Bronchoscopic Cryotherapy

경상국립대학교병원
정종환

Lecture Outline

1. **Bronchoscopic Cryotherapy의 기본 원리**
   Joule-Thomson · Freeze-Thaw · Cryoextraction · Probe 종류

2-1. **Cryoextraction for Blood Clot / Foreign Body**
   ICU·ECMO에서의 응급 기도확보

2-2. **Peripheral Lung Biopsy with Cryobiopsy**
   r-EBUS · Robotic · ENB와의 결합

2-3. **Mediastinal LN Biopsy via EBUS-guided Cryobiopsy**
   Lymphoma · Sarcoidosis · 분자검사

2-4. **Lung Cancer Cryoablation**
   Transbronchial · Cryo-Immunotherapy

2-5. **Malignant CAO Cryorecanalization**
   즉시 효과 · cartilage 보존

PART 1

기본 원리

Basic Principles of Bronchoscopic Cryotherapy

Cryotherapy의 역사와 현재의 위상

1968
Rigid bronchoscope를 통한 endobronchial cryosurgery가 최초 보고

2004
Hetzel:
Cryorecanalization 개념

2009
Babiak:
TBCB 기법 정식 도입

2021–23
Landmark RCTs
(Zhang ERJ, Fan Lancet)

2024
Transbronchial cryoablation FIH

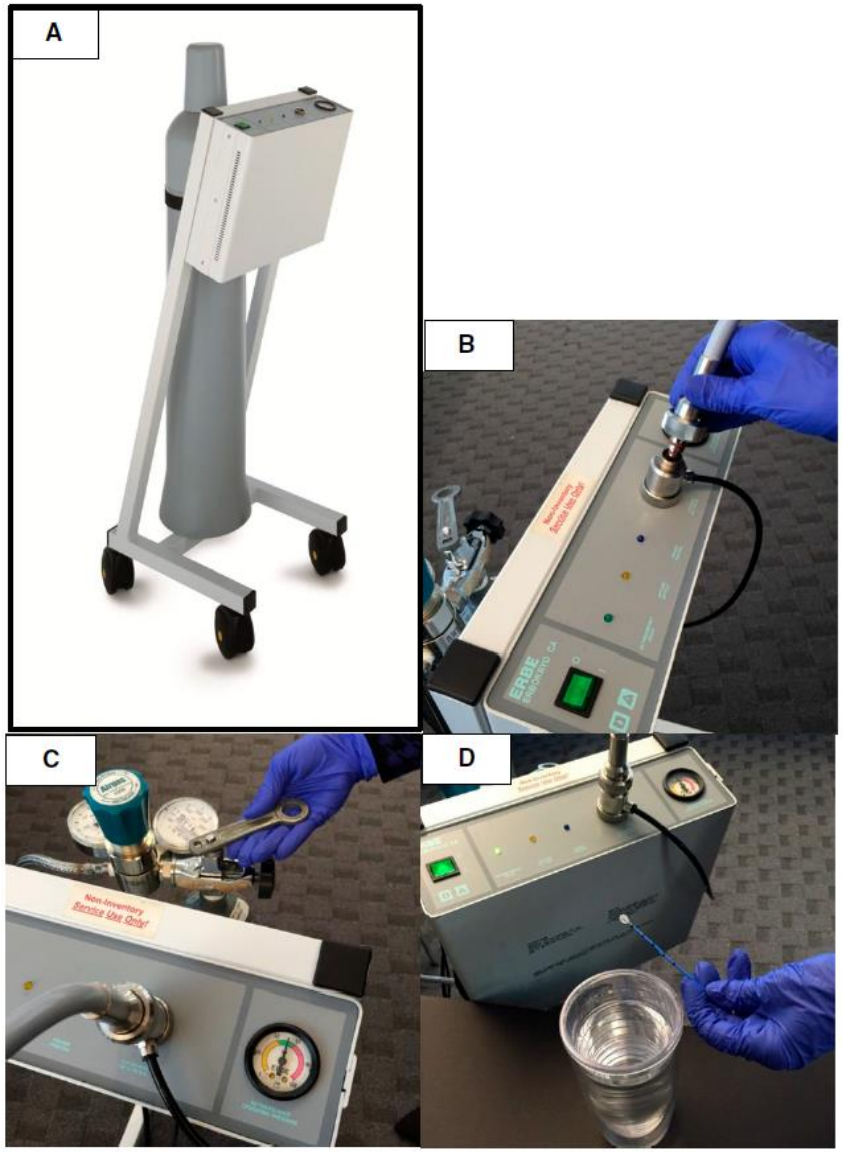
진단 (Diagnosis)
Cryobiopsy:
ILD, PPL, Mediastinal LN

치료 (Therapy)
Cryoablation,
Cryorecanalization

응급 (Emergency)
Cryoextraction:
blood clot, foreign body

DiBardino DM, et al. Ann Am Thorac Soc 2016;13(8):1405-1415. · Babiak A, et al. Respiration 2009;78(2):203-208.

Joule-Thomson Effect



사용 가스별 도달 온도

N_2O (Nitrous Oxide)

−89.5°C

표준 cryoprobe (Erbe 등)

CO_2

−78.5°C

일부 single-use probe

Liquid N_2 (LN_2)

−196°C

Spray cryotherapy (truFreeze)

압축 가스의 단열 팽창 → 극저온

고압 가스 → 좁은 오리피스 → 단열 팽창 → 열 흡수 → 급격한 온도 강하

DiBardino DM, et al. Ann Am Thorac Soc 2016;13(8):1405-1415. · Thomas R, Phillips MJ. ERS Monograph 2017, Ch.10.

Multimodal Cell Death

직접 손상

Direct Injury

세포 내·외 ice crystal 형성

세포소기관 파괴

막 파열 — 즉시 효과

허혈성 괴사

Vascular Injury

국소 vasoconstriction

Microthrombosis 형성

Delayed ischemic necrosis

면역학적 효과

Immunologic

동결로 손상된 세포 항원 노출

antitumor immune response 유발

(cryoimmunotherapy의 이론적 근거)

약 90% 세포 사멸을 위한 기준 · −40°C 이하, 분당 −100°C의 빠른 동결, 느린 해동, 반복 freeze-thaw cycle

DiBardino DM, et al. Ann Am Thorac Soc 2016. · Velez A, et al. Front Immunol 2023;14:1203539.

조직 감수성 — Cryotherapy의 안전성 비결

Cryosensitive (감수성 ↑)

수분·혈관 풍부

종양 조직 (highly vascular)

Granulation tissue

점막 / 내피세포

신경 (nerve fiber)

피부 / 점막상피

Cryoresistant (저항성 ↑)

수분·혈관 적음

Cartilage (기관 연골)

지방조직 (adipose tissue)

결합조직 / 섬유화 조직

Nerve sheath (신경 외막)

Fibrosis tissue

임상적 의의 : 기관지 cartilage가 보존되므로 thermal modality(laser, electrocautery)에 비해 perforation, stricture 위험이 현저히 낮음

DiBardino DM, et al. Ann Am Thorac Soc 2016. · Mathur PN, et al. Chest 1996;110:718-723.

두 가지 핵심 기법

① Freeze-Thaw Method

(Cryodevitalization)

Probe를 병변에 접촉 → 1-3분 동결 → 자연 해동 → 반복

즉시 효과 없음 — 1-2주 후 조직 괴사·박리

재시술이 필요할 수 있음

응급 기도폐쇄에는 부적합

적용: superficial tumor, granulation tissue, CIS

② Cryoextraction / Cryoadhesion

(En-bloc removal)

Probe 동결 후 해동 전 빠르게 후퇴

동결 조직이 probe에 부착되어 함께 빠짐

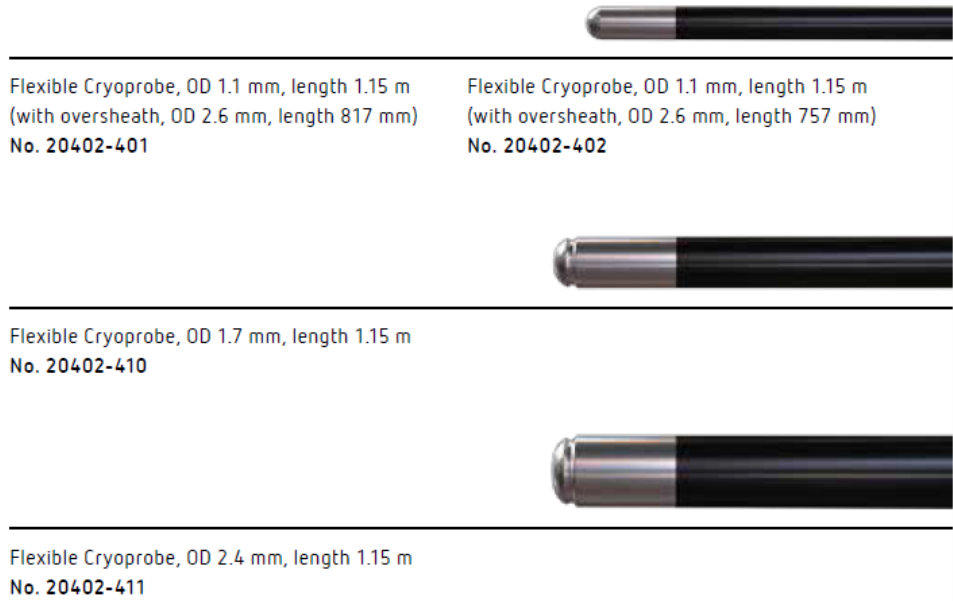
즉시적 효과, en bloc 제거 가능

적용: cryobiopsy, blood clot/foreign body 제거, cryorecanalization (malignant CAO)

Hetzel M, et al. J Thorac Cardiovasc Surg 2004;127(5):1427-1431. · Hetzel J, et al. Respiration 2008;76:193-197.

Cryoprobe의 종류와 특성

직경	Working Channel	주요 용도	특징
1.1 mm *single-use*	**≥ 1.2 mm** mini-scope, GS, EBUS	Peripheral cryobiopsy EBUS mediastinal cryobiopsy	*가장 유연· GS 호환* *검체GS 통해 회수 가능*
1.7 mm *single-use*	**≥ 2.0 mm** 표준 진단용 scope	ILD cryobiopsy peripheral pulmonary lesion	*최근ILD biopsy 표준* *(Hetzel 등)*
1.9 mm *reusable*	**≥ 2.6 mm** Therapeutic scope	ILD cryobiopsy peripheral pulmonary lesion	*전통적ILD probe* *larger sample*
2.4 mm *rigid/flex*	**Therapeutic** Rigid scope 내부	Cryorecanalization Central tumor	*Largest sample* *강력한cryoadhesion*



Flexible Cryoprobe, OD 1.1 mm, length 1.15 m (with oversheath, OD 2.6 mm, length 817 mm)
No. 20402-401

Flexible Cryoprobe, OD 1.1 mm, length 1.15 m (with oversheath, OD 2.6 mm, length 757 mm)
No. 20402-402

Flexible Cryoprobe, OD 1.7 mm, length 1.15 m
No. 20402-410

Flexible Cryoprobe, OD 2.4 mm, length 1.15 m
No. 20402-411

Erbe Elektromedizin GmbH specifications. · *Steinack C, et al. Respiration 2025;104(8):603-614.*

ERBE USA. *ERBECRYO® 2*. 2023.

Freezing Duration

검체 크기를 좌우하는 핵심 변수

검체 크기 영향 인자

Probe 직경 ↑ → 큰 검체

Freezing time ↑ → 큰 검체

Contact pressure ↑

Tissue water content (vascular tissue ↑)

Trade-off

너무 길면 → **bleeding · pneumothorax 위험 ↑**

너무 짧으면 → **검체 부적절, 진단율 ↓**

Probe	ILD (TBLC)	PPL	Mediastinal LN
1.9 mm	**5 – 7초**	**3 – 5초**	**N/A**
reusable	CHEST 2020 guideline Ing animal study: 최적 3초	ILD보다 짧게 적용 (조직 수분 함량 차이)	EBUS working channel에 삽입 불가
1.7 mm	**5초**	**4 – 6초**	**데이터 제한적**
single-use	Koike J Thorac Dis 2025 (n=25, 안전+진단 충분)	Steinack RCT 2025 (Respiration, n=54)	1.1 mm vs 1.7 mm RCT 진행 중 (중국 다기관)
1.1 mm	**6 – 8초**	**7 – 10초**	**3 – 5초**
single-use	Jilin Univ 2025 (n=52) 검체 5mm, severe bleeding 3.8%	Steinack RCT 2025 Kho: mean 6초 (3 passes)	Kho 2024: 최적 3–4초 Kamath review: median 4초 2–3 cryo-passes 권장

Trade-off · Probe가 작을수록 긴 동결 필요하나 합병증↓

Mediastinal LN은 LN 내 시간 최소화가 핵심 (짧은 동결 + 빠른 후퇴)

Hetzel J, et al. Respiration 2020;99(3):248-256. · Maturu VN, et al. Lung India 2023.

Koike. J Thorac Dis 2025. · Steinack. Respiration 2025;104(8):603-614. · Kho. Sci Rep 2024. · Kamath. Mediastinum 2025;9:5. · Maldonado. Chest 2020;157:1030.

Respiration

Interventional Pulmonology

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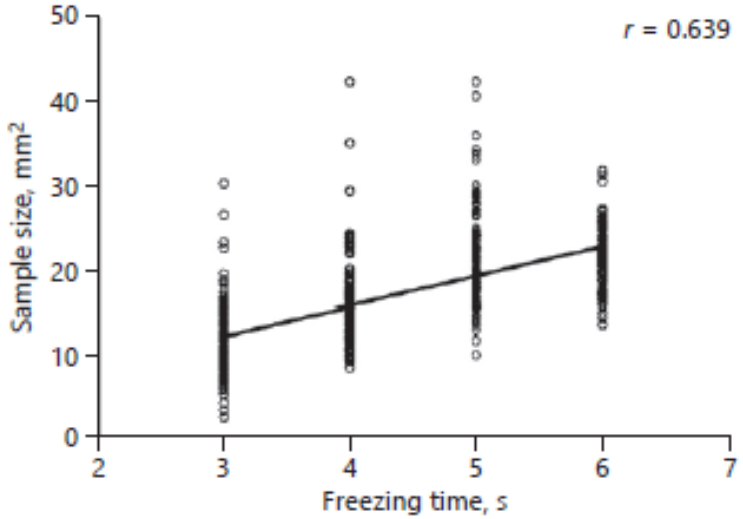
Optimize Initial Freezing Time of Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Disease: A Prospective Randomized Parallel Group Study

Xiaobo Chen[a] Yongshun Ye[b] Qian Han[a] Zhenyu Liang[a] Weiquan Xiao[a]
Difei Chen[a] Liya Lu[c] Yingying Gu[d] Nanshan Zhong[a] Shiyue Li[a]

Prospective randomized parallel-group study

1.9-mm cryoprobe -> ILD TBLC

총 100명을 25명씩 4군으로 배정 → freezing time 3, 4, 5, 6초



	3 s group	4 s group	5 s group	6 s group
Patients, *n*	25	25	25	25
Bleeding, *n* (%)				
0–1 grade	105 (89)	92 (73.6)	84 (68.3)	63 (54.8)
2 grade	13 (11)	33 (26.4)	39 (31.7)	52 (45.2)
Pneumothorax, *n* (%)	0	1 (4)	1 (4)	1 (4)
Pathological diagnosis, *n* (%)				
Definitive	15 (60)	19 (76)	21 (84)	23 (92)
Possible	2 (8)	5 (20)	2 (8)	1 (4)
Failed	8 (32)	1 (4)	2 (8)	1 (4)
Multidisciplinary diagnosis, *n* (%)	16 (64)	22 (88)	22 (88)	24 (96)*

* $p < 0.05$, significant difference among 4 groups, but no difference among 4 s, 5 s, and 6 s groups.

Diagnostic yield of MDD → showing **no significant differences among 4s, 5s, 6s groups**

Freezing time 증가 → grade 2 이상의 bleeding risk 증가

we recommended **4s** as the initial freezing time of TBCB

Respiration 2022;101:299–306.

ERJ OPEN RESEARCH
RESEARCH LETTER
S.S. KHO ET AL.

Exploring the optimal freeze time and passes of the ultrathin cryoprobe in transbronchial cryobiopsy of peripheral pulmonary lesions

ERJ Open Res 2024; 10: 00506-2023

Research letter/short report

Retrospective, single-centre

69 cases using the **1.1-mm** ultrathin cryoprobe → rEBUS-guided PPL-TBCB

81 cases using the **1.9-mm** reusable cryoprobe → rEBUS-guided PPL-TBCB

1.1mm cryoprobe

TABLE 1 Factors influencing diagnostic yield and bleeding rate of ultrathin cryoprobe (N=69)

	Diagnostic yield		
	Conclusive	Inconclusive	p-value
Mean target size			
<2 cm	21/27 (77.8)	6/27 (22.2)	0.767
⩾2 cm	34/42 (81.0)	8/42 (19.0)	
rEBUS orientation			
Concentric	27/31 (87.1)	4/31 (12.9)	0.232
Nonconcentric	28/38 (73.7)	10/38 (26.3)	
Cryobiopsy pass			
2-passes cut-off			
<2 passes	6/8 (75.0)	2/8 (25.0)	0.660
⩾2 passes	49/61 (80.3)	12/61 (19.7)	
3-passes cut-off			
<3 passes	15/23 (65.2)	8/23 (34.8)	0.034
⩾3 passes	40/46 (87.0)	6/46 (13.0)	
Freeze time			
4-s cut-off			
<4 s	10/11 (90.9)	1/11 (9.1)	0.314
⩾4 s	45/58 (77.6)	13/58 (22.4)	
6-s cut-off			
<6 s	29/36 (80.6)	7/36 (19.4)	0.855
⩾6 s	26/33 (78.8)	7/33 (21.2)	
8-s cut-off			
<8 s	42/51 (82.4)	9/51 (17.6)	0.358
⩾8 s	13/18 (72.2)	5/18 (27.8)	
10-s cut-off			
<10 s	51/64 (79.7)	13/64 (20.3)	0.987
⩾10 s	4/5 (80.0)	1/5 (20.0)	
Total specimen size			
<8 mm	25/34 (73.5)	9/34 (26.5)	0.208
⩾8 mm	30/35 (85.7)	5/35 (14.3)	

ERJ Open Res 2024; 10: 00506-2023.

1.1mm cryoprobe

	Bleeding complication		
	Bleeding	No bleeding	p-value
Cryobiopsy pass			
2-passes cut-off			
<2 passes	6/8 (75.0)	2/8 (25.0)	0.144
⩾2 passes	29/61 (47.5)	32/61 (52.5)	
3-passes cut-off			
<3 passes	15/23 (65.2)	8/23 (34.8)	0.089
⩾3 passes	20/46 (43.5)	26/46 (56.5)	
Freeze time			
4-s cut-off			
<4 s	5/11 (45.5)	6/11 (54.5)	0.703
⩾4 s	30/58 (51.7)	28/58 (48.3)	
6-s cut-off			
<6 s	21/36 (58.3)	15/36 (41.7)	0.187
⩾6 s	14/33 (42.4)	19/33 (57.6)	
8-s cut-off			
<8 s	29/51 (56.9)	22/51 (43.1)	0.086
⩾8 s	6/18 (33.3)	12/18 (66.7)	
10-s cut-off			
<10 s	31/64 (48.4)	33/64 (51.6)	0.174
⩾10 s	4/5 (80.0)	1/5 (20.0)	

Data are presented as n/N (%) unless otherwise stated. rEBUS: radial endobronchial ultrasound. Bold type represents statistical significance.

ERJ Open Res 2024; 10: 00506-2023.

reach into the target site may hold greater importance [3, 8, 9]. This was reflected in our finding that specimen size does not differ significantly between conclusive and inconclusive cases in our PPL-TBCB cohort. Nevertheless, while the optimal number of cryobiopsy passes and freezing time for the ultrathin cryoprobe in PPLs remains unknown, our findings suggest that a mean activation time of 6 s and three passes may yield a diagnostic yield comparable to that of the 1.9-mm cryoprobe. Interestingly, in cases where only one activation was performed, we were able to reach a conclusive diagnosis in 75% of cases.

In conclusion, PPL-TBCB may not require larger specimen sizes, as quality of tissue outweighs the quantity of tissue for accurate diagnosis. Comparable diagnostic yields in PPL-TBCB can be achieved by ~6 s of freezing time and three or more passes using the 1.1-mm cryoprobe with rEBUS guidance. The use of the 1.1-mm cryoprobe is associated with improved accessibility, shorter procedural time and potentially reduced incidence of severe bleeding. In the effort to enhance PPL diagnostic accuracy, further prospective studies are needed to establish standardised protocols for the optimal use of the ultrathin cryoprobe in PPLs.

1.1mm cryo-biopsy for PPL → **freezing time 6초 전후, 3회 이상 pass**를 권유 (1.9mm에 상응하는 outcome)

ERJ Open Res 2024; 10: 00506-2023.

Respiration

Interventional Pulmonology

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Diagnosis of Peripheral Pulmonary Lesions Using Forceps and 1.1- or 1.7-mm Cryoprobes: A Randomised Trial

Carolin Steinack[a] Jan Hendrik Rüschoff[b] Maurice Roeder[a]
Silvan Manuel Vesenbeckh[a] Silvia Ulrich[a] Martina Haberecker[b]
Miriam Nowack[b] Malcolm Kohler[a] Daniel P. Franzen[a,c] Thomas Gaisl[a]

[a]Department of Pulmonology, Interventional Lung Center, University Hospital Zurich, Zurich, Switzerland; [b]Department of Pathology and Molecular Pathology, University Hospital Zurich, Zurich, Switzerland; [c]Department of Internal Medicine, Spital Uster, Uster, Switzerland

Single-centre, investigator-initiated, open label, randomised trial

Forcep & Cryobiopsy with a **1.1-mm (freezing time 7–10s, n=29) or 1.7-mm cryoprobe (freezing time 4–6s, n=25)**

Table 2. Diagnostic yield, specimen properties, and adverse events in the entire cohort

Group	1.1-mm cryoprobe	1.7-mm cryoprobe	*p* value
N (%)	29 (53.7%)	25 (46.3%)	
Overall diagnostic yield	22 (75.9%)	22 (88.0%)	0.261
Lesion size ≤10 mm	1 (100%)	0 (0.0%)	-
Lesion size >10–20 mm	6 (50.0%)	3 (75.0%)	0.417
Lesion size >20 mm	15 (93.8%)	19 (100%)	0.282
Diagnostic yield for malignancies	23 (87.0%)	18 (94.4%)	0.435
Overall diagnostic yield CBs			0.198
No definitive diagnosis	9 (31.0%)	4 (16.0%)	
Definitive diagnosis	20 (69.0%)	21 (84.0%)	
Overall diagnostic yield FB			0.599
No definitive diagnosis	16 (55.2%)	12 (48.0%)	
Definitive diagnosis	13 (44.8%)	13 (52.0%)	
Diagnosis			0.493
Lung, adenocarcinoma	15 (51.7%)	13 (52.0%)	
Inflammatory	3 (10.3%)	3 (12.0%)	
Organising pneumonia	2 (6.9%)	4 (16.0%)	
Lung, squamous cell cancer	3 (10.3%)	1 (4.0%)	
Lung, carcinoid	3 (10.3%)	0 (0.0%)	
Lymphoma	1 (3.4%)	1 (4.0%)	
Pneumonitis	0 (0.0%)	1 (4.0%)	
Hepatocellular carcinoma	1 (3.4%)	0 (0.0%)	
Thyroid carcinoma	0 (0.0%)	1 (4.0%)	
Lung, large cell cancer	1 (3.4%)	0 (0.0%)	
Renal cell carcinoma	0 (0.0%)	1 (4.0%)	
Cryobiopsy long-axis diameter, mm	4.1±1.9	5.8±4.4	0.071
Cryobiopsy short-axis diameter, mm	2.8±1.4	3.4±1.3	0.111
Tumour long-axis diameter on cryo-specimens, mm	2.7±1.6	3.3±1.7	0.282
Tumour short-axis diameter on cryo-specimens, mm	2.1±1.2	2.3±1.3	0.580
Number of CBs			0.300
1	4 (13.8%)	5 (20.0%)	
2	6 (20.7%)	10 (40.0%)	
3	19 (65.5%)	10 (40.0%)	
Artifact-free lung parenchyma			0.148
25–49% of specimen	3 (11.5%)	1 (4.2%)	
50–74% of specimen	5 (19.2%)	1 (4.2%)	
75–100% of specimen	9 (34.6%)	18 (75.0%)	
>50 alveolar spaces on cryo-specimens			0.202
No	13 (44.8%)	7 (28.0%)	
Yes	16 (55.2%)	18 (72.0%)	
Procedural-related bleeding			0.847
No	26 (89.7%)	22 (88.0%)	
Yes	3 (10.3%)	3 (12.0%)	

Values are displayed as *n* (%), mean ± SD, or median [IQR].

