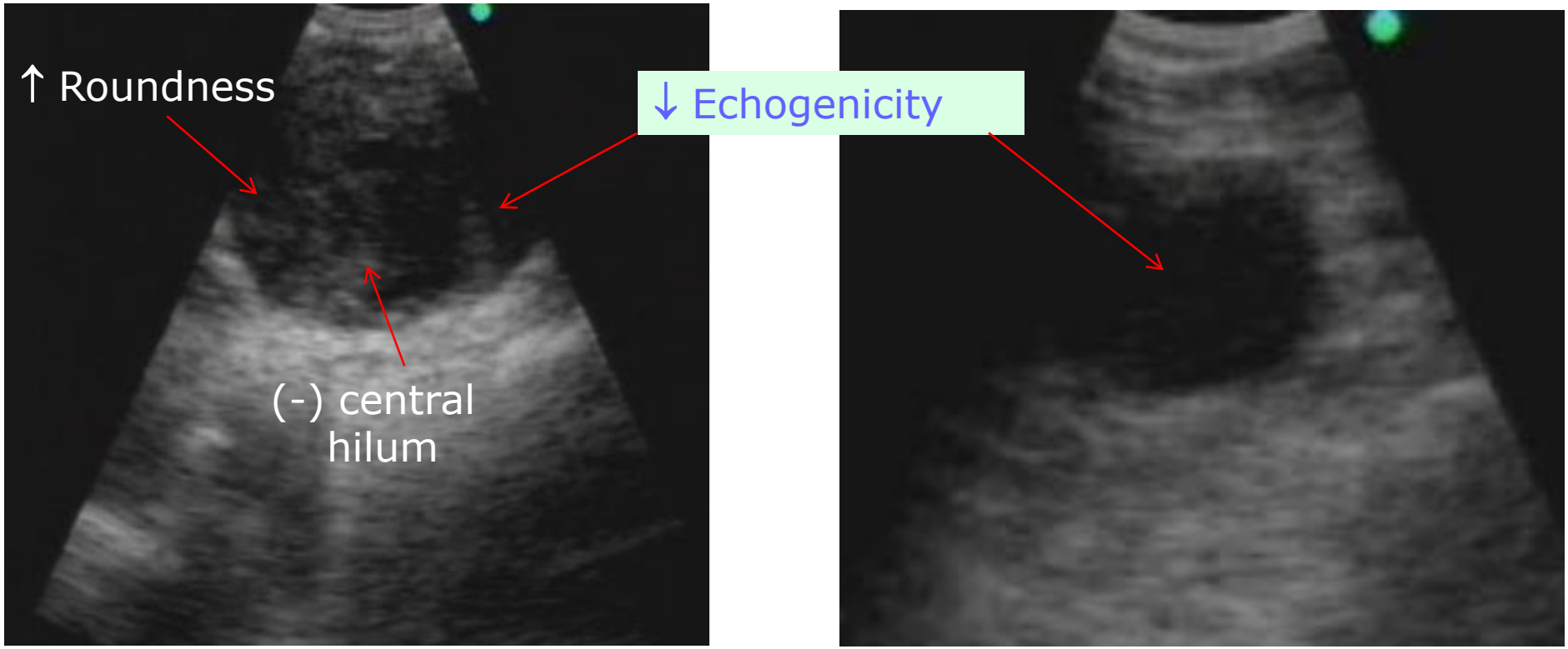
Features of benign LN





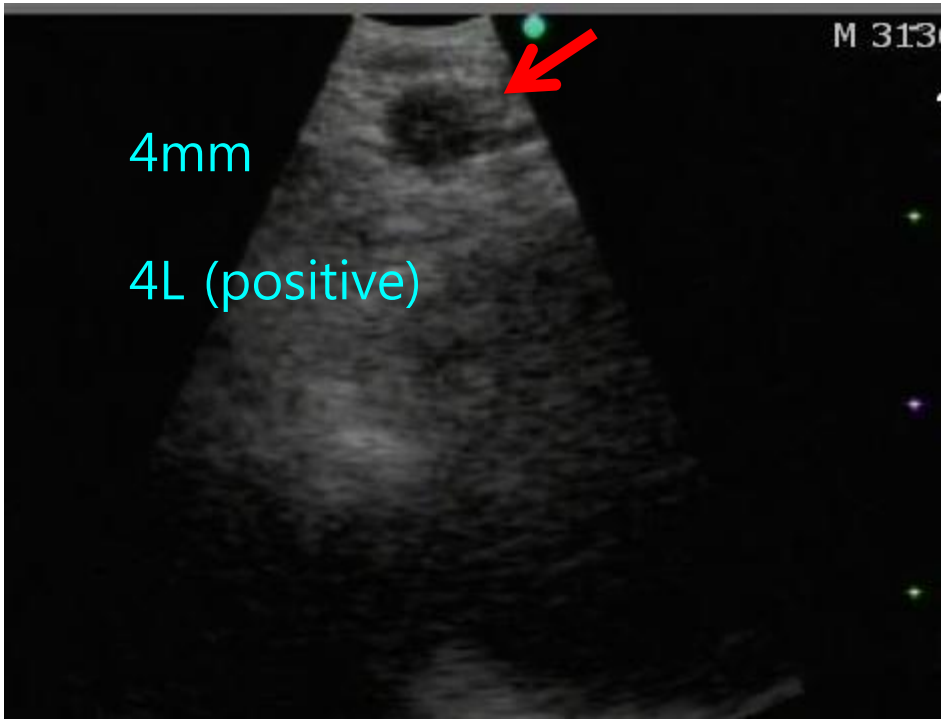
Understanding of EBUS Images

Features of malignant LN

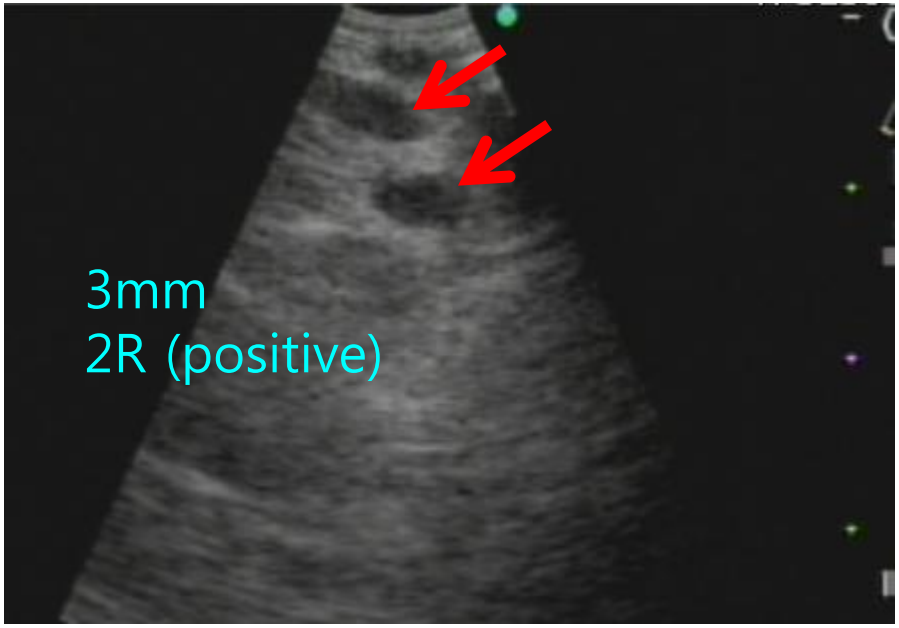


Understanding of EBUS Images

Features of malignant LN



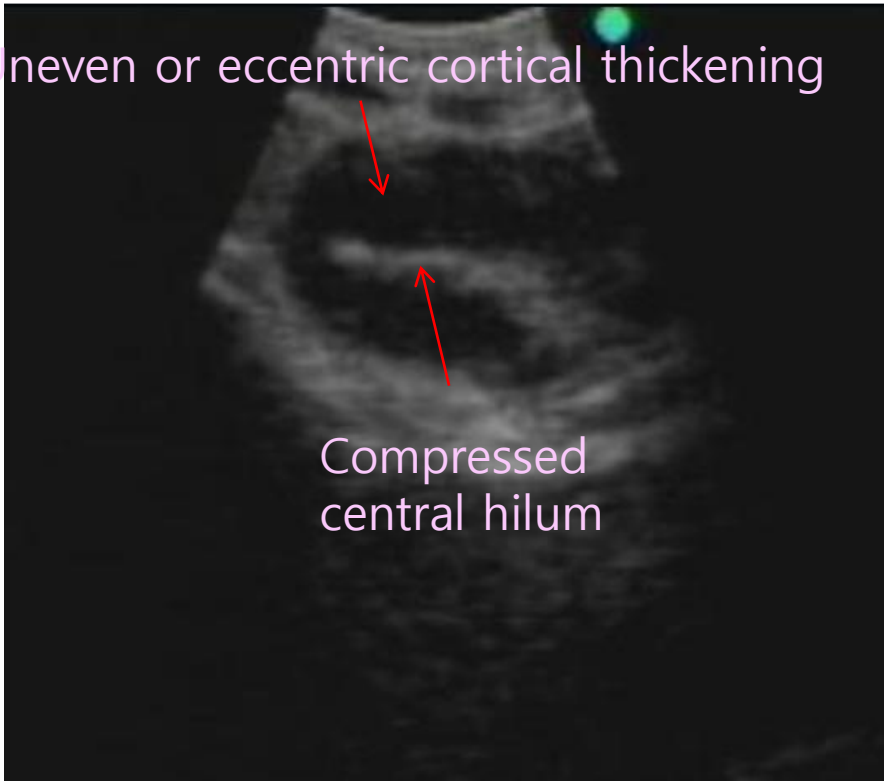
Small LN with typical features of Malignant node



