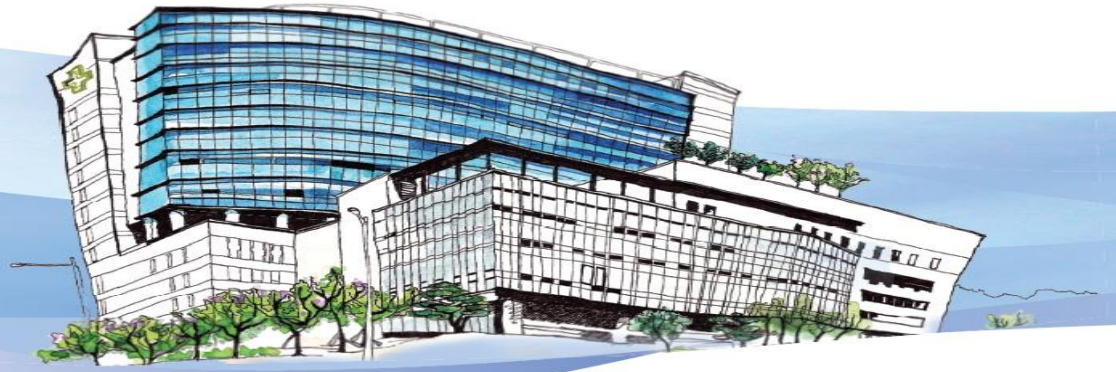


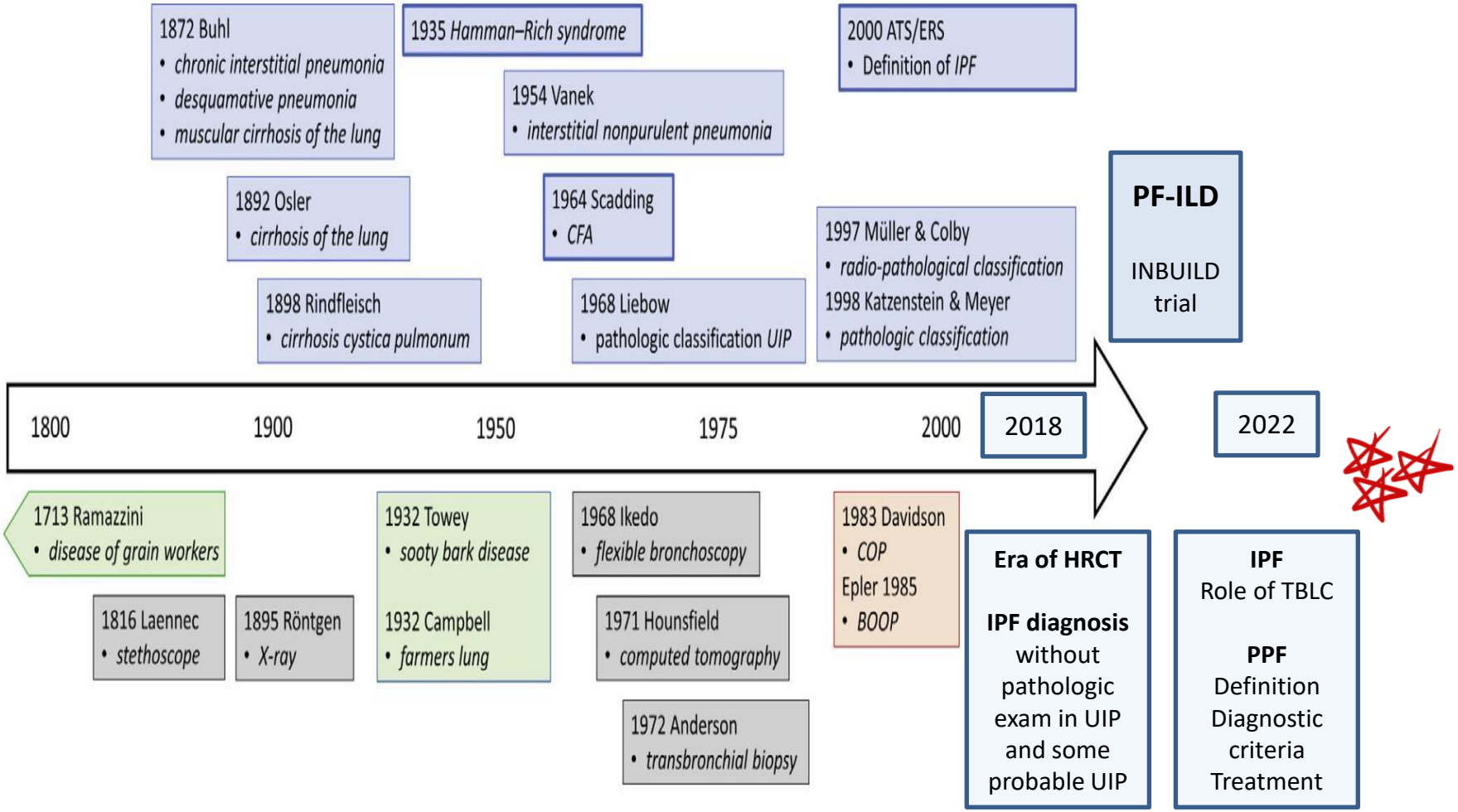
Transbronchial Lung Cryobiopsy for ILD

해운대백병원

이재하

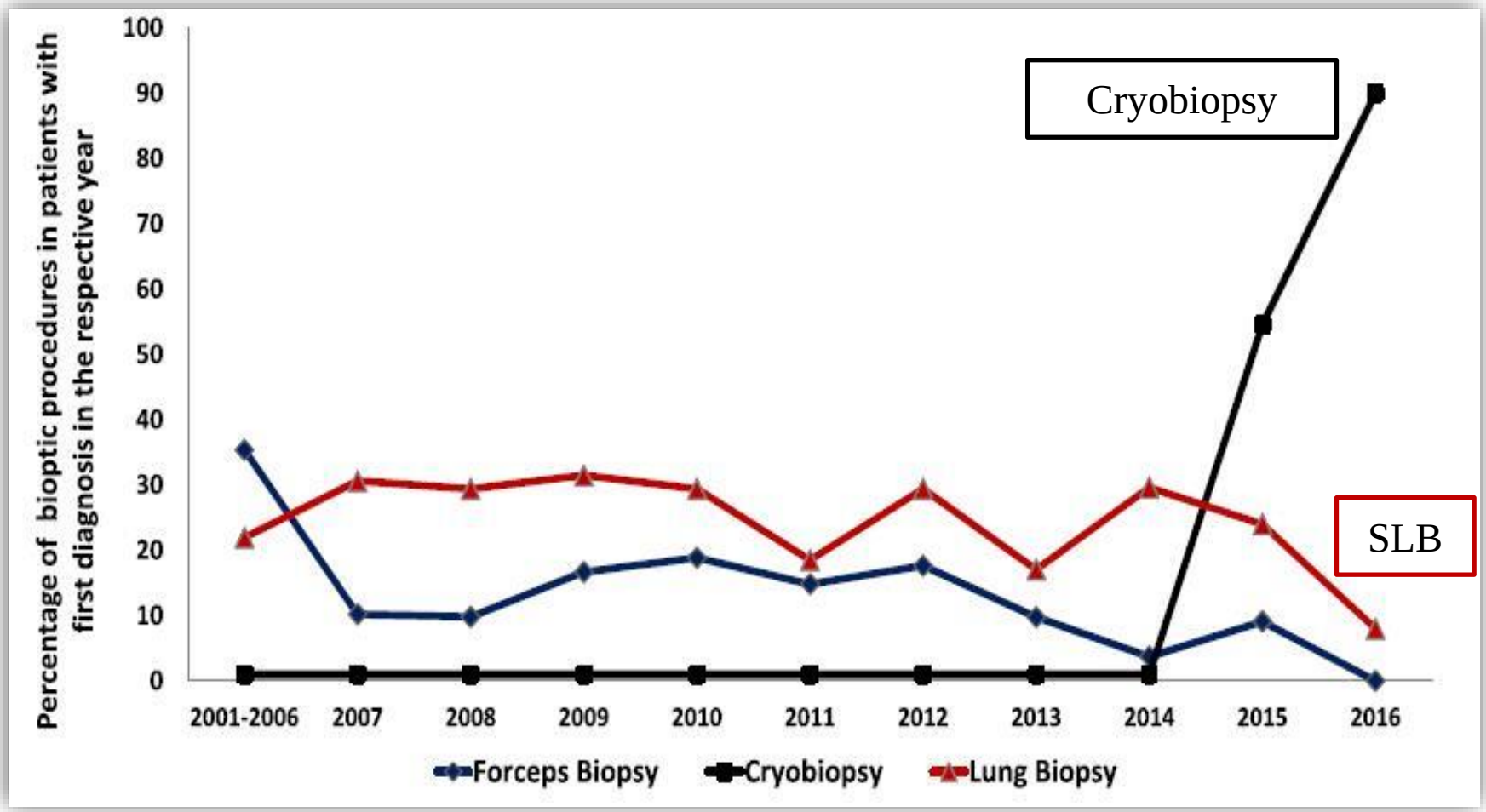
INJE UNIVERSITY
HAEUNDAE PAIK HOSPITAL

History of Interstitial lung disease



Clin Chest Med(2021) 42;229-239

Procedure in IPF at the first diagnosis



Respirology Research (2018) 19:141

TBLC vs SLB in guidelines (2018)