1.1-mm (freezing time 7–10s)

vs 1.7-mm (freezing time 4–6s)

→ diagnostic yield, specimen quality, molecular pathology suitability, bleeding 면에서 유의한 차이가 없었다.

Respiration 2025;104:603–613.

PART 2-1

Cryoextraction

Blood Clot · Foreign Body — Bedside Lifesaver

응급 기도폐쇄에서 Cryoextraction의 역할

적응증

Endobronchial blood clot

Tenacious mucus plug

Foreign body (수분 함량 ↑)

Plastic bronchitis cast

Aspirated food / pill

기존 도구의 한계

Forceps — clot fragmentation

Suction — rebleeding 위험

Snare/Basket — 곡면 적용 어려움

Rigid bronchoscope — 즉시 준비 어려움

Cryoextraction의 장점

En-bloc 제거 (cryoadhesion) · Bedside flexible bronchoscopy 가능 · ECMO 환자에서도 안전 · 동결 시 vasoconstrictive hemostasis 효과

Sriratanaviriyakul N, et al. J Bronchology Interv Pulmonol 2015;22(4):288-293. · Schmidt LH, et al. J Thorac Dis 2019;11(11):4319-4327.

ORIGINAL INVESTIGATION

Safety and Clinical Utility of Flexible Bronchoscopic Cryoextraction in Patients With Non-neoplasm Tracheobronchial Obstruction

A Retrospective Chart Review

Narin Sriratanaviriyakul, MD,†‡ Francis Lam, MD,†‡*
Brian M. Morrissey, MD,†‡ Nicholas Stollenwerk, MD,*†‡*
Michael Schivo, MD,†‡ and Ken Y. Yoneda, MD*†‡*

Retrospective chart review

38 cryotherapy sessions performed on 30 subjects

J Bronchol Intervent Pulmonol 2015;22:288–293

TABLE 1. Patient Data

Characteristic	Sessions	Patients
Patient population		
Total sessions and patients	38	30
Age range, y (mean)		28-73 (52.6)
Male/female		20/10
Airway		
Nonintubated	5	5
Endotracheal tube	32	24
Tracheostomy	1	1
Indication		
Blood clots	26	20
Mucous plugging	6	5
Foreign body	4	4
Plastic bronchitis	2	1

TABLE 3. Clinical Outcome by Session

Indication	Airway Patency* (%)	Improvement in Oxygenation/ Ventilation* (%)	Complications* (%)
Blood clots	24/26 (92)	14/21 (66.7)	1/26 (3.8)
Mucous plugging	4/6 (66.7)	4/6 (66.7)	0 (0)
Foreign body	2/4 (50)	3/4 (75)	0 (0)
Plastic bronchitis	2/2 (100)	NA	0 (0)
Total	32/38 (84.2)	21/31 (67.7)	1/38 (2.6)

*Number of sessions.
NA indicates not available.

FIGURE 1. Airway cast of a case with hemoptysis.

FIGURE 2. Airway cast of a case with plastic bronchitis.

시술 술기와 주의점

시술 절차

1. Probe tip을 clot/이물에 직접 접촉
2. N_2O 분사 → –90°C까지 5–10초 동결
   adhesion 확인
3. Bronchoscope과 probe 함께
   빠르게 후퇴 (en bloc)
4. 필요시 반복
   (Schmidt: 27 sessions 중 7회 반복)

Probe · 1.9 또는 2.4 mm flexible (대용량 WC 필요)

주의사항

Massive hemoptysis 후 안정화된 clot 제거 시
→ **Rebleeding 가능**
→ *APC, electrocautery, balloon tamponade 준비 필수*

식도 인접 부위에서 깊은 동결 시
→ **Fistula 위험**

병행 요법 (Multimodality)
→ *Cryoextraction + APC 조합으로*
massive bleeding + clot 동시 처리

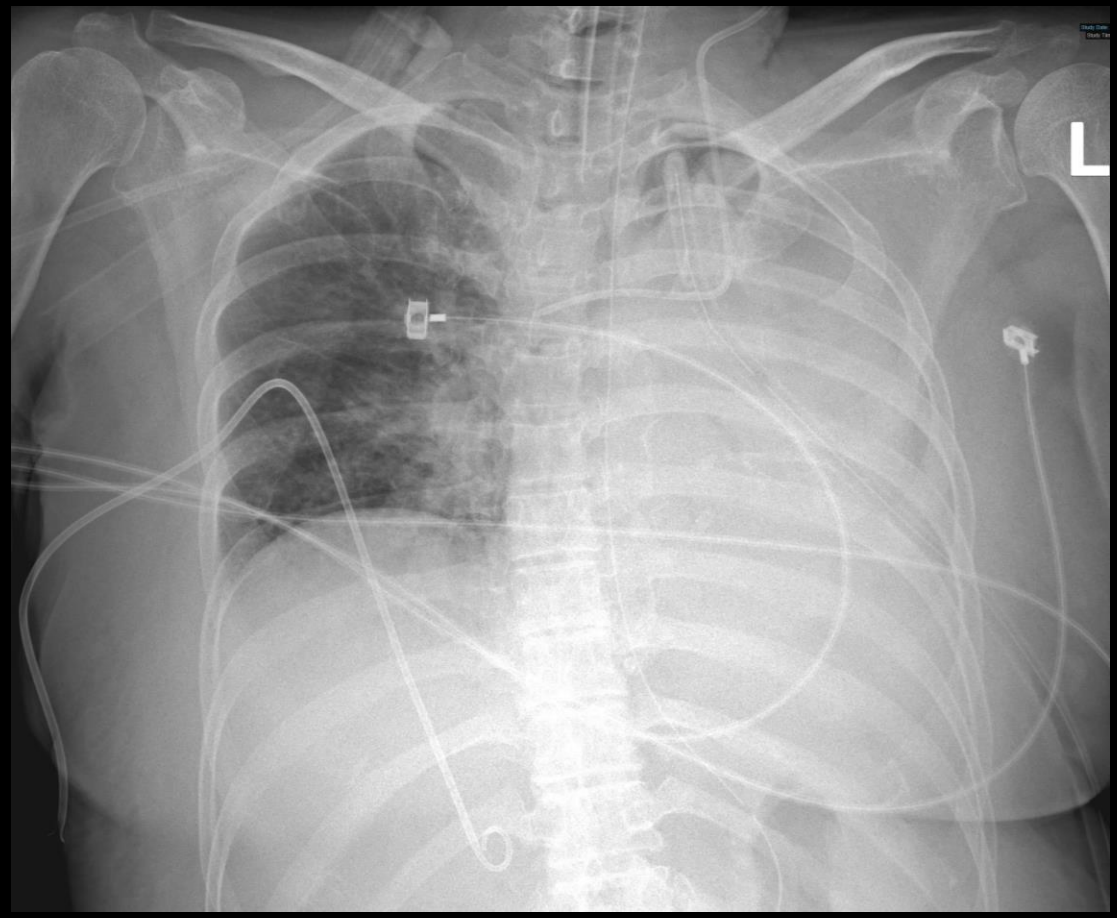
Schmidt LH. J Thorac Dis 2019. · Mahanani DA, et al. Respir Med Case Rep 2016;19:74-77.

Case #1 : 67/F blood clot extraction

2026.4
STEMI with Acute HF -> PCI, VA-ECMO

VA-ECMO → weaning
: hemoptysis, Lt. lung total atelectasis
SpO2 80~85% (ventilator FiO2 1.0)

→ 일요일 아침 응급 BFS 의뢰됨

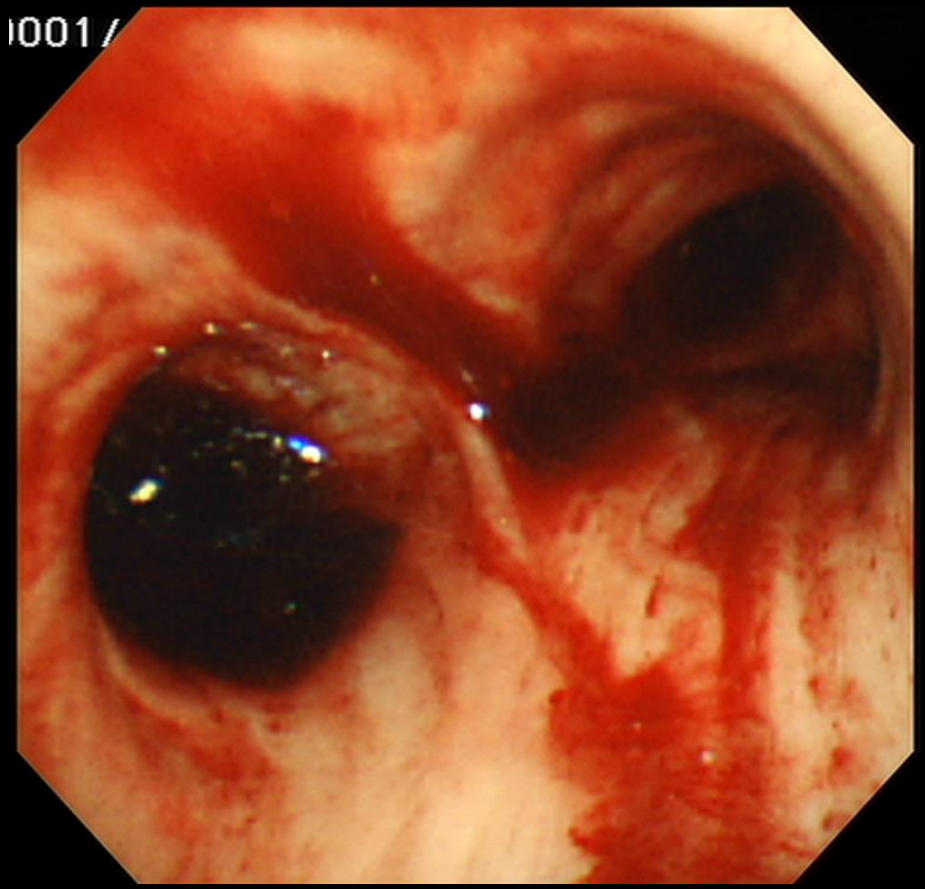


Case #1 : 67/F blood clot extraction

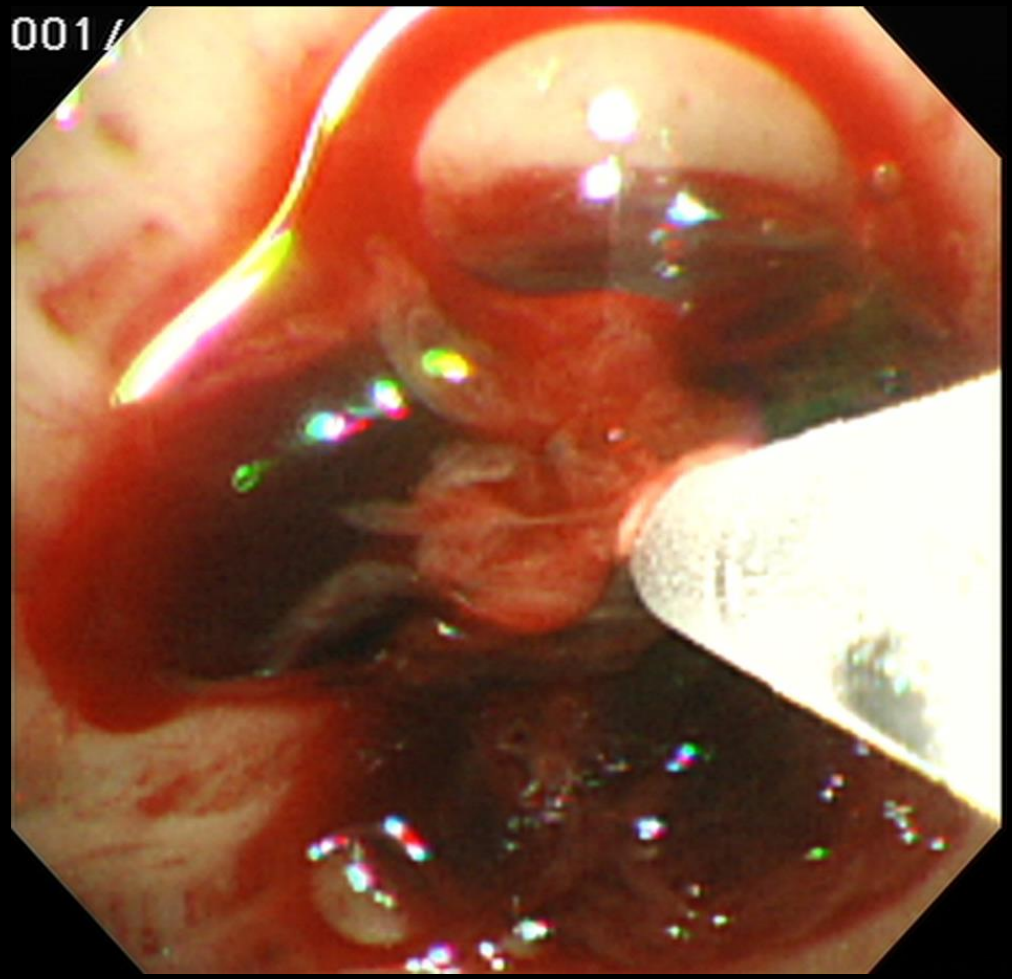
BFS
Total obstruction by blood clot in Lt. main bronchus

SpO2 80~85% (ventilator FiO2 1.0)
E-tube 7.5mm

VV-ECMO ?? 시술 대기 시간 vs 빠른 재개통 가능할 듯?
E-tube change (8.0mm) ?? Arrest risk

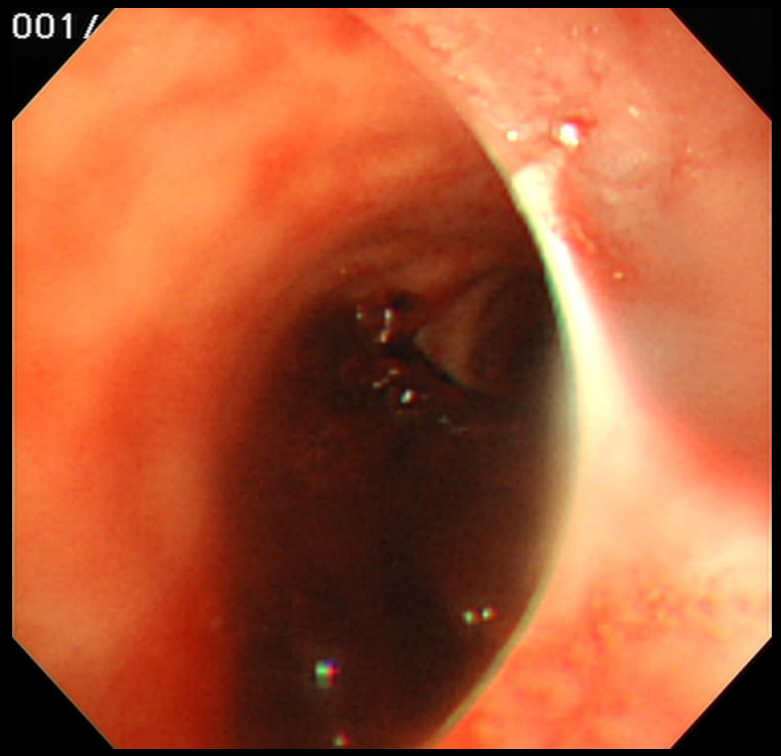


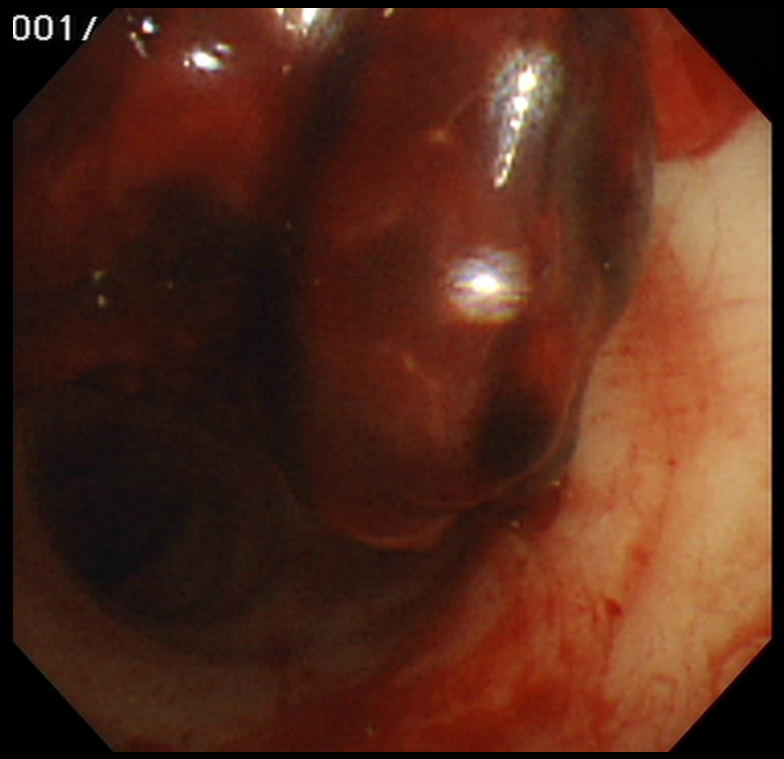
Case #1 : 67/F blood clot extraction

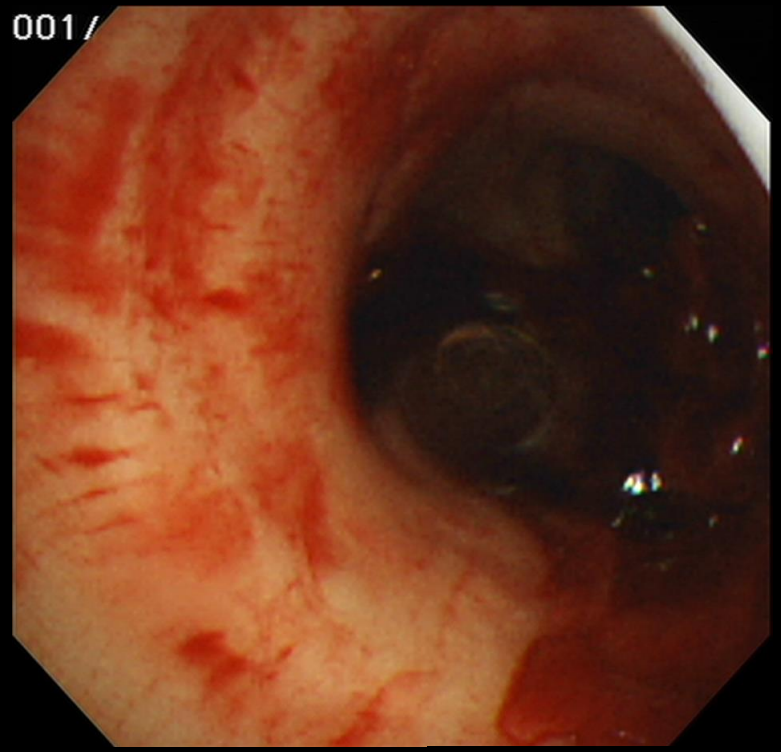


그냥 Cryo-extraction try !!