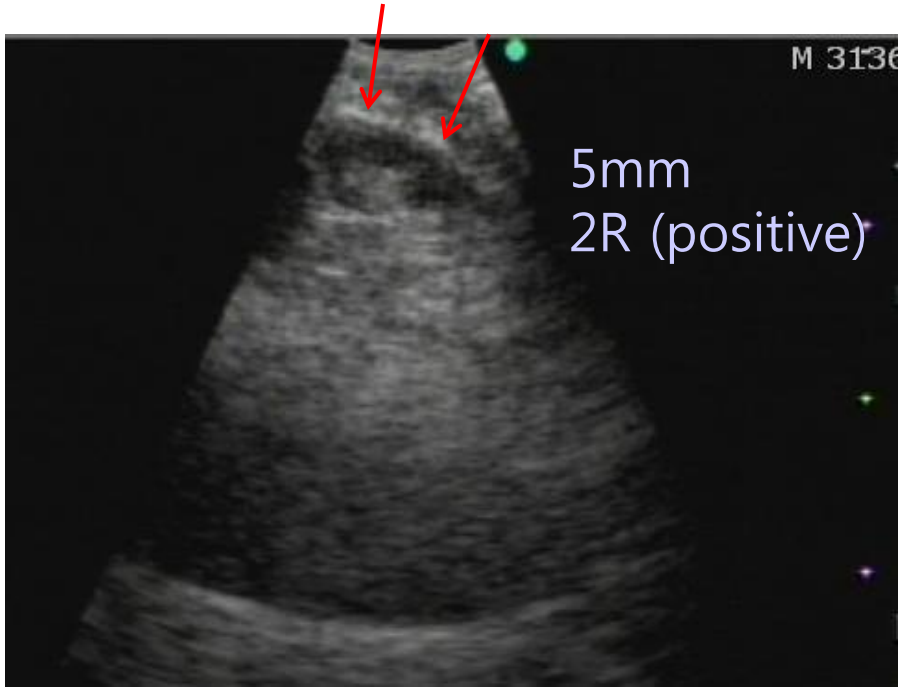
Multiple small dark nodes

Understanding of EBUS Images

Features of malignant LN

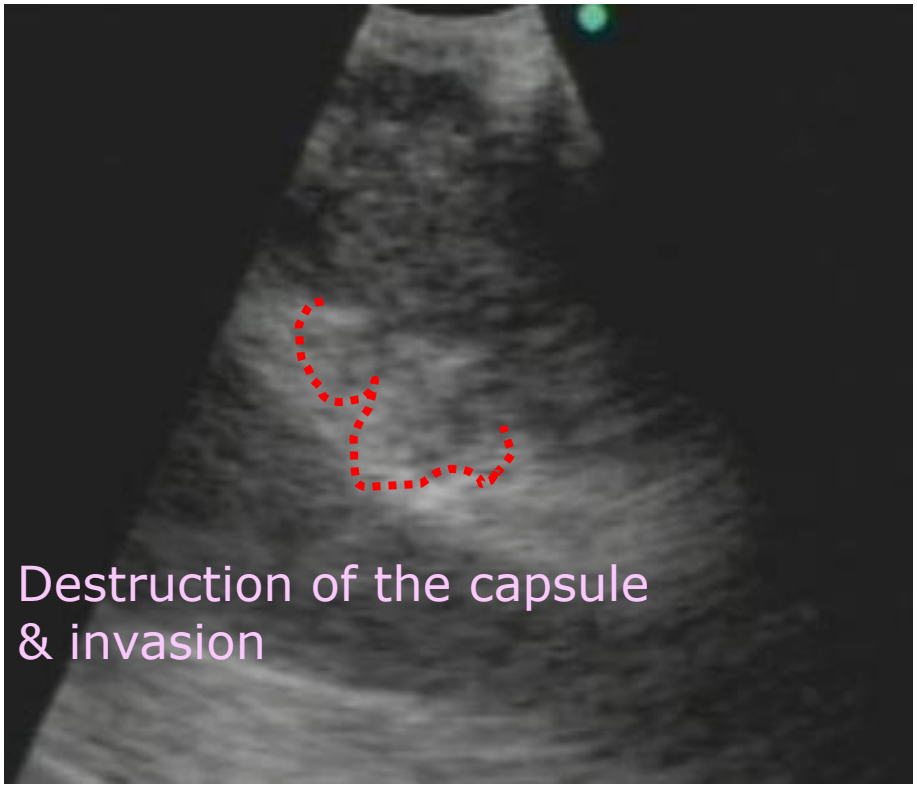


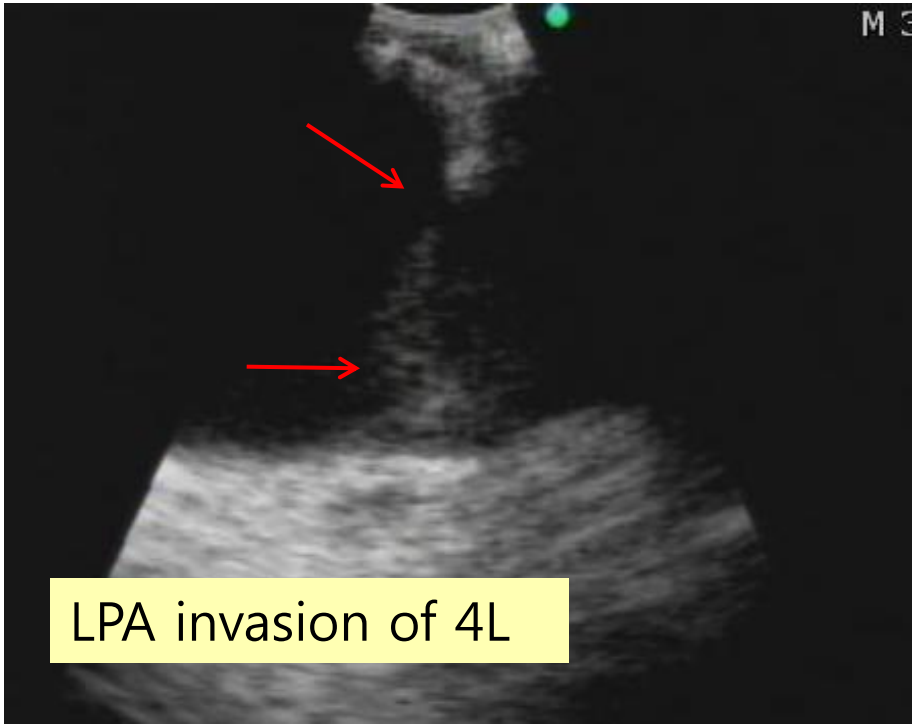
Eccentric cortical thickening



Understanding of EBUS Images

Features of malignant LN; extranodal invasion





Understanding of EBUS Images

Fujiwara et al,
1061 LNs

Combined NPV
of all 4 features : 98%

Morphologic Category	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnosis accuracy
Size ; more10mm	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
Echogenecity ; heterogenous	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

Chest. 2010 Sep;138(3):641-7

Understanding of EBUS Images

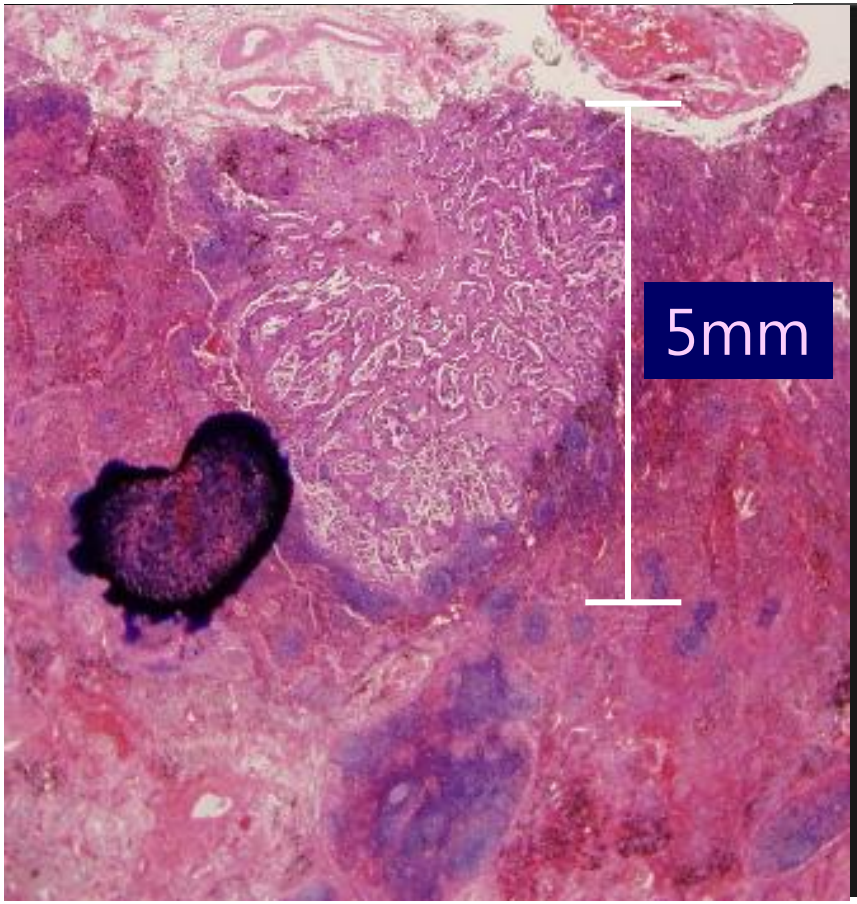
Table 4—*ORs Describing the Risk of Malignancy by Nodal Characteristics*

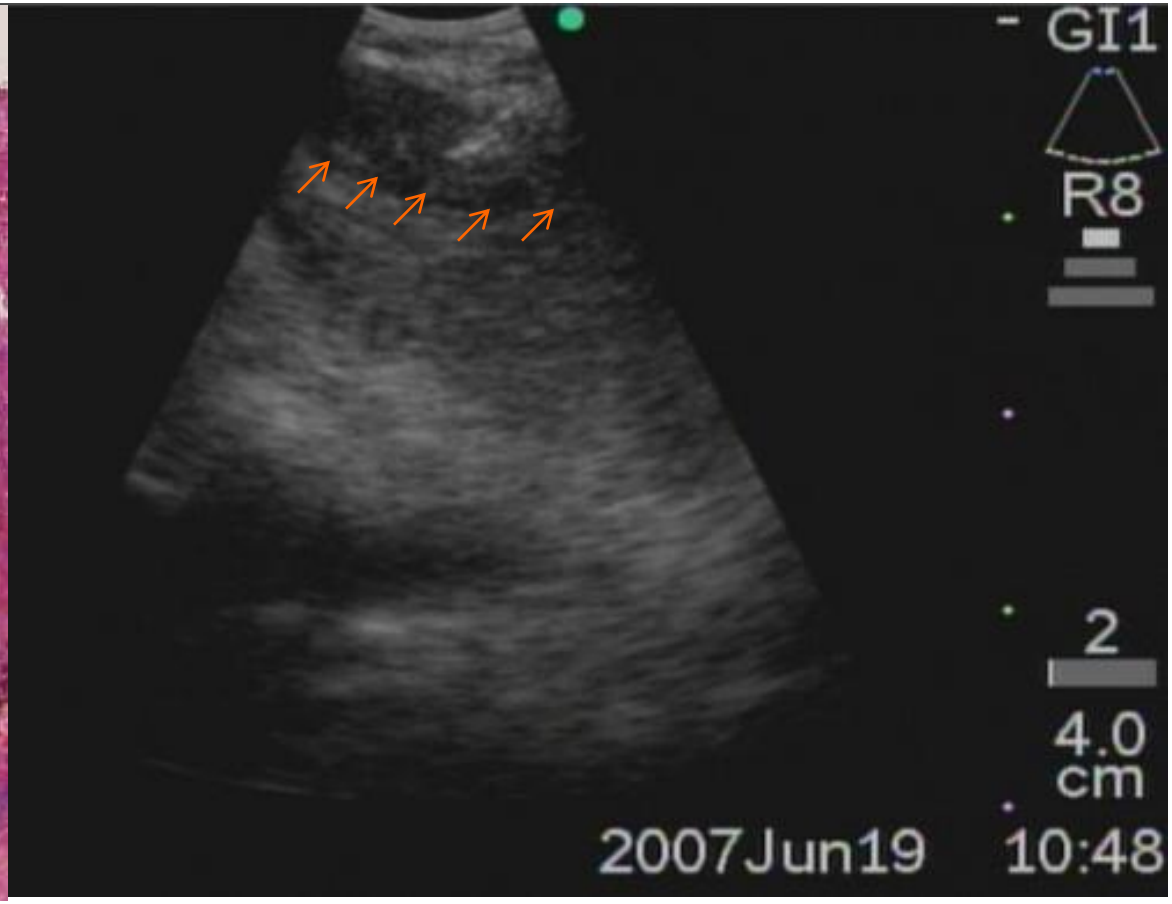
EBUS Pathology	Predictor	Variable	OR (95% CI)	*P* Value
Radiographic characteristics	PET scan activity	Normal	Ref	…
		Increased	3.48 (1.40-8.64)	.0072[a]
	CT scan lymph node size	< 10 mm	Ref	…
		10-20 mm	2.89 (1.11-7.52)	.029[a]
		> 20 mm	34.38 (6.02-196.48)	< .0001[a]
Ultrasound characteristics	Size	Continuous: change of 5 mm	1.57 (1.23-1.99)	.0002[a]
		< 10 mm	Ref	…
		10-20 mm	3.39 (1.77-6.46)	.0002[a]
		> 20 mm	10.28 (4.31-24.50)	< .0001[a]
	Shape	Triangular	Ref	…
		Oval	3.50 (1.54-7.96)	.0028[a]
		Round	4.16 (1.67-10.36)	.0022[a]
		Draping	1.49 (0.46-4.89)	.51
	Echogenicity	Hyperechoic	Ref	…
		Hypoechoic	1.47 (0.51-4.30)	.48
		Isoechoic	0.61 (0.11-3.32)	.56
	Borders	Well-defined	Ref	…
		Indistinct	0.98 (0.58-1.66)	.93
Procedural characteristics	Biopsy location	Center	Ref	…
		Periphery	0.97 (0.56-1.66)	.91

Memoli et al Chest. 2012 140(6): p. 1550-6.