	2018 Guideline	
	HRCT Pattern of Probable UIP*, Indeterminate for UIP, and Alternative Diagnosis	HRCT Pattern of UIP*
BAL cellular analysis	We suggest performing BAL cellular analysis (conditional)	We suggest *NOT* performing BAL cellular analysis (conditional)
Surgical lung biopsy	We suggest performing surgical lung biopsy (conditional)	We recommend *NOT* performing surgical lung biopsy (strong)
Transbronchial lung biopsy	No recommendation was made either for or against transbronchial lung biopsy	We recommend *NOT* performing transbronchial lung biopsy (strong)
Lung cryobiopsy	No recommendation was made either for or against cryobiopsy	We recommend *NOT* performing cryobiopsy (strong)

AJRCCM 2018; 198

[Thoracic Oncology Guidelines and Consensus Statements]

CHEST

Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Diseases

CHEST Guideline and Expert Panel Report

- In patients with suspected interstitial lung disease (ILD), we suggest that transbronchial cryobiopsy (TBC) can be used to provide histopathologic findings for multidisciplinary discussion diagnosis

  (Weak Recommendation, Very Low-Quality Evidence)

- The choice between **TBC** and surgical lung biopsy **(SLB)** should be based on **local availability** and **expertise**, **benefit-risk assessments**, and **patient preference following informed consent.**

CHEST 2020;157(4)2:1030-1042

IPF and PPF guideline (an Update 2022)

- We suggest that TBLC be regarded as an acceptable alternative to SLB for making a histopathological diagnosis in patients with ILD of undetermined type in medical centers with experience performing and interpreting TBLC (conditional recommendation, very low quality evidence).

- Increased evidence of additional studies after the 2018 guideline

AJRCCM 2022;205(9):e18-e47

IPF and PPF guideline (an Update 2022)

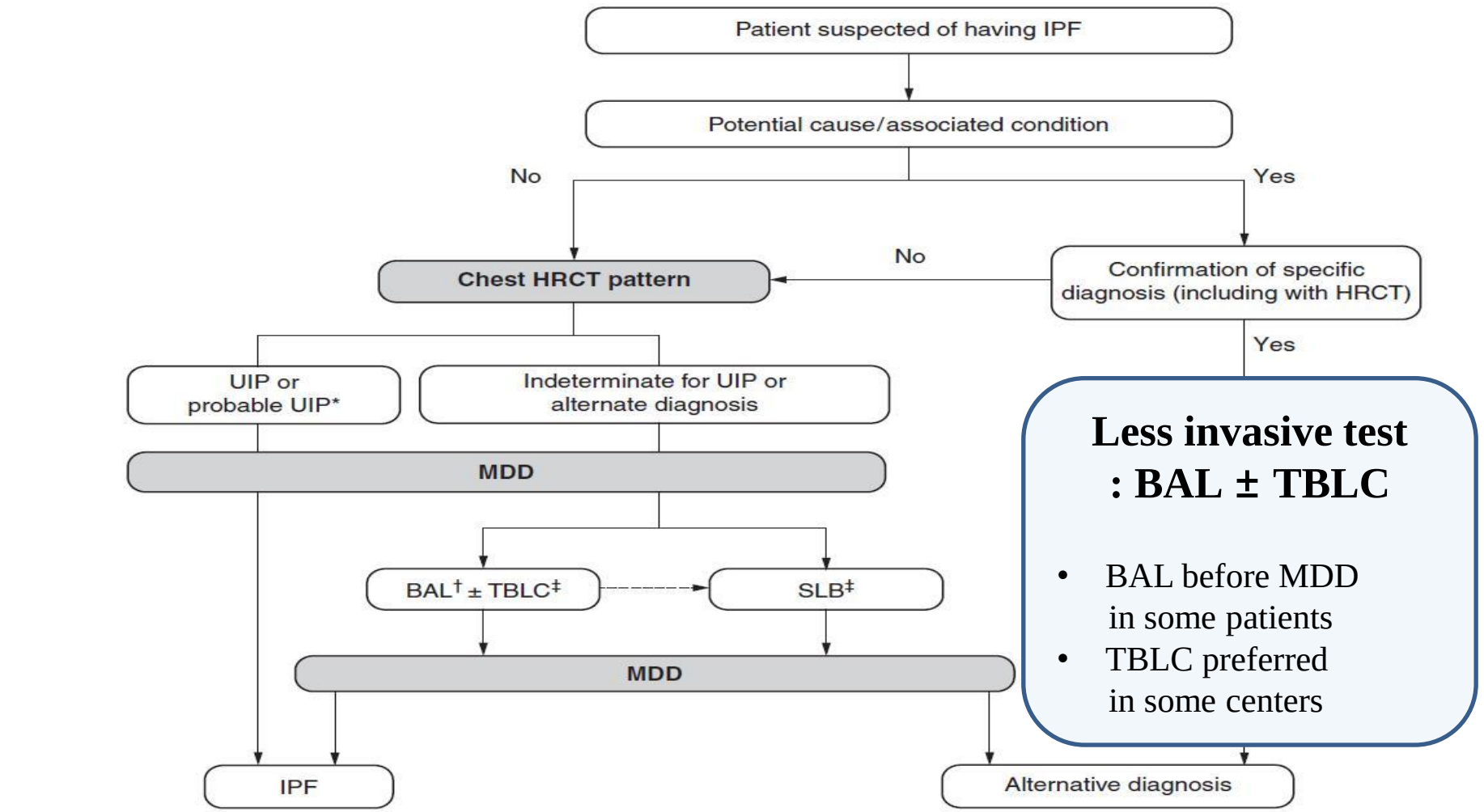
- **Diagnostic yield**: 79% (no difference across subgroup), 85% (when three or more samples) / 77% (when fewer samples)

- **Diagnostic agreement between SLB and TBLC**: 70.8 % (76.9% after MDD), 38% (small study)

- **Complications**: Pneumothorax in 9% (←20-25%) and any bleeding in 30% (severe bleeding (1.6%) – usually well controlled by endobronchial balloon blocker, procedural mortality (0.6% vs 1-15%), acute exacerbation (1.4%), respiratory infections and persistent air leakage: rare)

AJRCCM 2022;205(9):e18-e47

IPF and PPF guideline (an Update)



AJRCCM 2022;205(9):e18-e47

Relative contraindications for TBLC

- Severe lung function derangement (FVC<50%, DLco <35%)
- Moderate to severe pulmonary hypertension (estimated systolic pulmonary arterial pressure>40mmHg)
- Uncorrectable bleeding risk
- Significant hypoxemia (PaO2<55-60mmHg)

- Emerging data regarding the safety and diagnostic yield of TBLC in patients in whom SLB would not be performed because of significant lung function impairment or comorbidities