Case #1 : 67/F blood clot extraction



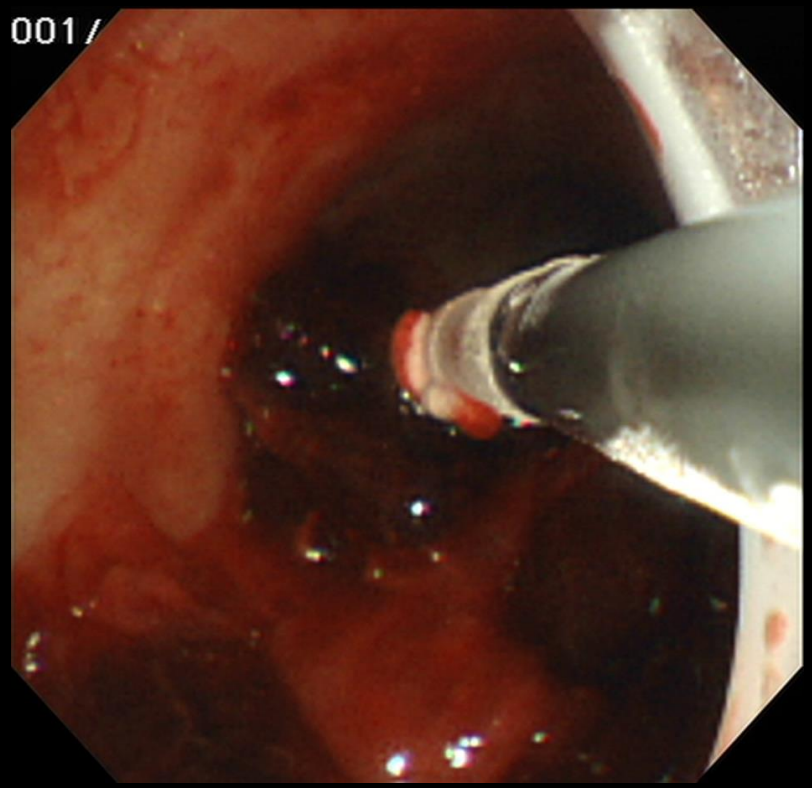


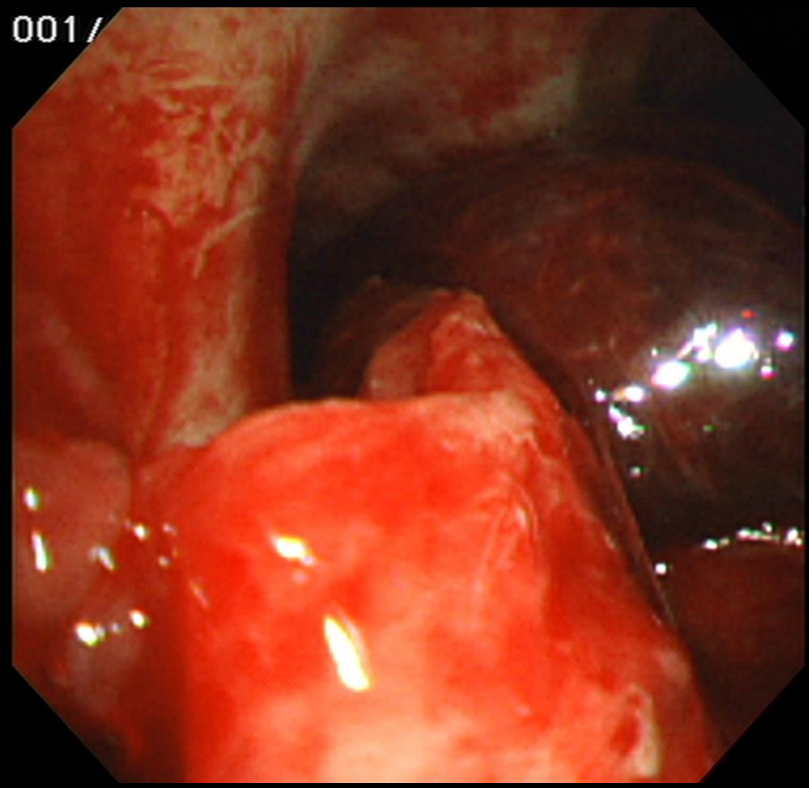


Blood clot extraction시 E-tube tip에 걸려 Rt. main bronchus도 막음

→ SpO2 측정되지 않음.. impending arrest

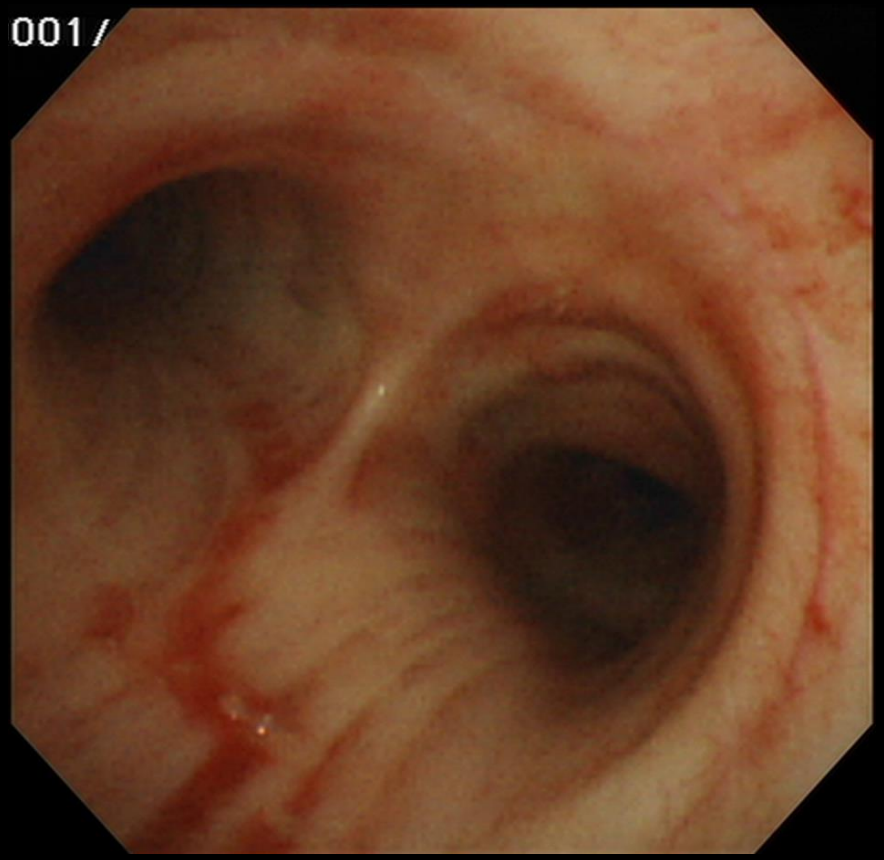
Case #1 : 67/F blood clot extraction

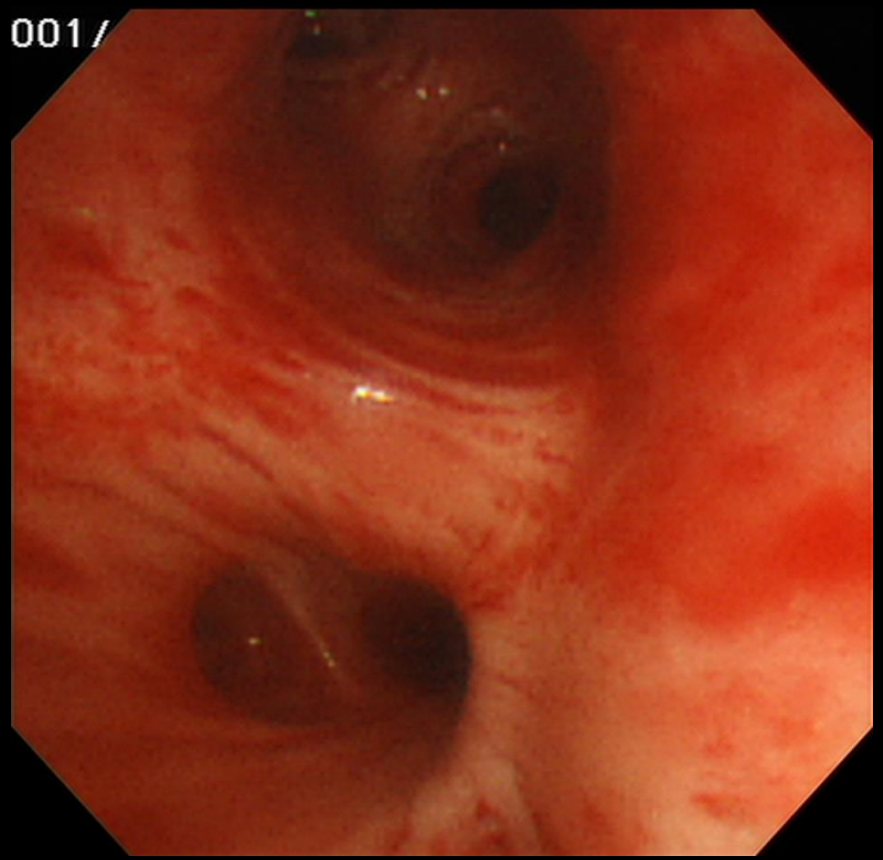




Lt. side down position & ambu bagging
→ cryo-extraction in Rt. main bronchus

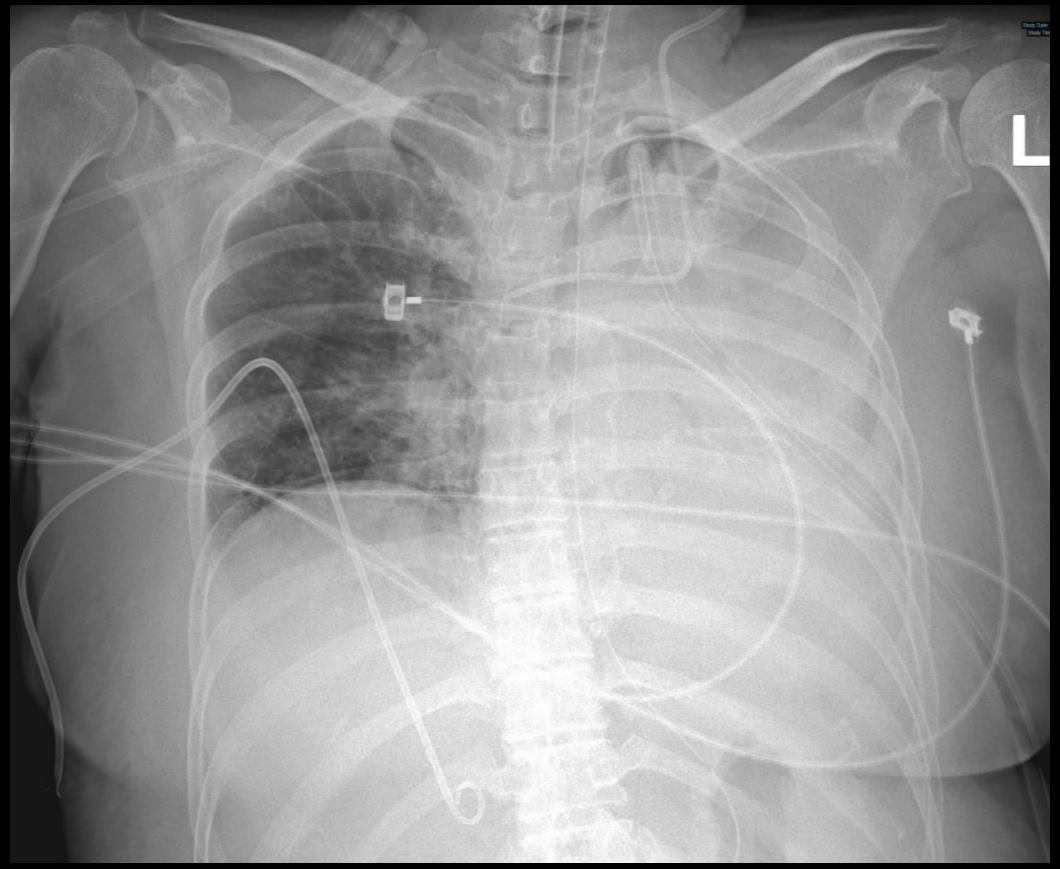
Case #1 : 67/F blood clot extraction

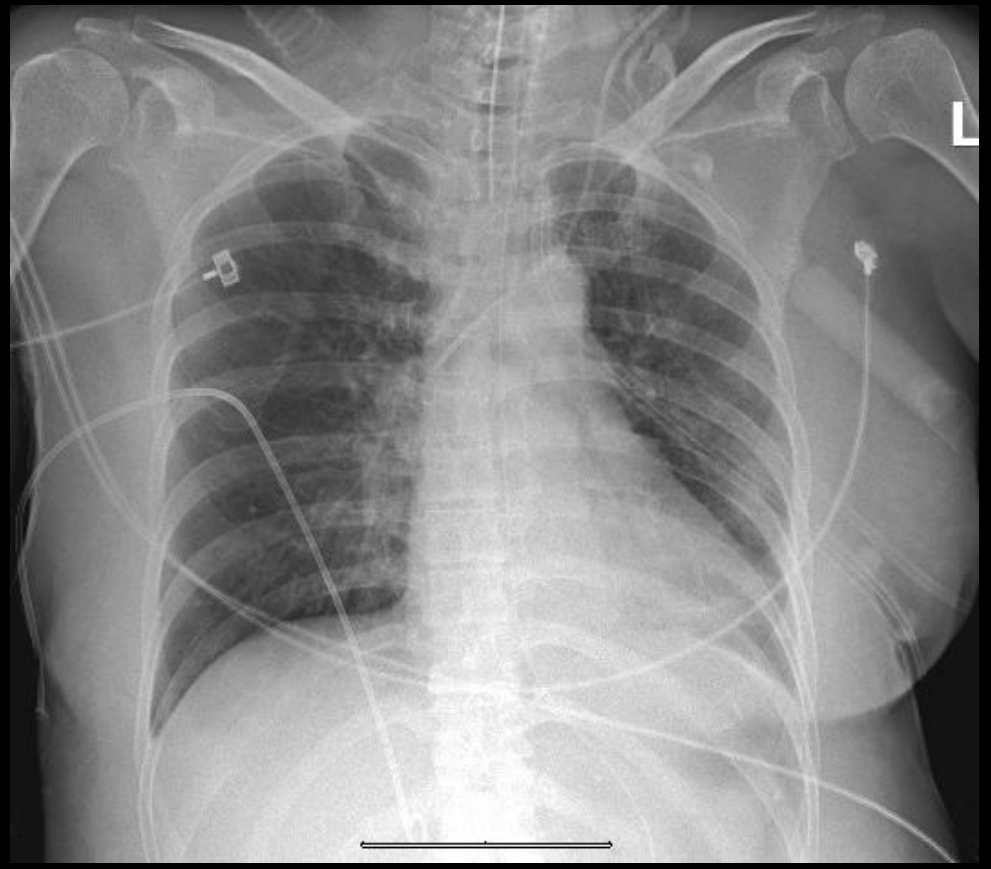




Successful cryo-extraction in Lt. main bronchus

Case #1 : 67/F blood clot extraction





Successful cryo-extraction in Lt. main bronchus

→ 예상치 못한 응급 상황이 발생할 수 있으니, 시술 전 가능한 조치는 다 시행을 하는 것이 좋다!!

PART 2-2

Peripheral Lung Cryobiopsy

with r-EBUS · Robotic · ENB

PPL 진단의 미충족 needs

Forceps Biopsy의 한계

Small specimen — 약 4 mm³

Crush artifact 빈발

Eccentric / adjacent lesion 진단율 ↓

분자검사 부적합률 ↑↑

EGFR / ALK / ROS1 / PD-L1 fail 다발

Cryobiopsy의 강점

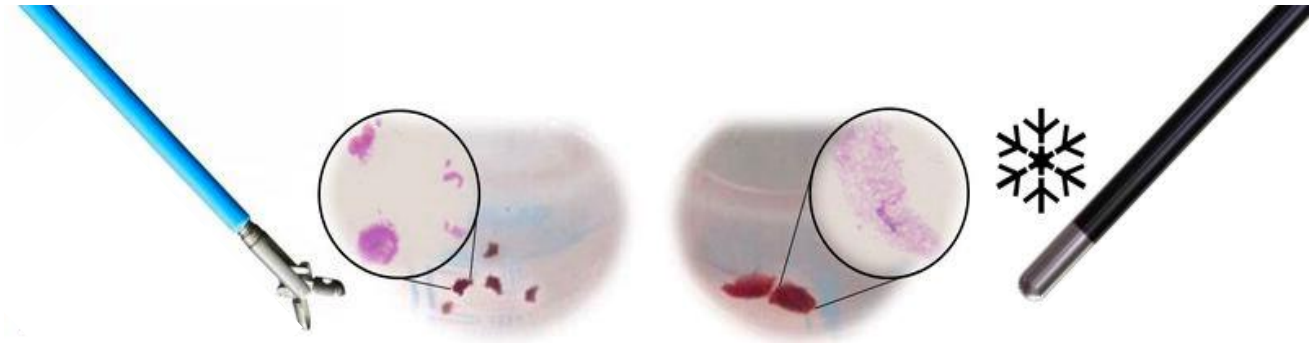
360° 동결 — eccentric/adjacent 채취 가능

검체 크기 4–15배 (Chung: 60 vs 4 mm³)

Crush artifact 거의 없음

NGS / IHC / PD-L1 모두 충분

분자검사 적합성 ↑↑



LDCT 폐암 검진 시대 · SPN 발견 ↑↑ → 진단 정확도 + 분자검사 충분량 요구 폭증

Kim SH, et al. Cancer Res Treat 2023;55(2):506-512. · Arimura K, et al. Respir Investig 2019;57:150-156.

[Thoracic Oncology Original Research]

CHEST

Diagnostic Outcomes and Safety of Cryobiopsy Added to Conventional Sampling Methods

An Observational Study

Yuji Matsumoto, MD; Toshiyuki Nakai, MD; Midori Tanaka, MD; Tatsuya Imabayashi, MD; Takaaki Tsuchida, MD; and Yuichiro Ohe, MD

Retrospective study

Conventional biopsies + **Cryobiopsy** vs Conventional biopsies

Chest. 2021 Nov;160(5):1890-1901.

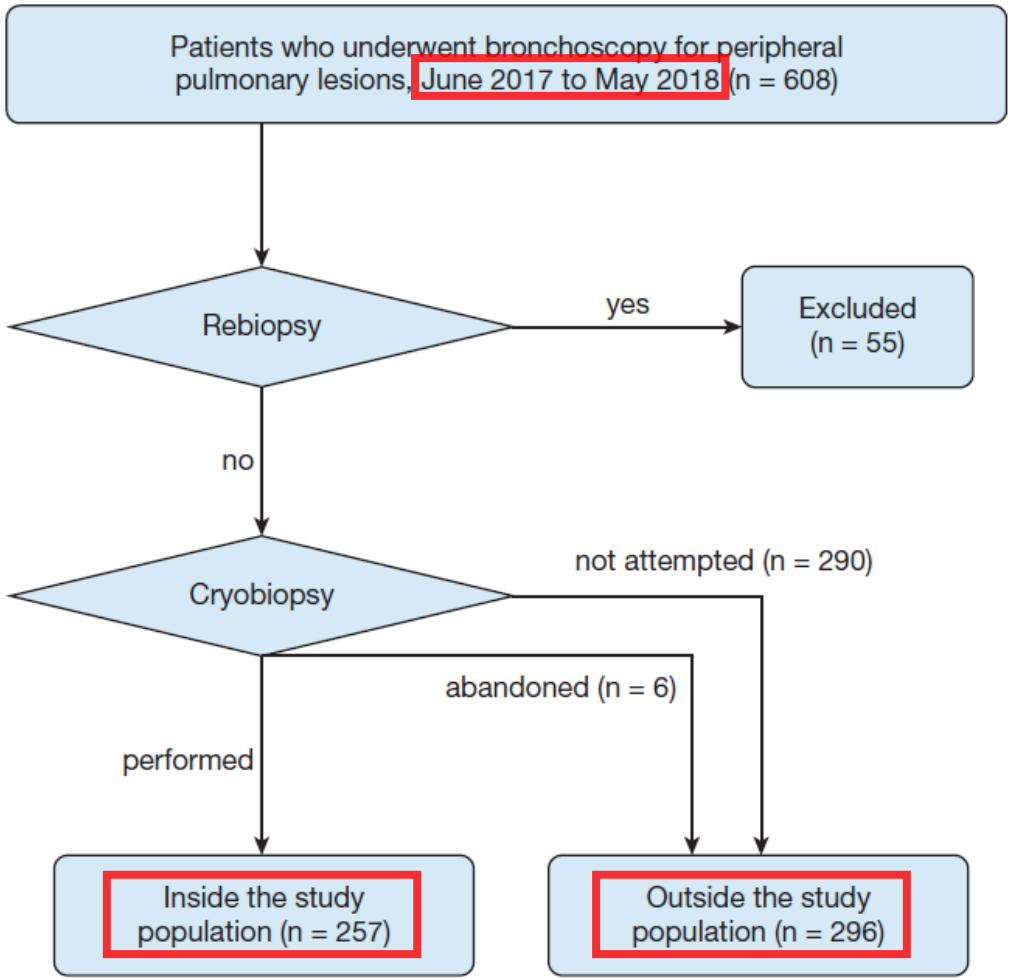


Figure 1 – *Flow diagram displaying patient selection.*

Chest. 2021 Nov;160(5):1890-1901.

TABLE 1] Baseline Characteristics Comparing Inside and Outside the Study Population

Variable	With Cryobiopsy (Inside the Study)	Without Cryobiopsy (Outside the Study)
Age, y	70 (33-86)	70 (29-88)
≤ 70	130 (50.6)	158 (53.4)
> 70	127 (49.4)	138 (46.6)
Sex		
Male	134 (52.1)	191 (64.5)
Female	123 (47.9)	105 (35.5)
Size, mm	22.9 (7.1-115.4)	24.9 (6.4-103.6)
≤ 20.0	98 (38.1)	109 (36.8)
> 20.0	159 (61.9)	187 (63.2)
Morphology		
Solid	152 (59.1)	245 (82.8)
Part-solid	92 (35.8)	44 (14.8)
Pure ground-glass	13 (5.1)	7 (2.4)
Lobe		
RUL and LUS	132 (51.3)	151 (51.0)
RML and lingula	39 (15.2)	27 (9.1)
RLL and LLL	86 (33.5)	118 (39.9)
Location		
Outer	192 (74.7)	210 (70.9)
Inner	65 (25.3)	86 (29.1)
Distance from the costal pleura, mm	8.2 (0-52.1)	5.9 (0-55.2)
≤ 10.0	147 (57.2)	178 (60.1)
> 10.0	110 (42.8)	118 (39.9)
Bronchus sign		
Positive	192 (74.7)	251 (84.8)
Negative	65 (25.3)	45 (15.2)
Related bronchial generation	7 (3-12)	7 (2-13)
≤ 6	111 (43.2)	147 (49.7)
> 6	146 (56.8)	149 (50.3)
Visibility on radiograph		
Visible	187 (72.8)	243 (82.1)
Invisible	70 (27.2)	53 (17.9)
Total	257 (100)	296 (100)

Chest. 2021 Nov;160(5):1890-1901.

TABLE 4] Transition of Diagnostic Outcomes With Cryobiopsy for Each Variable

Variable	Additional Diagnosable Cases by Cryobiopsy	Conventional Diagnosable Cases	*P* Value
Age, y			.263
≤ 70	14 (10.8)	103 (79.2)	
> 70	8 (6.3)	106 (83.5)	
Sex			.825
Male	11 (8.2)	111 (82.8)	
Female	11 (8.9)	98 (79.7)	
Size, mm			.102
≤ 20.0	12 (12.2)	73 (74.5)	
> 20.0	10 (6.3)	136 (85.5)	
Morphology			.463
Solid	14 (9.2)	123 (80.9)	
Part-solid	6 (6.5)	77 (83.7)	
Pure ground-glass	2 (15.4)	9 (69.2)	
Lobe			.524
RUL and LUS	9 (6.8)	105 (79.6)	
RML and lingula	3 (7.7)	34 (87.2)	
RLL and LLL	10 (11.6)	70 (81.4)	
Location			.803
Outer	17 (8.8)	153 (79.7)	
Inner	5 (7.7)	56 (86.2)	
Distance from the costal pleura, mm			.269
≤ 10.0	10 (6.8)	121 (82.3)	
> 10.0	12 (10.9)	88 (80.0)	
Bronchus sign			.011
Positive	12 (6.3)	169 (88.0)	
Negative	10 (15.4)	40 (61.5)	
Related bronchial generation			.502
≤ 6	8 (7.2)	95 (85.6)	
> 6	14 (9.6)	114 (78.1)	
Visibility on radiograph			.120
Visible	13 (7.0)	159 (85.0)	
Invisible	9 (12.9)	50 (71.4)	
R-EBUS finding			.001
Within	4 (3.0)	124 (92.5)	
Adjacent to	18 (14.9)	84 (69.4)	
Invisible	0 (0)	1 (50.0)	
Aspiration needle			.003
With	13 (16.1)	59 (72.8)	
Without	9 (5.1)	150 (85.2)	
ROSE			.344
With	17 (7.8)	179 (81.7)	
Without	5 (13.2)	30 (78.9)	
Total	22 (8.6)	209 (81.3)	...

Overall diagnostic yield was **89.9%** (81.3%+8.6%)

"adjacent to" → 진단율의 이득이 가장 크다
(69.4% vs **84.3%**)

Chest. 2021 Nov;160(5):1890-1901.

TABLE 5] Complications

Adverse Event	Cases
Bleeding	
Mild	101 (39.3)
Moderate	100 (38.9)
Severe	3 (1.2)
Life-threatening	0 (0)
Hypoxemia	11 (4.3)
Pneumothorax	2 (0.8)
Lung abscess	2 (0.8)
Cerebral infarction	1 (0.4)

Hemorrhage grade

Mild: blood suctioning required for < 1min

Moderate: suctioning required for > 1min, repeat wedging of the bronchoscope, or the application of cold saline, diluted vasoactive substances, or thrombin

Severe: selective intubation needed for < 20 min

Life-threatening: persistent selective intubation, or emergency care required.

Chest. 2021 Nov;160(5):1890-1901.