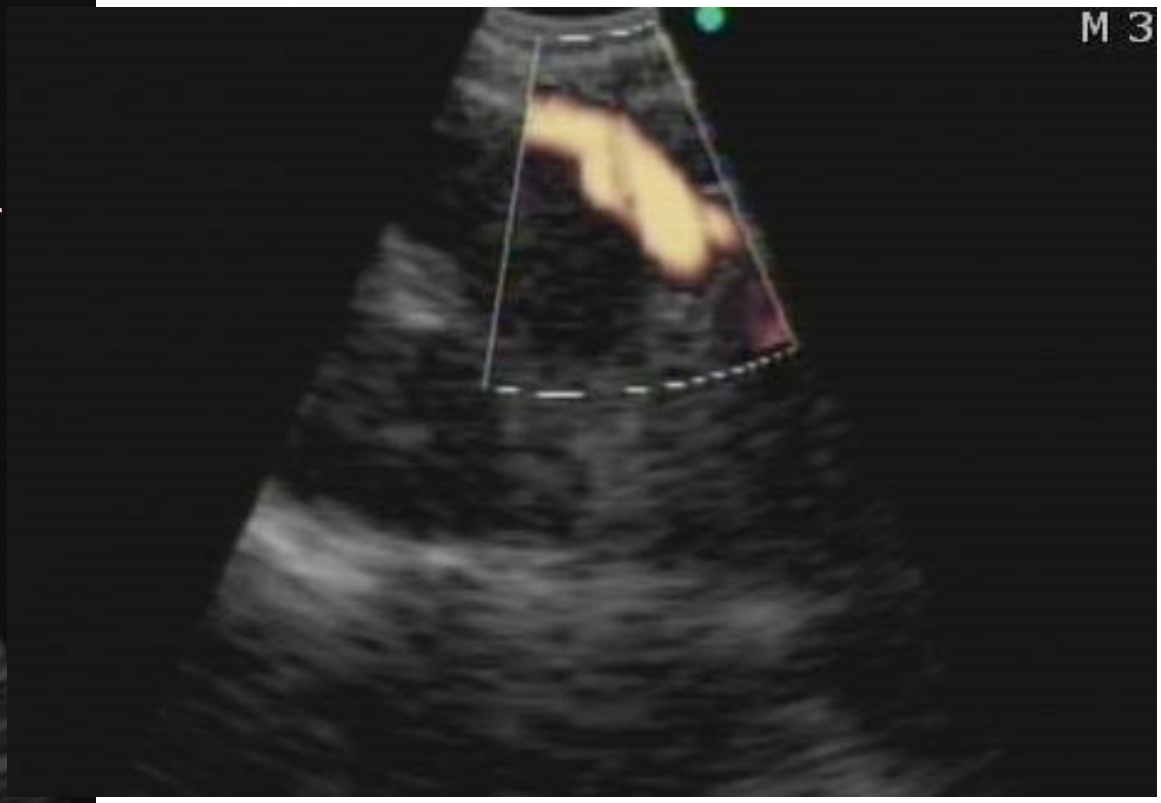
Echo-features of Mediastinal Lymph Nodes

F/61, Adenoca(T1), RLL, Metastasis on #7 diagnosed by EBUS-TBNA

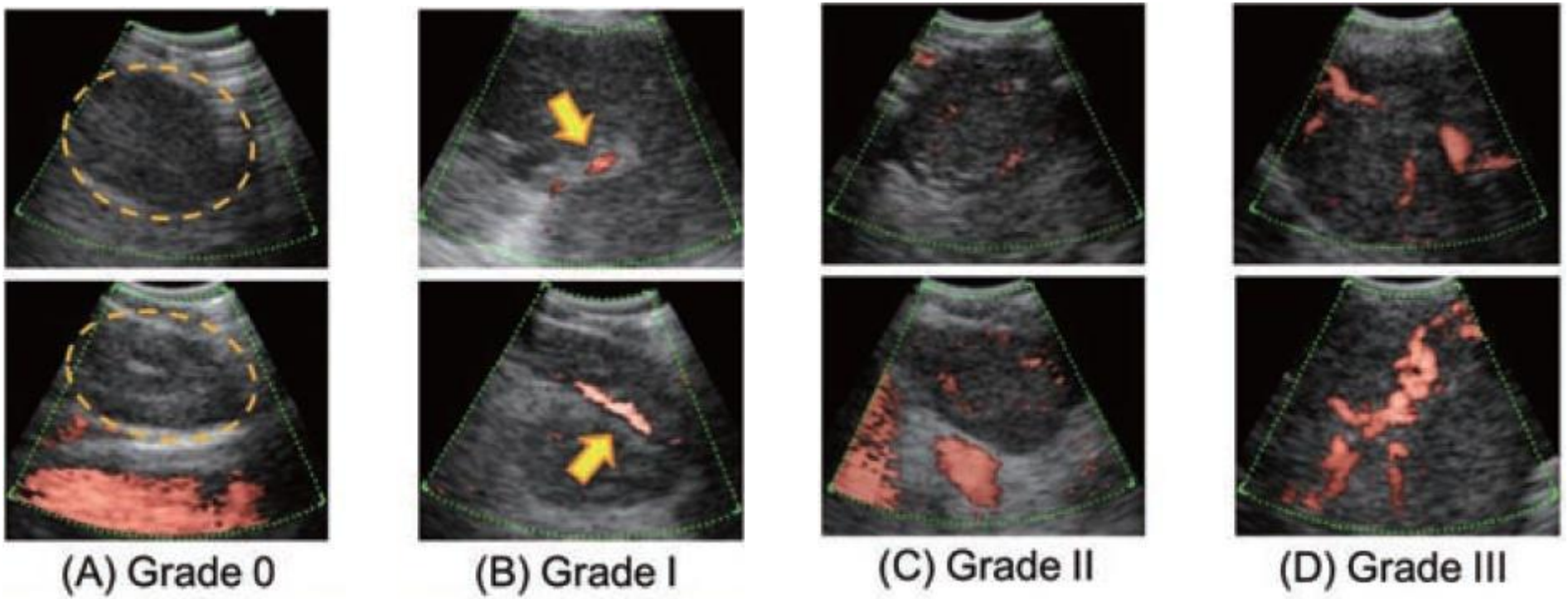




Doppler Mode



Doppler Mode ; Vascular Pattern in LNs



Retrospective 173 LNs
Grade 2& 3; sensitivity in detecting malignancy=87.7%

Nakajima et al. J Thorac Oncol. 2012;7: 1009–1014

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Lymph Node Selection During EBUS-TBNA

In Mediastinal Staging of Potentially Operable Lung Ca.

The possibility of a positive result

1) LN size or features on Chest CT
2) PET findings
3) Potential pathways of lymphatic metastasis
4) Echo features of LN

↓

Impact on deciding treatment

How Many Nodal Stations ?

Mediastinal staging in potentially operable lung cancer

Table 5—*Accessibility to Mediastinal Nodal Stations by EBUS-TBNA and EUS-B-FNA*

Nodal Stations With at Least One Node ≥5 mm[a]	Total	Accessible by EBUS-TBNA	Accessible by EUS-B-FNA	Accessible only by EBUS-TBNA	Accessible Only by EUS-B-FNA	Accessible by Both	Inaccessible by Both
1R	14	14	8	6	0	8	0
1L	1	1	1	0	0	1	0
2R	45	45	1	44	0	1	0
2L							
3A							
3P							
4R	107	107	1	106	0	1	0
4L	75	74	75	0	1	74	0
5	56	1[b]	11	0	10	1	45
6	12	0	0	0	0	0	12
7	107	107	106	1	0	106	0
8	8	3	8	0	5	3	0
9	13	0	13	0	13	0	0
Total	473	372 (78.6)	240 (50.7)	161 (34.0)	29 (6.1)	211 (44.6)	72 (15.2)

Nodal stations having at least one node with a short diameter of 5 mm on axial CT scans ; 2.5/ patient

[a]In 149 patients who underwent EBUS and EUS.

Hwangbo et al. Chest. ***138****(4): p. 795-802*

Studies on Roles of EBUS-TBNA in Lung Cancer Staging, NCC

NCC data, prospective studies in potentially operable NSCLC

	# of Pts	Inclusion	Sensitivity	NPV	Accuracy	# of LN
Study 1, 2008	95	LN≥ 5mm	93.8%	96.9%	97.9%	1.6
Study 2, 2009	117	LN≥ 5mm	90%	96.7%	97.4%	2.1
Study 3, 2010	143	All	84.4%	93.3%	95.1%	1.9
Study 4, NP	169	All	85.3%	88.9%	93.2%	2.9

A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer

Yasufuku et al. J Thorac Cardiovasc Surg 2011;142:1393-400

EBUS-TBNA followed by mediastinoscopy, n=153

	Sensitivity	NPV	Accuracy	# of LN
EBUS-TBNA	81%(43/53)	91%	93%	2.84
Mediastinoscopy	79%(42/53)	90%	93%	3.82

(McNemar's test, p=.78).

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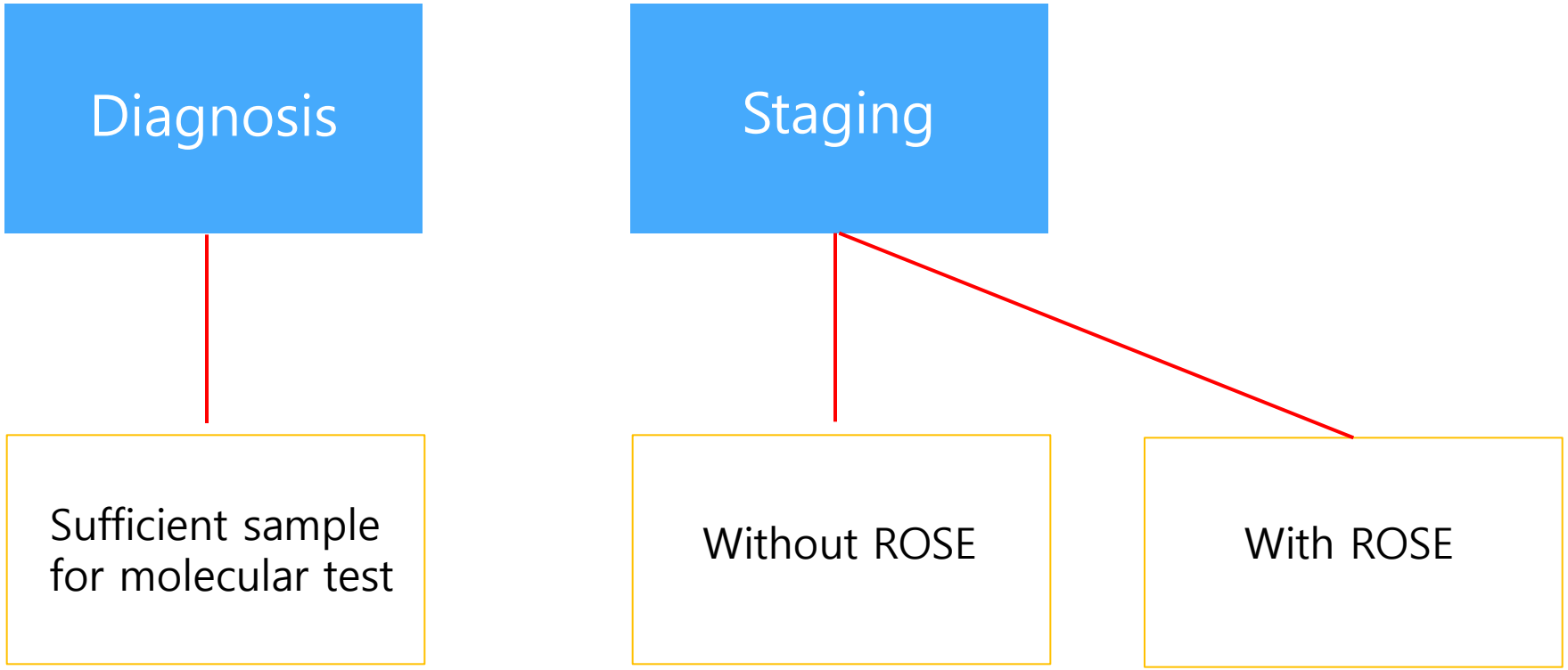
Number of Aspirations per Lesion

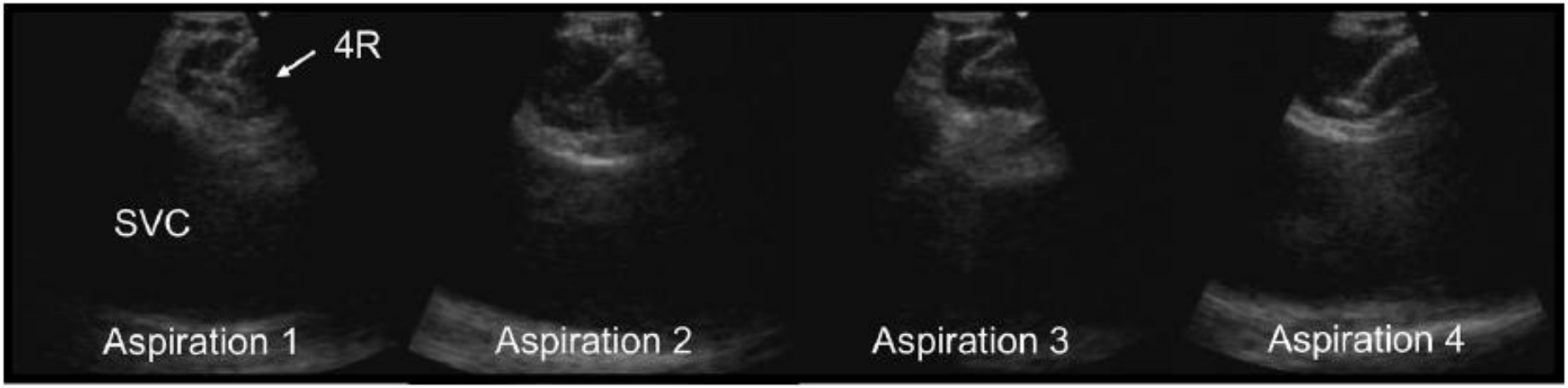


Real-time Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in Mediastinal Staging of Non-Small Cell Lung Cancer*