AJRCCM 2022;205(9):e18-e47

Characteristics in TBLC

Location	Duration	Patients	Setting/ Design	Cryoprobe	Samples	Type of Sedation	Fluoroscopy
United States	N/A	40	Retrospective	1.9 mm	Unknown	General anesthesia	Yes
Spain	5 yr	257	Prospective	1.9 mm/2.4 mm	Unknown	General anesthesia	Yes
United States	3 yr	36					Yes
Spain	2 yr	10					Yes
Belgium	1 yr						Yes
France	3 yr						Yes
Spain	3 yr						Yes
United States	3 yr						Yes
Turkey	N/A						Yes
United States	4 yr						Yes
India	2 yr					anesthesia	Yes
Spain	2 yr						Yes
Israel	2 yr						Yes
Germany	2 yr						Yes
Germany	1 yr						Yes
Spain	3 yr						Yes
Germany	N/A					anesthesia	Yes
Japan	1 yr						Yes
Portugal	3 yr						Yes
Denmark	1 yr						Yes
United States	1 yr						Yes
United States	3 yr						Yes
Portugal	2 yr						Yes
Spain	N/A						Yes
Iran	N/A						Yes
Iran	N/A						Yes
United States	1 yr						Yes
Italy	6 yr						Yes
Italy	4 mo						Yes
Italy	2 yr						Yes
Egypt	1 yr						Yes
Australia	N/A	1				ral anesthesia	Yes
Thailand	2 yr	74					Yes
Italy	1 yr	58	Retrospective	2.4 mm	1	Deep sedation	Yes
Australia	N/A	65	Prospective	1.9 mm/2.4 mm	3–7	General anesthesia	Yes
Israel	8 yr	14	Retrospective	2.4 mm	3–7	Deep sedation	Yes
United States	2 yr	74	Retrospective	1.9 mm	3	Deep sedation	Yes
Germany	2 yr	109	Retrospective	1.9 mm/2.4 mm	1–8	General anesthesia	Yes
Italy	3 yr	266	Retrospective	2.4 mm	1	Deep sedation	Yes

- **39 studies (2013 ~2020)**
- **5 prospective and 35 retrospective**
- **Fluroscopy – 100%**
- **General Anesthesia – 18 (46.2%)**
- **Deep Sedation – 18 (46.2%)**
- **Both of GA/DS – 3 (7.6%)**

AnnalsATS 202102-198OC

Deep sedation vs G/A

Deep sedation

- Midazolam (2~5mg IV) + Fentanyl (50~100mcg IV) + PRN adding
- Bronchoscopy room or hybrid room with fluoroscopy guidance
- E-tube + Fogarty balloon catheter
- No anesthesiologist

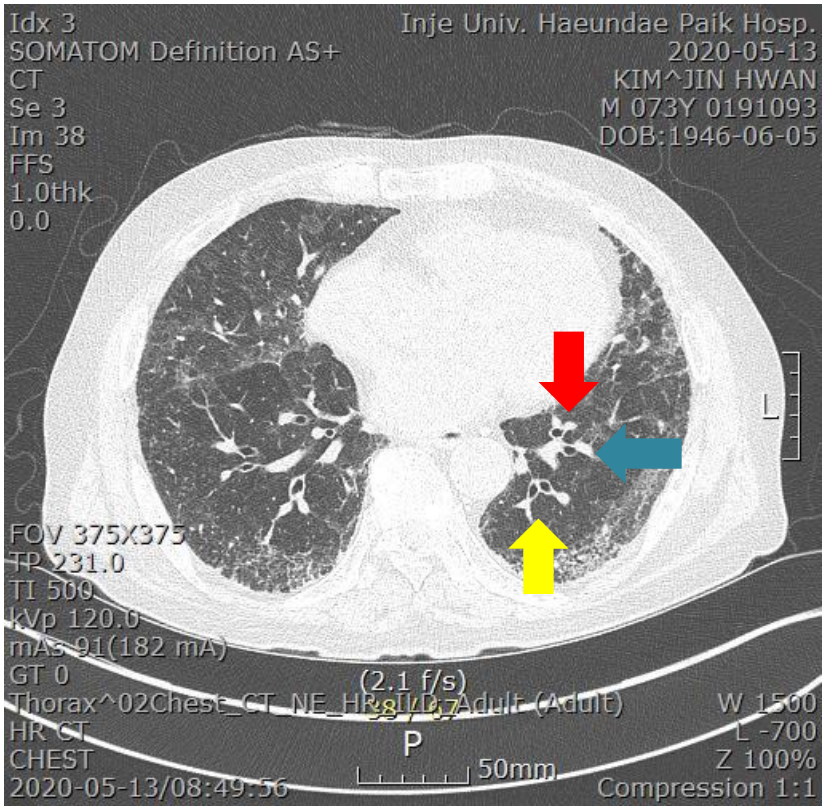
- Short procedure time (10~30min)
- Short recovery time

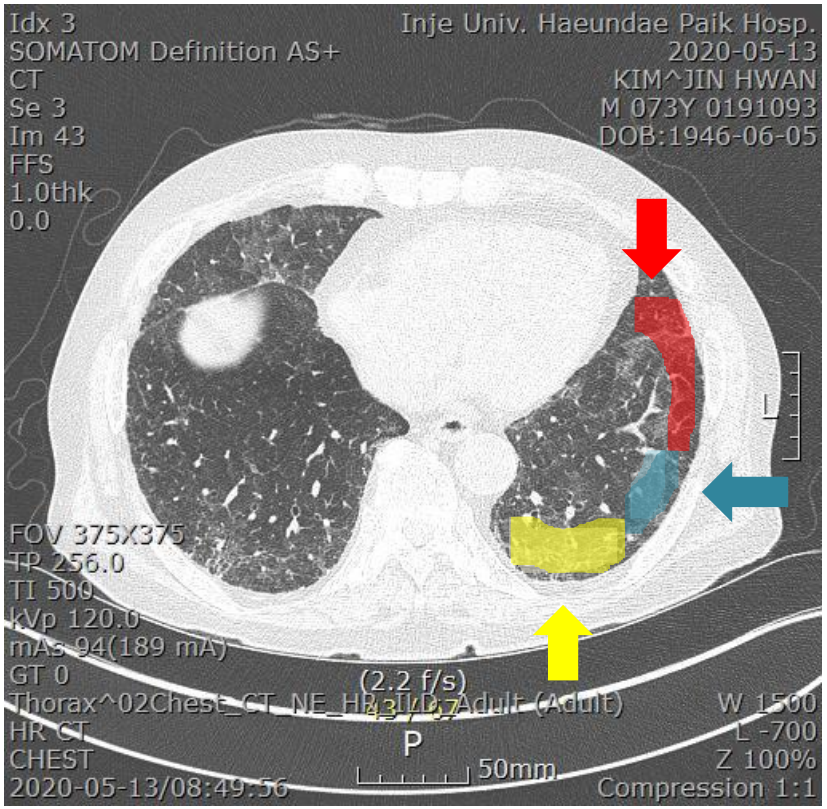
Method of TBLC: Single center experience