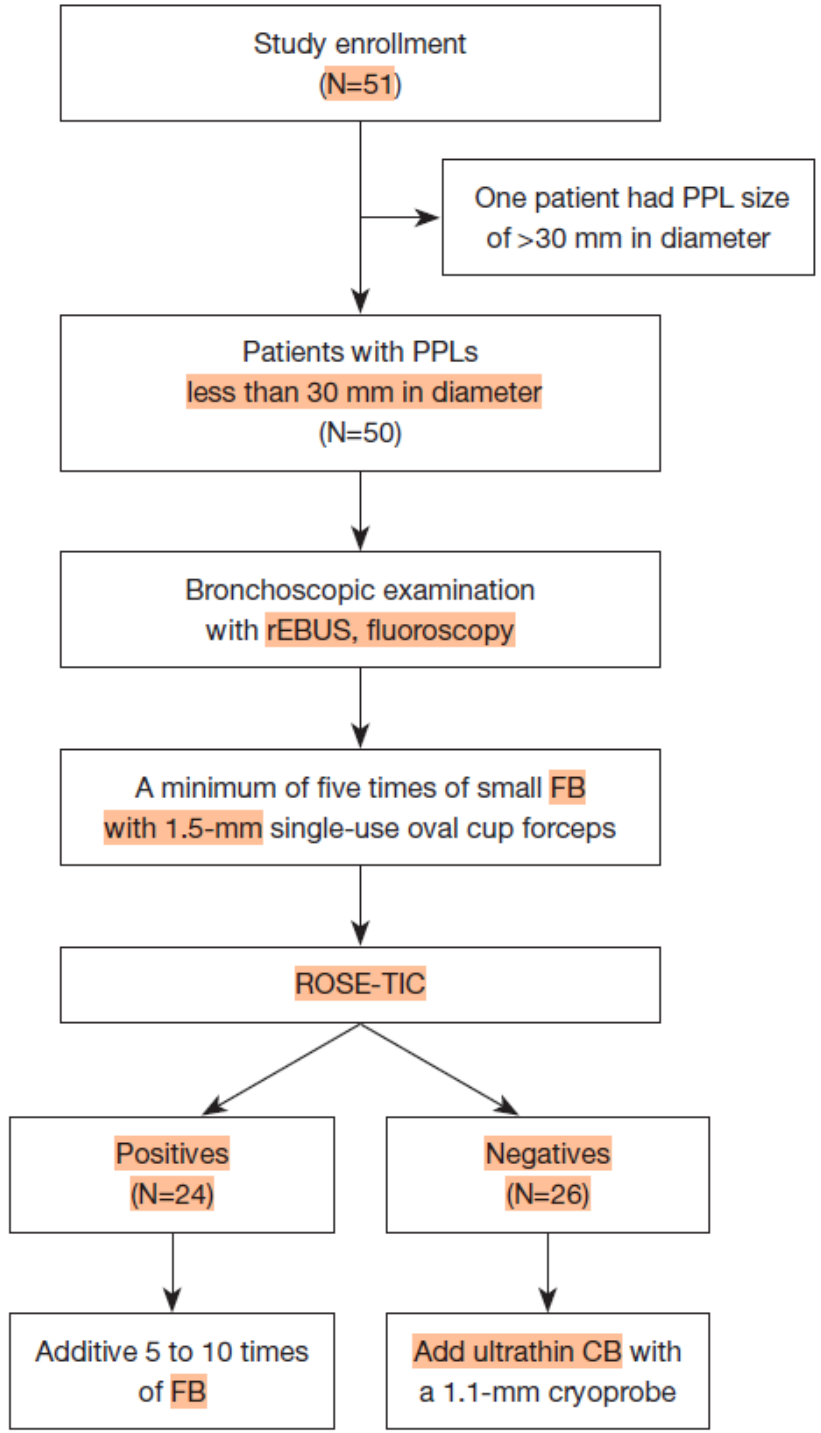
Original Article

Additional 1.1-mm cryobiopsy trial guided by rapid on-site cytologic evaluation of touch imprint cytology result of small forceps biopsy in peripheral pulmonary lesions: a prospective single-center study

Yuki Takigawa[1]^, Ken Sato[1], Suzuka Matsuoka[1], Mayu Goda[1], Keisuke Shiraha[1], Takeru Ichikawa[1], Shoichiro Matsumoto[1], Tomoyoshi Inoue[1], Miho Fujiwara[1], Jun Nishimura[1], Hiromi Watanabe[1], Kenichiro Kudo[1], Akiko Sato[1], Tetsuya Isoda[2], Yoko Shinno[2], Keiichi Fujiwara[1], Takuo Shibayama[1]

Single-center prospective study
PPLs <30 mm were enrolled
1.5-mm **forcep biopsy** vs 1.1-mm **cryo-biopsy** → Rapid on-site cytologic evaluation of touch imprint cytology **(ROSE-TIC)**

Transl Lung Cancer Res 2025;14(12):5273-5282.

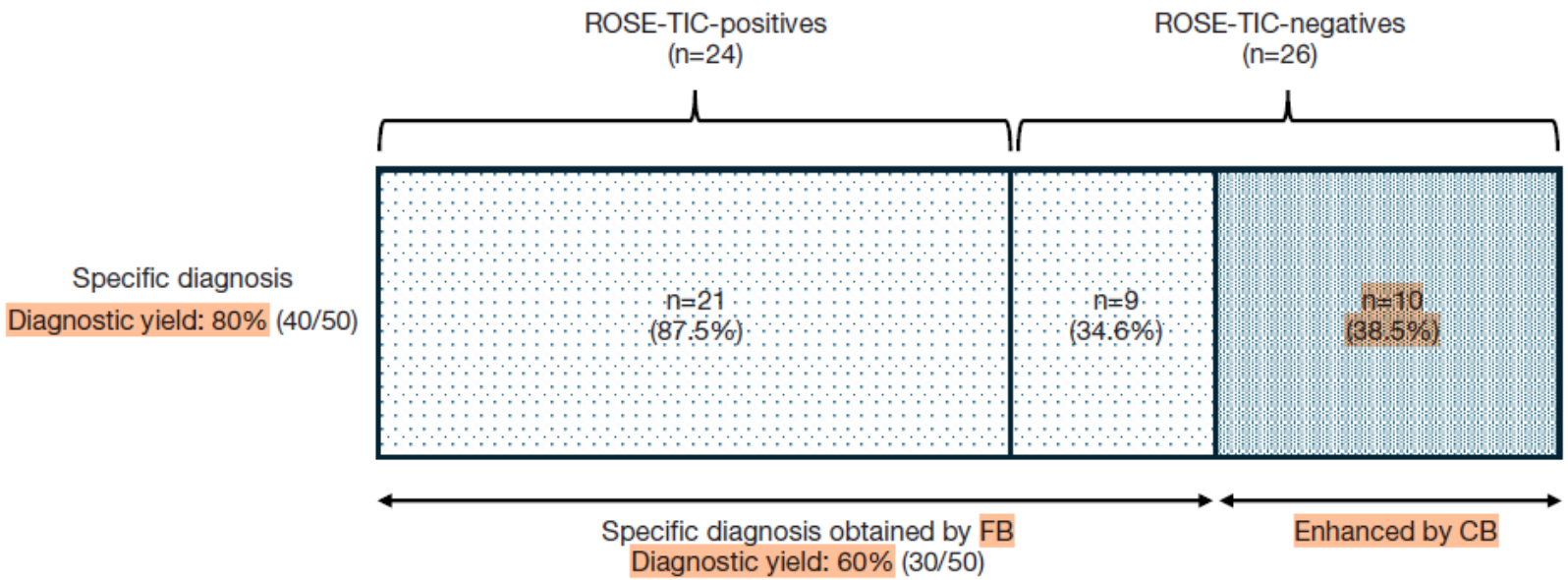


Transl Lung Cancer Res 2025;14(12):5273-5282.

Table 4 Histopathological diagnostic yield by ROSE-TIC results

Diagnosis	ROSE-TIC-positives (n=24)	ROSE-TIC-negatives (n=26)		Overall (n=50)
	FB[†]	FB	FB + CB	
Specific	21	9	19	40
Non-specific	3	17	7	10
Total	24	26	26	50
Diagnostic yield (%)	87.50	34.62	73.08	80.00

[†], including cytological findings (touch imprint cytology and forceps lens fluid), a specific diagnosis was made in 95.8% (n=23) of ROSE-TIC-positives. The ROSE-TIC-negative group showed no enhancement in cytological findings. CB, cryobiopsy; FB, forceps biopsy; ROSE-TIC, rapid on-site cytological evaluation of touch imprint cytology.



FB only와 비교하여 CB 추가 시 diagnostic yield가 **20% 상승** (60% → 80%)

Transl Lung Cancer Res 2025;14(12):5273-5282.

Table 5 Comparison of diagnostic yields according to visual parameters

Visual parameters	Total	FB		FB + CB		P value
		n	%	n	%	
Diameters of the PPLs						
<20 mm	38	20	53	28	74	0.003*
20–30 mm	12	10	83	12	100	0.50
rEBUS findings						
Within	23	19	83	23	100	0.12
Adjacent to	18	10	56	14	78	0.12
Blizzard	9	1	11	3	33	0.50
CT findings						
Solid	25	22	88	24	96	0.50
Partial Solid	17	7	41	13	76	0.040*
GGN	9	1	11	3	33	0.50

*, P<0.05. CB, cryobiopsy; CT, computed tomography; FB, forceps biopsy; GGN, ground-glass nodule; PPLs, peripheral pulmonary lesions; rEBUS, radial endobronchial ultrasound.

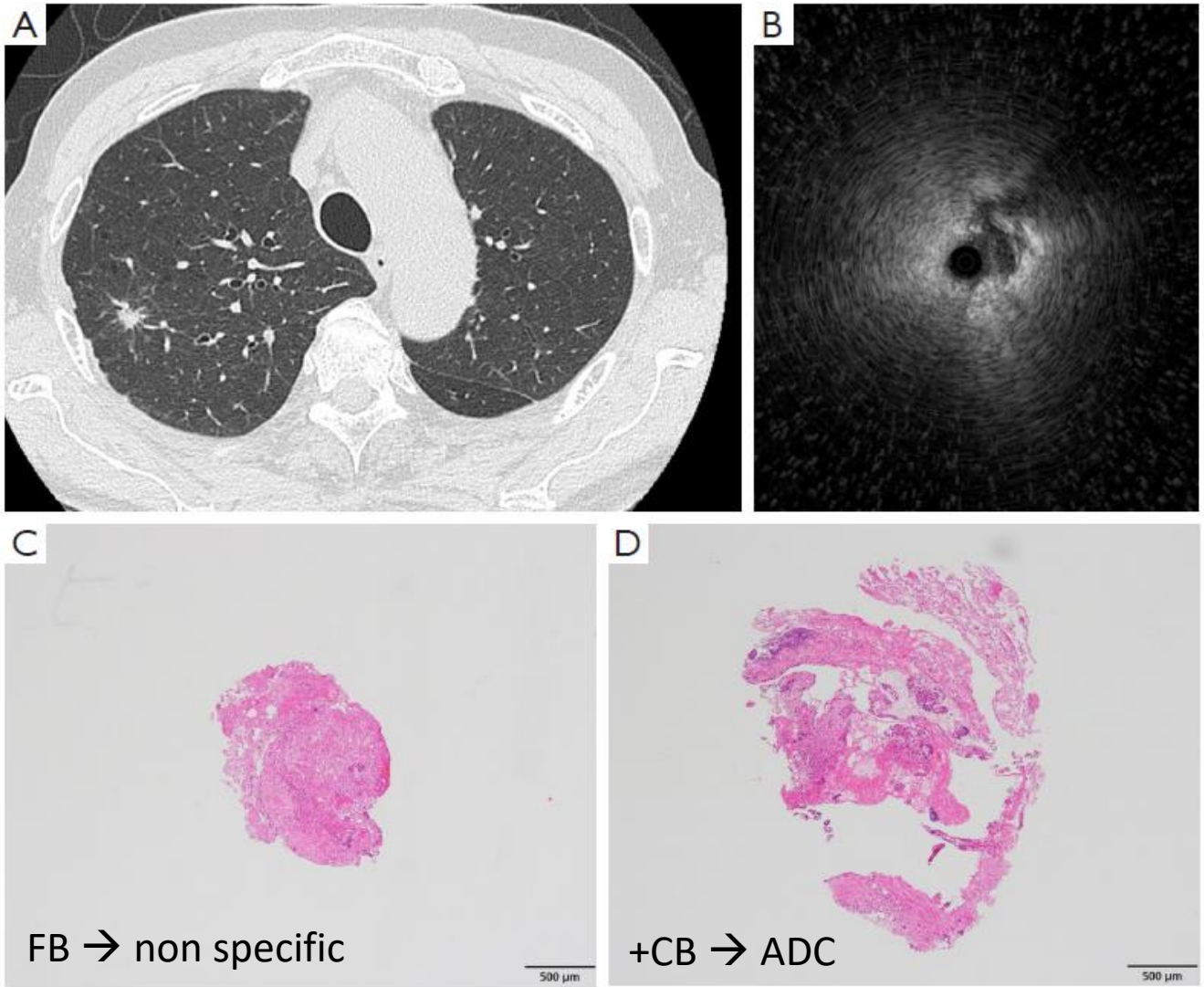


Figure 3 Effective case of additional cryobiopsy for ROSE-TIC negative lesion. (A) A case of an 8-mm right upper lobe pulmonary nodule. (B) EBUS-GS revealed the lesion adjacent to the bronchus. (C) Histopathological findings of forceps biopsy have no specific findings (hematoxylin and eosin staining). (D) Histopathological findings of cryobiopsy showed adenocarcinoma (hematoxylin and eosin staining). EBUS-GS, endobronchial ultrasound with guide sheath; ROSE-TIC, rapid on-site cytological evaluation of touch imprint cytology.

Transl Lung Cancer Res 2025;14(12):5273-5282.

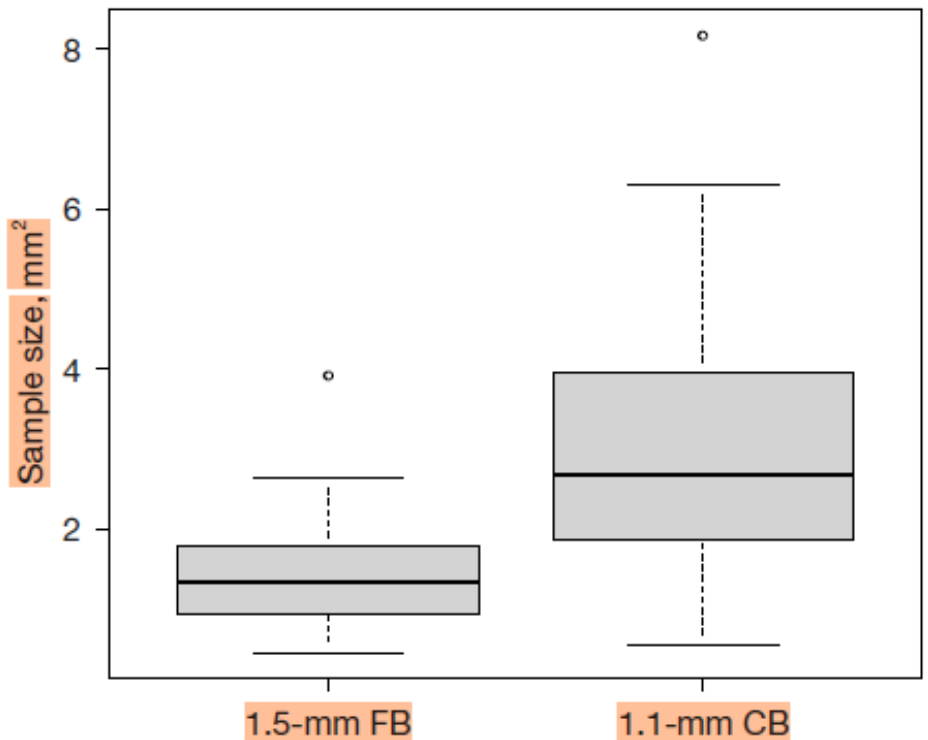


Figure 4 Comparison of the sample size between CB and FB. Statistical analysis was made by the Mann-Whitney *U* test. CB samples were significantly larger than FB samples (median: 2.70 *vs.* 1.35 mm^2; P<0.001). CB, cryobiopsy; FB, forceps biopsy.

Table 3 Complications of the bronchoscopic procedure

Complications	ROSE-TIC-positive (n=24)	ROSE-TIC-negative (n=26)	Total (n=50)
Bleeding			
Grade 0	19	17	36
Grade 1	3	6	9
Grade 2	2	3	5
≥ Grade 3	0	0	0
Pneumothorax	1	0	1
Pneumonia	0	1	1

ROSE-TIC, rapid on-site evaluation of touch print cytology.

Hemostatic strategies : **two-scope method**, **tube wedging**, and **non-intubated CB method**.

Transl Lung Cancer Res 2025;14(12):5273-5282.

Oki *et al. BMC Pulmonary Medicine* (2022) 22:361
https://doi.org/10.1186/s12890-022-02166-w

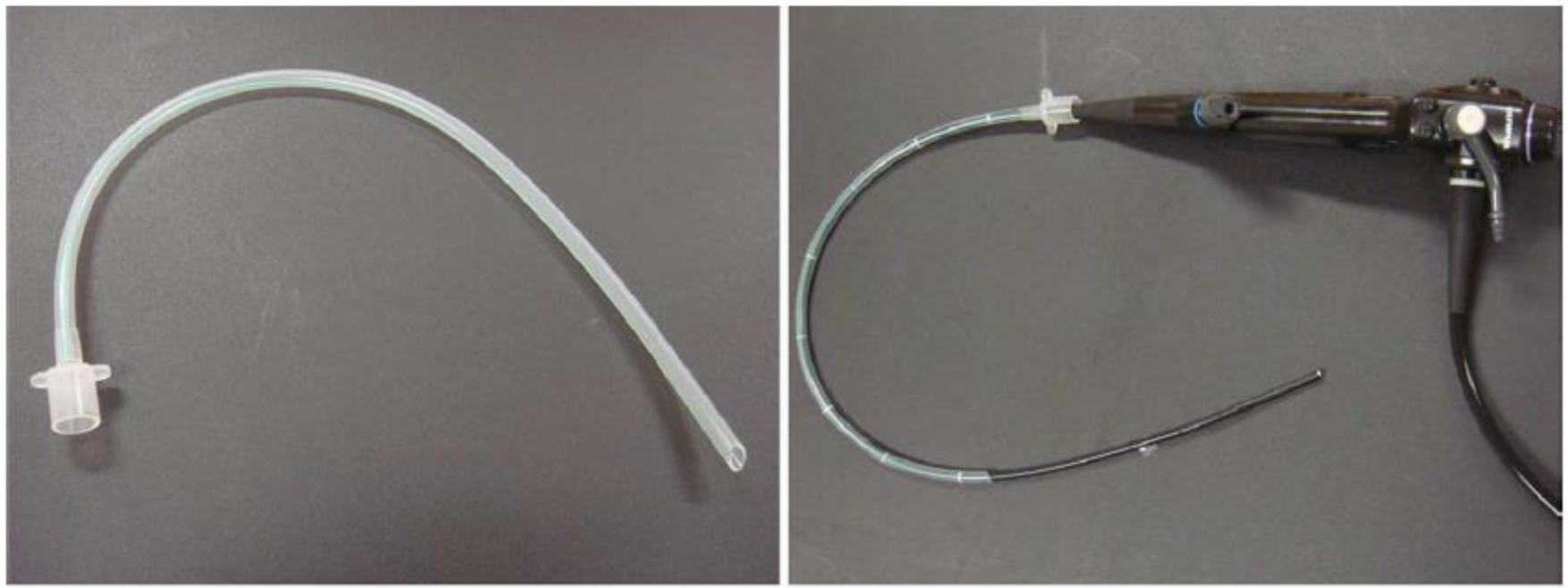
BMC Pulmonary Medicine

RESEARCH

Open Access

Thin bronchoscopic cryobiopsy using a nasobronchial tube

Masahide Oki[1*], Hideo Saka[1,2], Yoshihito Kogure[1], Hideyuki Niwa[1], Akane Ishida[1], Arisa Yamada[1], Atsushi Torii[1] and Chiyoe Kitagawa[1]



a b

Fig. 1 **a** A customized 5.0-mm silicone endotracheal tube with a connecter. **b** The tube was attached to a 4.0 mm bronchoscope

전신마취나 rigid bronchoscopy 없이 conscious sedation에서 transnasal로 시행 가능하다는 장점!!

Oki et al. BMC Pulmonary Medicine (2022) 22:361.