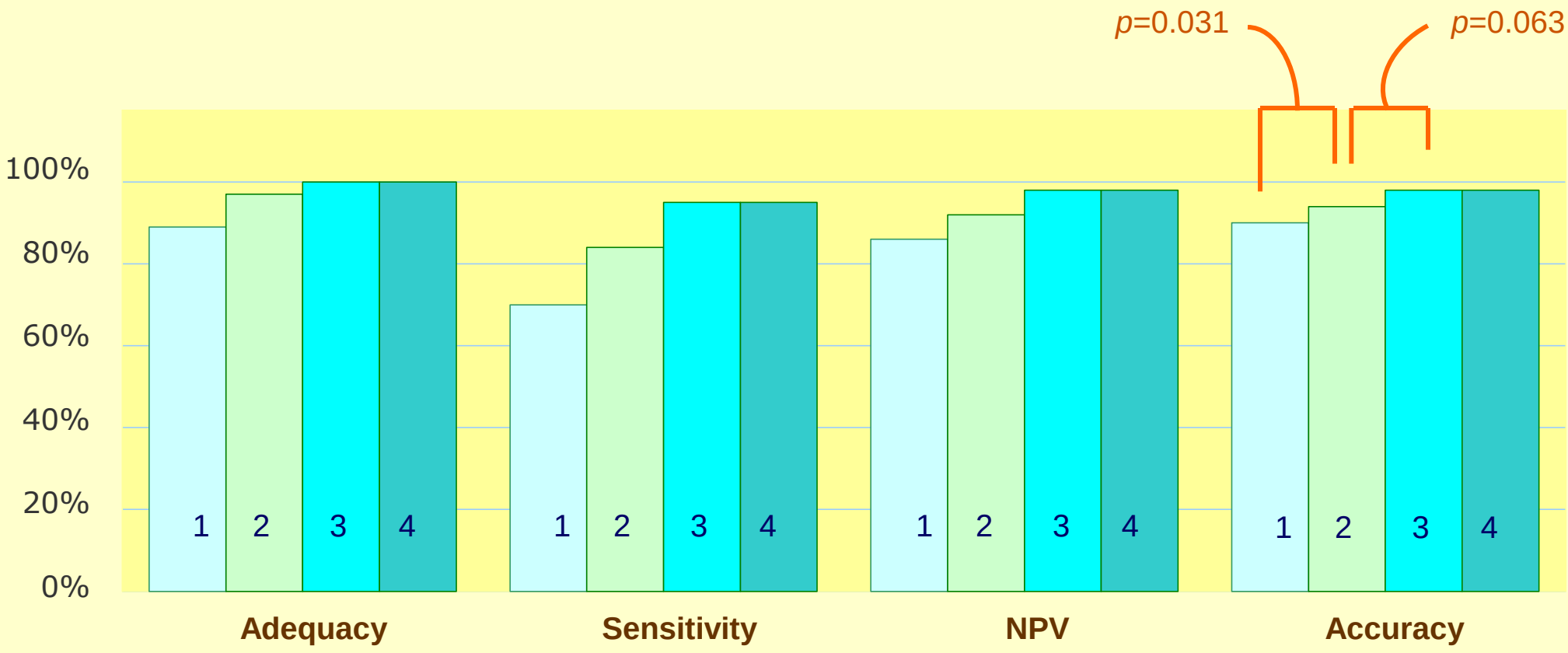
How Many Aspirations Per Target Lymph Node Station?

Lee et al CHEST 2008 134:368-74

Prospective, 102 potentially operable lung ca pts, 2006. 7-2007. 4
163 nodes, 4 aspirations per nodal station



Optimal results can be obtained in 3 aspirations per LN station in EBUS-TBNA for mediastinal staging of potentially operable NSCLC.



Lee et al Chest 2008 134-368-74

When at least one tissue core specimen is obtained by the 1st or 2nd aspiration, 2 aspirations per LN station can be acceptable

Variables	Aspirations, No.			
	1		2	
	Tissue Core	No Tissue Core	Tissue Core	No Tissue Core
Sensitivity	75.9 (22/29)	57.1 (8/14)	91.9 (34/37)	33.3 (2/6)
NPV	89.9 (62/69)	77.8 (21/27)	96.0 (72/75)	73.3 (11/15)
Accuracy	92.3 (84/91)	82.9 (29/35)	97.2 (106/109)	76.5 (13/17)

Lee et al Chest 2008 134-368-74

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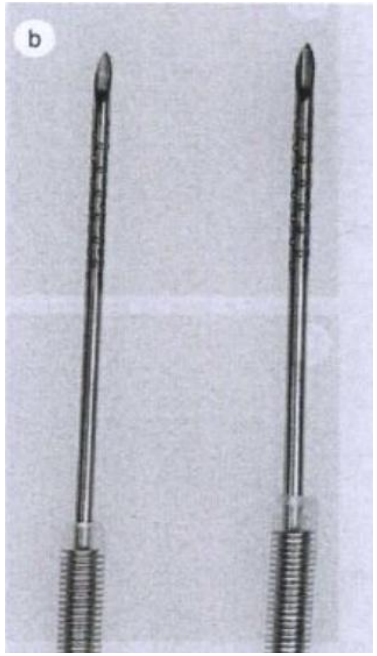
Comparison of 21G & 22G Needles



22G needle 21G needle

1299 pts, retrospective
American Chest Physicians Quality Improvement Registry

	21 Gauge (n=240 patients, 497 lymph nodes)	22 Gauge (n = 995 patients, 2271 lymph nodes)	Adjusted Odds Ratio (95% CI)	P-Value
By patient				
Diagnostic yield, n (%)	123 (51)	511 (51)	1.2 (0.9 – 1.8)	0.26[a]
By lymph node				
Diagnostic yield, n (%)	197 (40)	746 (33)	1.5 (0.7 – 3.1)	0.27[b]
Sample adequacy, n (%)	446 (90)	2054 (90)	1.4 (0.7 – 2.8)	0.37[c]

Yarmus et al Chest in press

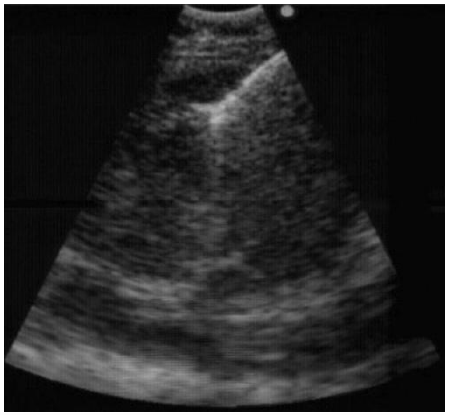
Comparison of 21G & 22G Needles

60 pts, randomized, adequate vs. inadequate p=0.40

Specimen category	21G	22G
I diagnostic	35(58%)	34(57%)
II Non diagnostic adequate	8(13%)	13(22%)
III Non diagnostic inadequate	15(25%)	7(12%)
IV No specimens	2(%)	6(10%)

Oki et al J Bronchol Intervent Pulmonol 2011 (18) p306

EBUS Mini-forceps



50 pts with low likelihood of NSCLC

Table 2. Diagnostic Yield

	EBUS-TBNA (%)	EBUS-MFB (%)	*p* value MFB vs TBNA
Overall Yield	60/74 (81)	67/74 (91)	0.09
Nonmalignant disease	43/49 (88)	43/49 (88)	
Granulomatous disease	29/33 (88)	29/33 (88)	
Other nonmalignant	14/16 (88)	14/16 (88)	
Malignant disease	17/25 (68)	24/25 (96)	0.008
Non-small cell lung carcinoma	4/5 (80)	5/5 (100)	
Small cell lung carcinoma	6/8 (75)	8/8 (100)	
Breast carcinoma	4/4 (100)	4/4 (100)	
Renal cell carcinoma	1/1 (100)	1/1 (100)	
Sarcoma			
Lymphoma	Lymphoma 0/4	4/4	
Other malignant	2/2 (100)	2/2 (100)	

Chrissian et al Ann Thorac Surg 2011;92:284 –9

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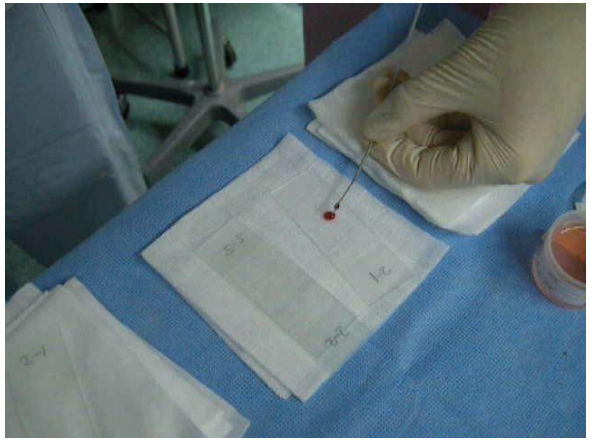
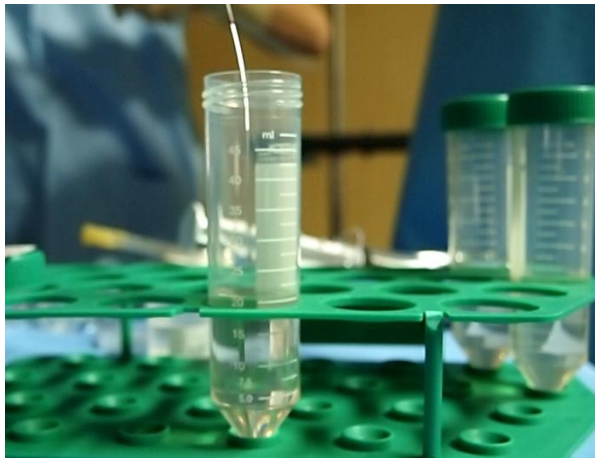
Sample Handling

1.



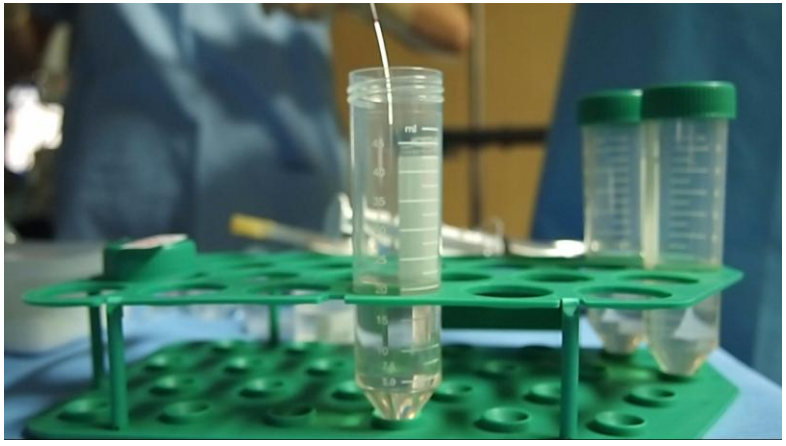
Cytology slide

Tissue core in 10% formalin



Cell-block

2.

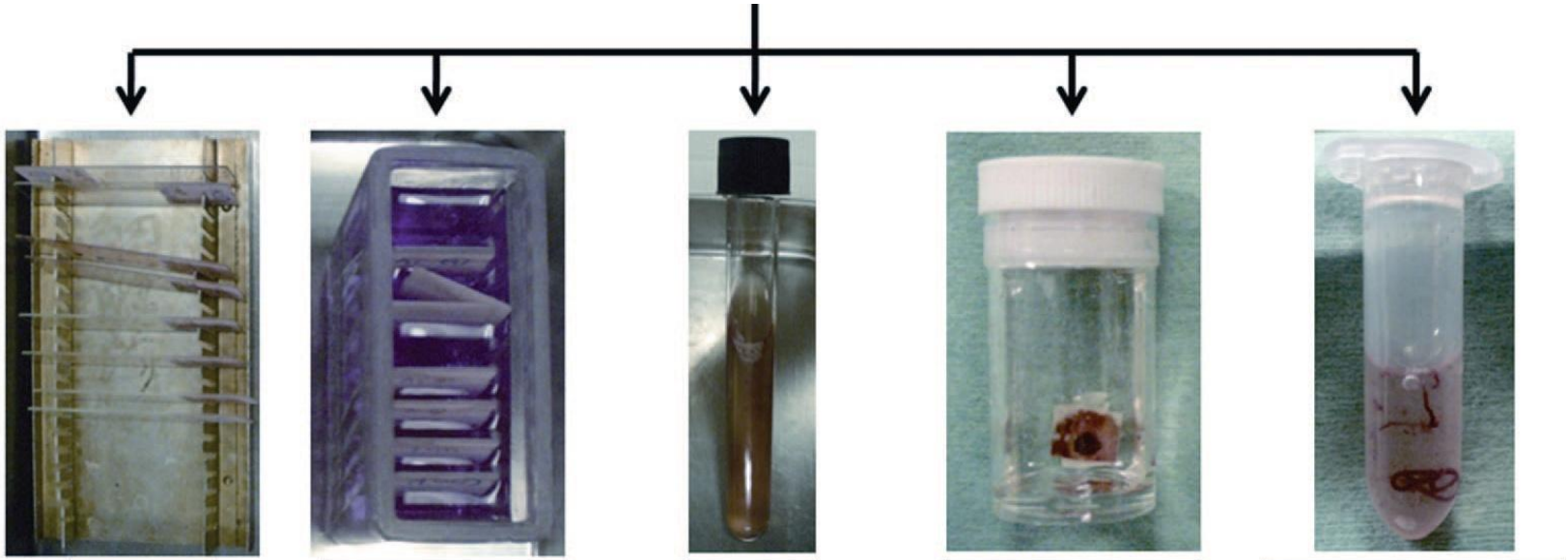


Cell-block

Others; in saline for microbiology
or flow cytometry
storage in -80°

Sample Handling

How I Do It: Yasufuku et al J Thorac Oncol. 2011;6: 203–206)