Method of TBLC: Single center experience

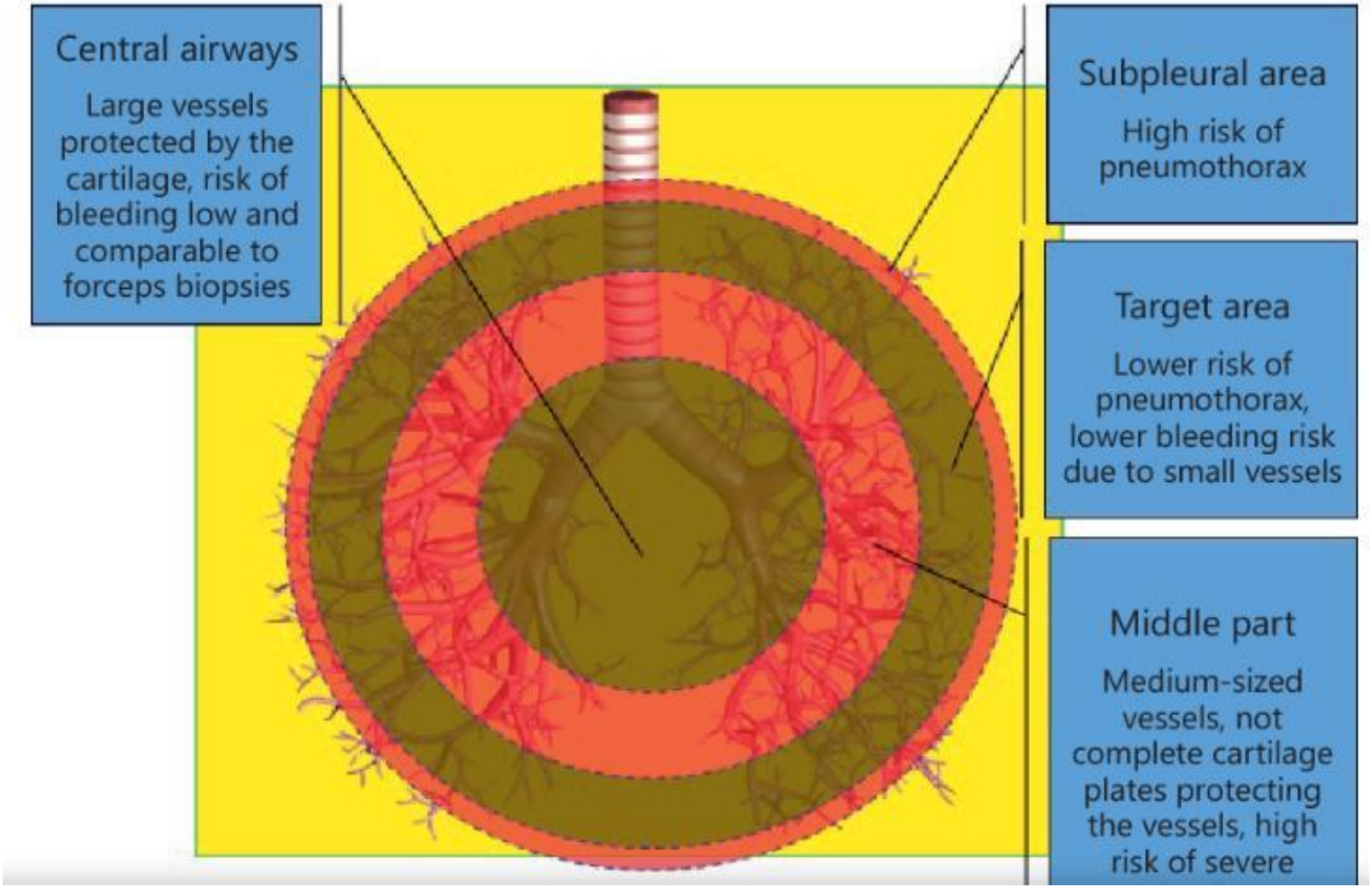
Method of TBLC: Single center experience

Biopsy target lesion (B8-9-10)