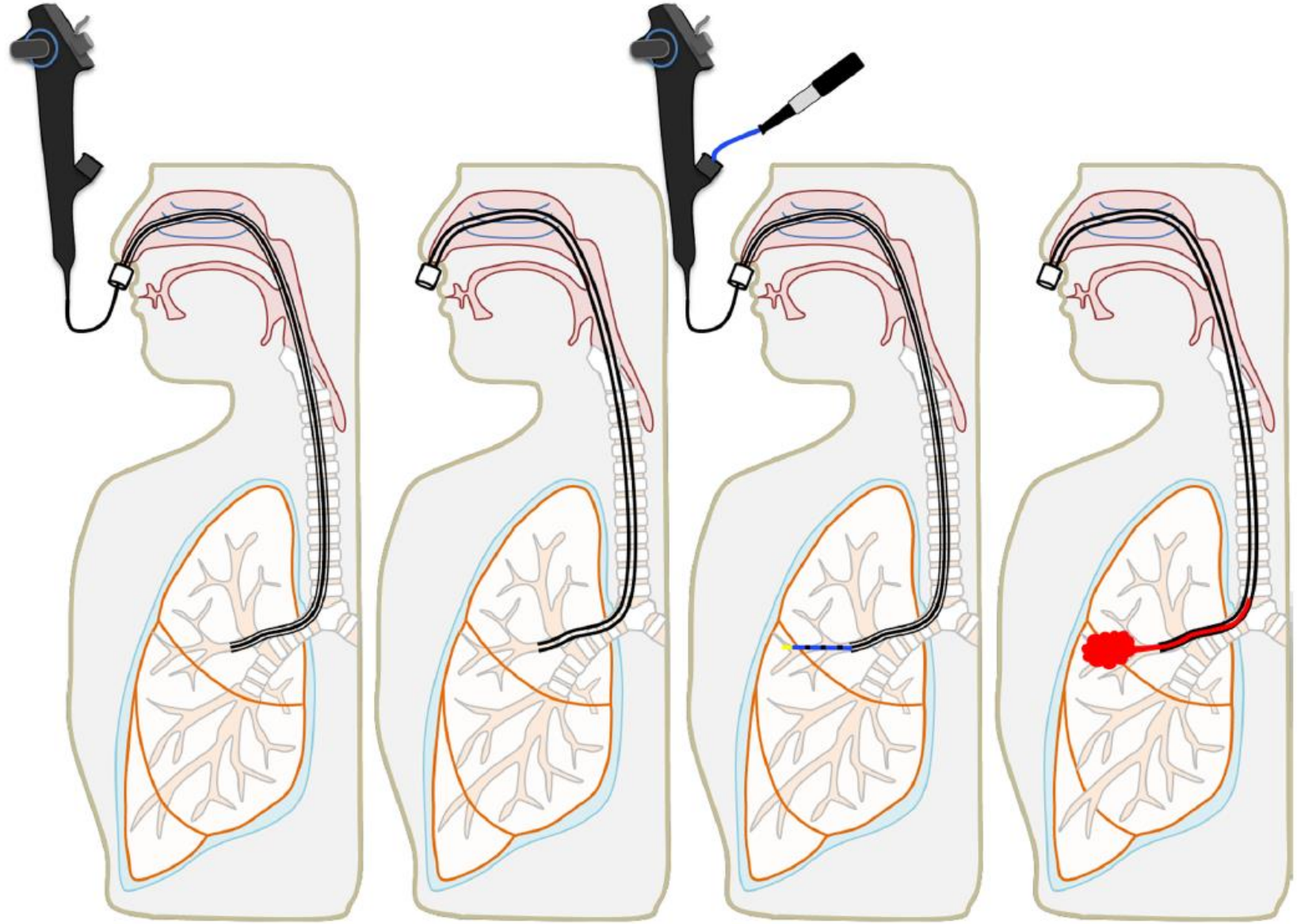


Fig. 2 Wedged-tube cryobiopsy. **a** Advancement of the long bronchial tube through the nose to the target bronchus under thin bronchoscopic control. **b** Wedged bronchial tube. **c** Cryobiopsy. **d** Prevention of blood flooding into the central airway by draining with the bronchial tube

Table 4 Safety

Variables	Value
Complications	
Bleeding	
Grade 0; no bleeding	15 (20.5)
Grade 1; mild bleeding	58 (79.5)
< 50 mL	53
> 50 mL	5
Grade 2, 3; moderate, severe bleeding	0 (0)
Pneumothorax	2[a] (2.7)
Pneumomediastinum	1 (1.4)
Pneumonia	1 (1.4)
Supplemental oxygen during bronchoscopy	
Yes	35 (47.9)
No	38 (52.1)

Data are presented as no. or no. (%) unless otherwise stated

[a] These patients did not require thoracic drainage

Respiration

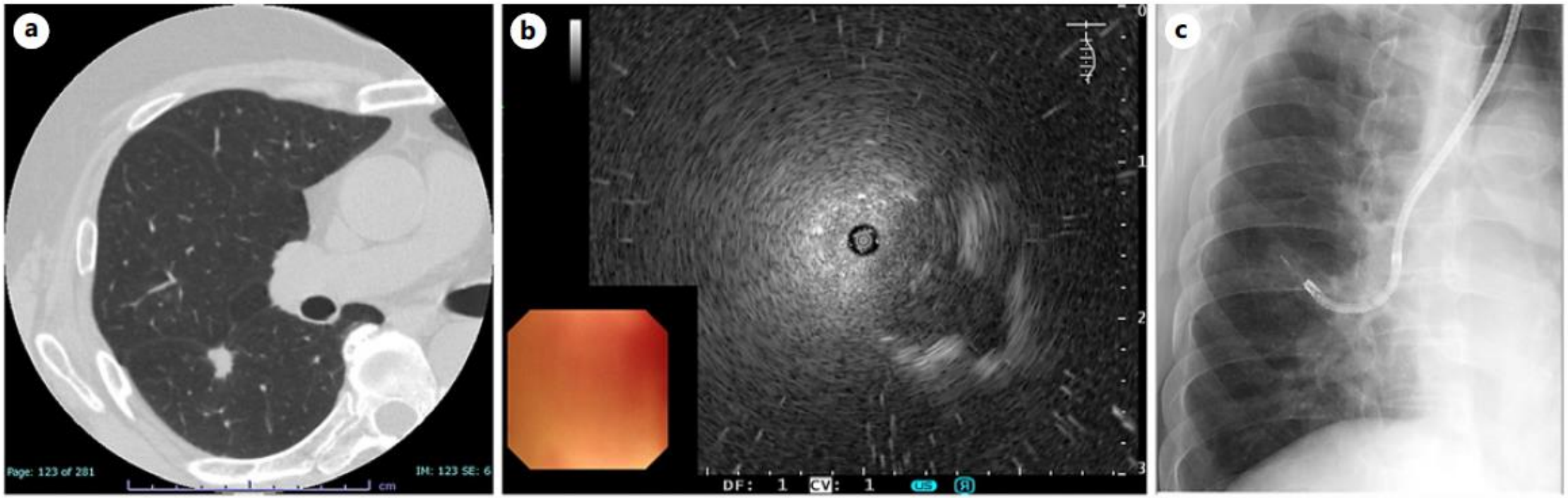
Interventional Pulmonology

Respiration 2023;102:503–514
DOI: 10.1159/000531010

Received: January 9, 2023
Accepted: May 3, 2023
Published online: June 28, 2023

Diagnostic Utility and Safety of Non-Intubated Cryobiopsy Technique Using a Novel Ultrathin Cryoprobe in Addition to Conventional Biopsy Techniques for Peripheral Pulmonary Lesions

Toshiyuki Nakai[a] Tetsuya Watanabe[a] Yuto Kaimi[b] Kazuhiko Shiomi[b] Kanae Ando[b] Atsushi Miyamoto[a] Koichi Ogawa[a] Yoshiya Matsumoto[a] Kenji Sawa[a] Kanako Sato[a] Kazuhisa Asai[a] Yuji Matsumoto[c, d] Yu Mikami[e] Masahiko Ohsawa[b] Tomoya Kawaguchi[a]



It was frozen for **2 or 3 s** for the frozen tissue specimens **to pass through the 2.0-mm working channel** [8, 9]. The freezing time for the initial cryobiopsy was set at 2 s and increased to 3 s depending on the amount of specimens obtained.

The tissue specimens attached to the frozen tip were collected by the assistant by **extracting the cryoprobe through the working channel**, while the **operator wedged the bronchoscope** into the peripheral bronchus and **fixed it in place.**

Respiration 2023;102:503–514.

Lung (2022) 200:737–745
https://doi.org/10.1007/s00408-022-00578-3

INTERVENTIONAL PULMONOLOGY

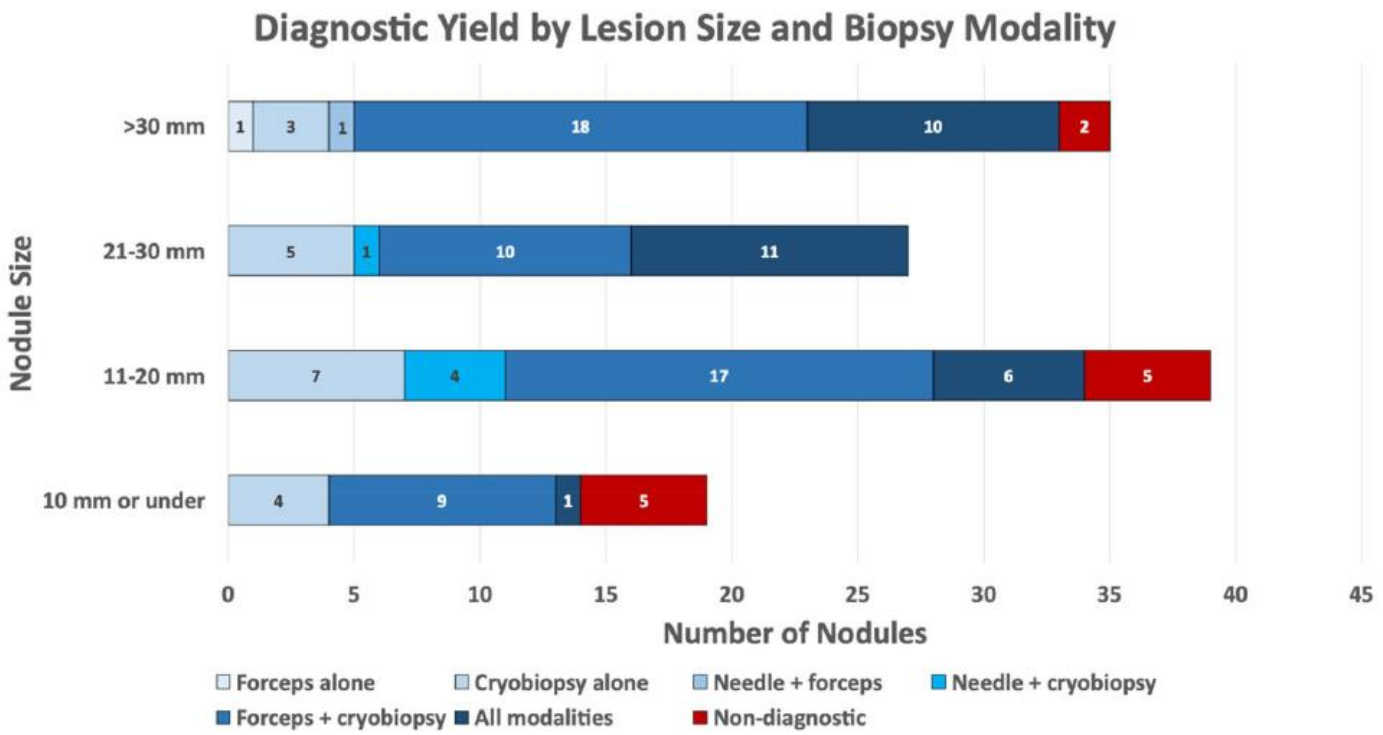
Check for updates

Novel Robotic-Assisted Cryobiopsy for Peripheral Pulmonary Lesions

Catherine L. Oberg[1,4] · Ryan P. Lau[2] · Erik E. Folch[3] · Tao He[1] · Reza Ronaghi[1] · Irawan Susanto[1] · Colleen Channick[1] · Rodrigo Garcia Tome[1] · Scott Oh[1]

Retrospective analysis of **120** peripheral pulmonary lesions

Biopsied via **robotic bronchoscopy** using **needle aspirate**, **forceps**, and **cryobiopsy**



Yield per tool, diagnostic cases	$n = 108$
Needle alone	0 (0%)
Forceps alone	2 (1.9%)
Cryobiopsy alone	19 (17.6%)
Needle + forceps	1 (0.9%)
Needle + cryobiopsy	5 (4.6%)
Forceps + cryobiopsy	53 (49.1%)
Needle + forceps + cryobiopsy	28 (25.9%)
Molecular analysis	$n = 49$
Local IHC/FISH adequacy	49 (100%)
Needle	2 (100%)
Forceps	18 (100%)
Cryobiopsy	29 (100%)
NGS adequacy	45 (81.6%)
Needle	1 (50%)
Forceps	15 (83.3%)
Cryobiopsy	29 (100%)

*IHC—immunohistochemistry, FISH—fluorescence in situ hybridization, NGS—next-generation sequencing

Cryobiopsy 단독으로 진단된 % → **약 18%**

Lung (2022) 200:737–745.

Lung Cancer 196 (2024) 107967

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Research Paper

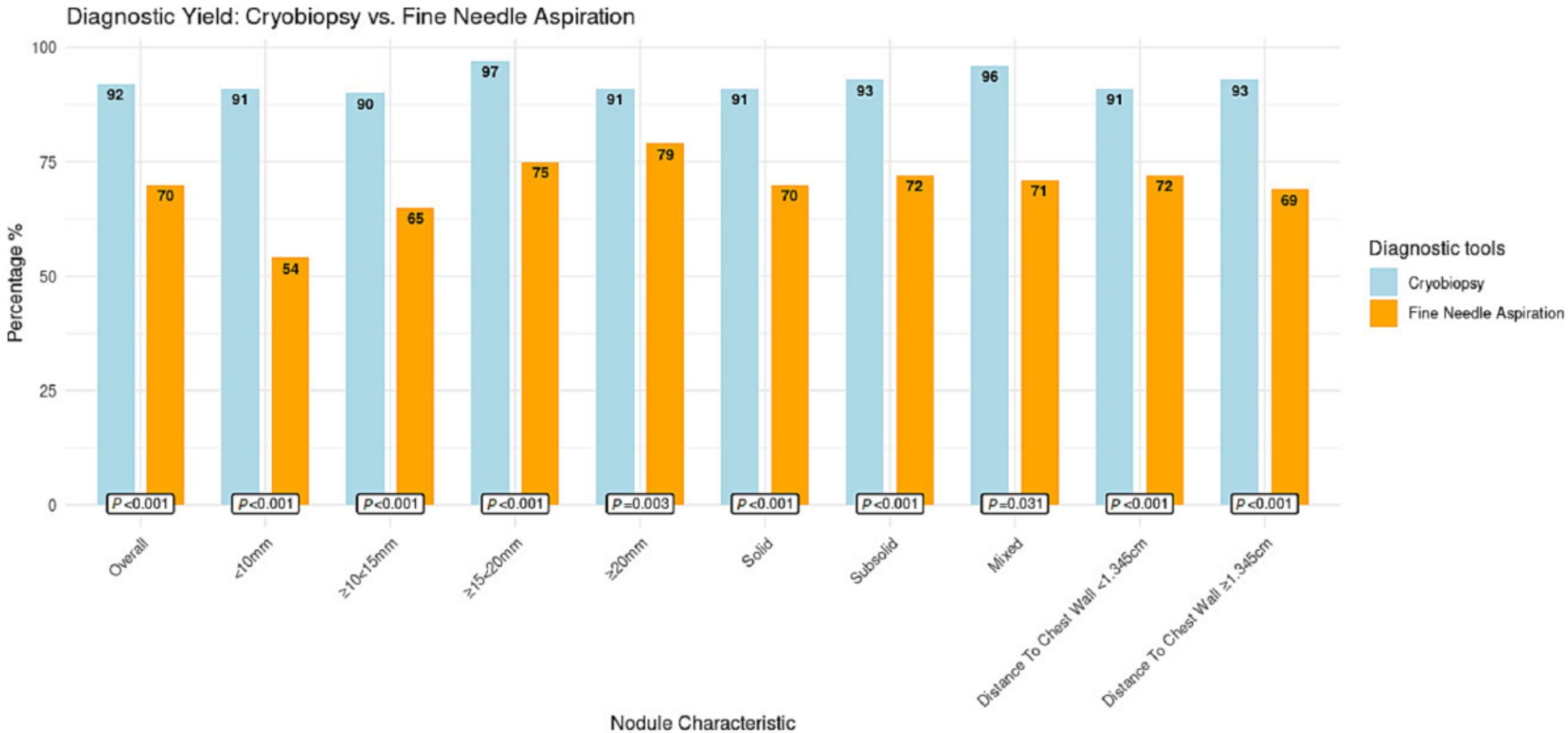
Cryobiopsy versus fine-needle aspiration for shape-sensing robotic-assisted sampling of small lung nodules

David Abia-Trujillo [a,*], Rodrigo Funes-Ferrada [a], Alejandra Yu Lee-Mateus [a], Alanna Barrios-Ruiz [a], Andras Khoor [b], Neal M. Patel [a], Britney N. Hazelett [a], Kelly S. Robertson [a], Sebastian Fernandez-Bussy [a]

Retrospective cohort study

256 patients, with a combined 284 procedures, and **324 nodules sampled**.

Biopsied via **robotic bronchoscopy** using **needle aspirate**, **cryobiopsy**



Lung Cancer 196 (2024) 107967.

PART 2-3

Mediastinal Cryobiopsy

EBUS-guided TBMC — Lymphoma & Sarcoidosis

Respiration

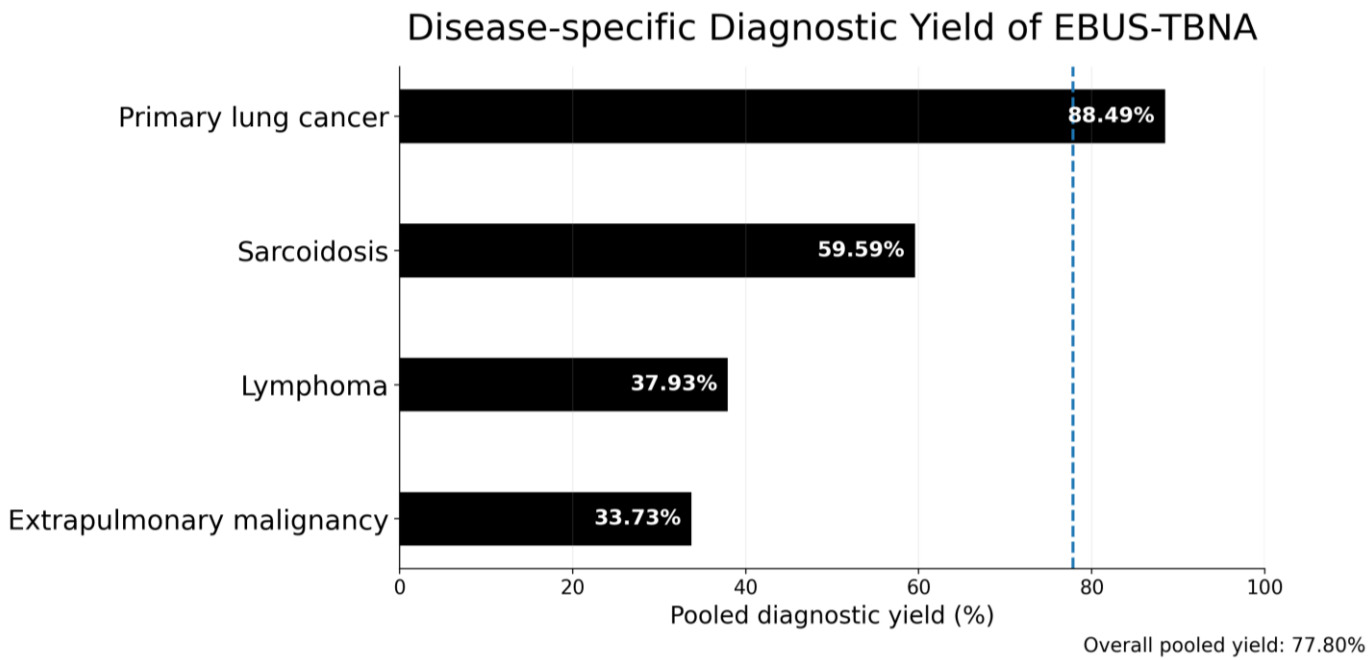
Interventional Pulmonology

Respiration 2024;103:752–764
DOI: 10.1159/000540859

Received: May 31, 2024
Accepted: August 8, 2024
Published online: August 13, 2024

Comparison between Endobronchial Ultrasound-Guided Transbronchial Node Biopsy and Transbronchial Needle Aspiration: A Meta-Analysis

Wuchen Yang[a, b] Huizhen Yang[b] Quncheng Zhang[b] Felix J.F. Herth[c, d]
Xiaoju Zhang[b]



EBUS-TBNA의 제한점!!

Lung cancer 진단에는 우수하나 lymphoma or benign disease 진단에는 제한점이 많다.

: lung cancer는 cytology에서 명확한 malignant cell만 보여도 진단이 가능한 경우가 많지만,

lymphoma or benign disease는 **림프절 architecture의 손실, 세포 분포 및 특이적인 조직학적 pattern 확인이 어려움.**

Respiration 2024;103:752–764

Review Article

Proposal for a standardized methodology for performing endobronchial ultrasound-guided mediastinal cryobiopsy: a four-step approach

Miguel Angel Ariza Prota[1^], Javier Pérez Pallarés[2], Emanuela Barisione[3], Sammy Onyancha[4], Nadia Corcione[5], Hector Enrique Torres Rivas[6], Luis Fernández Fernández[6], Marta García Clemente[1], Francisco Julián López González[1]

Step 1: the planning (select the best place, choose it wisely)

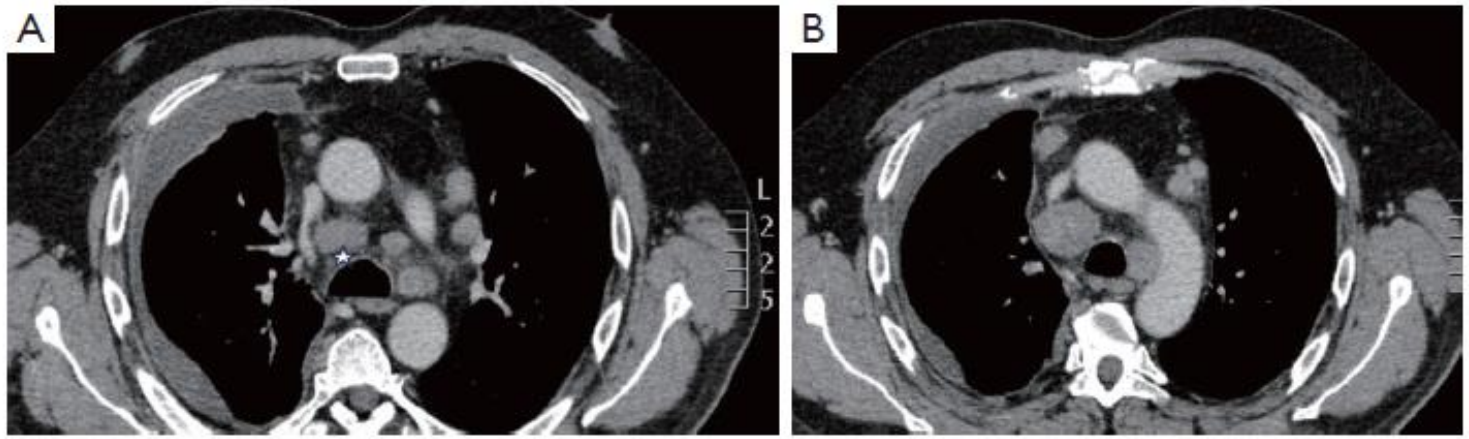


Figure 1 Thorax CT from different levels for the same patient. (A) Asterisk showing the space between 4R station and the tracheobronchial wall. (B) CT showing how the space between the 4R station and the right paratracheal wall decreases as we move down the trachea. CT, computed tomography.

Wall에 가장 가까운 LN의 level을 찾는다.

접근 난이도 : 쉬움 → 어려움
11L, 11Ri, 7, 11Rs, 4R, 2L, 2R, 10R, 10L, 3p, 4L

Step 2: the puncture (the first puncture will guide the rest of the process)

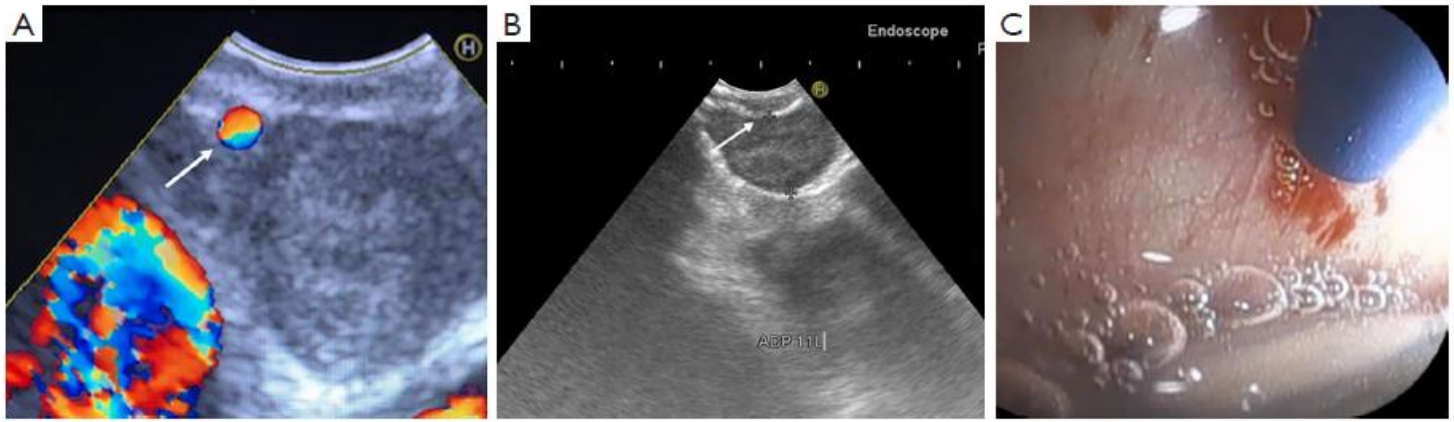


Figure 2 Lymph node stations and Doppler-mode on the ultrasound image. (A) Arrow showing a vessel in the proximal zone of the lymph node. (B) Arrow showing the location with the thinnest mucosa and lymph node capsule. (C) Needle sheath avoiding cartilage before performing the puncture. ADP, adenopathy.