air-dry
- Diff-Quick®
- Giemsa

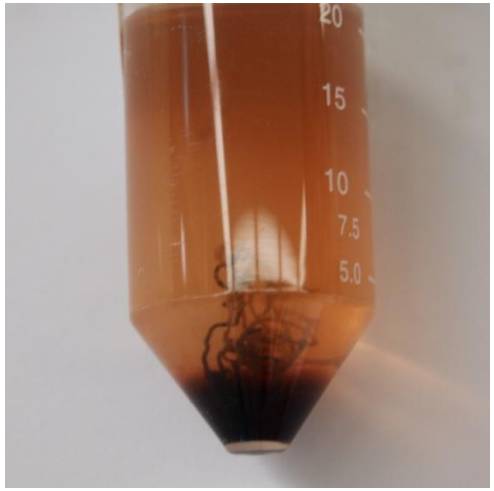
95% ethanol
- Papanicolaou

saline
- Microbiology
- Cell block
- Flow cytometry
- DNA/RNA

10% formalin
- Histology
- IHC
- FISH
- DNA/RNA

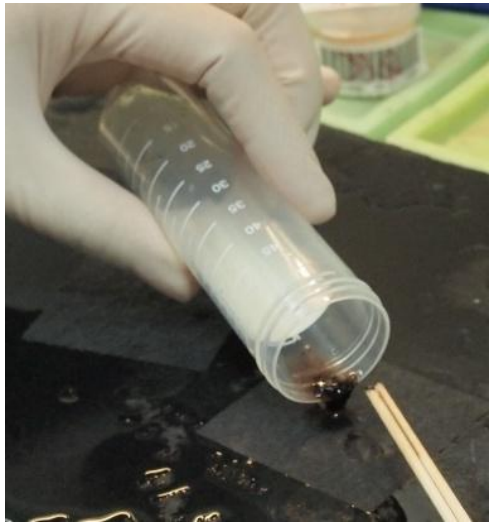
storage in -80°C
- DNA/RNA
- Protein

Sample Preparation



centrifuge →

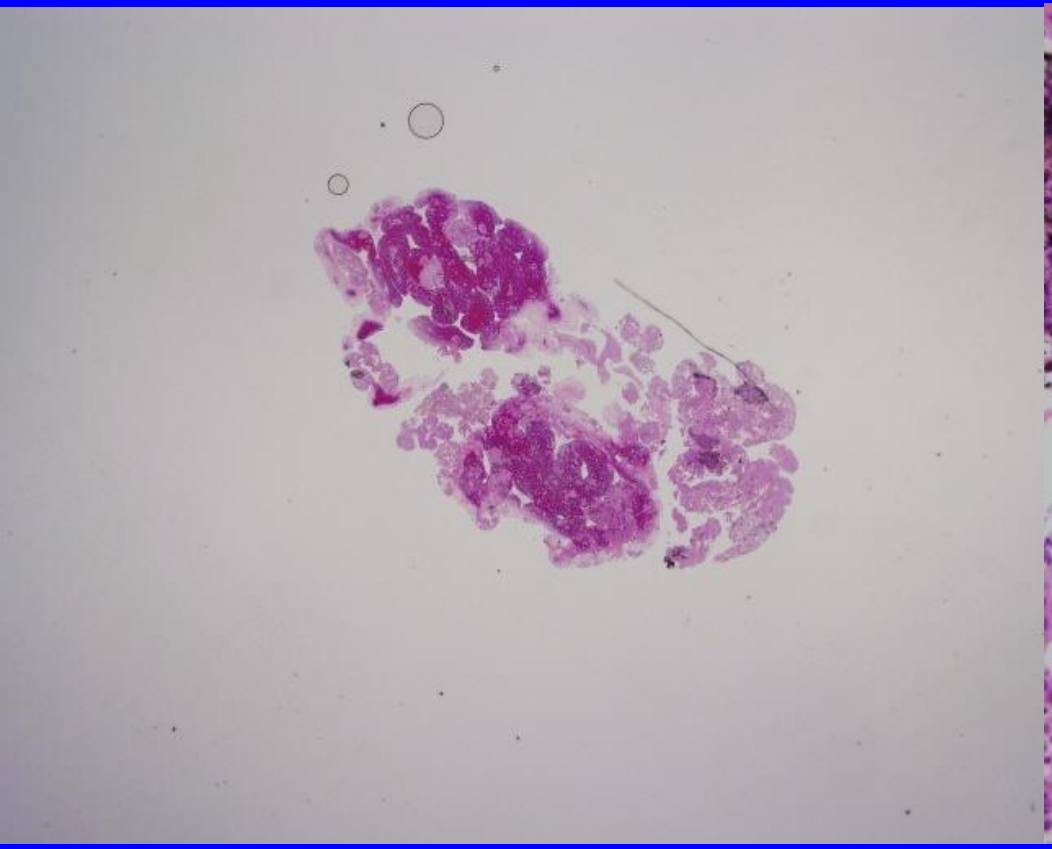
→

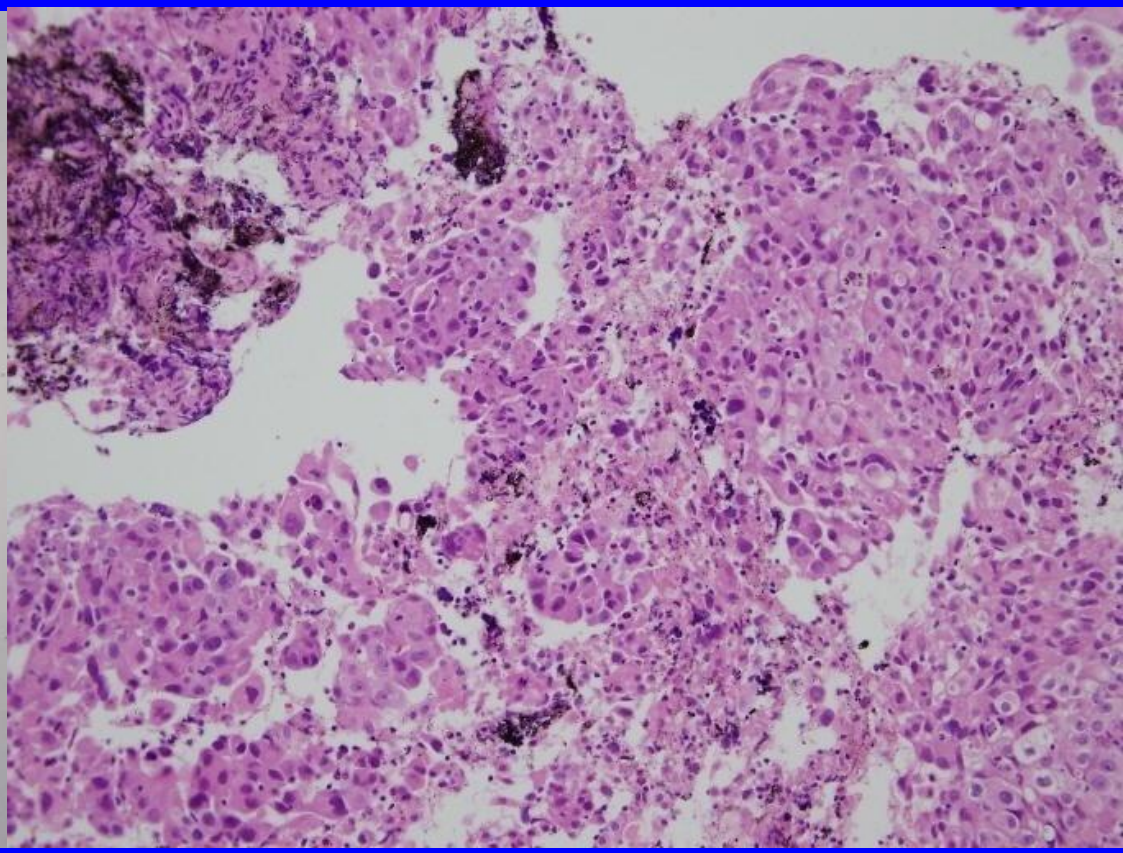


→

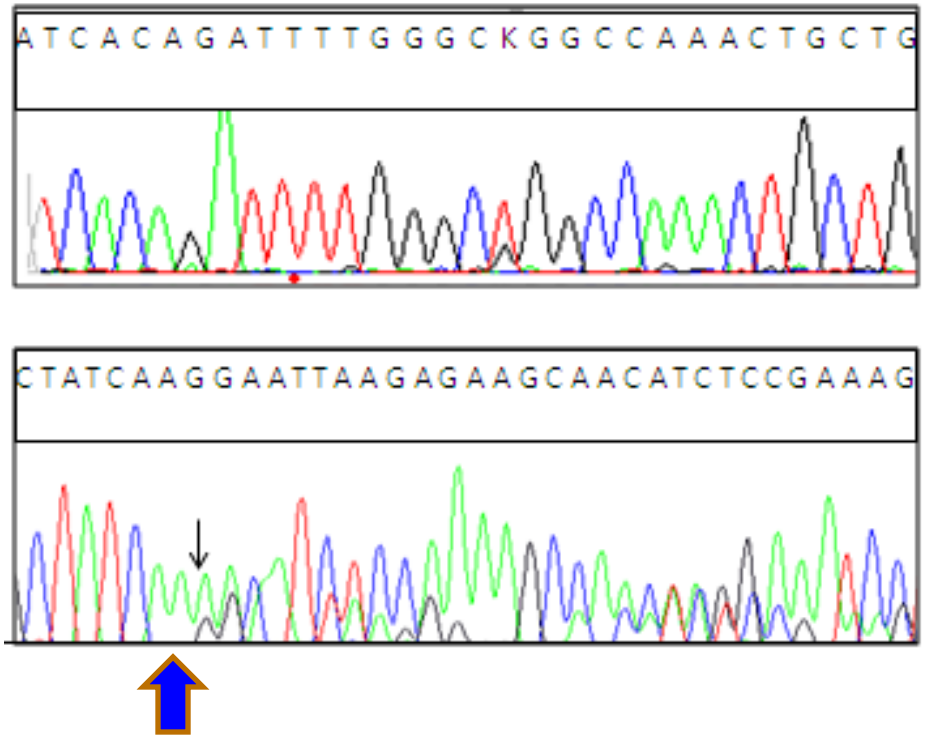
→

EBUS-TBNA specimen; by cell-block



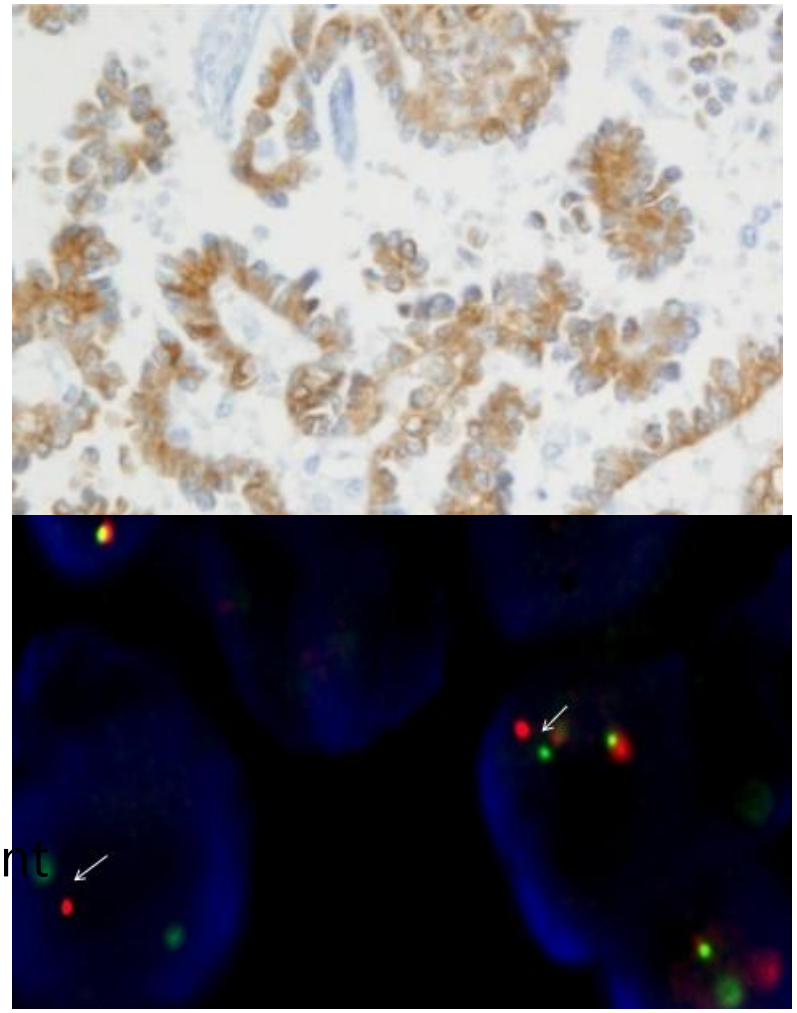


EBUS-TBNA; EGFR mutation Analysis & biomarker studies



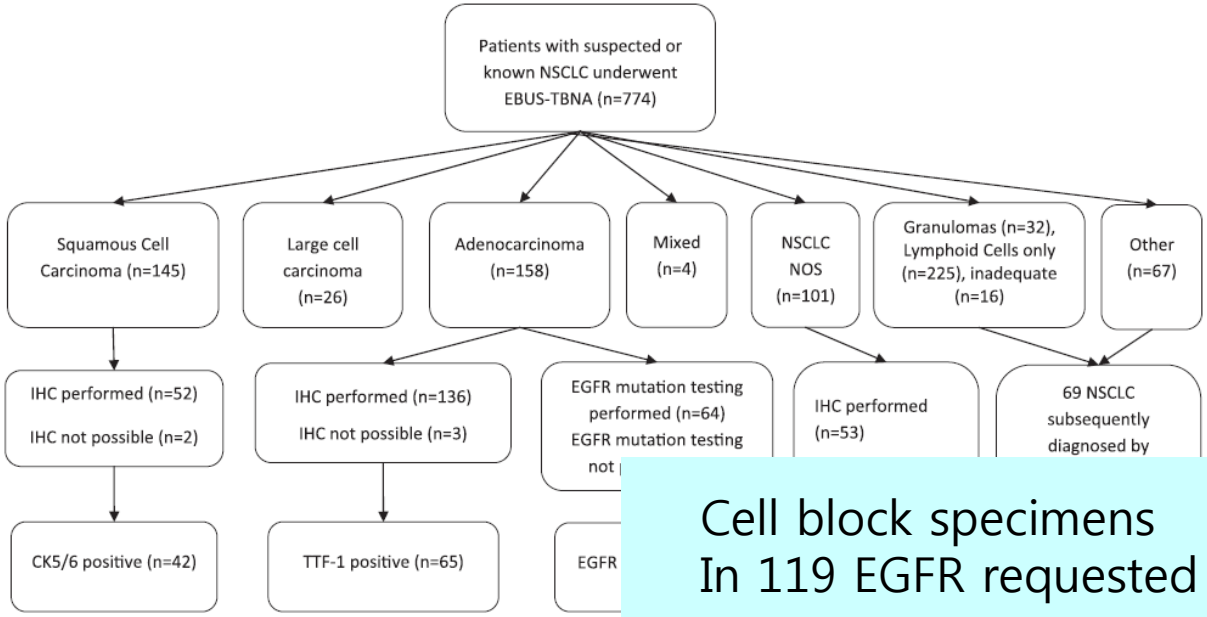
EGFR mutation

ALK rearrangement



Suitability of Endobronchial Ultrasound-guided Transbronchial Needle Aspiration Specimens for Subtyping and Genotyping of Non–Small Cell Lung Cancer

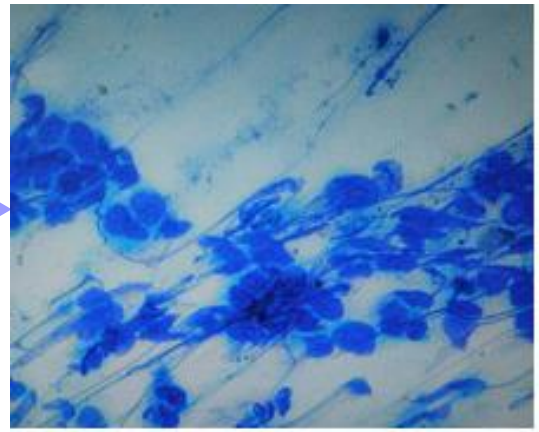
A Multicenter Study of 774 Patients



Cell block specimens
In 119 EGFR requested pts→ possible in 90%(107)

Navani et al. Am J Respir Crit Care Med 2012 Vol 185, Iss. 12, pp 1316–1322

Rapid On-site Cytopathologic Examination (ROSE)



- In the bronchoscopy unit
- Preliminary rapid diagnosis
- Affect on more procedures; ↓ number of aspirations, other procedures
- Cost, time

Rapid On-Site Cytologic Evaluation During Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for Nodal Staging in Patients With Lung Cancer

Table 4. Comparison of the Result of Rapid On-Site Evaluation (Diff-Quick) and Final Diagnosis