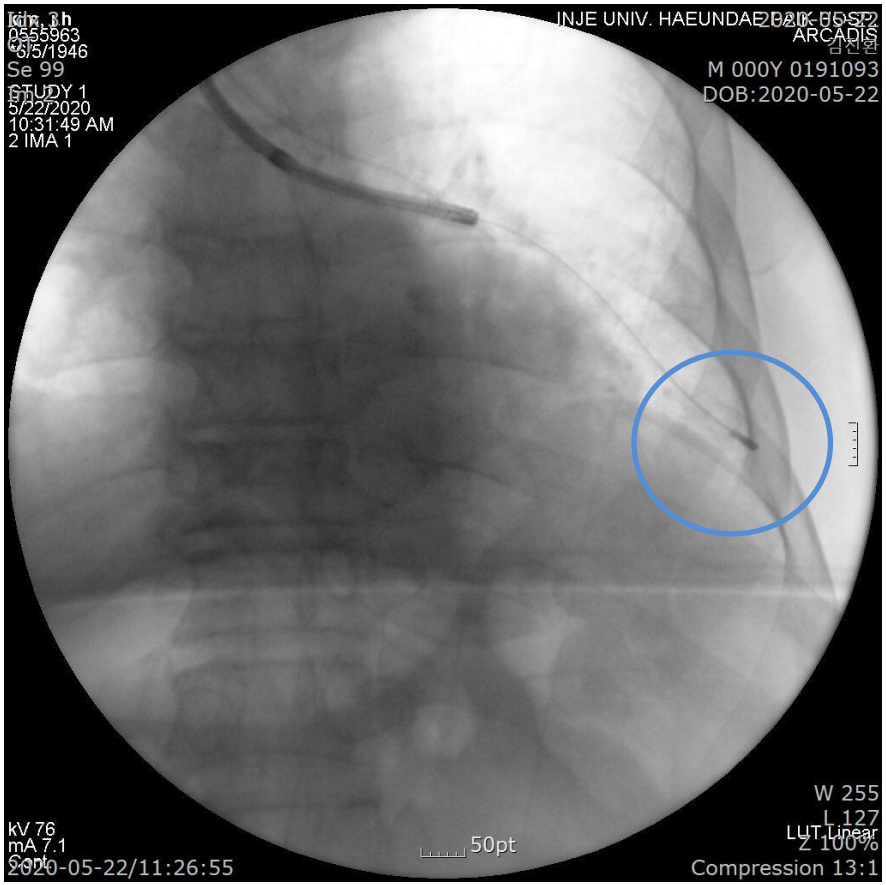


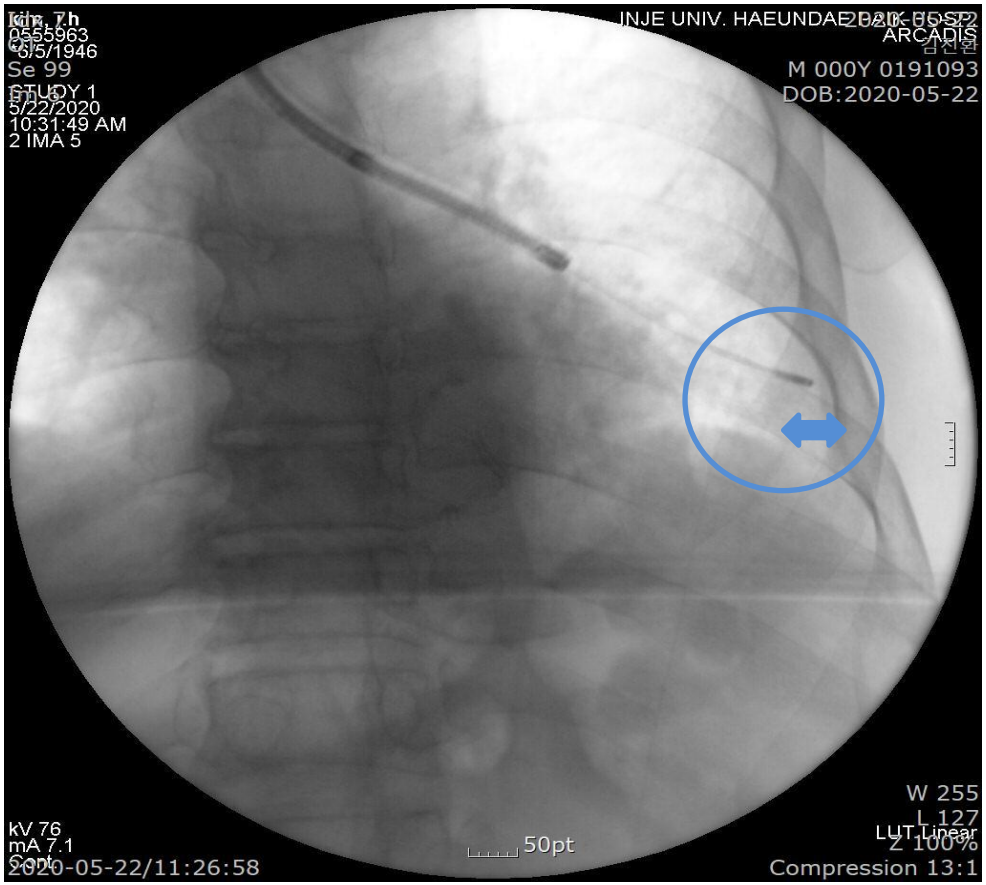


Biopsy target lesion



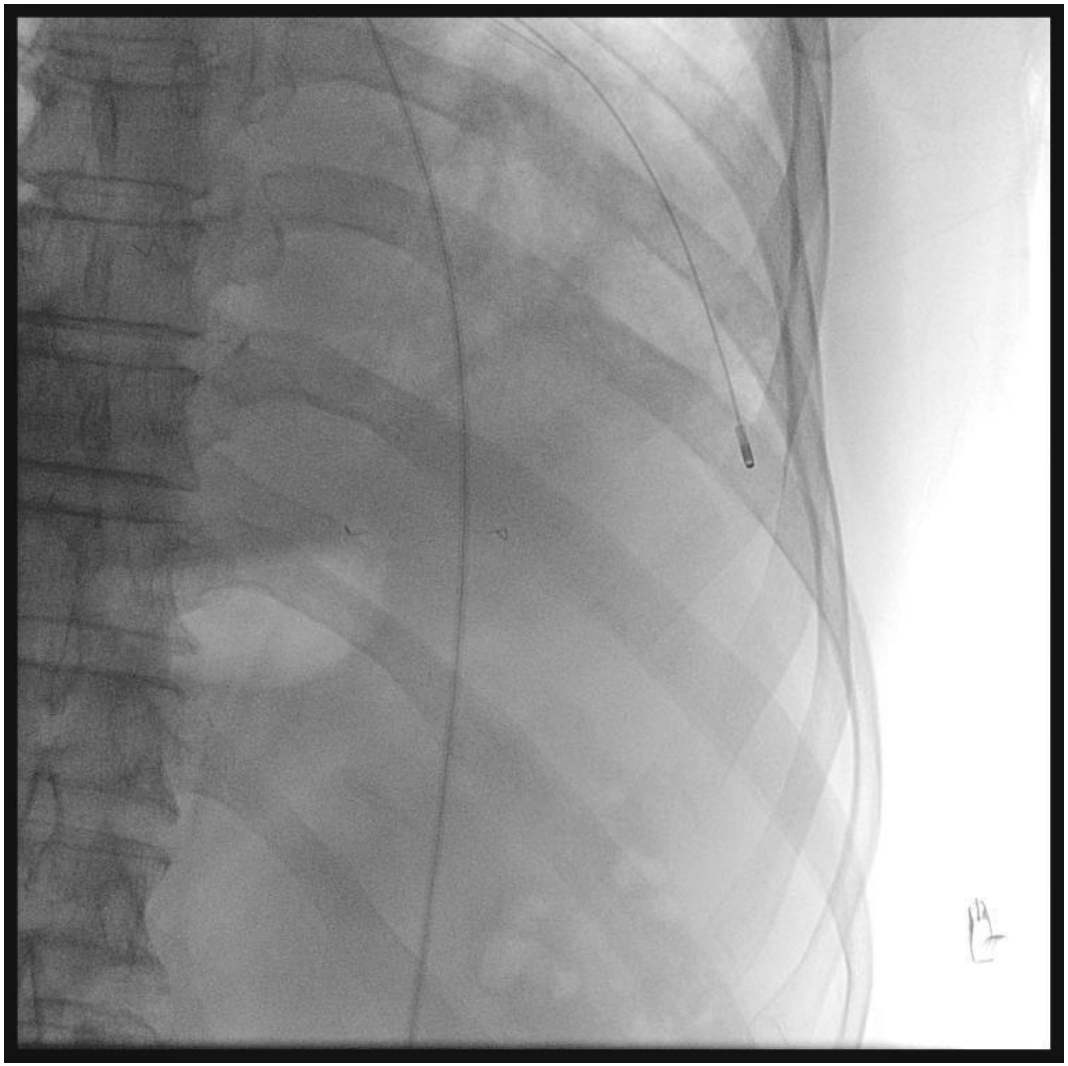
Fluroscopy guidance



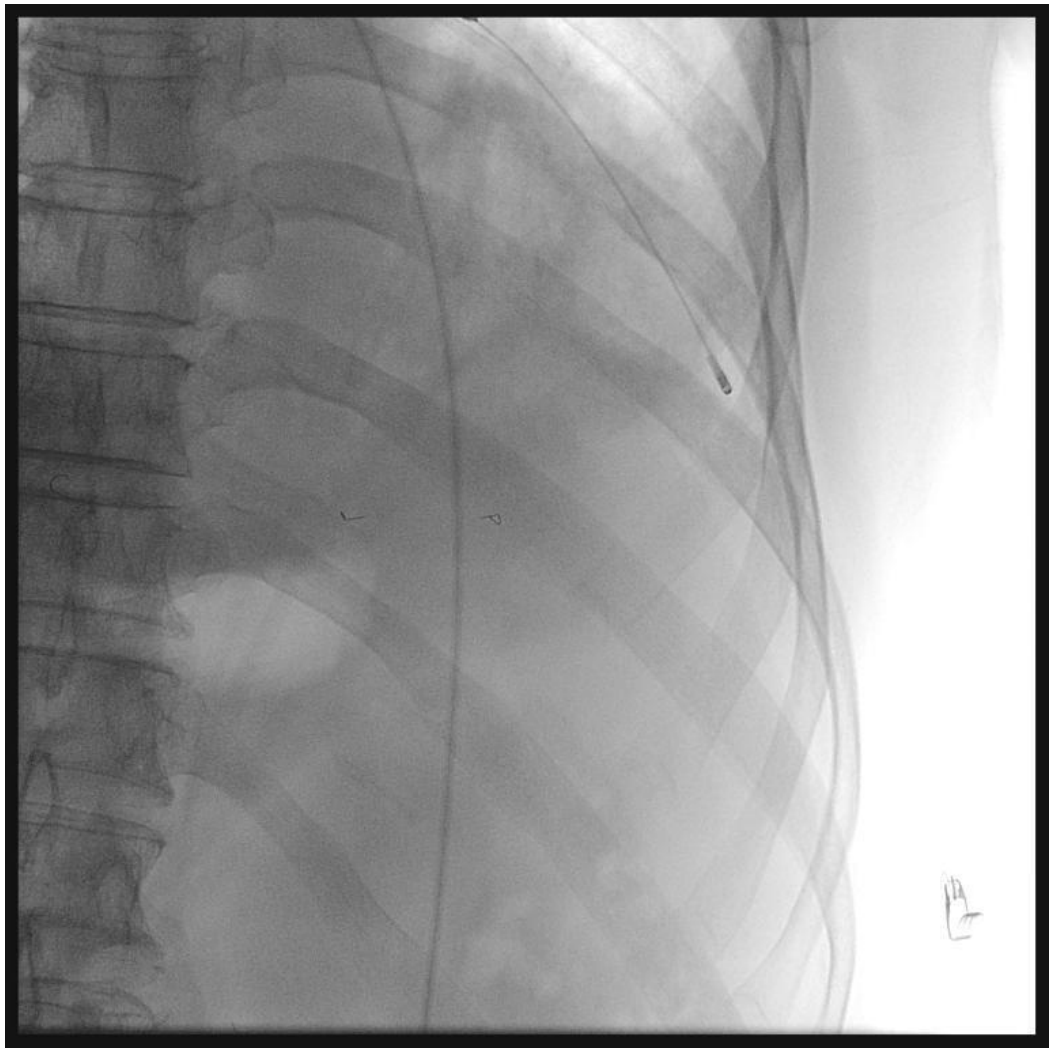


Rotation of fluroscopy

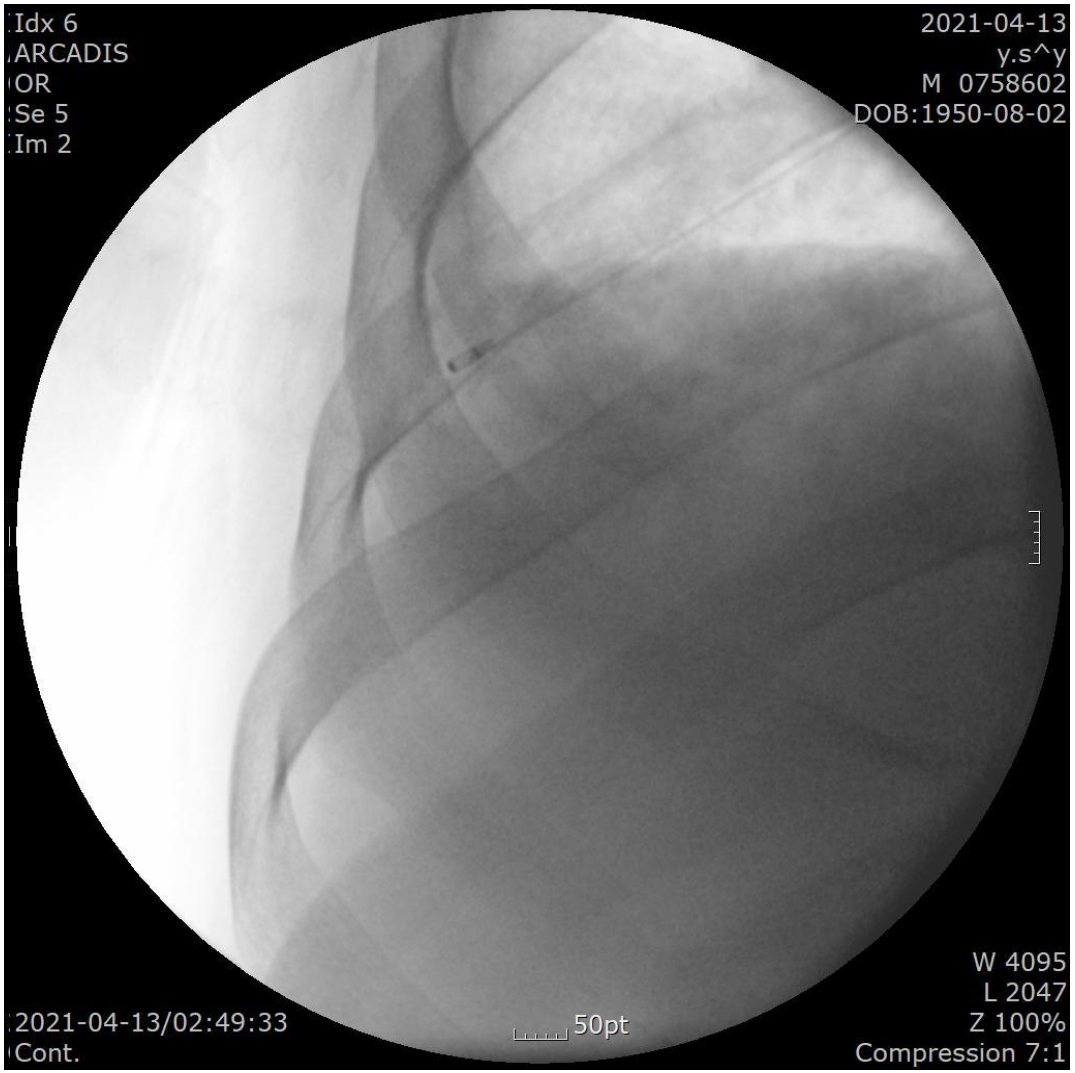
Rotation of fluroscopy



Rotation of fluroscopy



Rotation of fluroscopy



Single center experience of TBLC in Korea
Baseline characteristics

Characteristic	Value (n=27)
Age, yr	65.1 (63.0–71.0)
Male sex	20 (74.1)
Weight, kg	67.0 (58.0–75.0)
Height, cm	1.67 (1.59–1.70)
Body mass index, kg/m^2	25.1 (22.5–28.4)
Ever-smokers	20 (74.1)
Pack-years	40.0 (26.3–48.8)
BAL	
WBC, cell/μL	1,100.0 (400.0–1,900.0)
Macrophage, %	69.5 (48.0–90.0)
Neutrophil, %	5.5 (2.3–26.3)
Lymphocyte, %	8.0 (4.0–22.3)
Pulmonary function test	
FVC, % predicted	78.0 (66.0–92.0)
FEV_1, % predicted	84.0 (76.0–100.0)
DLco, % predicted	63.0 (48.0–69.0)
Six-minute walk test	
Distance, m	480.0 (445.5–544.5)
Initial SpO_2, %	96.0 (95.5–97.5)
Nadir SpO_2, %	92.0 (87.0–95.0)
Arterial oxygen pressure, mm Hg	92.0 (66.9–99.8)
ProBNP, pg/mL	73.4 (17.4–101.1)
LDH, U/L	236.5 (197.5–304.8)
CRP, mg/dL	0.17 (0.1–0.4)
IL-6, pg/mL	4.4 (2.3–7.9)

TRD 2022 Oct;85(4):341-348

Single center experience of TBLC in Korea
Details of TBLC

Characteristics	
Hospital length of stay (day)	3.0 (3.0-4.0)†
Fogarty catheter	2 (7.4)
Univent endobronchial tube	25 (92.6)
7.0 Fr	10 (40.0)
7.5 Fr	15 (60.0)
Flexible bronchoscopy	27 (100)
Cryoprobe	
1.7 mm (disposable)	15 (55.6)
1.9 mm (reusable)	12 (44.4)
Duration of procedure (minutes)	20.0 (15.0-30.0)†
Biopsy location	
RLL	17 (62.9)
LLL	10 (37.1)
B8*	33 (63.5)
B9	18 (34.6)
B6	1 (1.9)

Characteristics	
Number of specimens	2.0 (2.0-2.0)†
Biopsy size (cm)	
Smallest axis diameter	0.3 (0.2-0.3)†
Largest axis diameter	0.5 (0.5-0.7)†
Bleeding	
No bleeding	10 (19.2)
Mild bleeding	19 (36.5)
Moderate bleeding	20 (38.5)
Severe bleeding	3 (5.8)
Pneumothorax	7 (25.9)
Chest tube drain (+)	2 (7.4)
Chest tube drain (-)	5 (18.5)