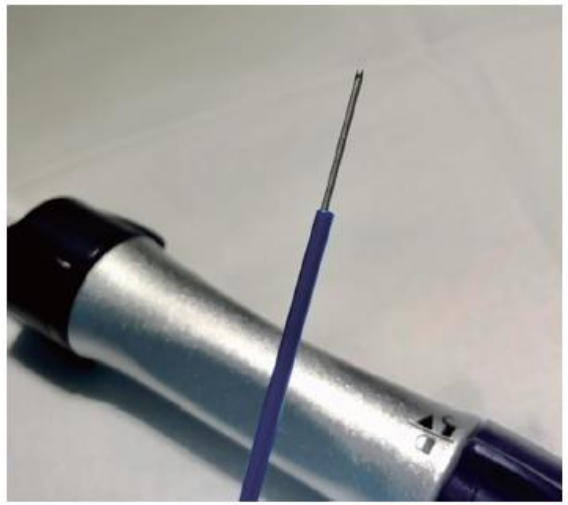


Figure 4 22-gauge SonoTip TopGain crown cut tip needle.

22G SonoTip TopGain **crown-cut needle** 권고 : 더 뚜렷한 puncture trace 확인 가능

Step 3: "the tunnel" : 검체 채취보다 cryoprobe 삽입로 확보가 목적

Figure 5 Arrows on the ultrasound image showing the trace left by the TBNA needle inside the lymph node. TBNA, transbronchial needle aspiration.

Figure 6 Arrow pointing at the broken lymph node capsule.

- 같은 위치에서 두번째 TBNA를 시행 → mucosa–submucosa–lymph node capsul을 통과하는 tunnel을 만든다
- **Aspiration은 하지 않는다!!** Why?> proximal lymph node 부위의 trauma와 bleeding을 줄이기 위해서
- 8–12회 정도 needle movement
- 이후 needle 길이를 약 1 cm 줄여 proximal capsule 부위에 집중
- needle이 저항 없이 들어갔다 나올 수 있으면 capsule이 충분히 열렸다고 판단

Step 4: the cryobiopsy

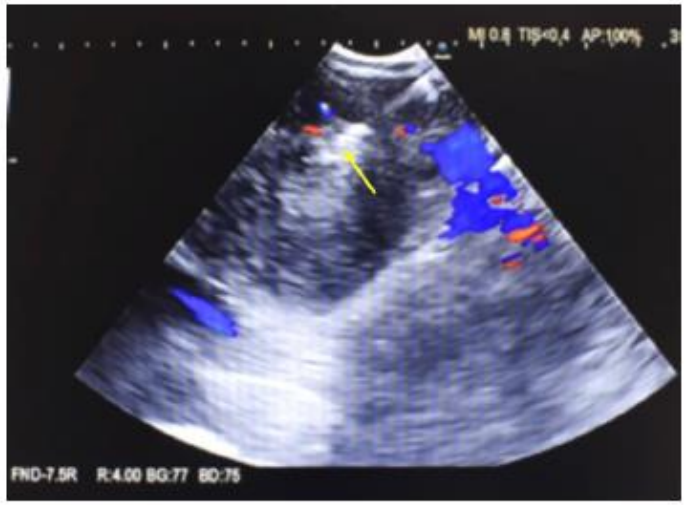


Figure 9 Arrow in the ultrasound image and Doppler mode pointing the tip of the cryoprobe in the correct and desired position.

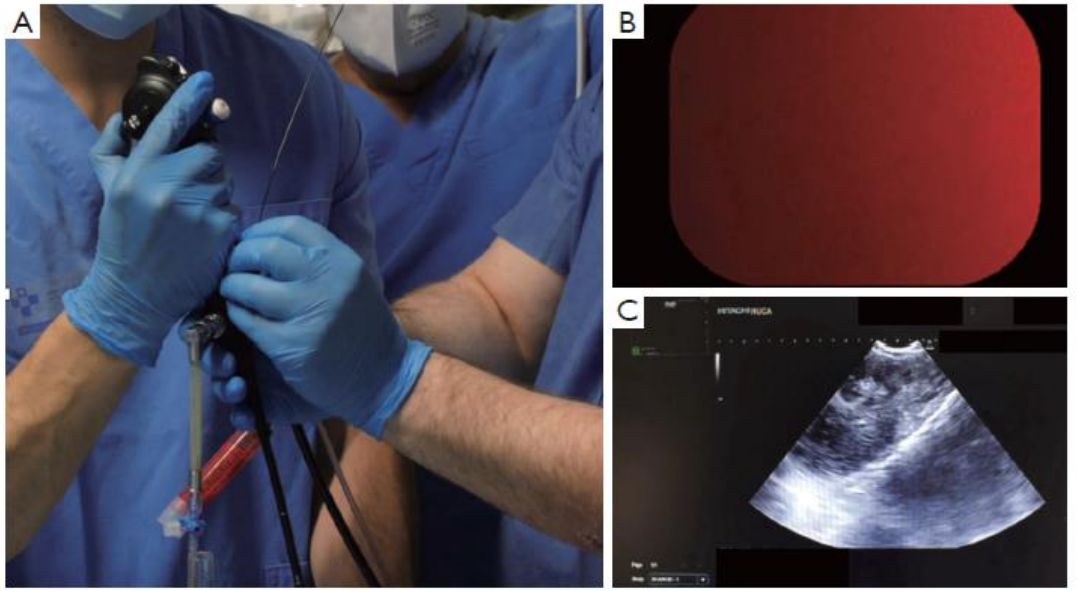


Figure 8 Introduction of the cryoprobe. (A) 1.1 mm cryoprobe being introduced gently into the working channel of the EBUS bronchoscope. (B) No endoscopic vision for letting us locate the previous puncture site. (C) Ultrasound image showing the needle trace inside the lymph node. EBUS, endobronchial ultrasound.

- needle trace와 broken capsule을 초음파로 다시 확인
- 1.1 mm cryoprobe를 **EBUS bronchoscope working channel**로 삽입
- EBUS scope lever를 **neutral position →3–5초 freezing**
- Cryoprobe와 EBUS scope를 함께 빼면서 frozen tissue를 회수

Step 4: the cryobiopsy

Figure 10 Ultrasound image of the cryoprobe. (A) Ultrasound image confirms the cryoprobe tip positioned distally within the lymph node. (B) Cryoprobe's tip located in the lymph node's medial area. (C) Cryoprobe's tip positioned in the proximal zone of the lymph node.

- **3 samples per station** : 1st distal area → 2nd medial area → 3rd capsule 근처 proximal area

Mediastinum 2024;8:30.

Step 4: the cryobiopsy

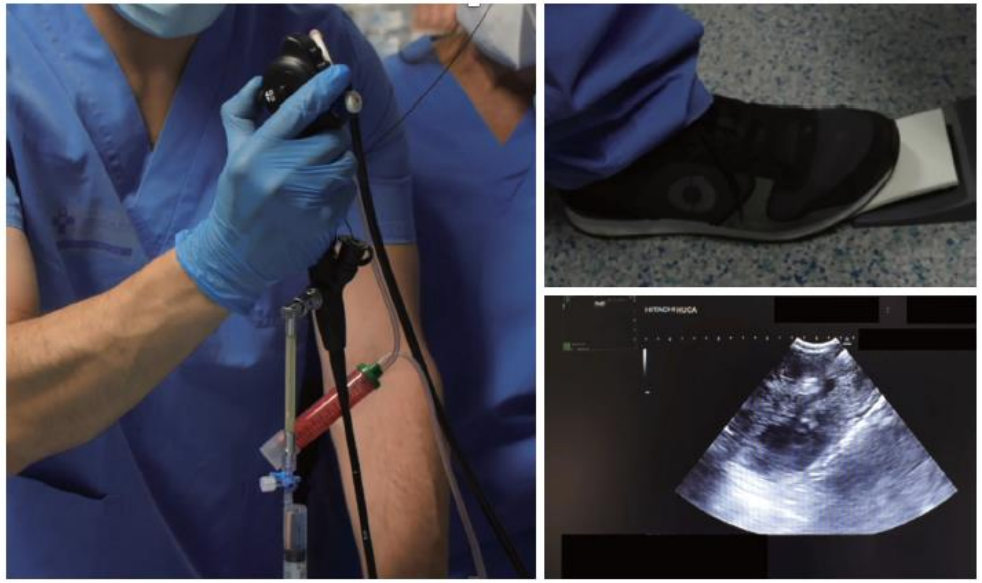


Figure 11 The Cryoprobe firmly grasped with the fourth and fifth fingers, once fixed, the lever of the EBUS scope should be in neutral position. The pedal needs to be pressed for 3–5 seconds until the sample is secured outside the airway. EBUS, endobronchial ultrasound.

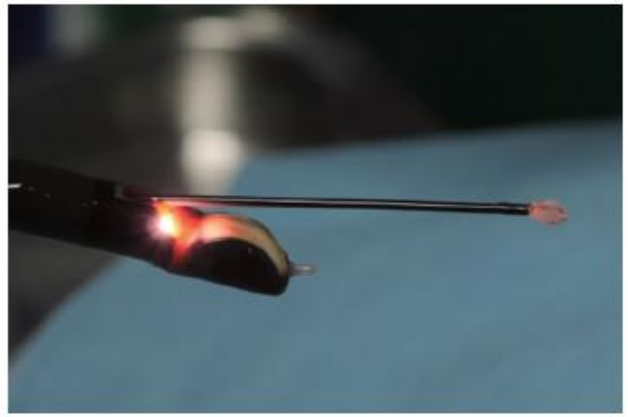


Figure 12 Cryobiopsy attached to the tip of the 1.1 mm cryoprobe.

Freezing time: 3–5초 권장

6초 이상 freezing을 하면 sample size가 더 증가하지 않고, pneumothorax나 pneumomediastinum 위험이 증가

Review Article

Mediastinal lymph node cryobiopsy guided by endobronchial ultrasound: a comprehensive review of methods and outcomes

Shiwani Kamath, Abdullah Jahangir, Salim Daouk, Houssein A. Youness

Interventional Pulmonary Program, Section of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Oklahoma Health Sciences Center and The Oklahoma City VA Health Care System, Oklahoma City, OK, USA

Contributions: (I) Conception and design: HA Youness; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: S Kamath, A Jahangir, S Daouk; (V) Data analysis and interpretation: S Kamath, A Jahangir, S Daouk; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Houssein A. Youness, MD, FCCP. Interventional Pulmonary Program, Section of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, University of Oklahoma Health Sciences Center and The Oklahoma City VA Health Care System, 800 Stanton L Young Blvd, Suite 8400, Oklahoma City, OK 73104, USA. Email: houssein-youness@ouhsc.edu.

Table 2 Overall yield for EBUS-TBC and EBUS-TBNA

Author, year	Cryobiopsy			TBNA		
	Population	Yield	Percentage	Population	Yield	Percentage
Cheng, 2024 (9)	154	141	91.6	154	118	76.6
Zhang, 2021 (8)	194	178	91.8	194	155	79.9
Fan, 2023 (10)	136	126	92.6	135	109	80.7
Poletti, 2024 (11)	48	46	95.8	48	26	54.2
Genova, 2022 (12)	5	3	60.0	5	4	80.0
Gershman, 2022 (13)	24	20	83.3	24	21	87.5
Gonuguntla, 2021 (14)	4	4	100.0	4	3	75.0
Ariza-Prota, 2022 (15)	4	4	100.0	4	3	75.0
Ariza-Prota, 2023 (16)	50	48	96.0	50	41	82.0
Salcedo, 2023 (17)	50	45	90.0	50	32	64.0

EBUS-TBC, endobronchial ultrasound-guided transbronchial cryobiopsy; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration.

Table 3 Yield in benign pathology

Study	No. of patients with benign pathology	Cryobiopsy yield (%)	TBNA yield (%)
Cheng, 2024 (9)	47	78.7	59.6
Zhang, 2021 (8)	47	80.9	53.2
Fan, 2023 (10)	48	94	66.7
Gonuguntla, 2021 (14)	2	100	100
Ariza-Prota, 2023 (16)	12	100	60

TBNA, transbronchial needle aspiration.

Sarcoidosis yield

Zhang et al. 100% vs 66%

Fan et al. 100% vs 75%

Cheng et al. 92% vs 75%

Lymphoma yield

Zhang et al. 88% vs 13%

Complications

The most common complication was bleeding. **Most studies reported minor bleeding** (grade 0–1).

Pneumothorax or pneumomediastinum was another reported complication noted on post-procedural radiography. These occurred at **a rate of <2%** and resolved without further intervention.

None of the above complications were statistically significant compared to the control group, suggesting that cryobiopsy offers no significant additional procedural risk.

PART 2-4

Cryoablation for Lung Cancer

Transbronchial Approach + Cryo-Immunotherapy

Lung Cancer Cryoablation의 Rationale

적응증

수술 불가/거부 Stage IA NSCLC

Oligometastasis / 다발성 cancer

ILD 동반 폐암 (수술/RT 부담)

재발성 lesion 반복 적용 가능

Percutaneous의 한계

Pneumothorax 25–34%

Hemothorax / 늑간동맥 손상

흉벽·종격동 인접 안전성 문제

Needle tract seeding (드묾)

Transbronchial Cryoablation의 장점

흉막 보존 (pneumothorax ↓↓) · Day-care 외래 시술 가능 · Multiple lesion 복수 ablation · RFA/MWA와 달리 항원 보존 (cryo-immunology)

Velez A. Front Immunol 2023;14:1203539. · Hinshaw JL. J Vasc Interv Radiol 2010;21:1424-1428.

OPEN ACCESS

Original research

Transbronchial cryoablation in peripheral lung parenchyma with a novel thin cryoprobe and initial clinical testing

Chuanjia Gu,[1,2,3] Haibin Yuan,[4] Chi Yang,[5,6] Fangfang Xie,[1,2,3] Junxiang Chen,[1,2,3] Lei Zhu,[7] Yifeng Jiang,[8] Jiayuan Sun [1,2,3]

stage IA peripheral lung cancer or metastases

1.9-mm thin flexible cryoprobe

CBCT-guided transbronchial cryoablation

first-in-human 연구

Gu C. Thorax 2024;79(7):633-643. · .

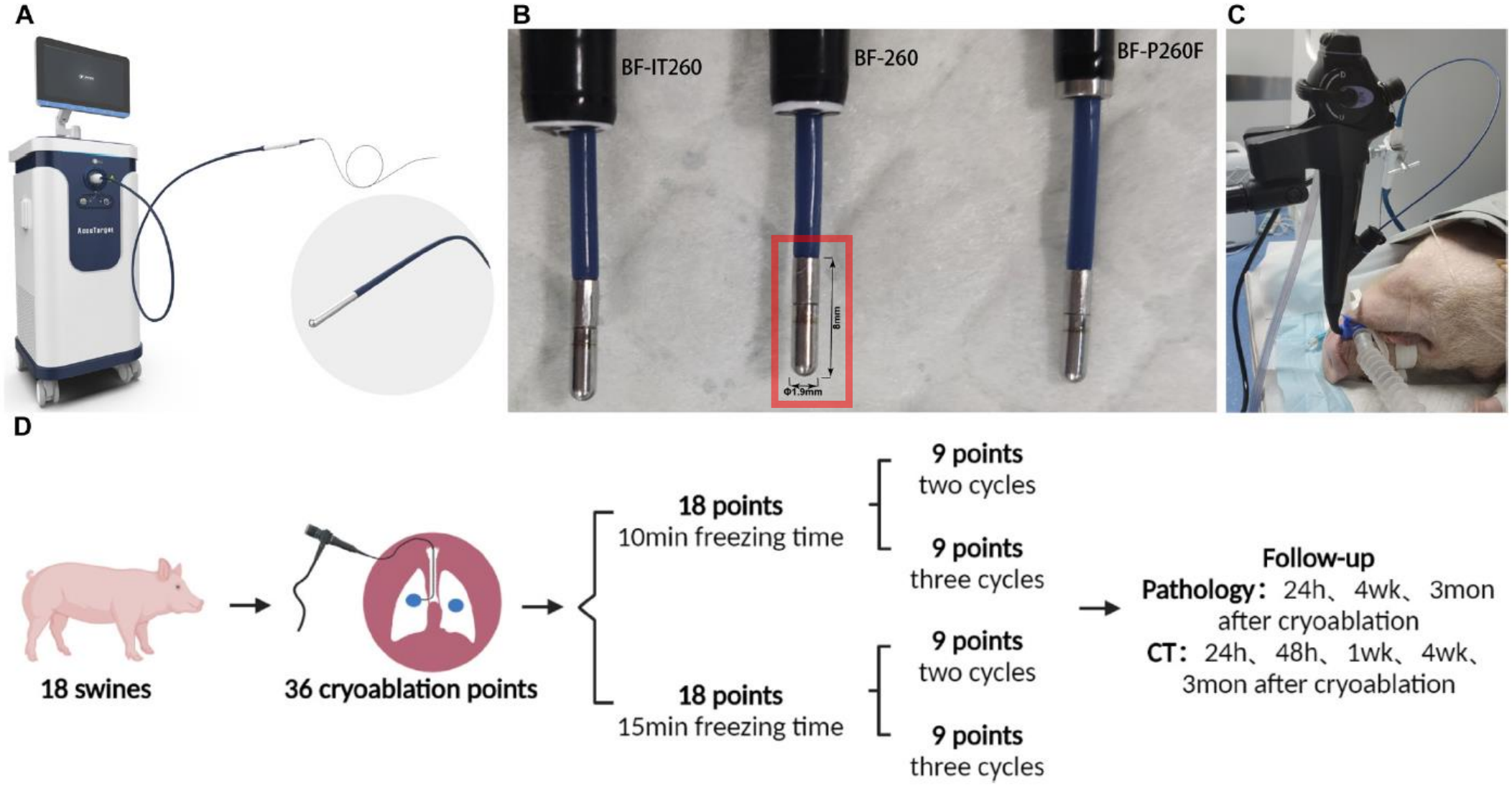


Figure 1 (A) Cryotherapy system and novel thin flexible cryoprobe. (B) Adaptability of the novel flexible cryoprobe to different models of bronchoscopes (BF-1T260, BF-260 and BF-P260F). (C) Experimental overview. (D) Experimental grouping and procedures created with BioRender.com.

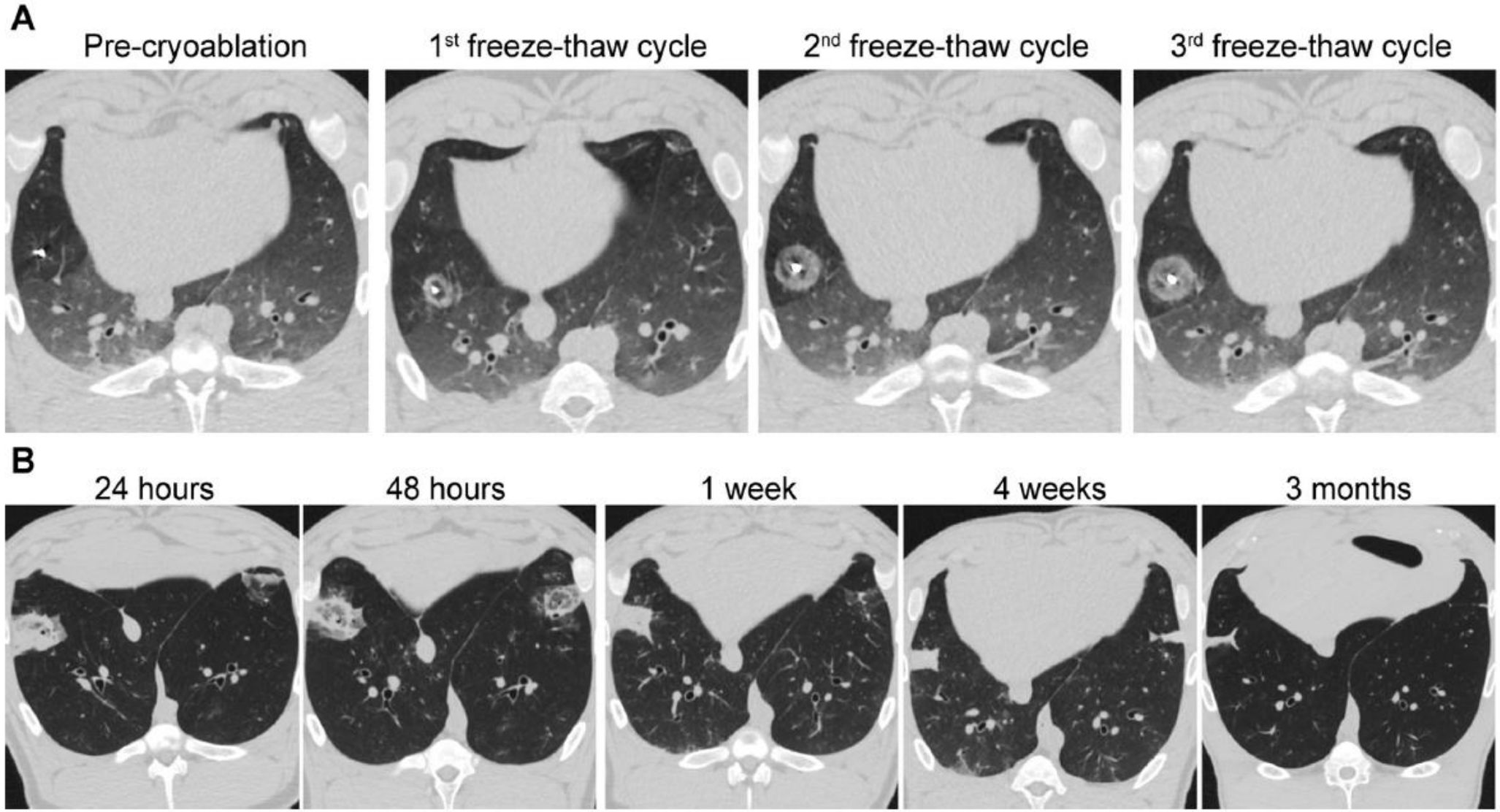


Figure 2 Representative CT findings of dynamic changes from the group 15 min for three cycles during cryoablation (A) and 3 months post cryoablation (B).