Rapid On-Site Evaluation (Diff-Quik)	EBUS-TBNA Results (H&E/Papanicolaou)		
	Positive	Negative	Total
Positive	194	0	194
Negative	25	219	244
Total	219	219	438

Concordance = 94.3%, sensitivity = 88.6%, specificity = 100%, negative predictive value = 89.8%.

Nakajima et al. Ann Thorac Surg 2012 in press

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Complications of EBUS-TBNA

0.15% by a meta-analysis

1.44 % by a large (n=1317) registry

1. Minute bleeding
2. Hematoma
3. Pnemo-mediastinum
4. Infection : ex) Mediastinitis, abscess, pericarditis
5. Granulation tissue
4 Related to bronchoscopy itself & other procedures
   ex) hypoxia, pneumothorax

Complications; Bleeding

- Minute endobronchial bleeding
- Mild mediastinal bleeding or lymph node bleeding
- Severe bleeding; very rare

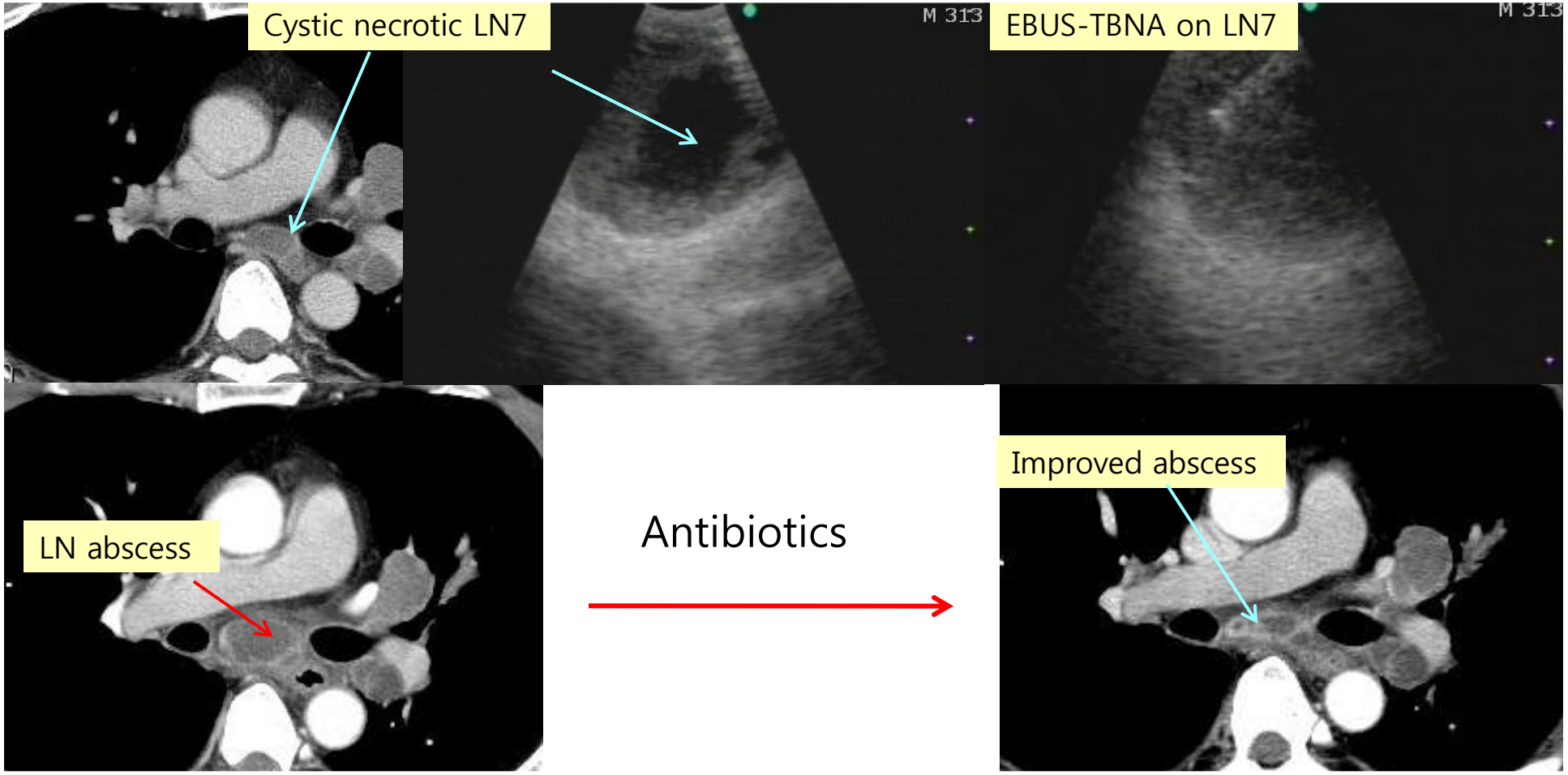
- 12 case series; safe EBUS-TBNA in patients using Clopidogrel

Stather et al Respiration 2012;83:330-4

- Avoid use of aspirin or anticoagulant if possible

Complications : Abscess on a Cystic Lymph Node

M/59, SCC LUL

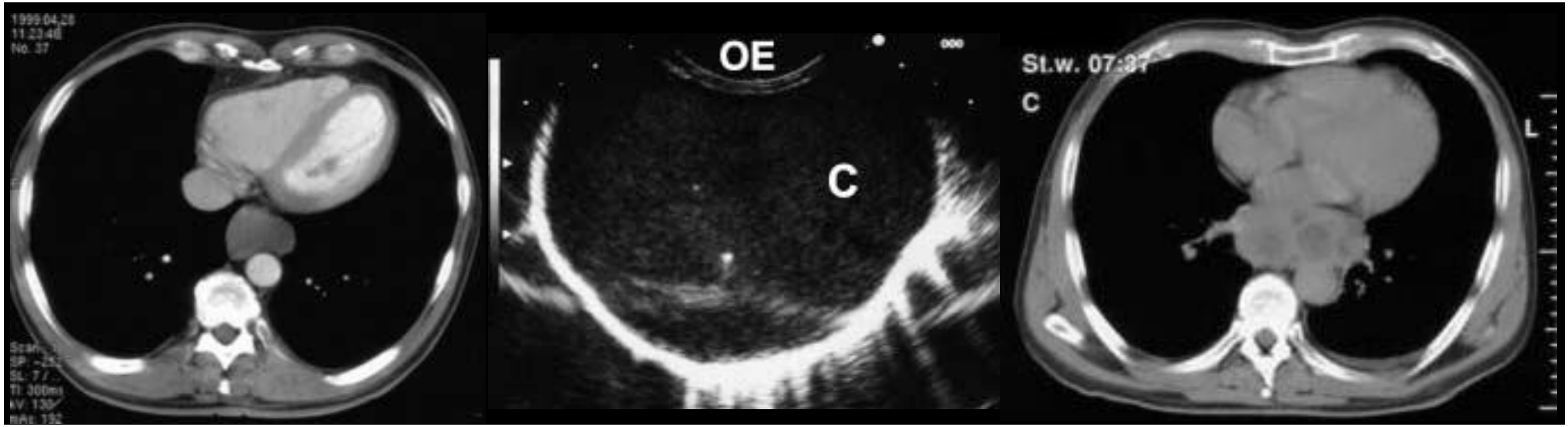


6 days after EBUS-TBNA

19 days after EBUS-TBNA

Infectious Complications following EUS-FNA

Mediastinitis Caused by EUS-FNA of a Bronchogenic Cyst



Annema et al Endoscopy 2003 35-p791

Infections on cystic pancreas lesions: up to 14%

→ EUS-FNA on cystic lesions : prophylactic antibiotics

Infectious Complications following EBUS-TBNA

- Prophylactic Antibiotics for EBUS-TBNA ?