Pneumonia	0 (0.0)
Acute exacerbation	1 (3.7)
Death	0 (0.0)

TRD 2022 Oct;85(4):341-348

Single center experience of TBLC in Korea
Clinico-radiologic-histopathologic analysis and result of MDD

Characteristics	N (%)
Radiologic pattern	
UIP	1 (3.7)
Probable	9 (33.3)
Indeterminate UIP	9 (33.3)
Alternative UIP	8 (29.7)
Histopathologic pattern	
UIP	0 (0.0)
Probable UIP	5 (18.5)
Indeterminate	9 (33.3)
Alternative	13 (48.2)
Specific alternative pattern	
Smoking related ILD	6 (22.2)
NSIP	3 (11.1)
Inhalation injury	2 (7.4)
PPFE	1 (3.7)
Lung cancer	1 (7.7)

Characteristics	N (%)
Final MDD diagnosis	
IPF	9 (33.3)
Smoking related ILD†	7 (25.9)
NSIP	5 (18.6)
Unclassifiable ILD*	4 (14.8)
PPFE	1 (3.7)
Lung cancer	1 (3.7)
Treatment	
Pirfenidone	11 (40.7)
Steroid	11 (40.7)
Immunosuppressive drug	4 (14.8)
No treatment	5 (18.5)

TRD 2022 Oct;85(4):341-348

Single center experience of TBLC in Korea

- 27 patients
- Decision of TBLC and final diagnosis by MDD
- General anesthesia in operation room
- Flexible bronchoscopy (4mm)
- Fluroscopy guidance with endobronchial balloon blocker
- Lower lobe (B6-10)
- TBLC team: Two pulmonologist (1 intervention specialist) and 3 nurses
- Median duration of procedure and hospitalization – less than 30minutes and 3days
- Final diagnostic yield – 85.2%
- Manageable complications

TRD 2022 Oct;85(4):341-348

Medical Costs after January 2022

항목	명칭	총액	급여			비급여
			본인 부담금	공단 부담금	전액본인부담	
주사료(행위료)	기관내주입	23,138	4,628	18,510		
주사료(약품비)	에피네프린	330	66	264		
	리도카인주사액	1,006	201	805		
검사료	굴곡성기관지경	114,850	22,970	91,880		
	기관지폐포세척술	44,738	8,948	35,790		

항목	명칭	총액	급여			비급여
			본인 부담금	공단 부담금	전액본인부담	
기관지내시경관련 비용		890,563	178,114	682,449	0	
마취관련 비용		482,400	64,679	258,721	0	159,000
그 외 비용		829,087	270,557	50,4210	0	84,320
Total		2,202,050	513,350	1.445,380	0	243,320

	간]					
	마취중말초산소포화도 감시	3,050	610	2,440		
	산소10L/1분당[전신마취시]	180	36	144		
	탄산가스흡수제	1,384	277	1,107		
	굴곡성기관지경 기관내삽관술[마취]	114,850	22,970	91,880		
치료재료대	Endotracheal Tube	13,990	2,798	11,192		
마취관련 비용		482,400	64,679	258,721		159,000