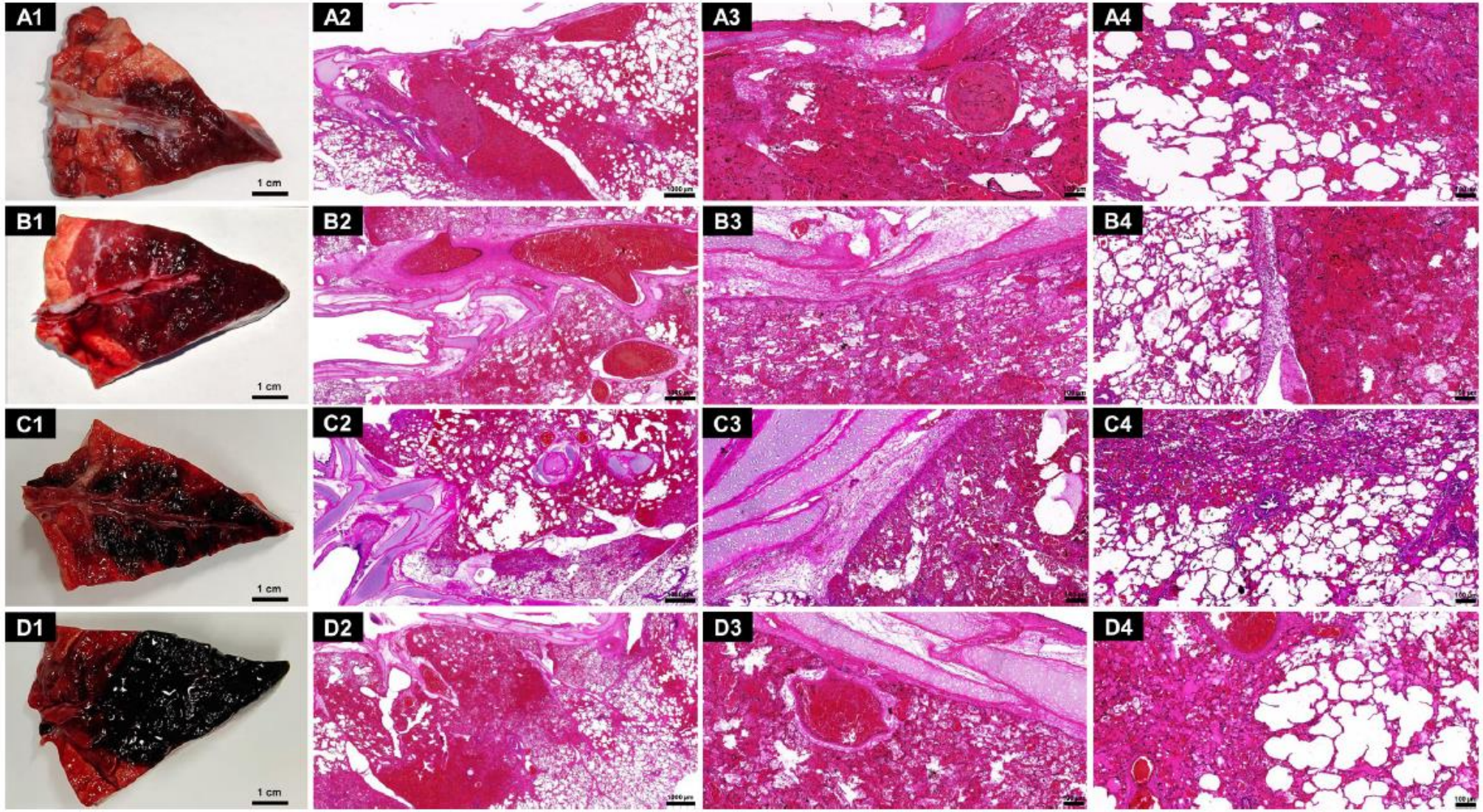


Figure 3 Representative histopathological findings at 24 hours after ablation in the groups 10 min for two cycles (A), 10 min for three cycles (B), 15 min for two cycles (C) and 15 min for three cycles (D). Gross pathology of the ablation zone along the bronchus at the area of cryoprobe insertion

Table 3 Patients and tumour characteristics receiving transbronchial cryoablation

Case	Gender	Location	Pathology	Density	Size (mm)	Distance to pleura (mm)	Comorbid disease or history
1	F	RUL	LUAD	mGGO	24.29×18.21	0.00	Multiple primary lung cancer, hypertension, cerebral infarction
2	F	RUL	LUAD	mGGO	13.58×13.23	19.50	After RML lobectomy for lung cancer, multiple primary lung cancer, hypertension, cerebral infarction
3	F	RLL	LUAD	Solid	19.84×16.49	14.16	Lung metastasis from colon cancer, after LUL lobectomy for lung cancer, hypertension
4	M	LLL	LUAD	Solid	15.49×12.65	12.47	CHD, Parkinson's disease
5	F	RLL	LUAD	mGGO	18.43×11.40	30.04	After RUL lobectomy for lung cancer, multiple primary lung cancer, hypertension
6	F	LLL	LUAD	pGGO	9.65×7.37	28.94	After RML lobectomy for lung cancer, multiple primary lung cancer
7	F	LUL	LUAD	Solid	14.47×12.94	31.63	Asthma, refusal to surgery
8	F	LUL	LUAD	mGGO	17.44×14.15	10.66	CHD, hypertension, diabetes
9	F	RLL	LUAD	pGGO	12.19×10.51	4.10	After LLL lobectomy for lung cancer, multiple primary lung cancer

CHD, coronary heart disease; F, female; LLL, left lower lobe; LUAD, lung adenocarcinoma; LUL, left upper lobe; M, male; mGGO, mixed ground-glass opacity; pGGO, pure ground-glass opacity; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

9 patients, 9 lesion → transbronchial cryoablation을 시행

stage IA peripheral lung cancer or pulmonary metastasis

수술이 어렵거나 수술을 거부한 환자

navigation bronchoscopy, radial EBUS, cone-beam CT 유도

첫 4명은 안전성을 고려해 **7분 freezing + 3분 thawing** → 이후 **freezing time을 10분**

Gu C. Thorax 2024;79(7):633-643.

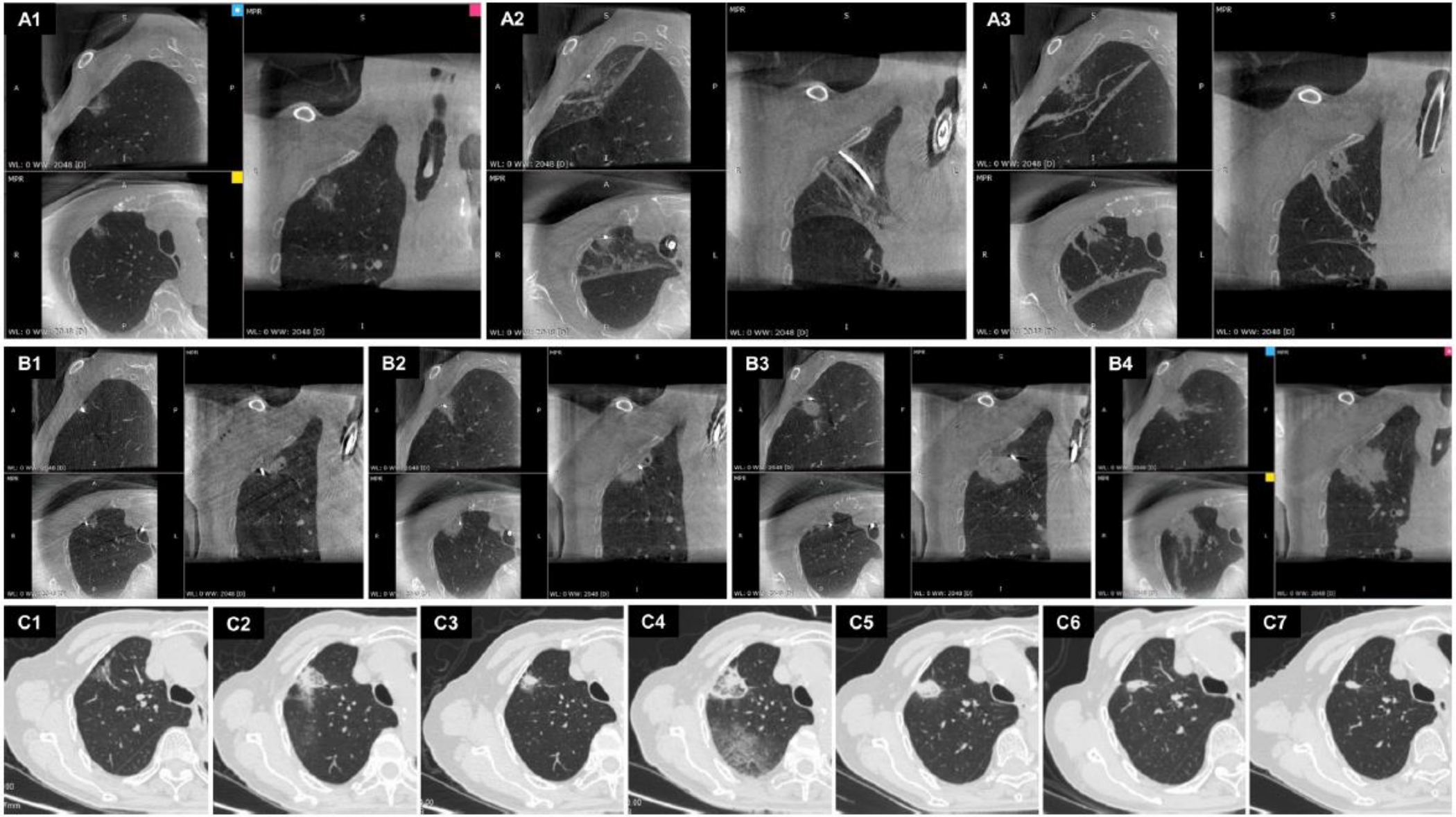


Figure 6 Cone-beam CT (CBCT)-guided transbronchial cryoablation in case 1. CBCT images during the first cryoablation showing the target lesion before the procedure (A1), interprocedural confirmation of the cryoprobe inside the target lesion (A2) and the lesion immediately after cryoablation (A3). CBCT images of the second cryoablation showing the cryoprobe in three different target bronchi during cryoablation (B1–B3) and the lesion covered completely within the ablation area immediately after cryoablation (B4). Chest CT before cryoablation (C1), 1 day (C2) and 1 month (C3)after the first cryoablation and 1 day (C4), 1 month (C5), 3 months (C6) and 12 months (C7) after the second cryoablation. MPR, multiplanar reconstruction ;

Gu C. Thorax 2024;79(7):633-643. · .

2 exhibited incomplete ablation and subsequent local progression at 6 months

→ Technical efficacy at 3 months : **77.78%** (7/9)
→ disease control rate of **100% at 3 months**

No postprocedural complications were observed.

Gu C. Thorax 2024;79(7):633-643. · .

PART 2-5

Cryorecanalization

Malignant Central Airway Obstruction

Malignant CAO의 임상적 부담

진행성 폐암의 약 **30%**에서 central airway 침범 · dyspnea, post-obstructive pneumonia, hemoptysis

치료 옵션	장점	단점
Mechanical debulking	즉시 효과	출혈, 천공 위험
Laser / Electrocautery	즉시 효과, 정밀	Airway fire, cartilage damage
APC	표면 출혈 제어	표면 효과만, 가스 색전
Cryorecanalization	즉시 효과 + cartilage 보존	출혈 7-10%, hemostasis 필요
Stent	Extrinsic compression 해결	Granulation, migration

Ernst A. Am J Respir Crit Care Med 2004. · Ost DE. Chest 2015;148:450-471.

J Korean Med Sci. 2023 Aug 14;38(32):e244
https://doi.org/10.3346/jkms.2023.38.e244
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Respiratory Diseases

Check for updates

Clinical Outcomes of Bronchoscopic Cryotherapy for Central Airway Obstruction in Adults: An 11-Years' Experience of a Single Center

Jong Hwan Jeong [1,2] **Jiwon Kim** [1] **Chang-Min Choi** [1] **and Wonjun Ji** [1]

[1]Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[2]Division of Pulmonology and Allergy, Department of Internal Medicine, Gyeongsang National University Hospital, Gyeongsang National University School of Medicine, Jinju, Korea

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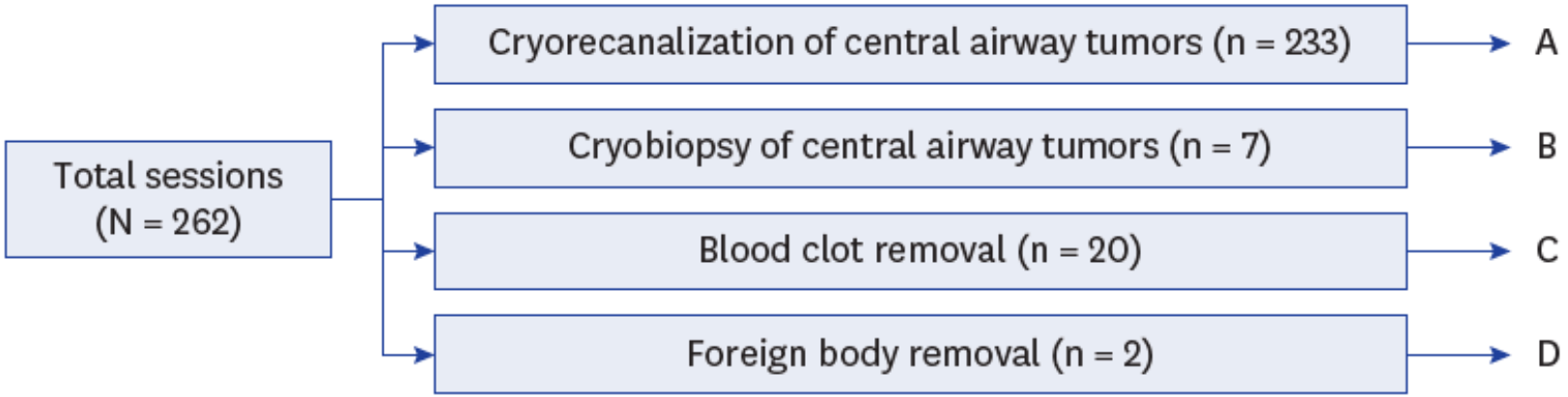

A: Analyses of factors associated with success rate (Table 3)
A + C: Assessment of outcomes according to etiology (Table 4)
A + B: Analyses of factors associated with moderate to severe intrabronchial bleedings (Table 6)

Fig. 2. Flow diagram of bronchoscopic cryotherapy sessions.

Retrospective, single-center study at Asan Medical Center, Seoul, Republic of Korea, from January 2009 to December 2020

J Korean Med Sci. 2023 Aug 14;38(32):e244.

Table 2. Procedure characteristics of cryotherapy sessions

Characteristics	Values (%)
Total number of sessions	262 (100.0)
Anesthesia	
Moderate sedation	209 (79.8)
General anesthesia	53 (20.2)
Respiratory failure before procedure	
No symptom	135 (51.5)
Dyspnea	37 (14.1)
Nasal O2 inhalation	64 (24.4)
Ventilator	26 (10.0)
Cause of cryotherapy	
Cryorecanalization of central airway tumors	233 (88.9)
Cryobiopsy of central airway lesions	7 (2.7)
Blood clot	20 (7.6)
Foreign body	2 (0.8)
Bronchoscopy	
Flexible bronchoscopy	232 (88.5)
Rigid bronchoscopy	30 (11.5)
Concomitant method	
Stent placement	12 (4.6)
Laser	54 (20.6)
Electrocoagulation knife	6 (2.3)
Photodynamic therapy	7 (2.7)
ECMO	18 (6.9)

Values are presented as number (%).
ECMO = extracorporeal membrane oxygenation.

Table 4. Outcomes according to etiology of cryorecanalization for central airway obstruction

Variables	No. of sessions	Reestablishment of airway patency			Symptom relief[a]	No. of patients	Survival after intervention, mon[b]
		Complete	Partial	None			
		No. (%)	No. (%)	No. (%)	No. (%)		Mean ± SD
Total	253	161 (63.6)	69 (27.3)	23 (9.1)	93/125 (74.4)	202	30.5 ± 39.2
Malignancy							
NSCLC	127	81 (63.8)	37 (29.1)	9 (7.1)	53/71 (74.6)	100	23.1 ± 34.3
SCLC	6	3 (50.0)	2 (33.3)	1 (16.7)	2/4 (50.0)	4	6.7 ± 6.1
Metastasis of thyroid cancer	8	3 (37.5)	5 (62.5)	0 (0.0)	0/0	3	13.1 ± 11.6
Metastasis of colon cancer	7	5 (71.4)	2 (28.6)	0 (0.0)	2/2 (100.0)	6	14.7 ± 12.9
Metastasis of RCC	35	21 (60.0)	9 (25.7)	5 (14.3)	10/13 (76.9)	22	29.9 ± 29.4
Metastasis of HCC	8	4 (50.0)	4 (50.0)	0 (0.0)	6/6 (100.0)	7	7.9 ± 7.1
Other malignancy	18	10 (55.6)	3 (16.7)	5 (27.8)	5/8 (62.5)	16	40.1 ± 50.9
Benign lesion	24	15 (62.5)	7 (29.2)	2 (8.3)	5/6 (83.3)	24	72.3 ± 45.0
Blood clot	20	19 (95.0)	0 (0.0)	1 (5.0)	10/15 (66.7)	20	-

SD = standard deviation, NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer, RCC = renal cell carcinoma, HCC = hepatocellular carcinoma.
[a]Data from 125 sessions are included, after excluding patients with no oxygen requirement or subjective symptoms of dyspnea before the procedure.
[b]For patients who underwent more than one intervention, calculations were based on the date of the first intervention. Patients with blood clots were excluded.

Table 3. Factors associated with success rate of cryorecanalization for central airway obstruction

Variables	Sessions	Reestablishment of airway patency			Univariate analysis[a]		Multivariate analysis[a]	
		Complete	Partial	None				
		No. (%)	No. (%)	No. (%)	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Total number of sessions	233	142 (60.9)	69 (29.6)	22 (9.4)				
Location								
Central[b]	178	109 (61.2)	54 (30.3)	15 (8.4)	Reference			
Peripheral[c]	55	33 (60.0)	15 (27.3)	7 (12.7)	0.631 (0.243–1.637)	0.344		
Distal airway atelectasis								
Absent	61	37 (60.7)	22 (36.1)	2 (3.3)	Reference		Reference	
Present	172	105 (61.0)	47 (27.3)	20 (11.6)	0.258 (0.058–1.137)	0.073	0.375 (0.076–1.842)	0.227
Length of airway invasion								
≤ 2 cm	101	67 (66.3)	29 (28.7)	5 (5.0)	Reference		Reference	
> 2 cm	132	75 (56.8)	40 (30.3)	17 (12.9)	0.352 (0.125–0.990)	0.048	0.486 (0.160–1.476)	0.203

OR = odds ratio, CI = confidence interval

[a]Factors associated with partial to complete reestablishment of airway patency were analyzed using univariate and multivariate logistic regression analyses.

[b]The location of the central type included the trachea, carina, both main bronchi, and right bronchus intermedius.

[c]The location of the peripheral type included the lobar bronchus.

Cryorecanalization

Table 5. Safety profile

Variables	Values
Cryorecanalization	233
Total bleeding	78 (33.5)
Mild	12 (5.6)
Moderate	65 (27.9)
Severe	1 (0.4)
Respiratory failure	1 (0.4)
Death	1 (0.4)
Cryobiopsy	7
Complication	0 (0.0)
Blood clot	20
Complication	0 (0.0)
Foreign body	2
Complication	0 (0.0)

Values are presented as number (%).

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Cryorecanalization

Table 6. Univariate and multivariate analyses of factors associated with moderate to severe intrabronchial bleeding (sessions N = 240)

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Female sex	1.227 (0.626–2.402)	0.551		
Old age (≥ 75 years)	2.646 (1.067–6.565)	**0.036**	1.943 (0.714–5.290)	0.194
Smoking history (≥ 30 PYs)	0.872 (0.491–1.549)	0.641		
FEV1 < 50%	1.464 (0.635–3.378)	0.371		
Comorbidity				
DM	2.235 (1.124–4.446)	**0.022**	2.820 (1.273–6.247)	**0.011**
HTN	2.045 (1.103–3.791)	**0.023**	1.609 (0.798–3.242)	0.183
COPD	1.477 (0.798–2.734)	0.214		
Chronic kidney disease	1.056 (0.200–5.582)	0.949		
Liver cirrhosis	2.714 (0.534–13.800)	0.229		
Location				
Trachea & carina	Reference		Reference	
Right main bronchus	0.799 (0.375–1.702)	0.561	0.745 (0.318–1.745)	0.498
Left main bronchus	0.822 (0.356–1.900)	0.647	0.926 (0.366–2.347)	0.872
Upper lobe	0.305 (0.092–1.003)	**0.051**	0.356 (0.102–1.250)	0.107
Middle lobe	2.056 (0.377–11.213)	0.405	1.282 (0.216–7.606)	0.785
Lower lobe	0.685 (0.232–2.022)	0.493	0.757 (0.243–2.358)	0.631
Etiology				
NSCLC	Reference			
SCLC	0.500 (0.057–4.422)	0.533		
Metastasis of thyroid cancer	2.500 (0.595–10.510)	0.211		
Metastasis of colon cancer	0.417 (0.049–3.578)	0.425		
Metastasis of RCC	0.741 (0.309–1.775)	0.501		
Metastasis of HCC	2.500 (0.595–10.510)	0.211		
Benign	0.833 (0.307–2.260)	0.720		
Other malignancy	0.667 (0.208–2.138)	0.495		
Stent placement	2.800 (0.870–9.016)	**0.084**	2.921 (0.808–10.557)	0.102
Respiratory failure before BC	3.767 (1.341–10.578)	**0.012**	3.546 (1.148–10.951)	**0.028**
Distal airway atelectasis				
Absent	Reference		Reference	
Present	0.540 (0.291–1.003)	**0.051**	0.417 (0.199–0.875)	**0.021**
Length of airway invasion				
≤ 2 cm	Reference			
> 2 cm	0.715 (0.404–1.265)	0.249		

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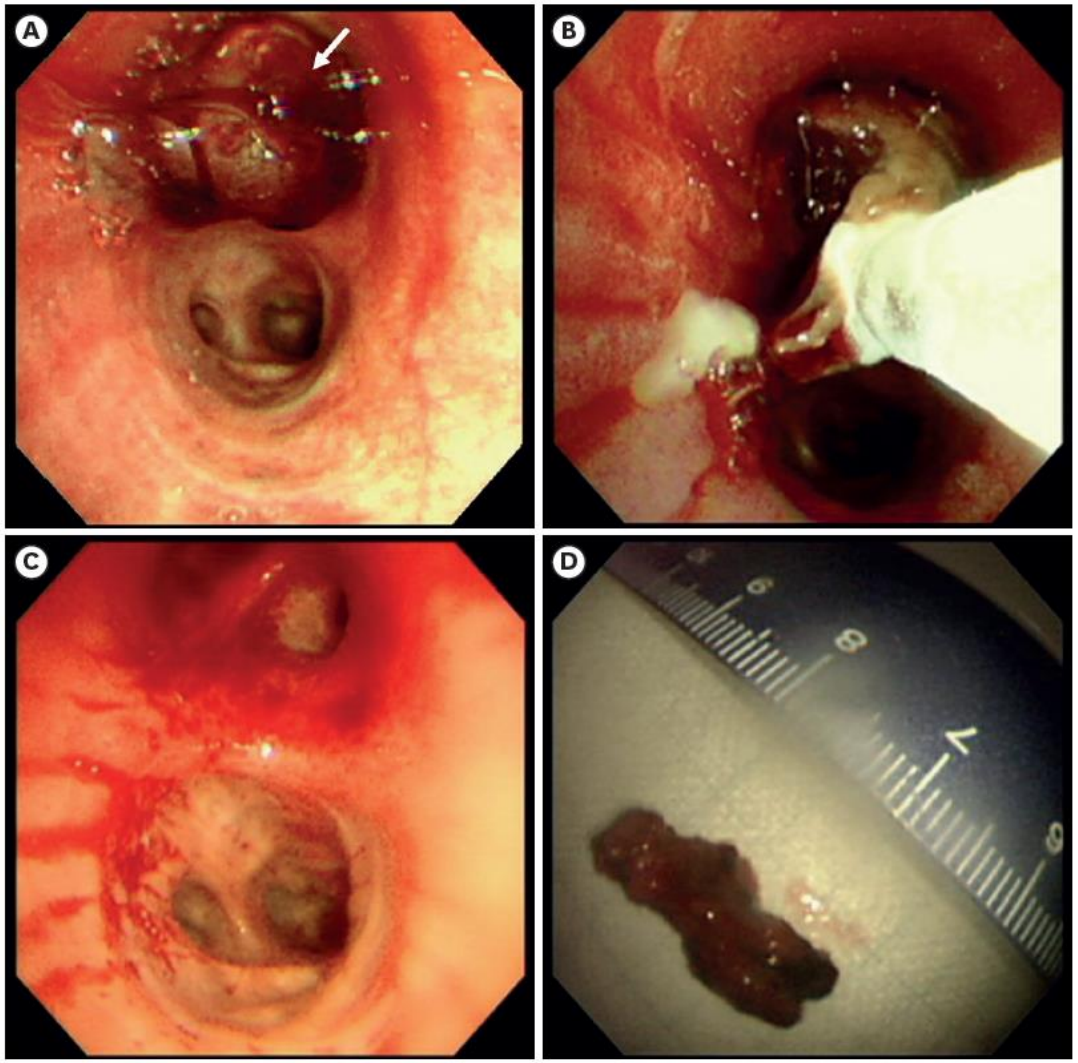

Fig. 1. Cryotherapy for endobronchial metastasis of renal cell carcinoma. (**A**) Huge exophytic tumor mass in left upper lobe bronchus (white arrow). (**B**) Freezing and extracting the tumor mass with cryoprobe. (**C**) Left upper lobe bronchus after cryotherapy. (**D**) Extracted tumor mass.