  No consensus

  Targeting oral organisms

  Special consideration ; cystic, avascular anthracotic or necrotic lesion

  immuno-compromised, DM

- Bacteremia following EBUS-TBNA 3/43(7%)

  oropharyngeal commensal organisms

  No clinical features of infection

Steinfort et al ERJ 2010;38

Complications, Consequences, and Practice Patterns of Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration: Results of the AQuIRE Registry

Outcome	No. of Events (N = 1,317)	Complication Rate (% with 95% CI)
Any complication within 24 h	19	1.44 (0.87-2.24)
Bleeding requiring intervention*	3	0.2 (0.05–0.7)
Pneumothorax	7	0.53 (0.21–1.1)
Clinically significant airway injury	1	
Sustained hypoxia	4	
Hypotension	1	
Cardiac arrest	0	
Arrhythmia	0	
Respiratory failure within 24 hours	3	0.23 (0.05-0.7)

Transbronchial biopsy performed			
No	1,117 (98.8)	13 (1.2)	
Yes	181 (96.8)	6 (3.2)	0.04

Eapen et al Chest in press

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Learning Curve

Table 3. Diagnostic Ability of Endobronchial Ul

	Sensitivity
Overall diagnosis	
First 10	44.4%
Next 46	94.1%
Total	83.7%
Cancer diagnosis	
First 10	16.7%
Next 46	96.2%
Total	81.3%

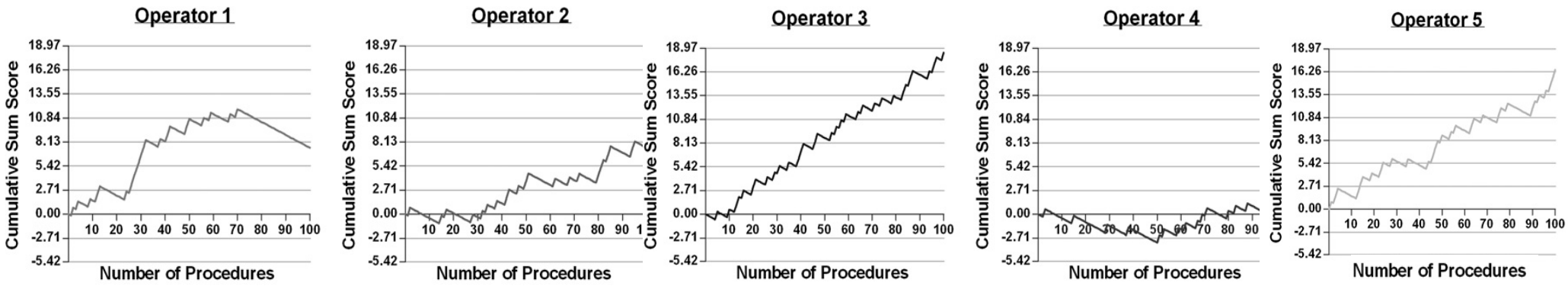
Goth et al. Ann Thorac Surg 2008; 86:1104-9

Table 2 The diagnostic yield of linear EBUS for all procedures, malignancy or benign disease

	Sensitivity (CI)
All procedures (n = 200)	87.41 % (80.76–91.99)
0–25 procedures	82.35 % (58.97–93.81)
26–50 procedures	81.25 % (56.99–93.41)
51–75 procedures	88.24 % (65.66–96.71)
76–100 procedures	87.5 % (63.98–96.5)
101–125 procedures	86.67 % (62.12–96.26)

Abu-Hijleh et al. Lung (2013) 191:109–115

Learning curves for endobronchial ultrasound using cusum analysis



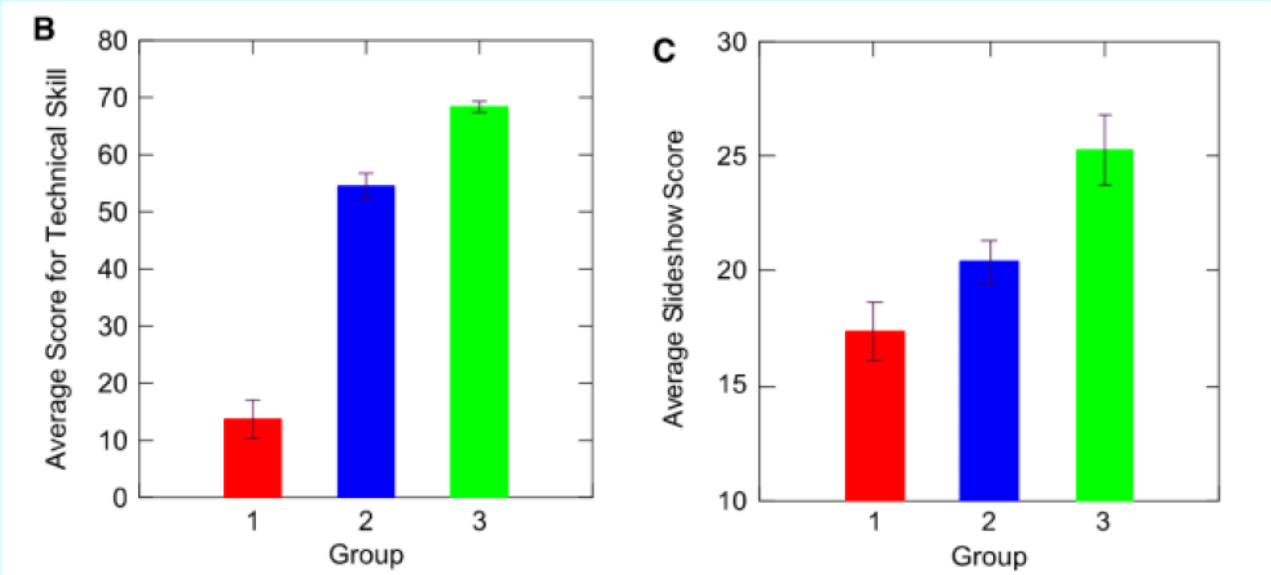
- 5 operators, first 100cases
  a wide range of time over competence is attained

- The pooled sensitivity; 67.4%
  (individual sensitivities 66.7, 70.7, 61.2, 80.3 and 59.7%).

Kemp et al.Thorax 2010;65:534e538.

Endobronchial Ultrasound Skills and Task Assessment Tool

- Assessing the validity evidence for a test of EBUS-TBNA operator skills
- 10 items; 1-7 Technical skills,
  8-10 25 images slide show
  EBUS images, anatomic orientation & correlation



Differences between groups

Beginner
Intermediates
experienced

Davoudi et al AJRCCM 2012 (186) 773-779

Summary

- ♥ EBUS-TBNA; well be done under conscious sedation
- ♥ Technical & practical considerations

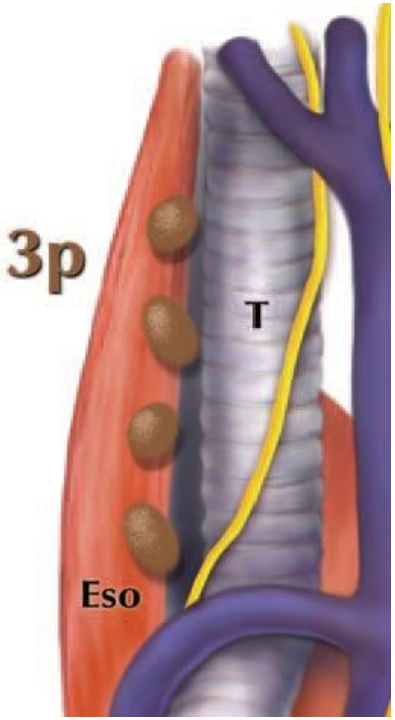
  proper sedation & local anesthesia

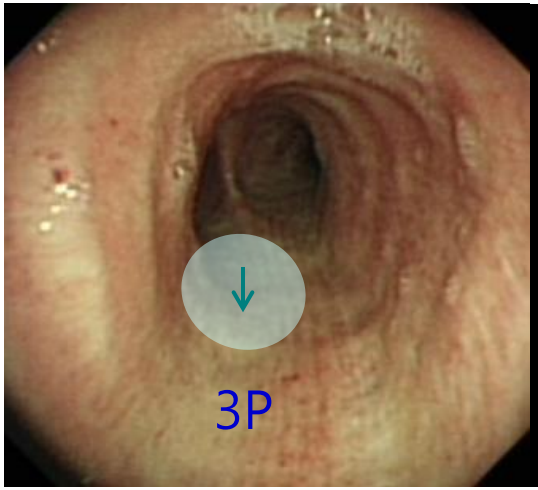
  bronchoscope & needle handling

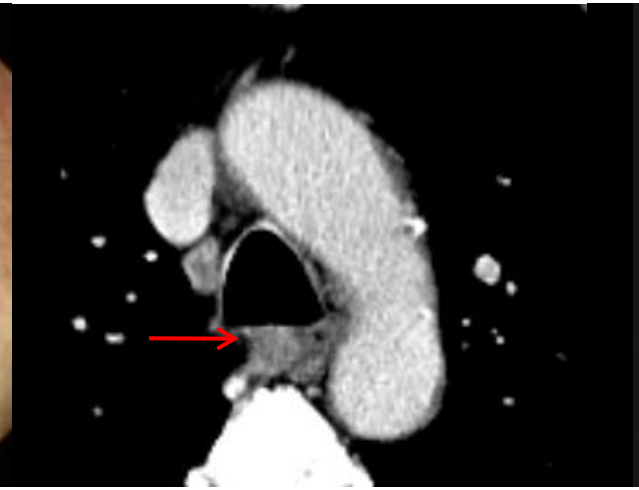
  understanding of US images & target selection

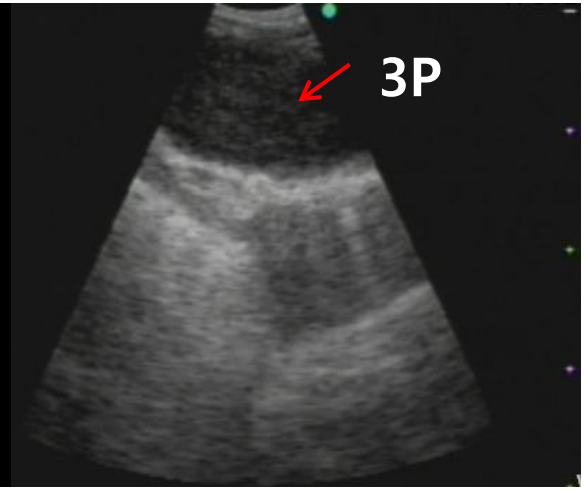
  sample handling
- ♥ Try to avoid complications

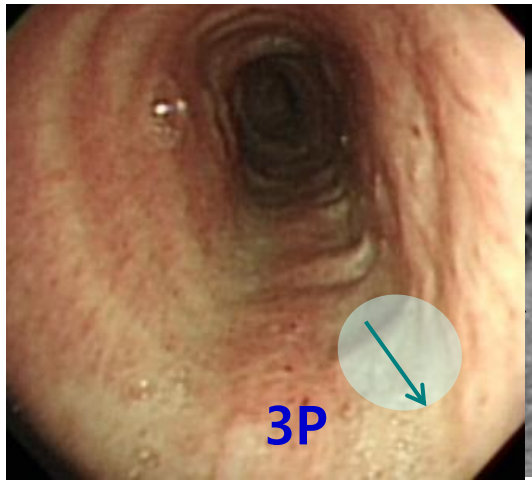
IASLC LN Classification ; Ambiguous Locations **Station 3p**