TBLC: Hurdles in Korea

- Decision of performing histopathologic analysis by VATS or TBLC

→ based on local availability and expertise, benefit-risk assessments, and patient preference following informed consent

- Learning curve of TBLC in ILD

→ Training (self-training, fellowship training, procedure course/work-shops, and training in experienced center)

- Pathologic analysis and final decision by MDD

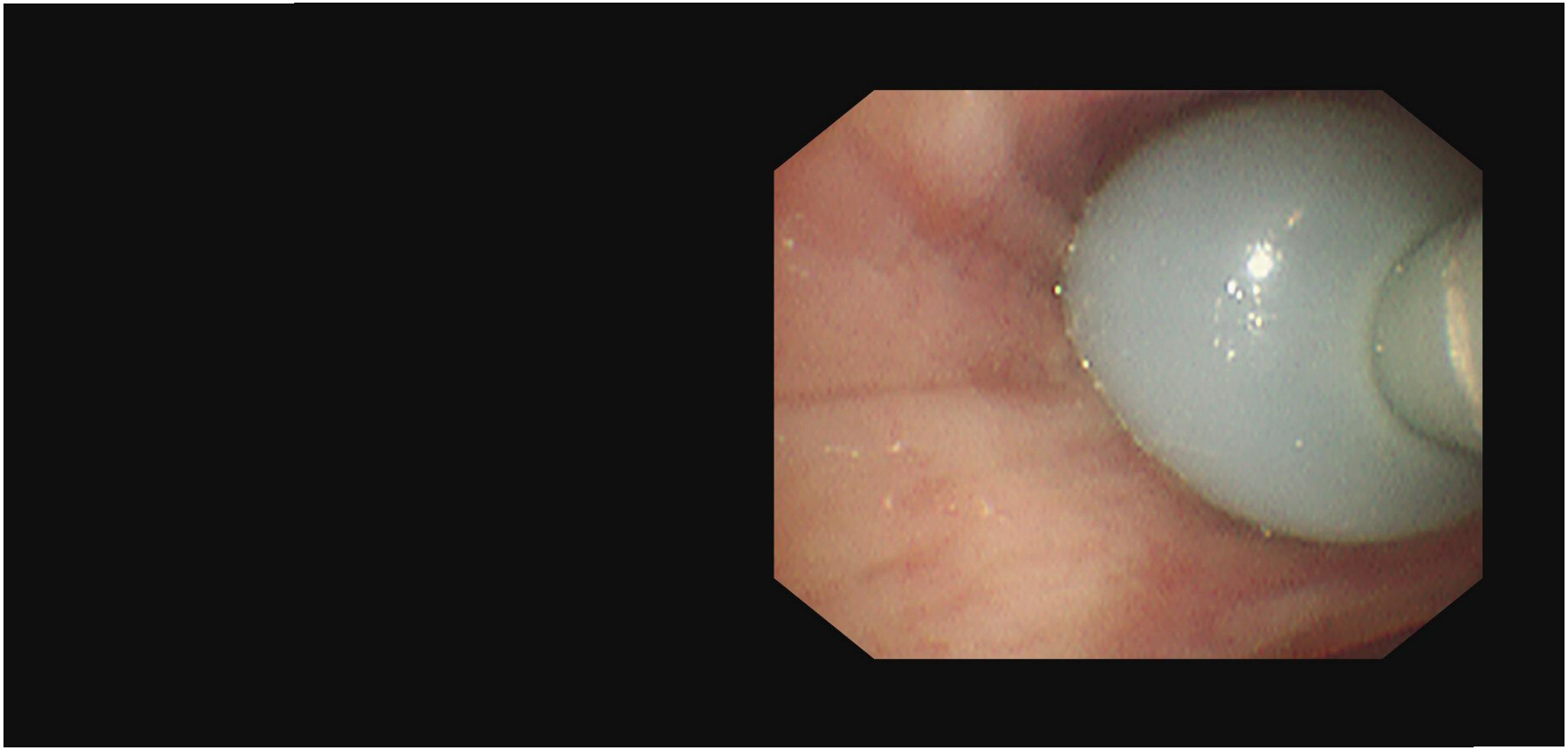
→ Sharing of experience (radiologic-histopathologic diagnosis)

Hands-on program

- 1. Scope 위치 확인 → B6-10 (A)
- 2. Balloon catheter 거치 (상위 level) (A and B)
- 3. Endobronchial balloon function 확인 (B)
- 4. Cryoprobe 진입 및 끝까지 진입 후 1-2cm withdrawal (A)
- 5. Cryoprobe 급속냉동 및 조직검사 (freezing time: 5-6 seconds, effect 2)
- 6. Cryoprobe 및 bronchoscopy withdrawal (A) 및 ballooning (B)
- 7. Balloon decompression 이후 출혈 정도 확인 (A and B)
- 8. 검체 관리 (with negative pressure for one minute)

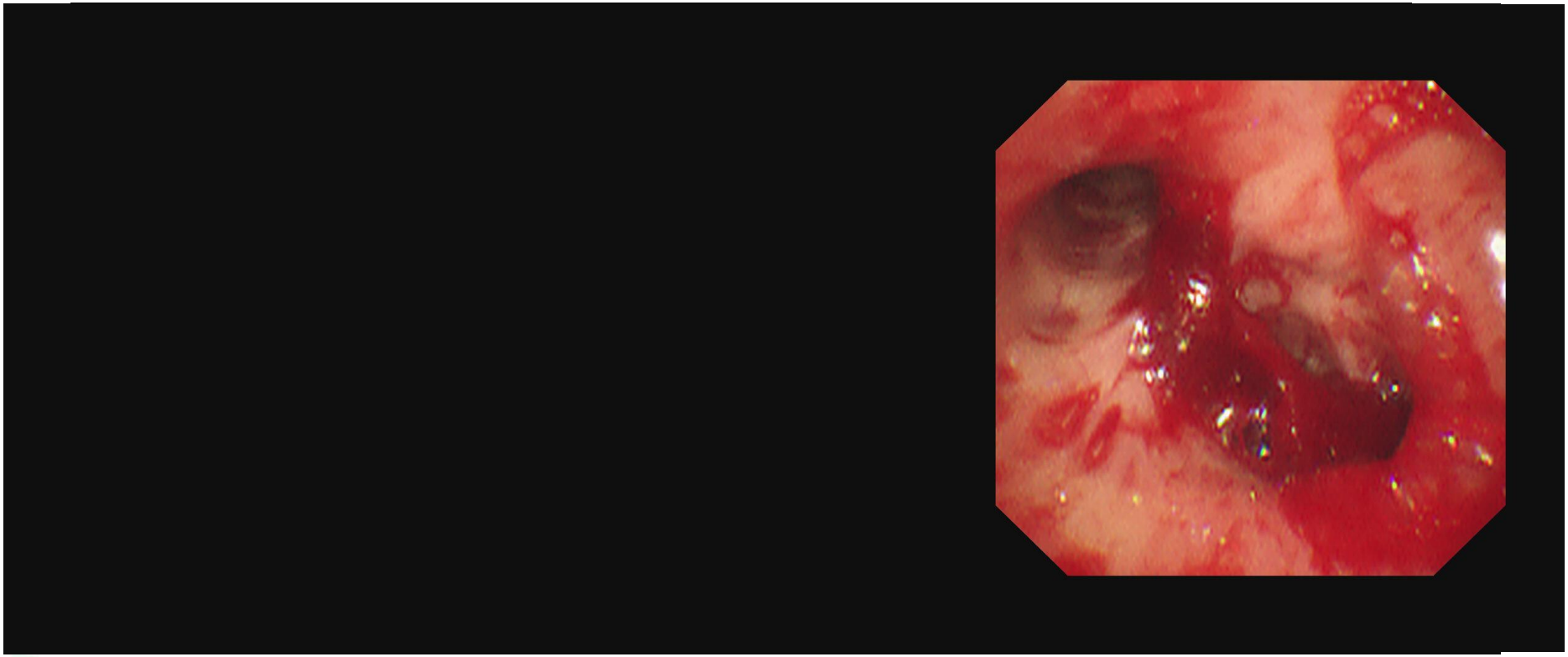
Hands-on program (Step 1)

- 1. Scope 위치 확인 → B6-10 (A)
- 2. Balloon catheter 거치 (상위 level) (A and B)
- 3. Endobronchial balloon function 확인 (B)