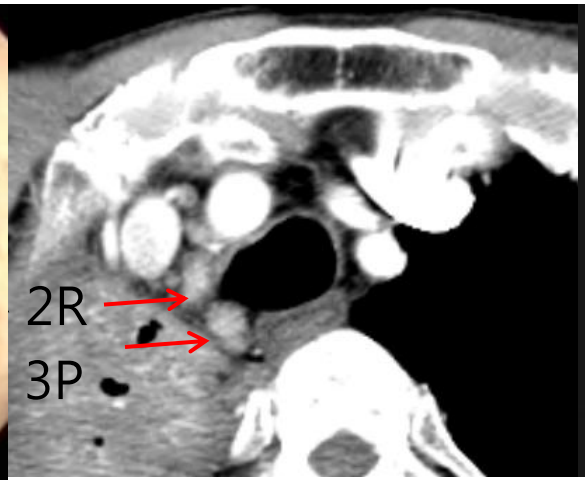


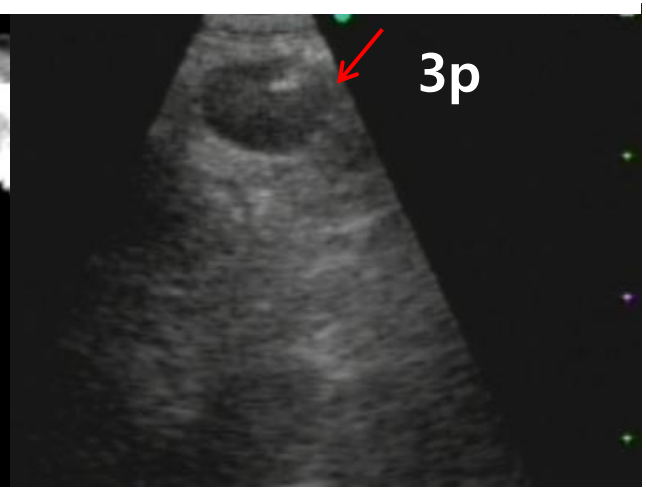










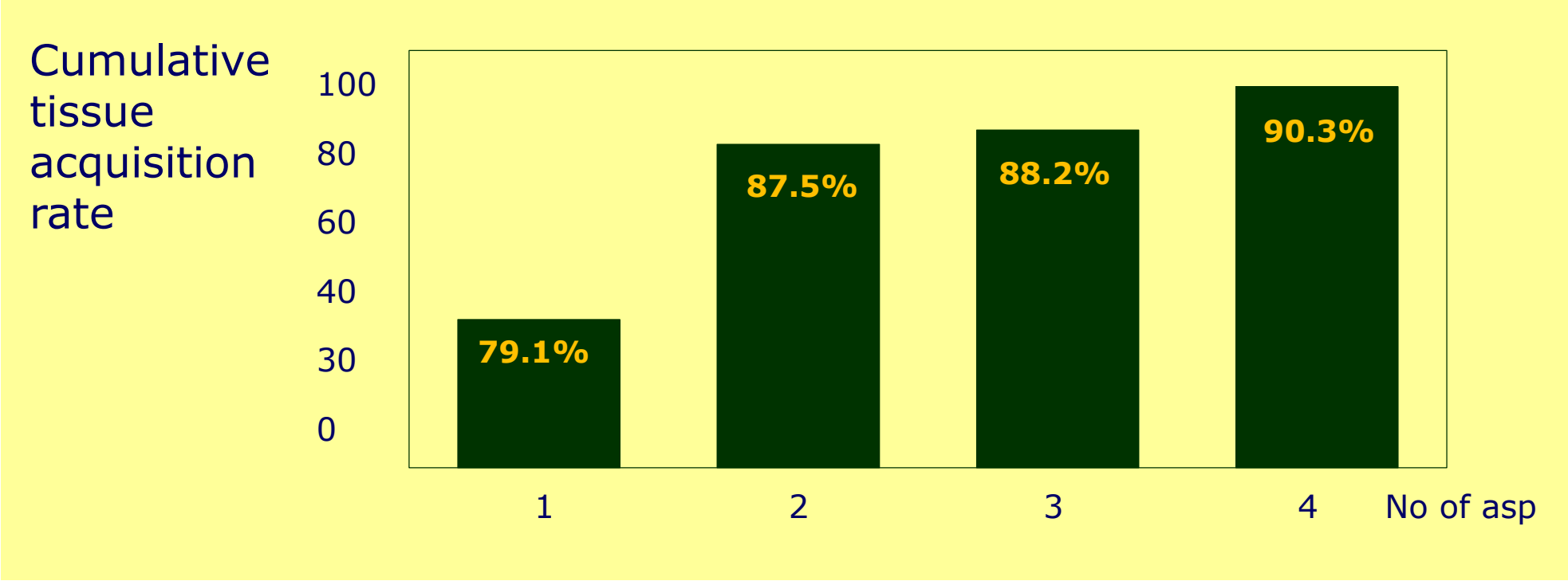


Tissue Acquisition Rate by EBUS-TBNA in Lung Ca Diagnosis

107 lung ca pts

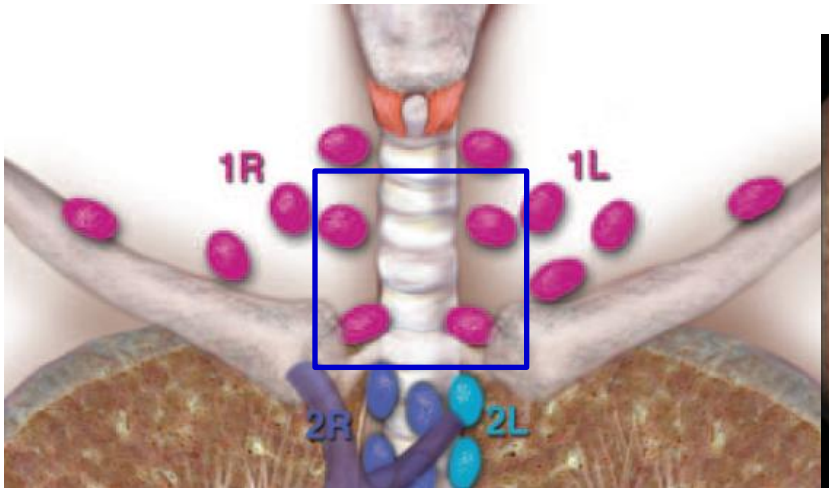
144 cancer lesions (26 mass, 118 LNs)

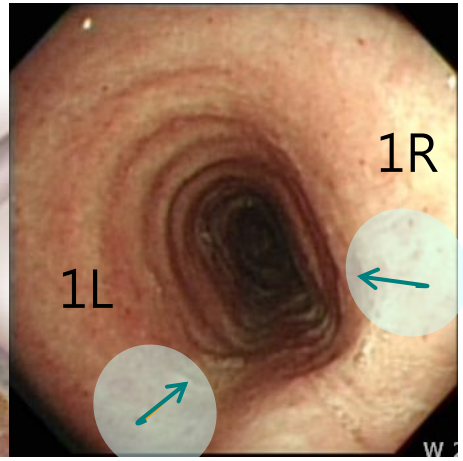
2.34 aspiration/ lesion, tissue acquisition 79.8%/aspiration

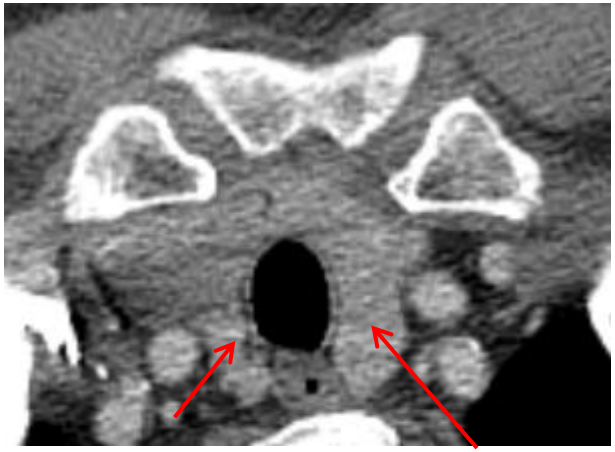


NCC data

IASLC LN Classification ; Ambiguous Locations **Station 1**

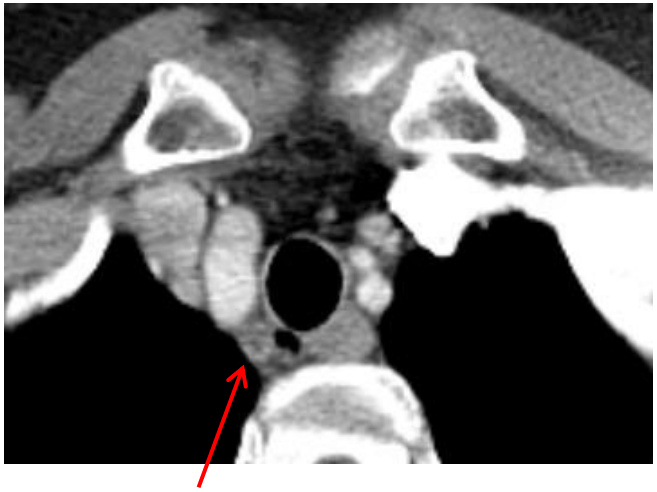






thyroid

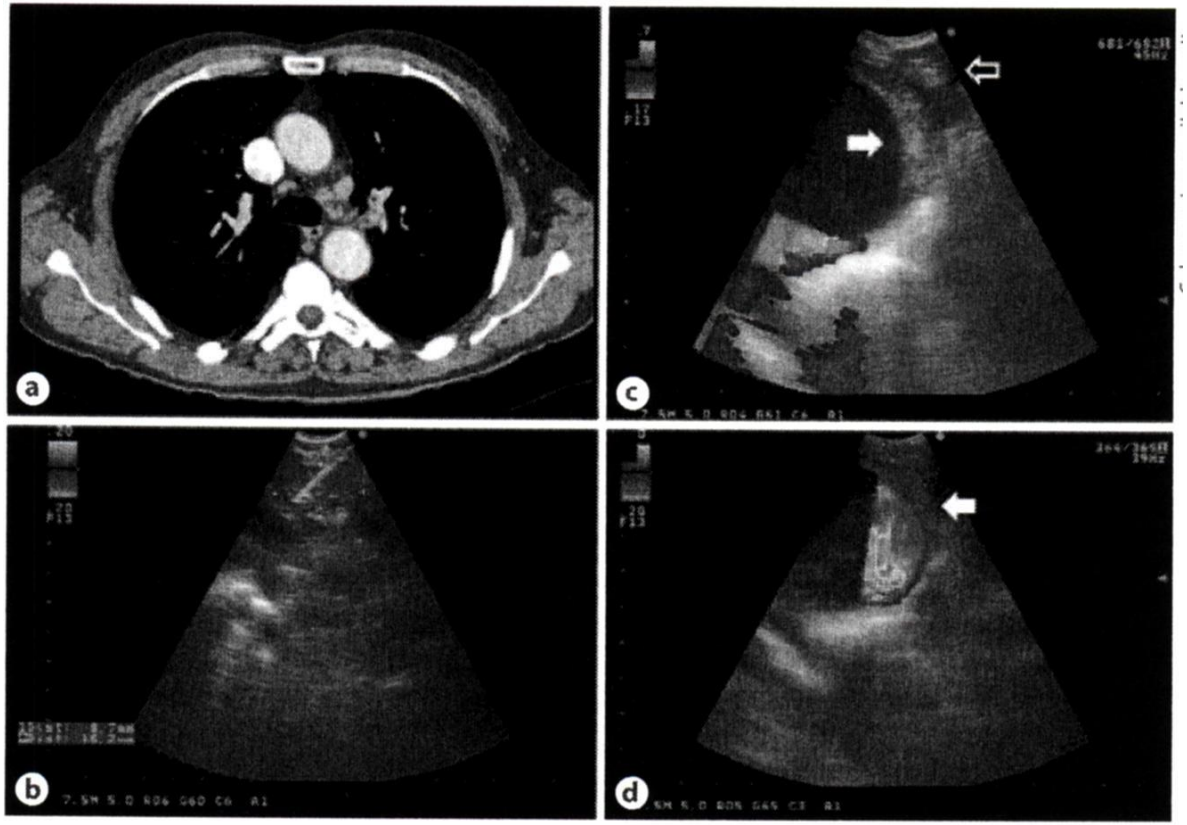
2R



1R

Complications; Bleeding

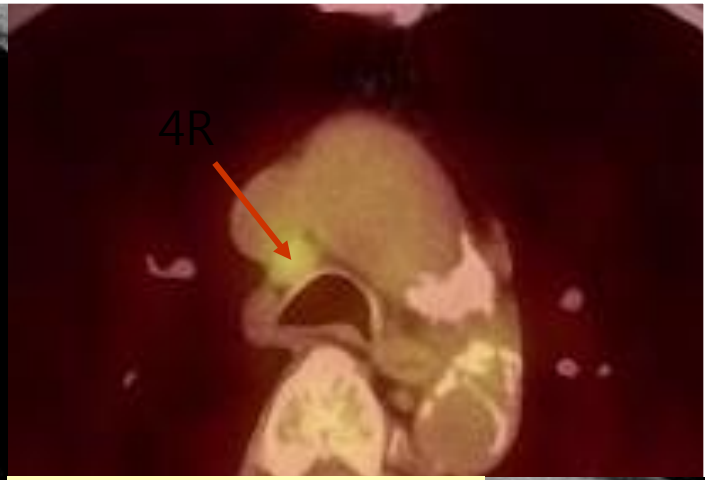
Intramural Hematoma of the Pulmonary Artery and Hemopneumomediastinum after Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration



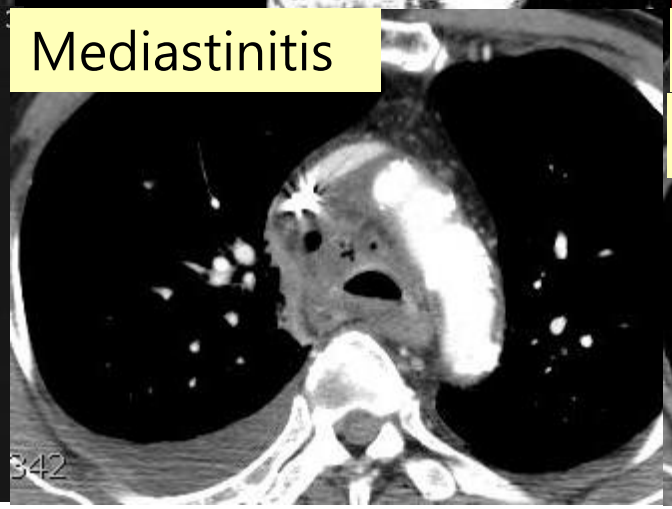
Botana-Rial M et al
Respiration. 2011 Nov 29

Complications : Mediastinitis

M/82, Adenoca, DM for 20 yrs, planning for proton therapy



Mediastinitis



Op & antibiotics

Actinomyces odontolyticus