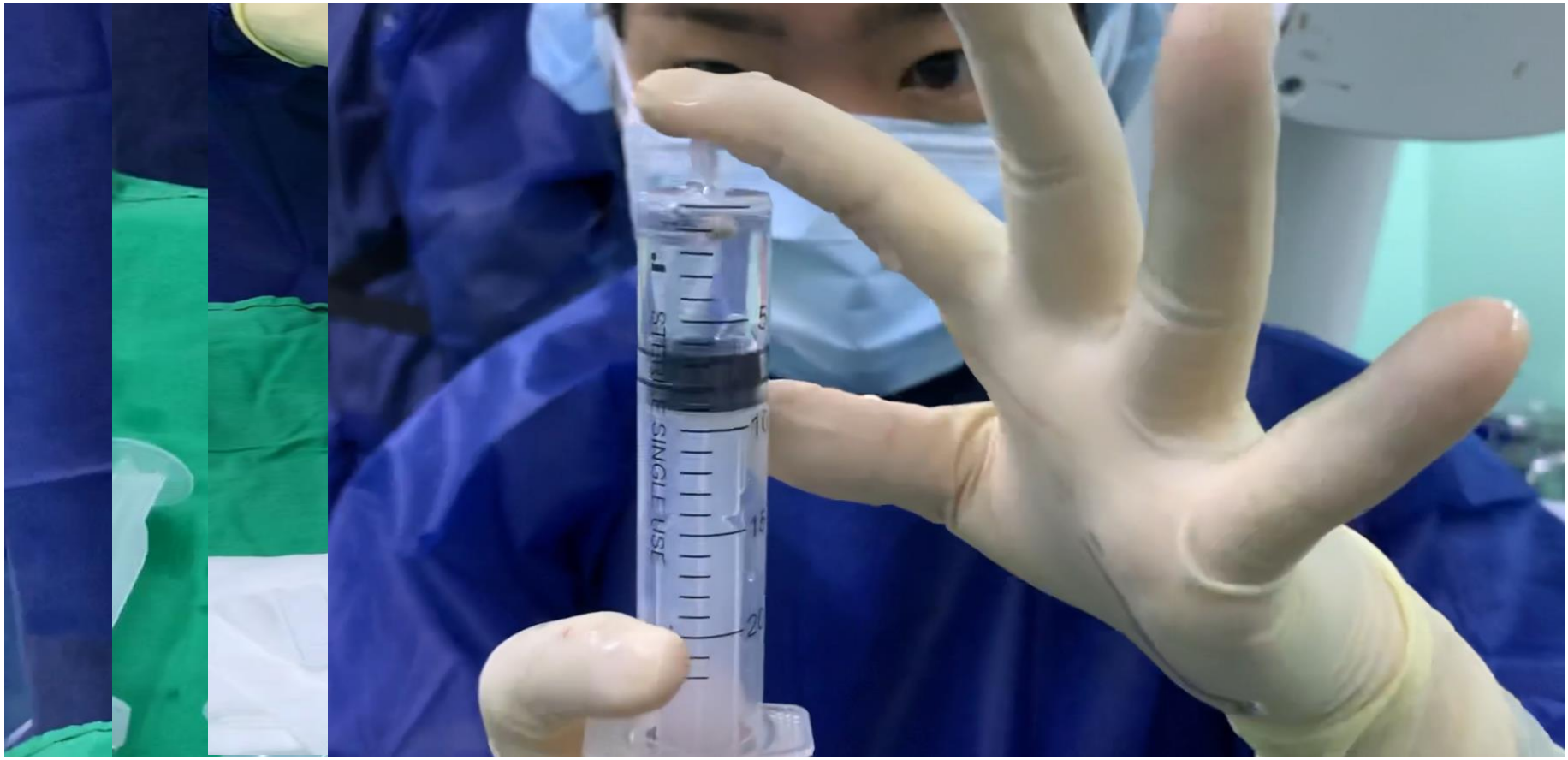
Hands-on program (Step 2)

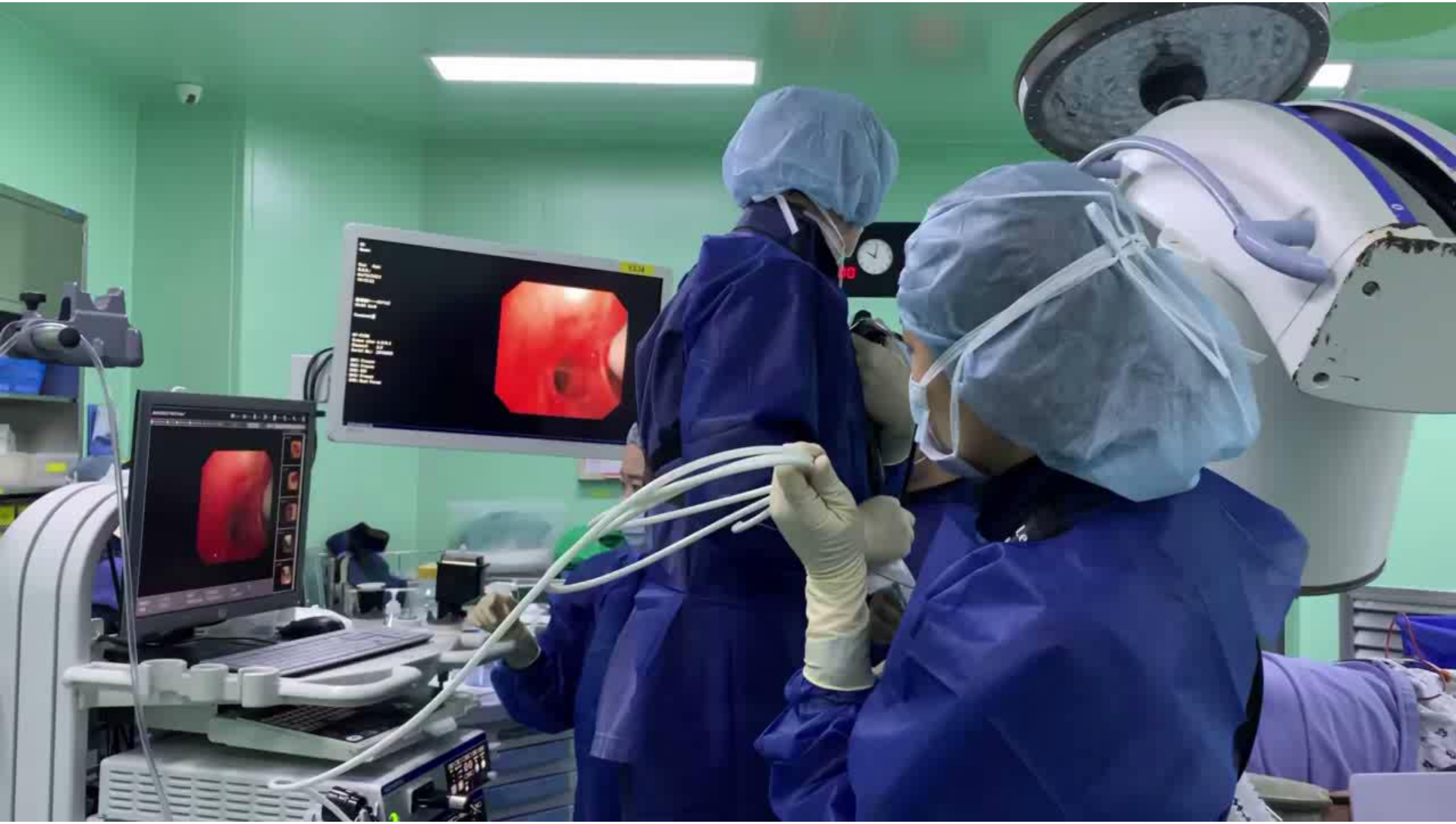
- 4. Cryoprobe 진입 및 끝까지 진입 후 1-2cm withdrawal (A)
- 5. Cryoprobe 급속냉동 및 조직검사 (freezing time: 5-6 seconds, effect 2)
- 6. Cryoprobe 및 bronchoscopy withdrawal (A) 및 ballooning (B)
- 7. Balloon decompression 이후 출혈 정도 확인 (A and B)



Hands-on program (Step 3)

- 8. 검체 관리 (with negative pressure for one minute)





감사합니다