Conclusion

- MCAO 환자들에 대해 Moderate sedation, flexible BFS를 통해서도 효과적이고 상대적으로 안전하게 cryo-recanalization 시행할 수 있다.

- distal airway atelectasis or extensive airway invasion (>2cm) 있더라도 cryo-recanalization을 시도해 볼 수 있다. (distal airway atelectasis 존재시 출혈 위험도는 오히려 낮음)

- DM, respiratory failure before BC가 있는 경우 bleeding risk가 높을 수 있으니 주의할 필요가 있다.

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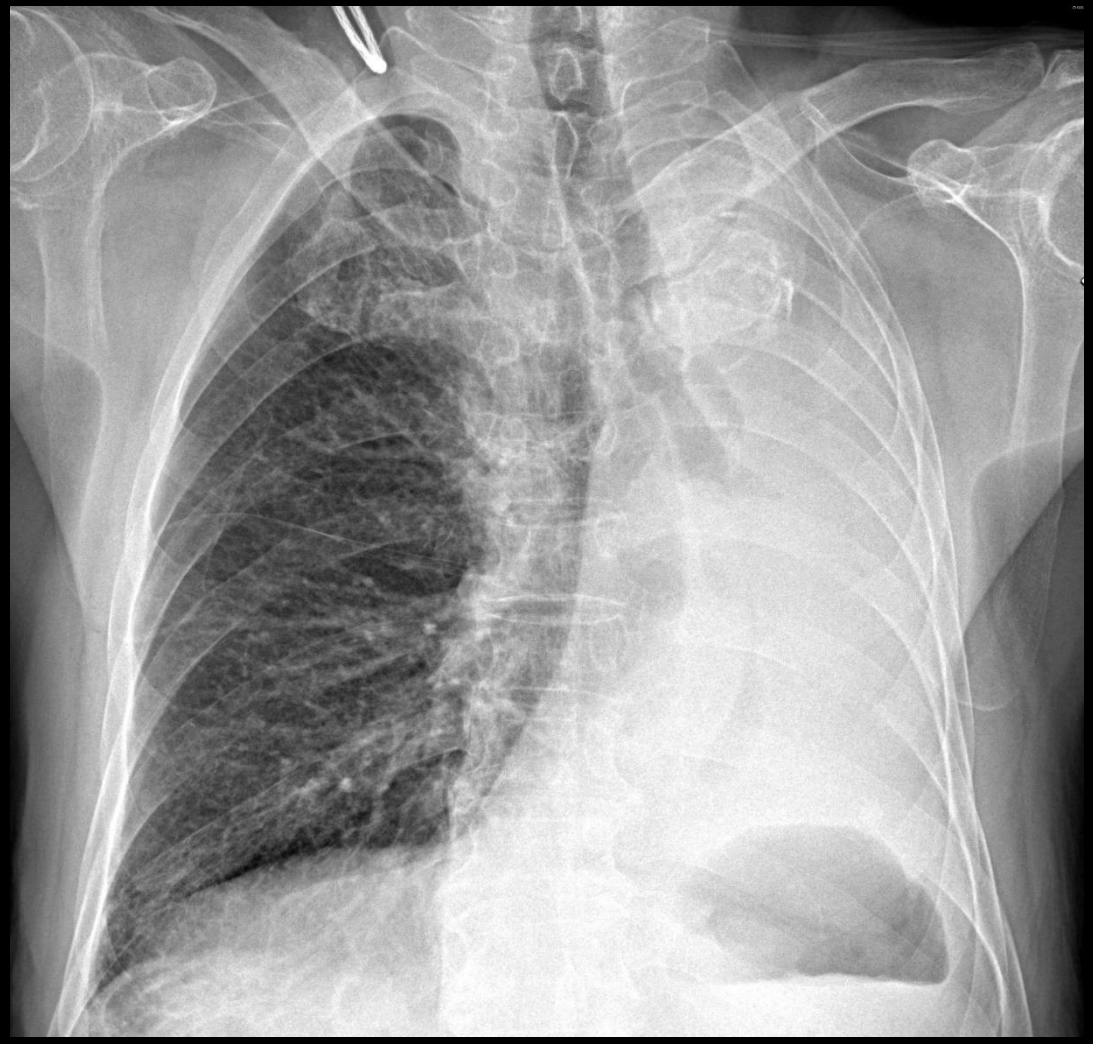
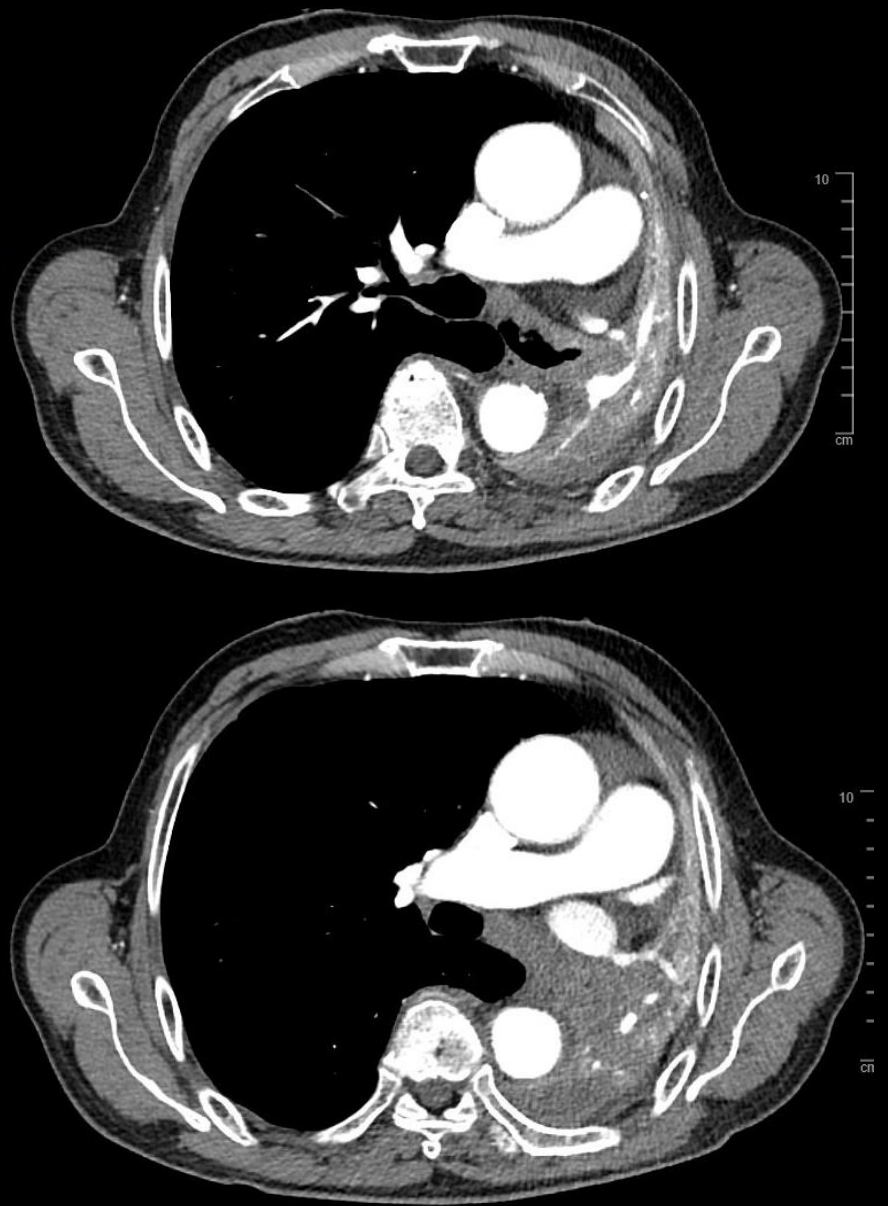
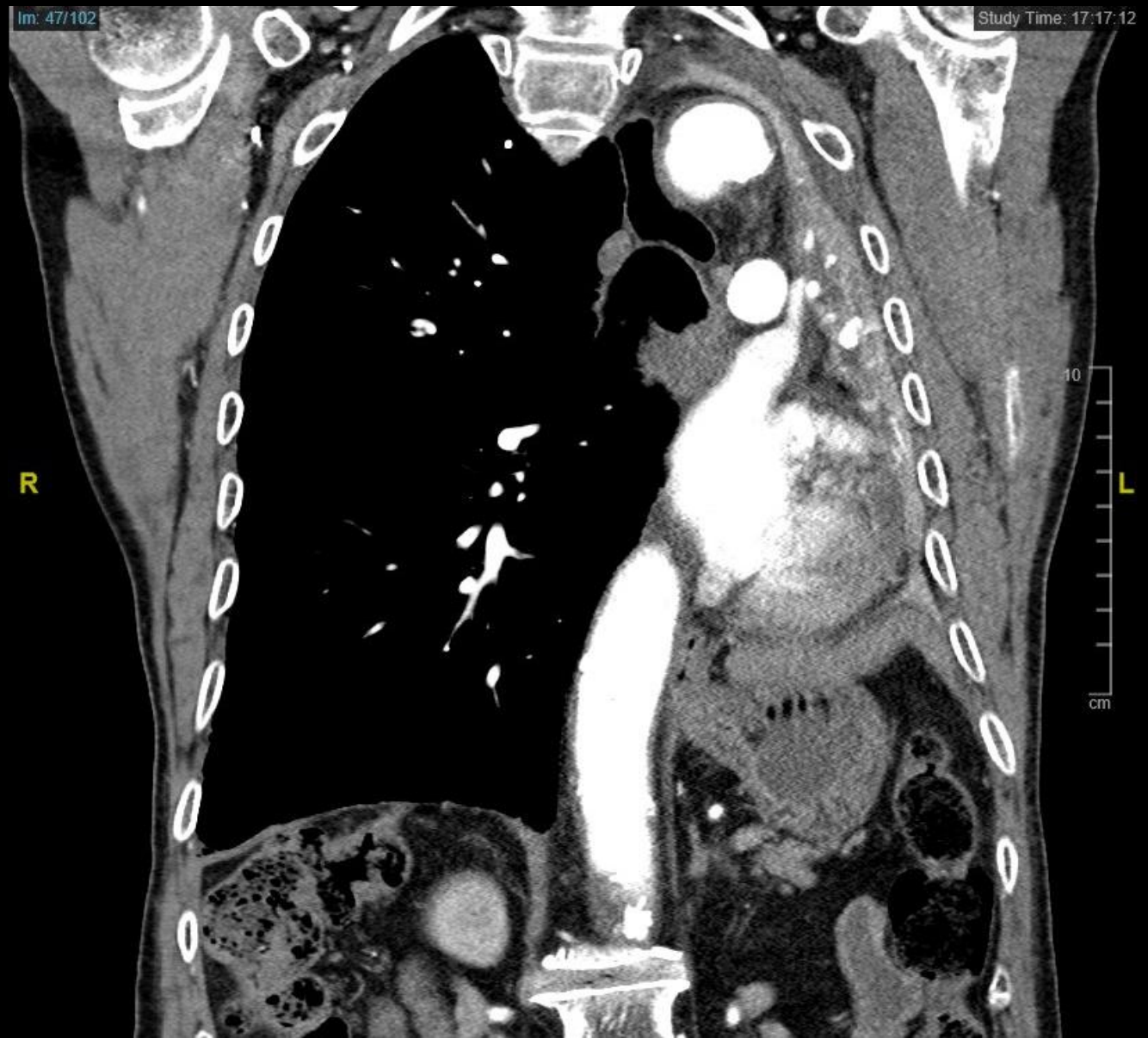
Case 2 : 86/M　dyspnea aggravation　1MA, HFNC

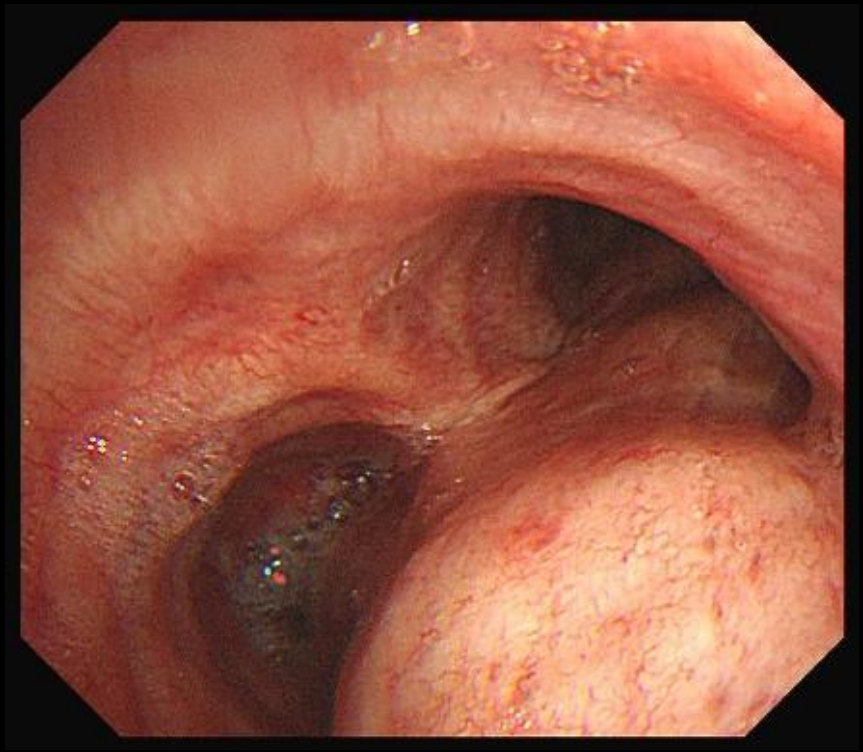


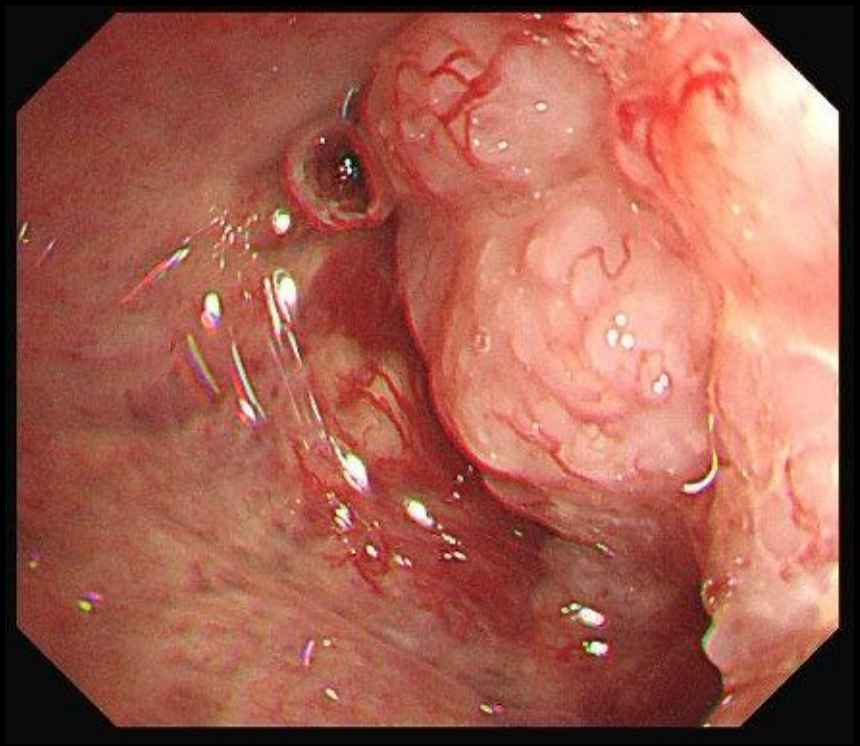


Case 2 : 86/M　dyspnea aggravation　1MA, HFNC

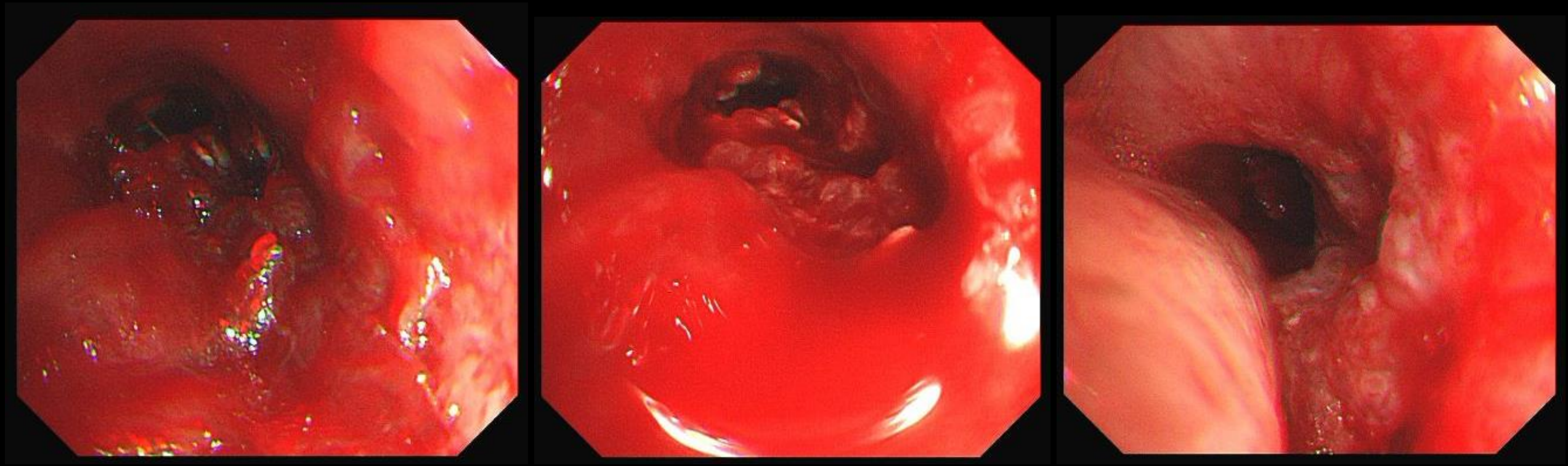


Case 2 : 86/M　BFS, Lt. main



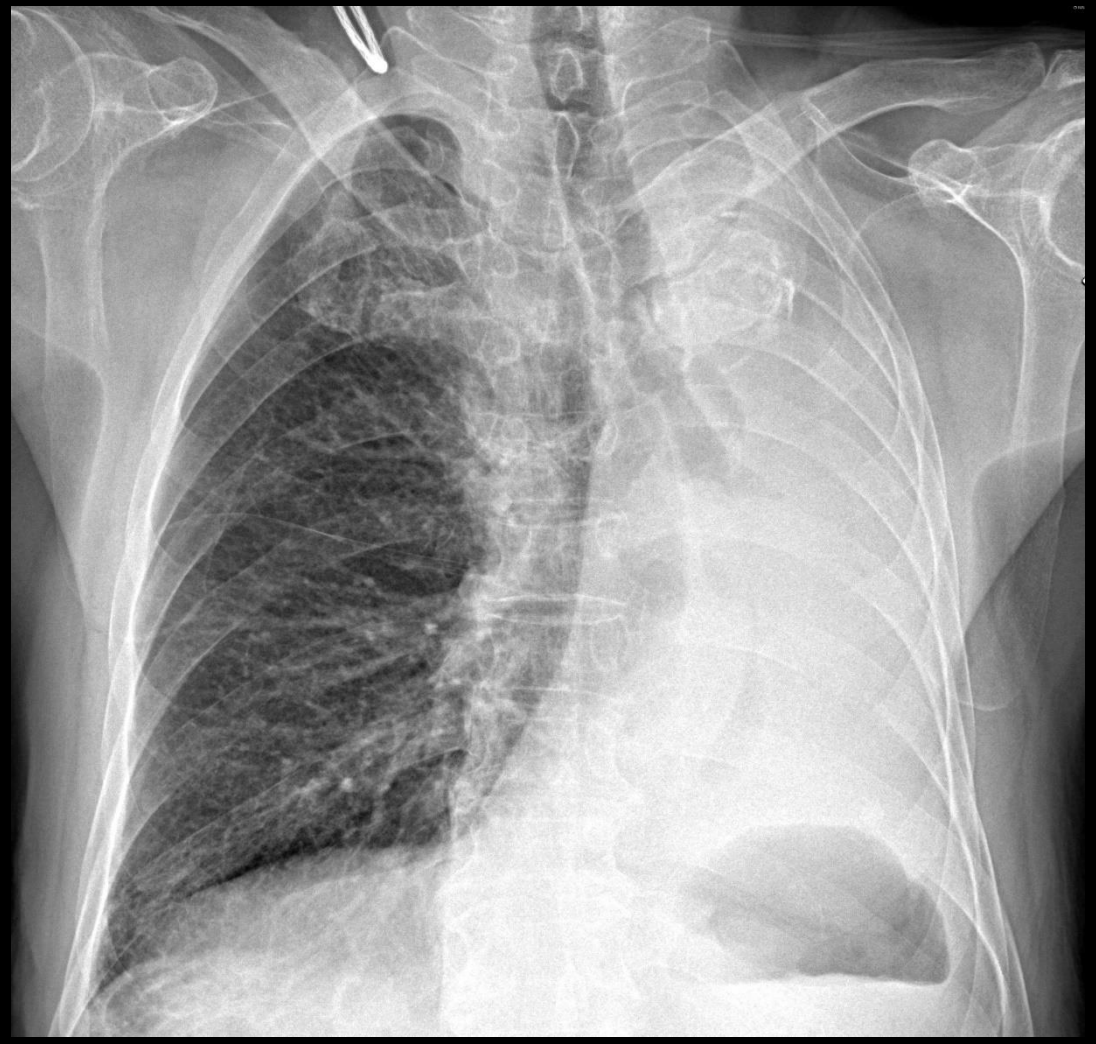


Case 2 : 86/M Cryo-extraction #1, Lt. main

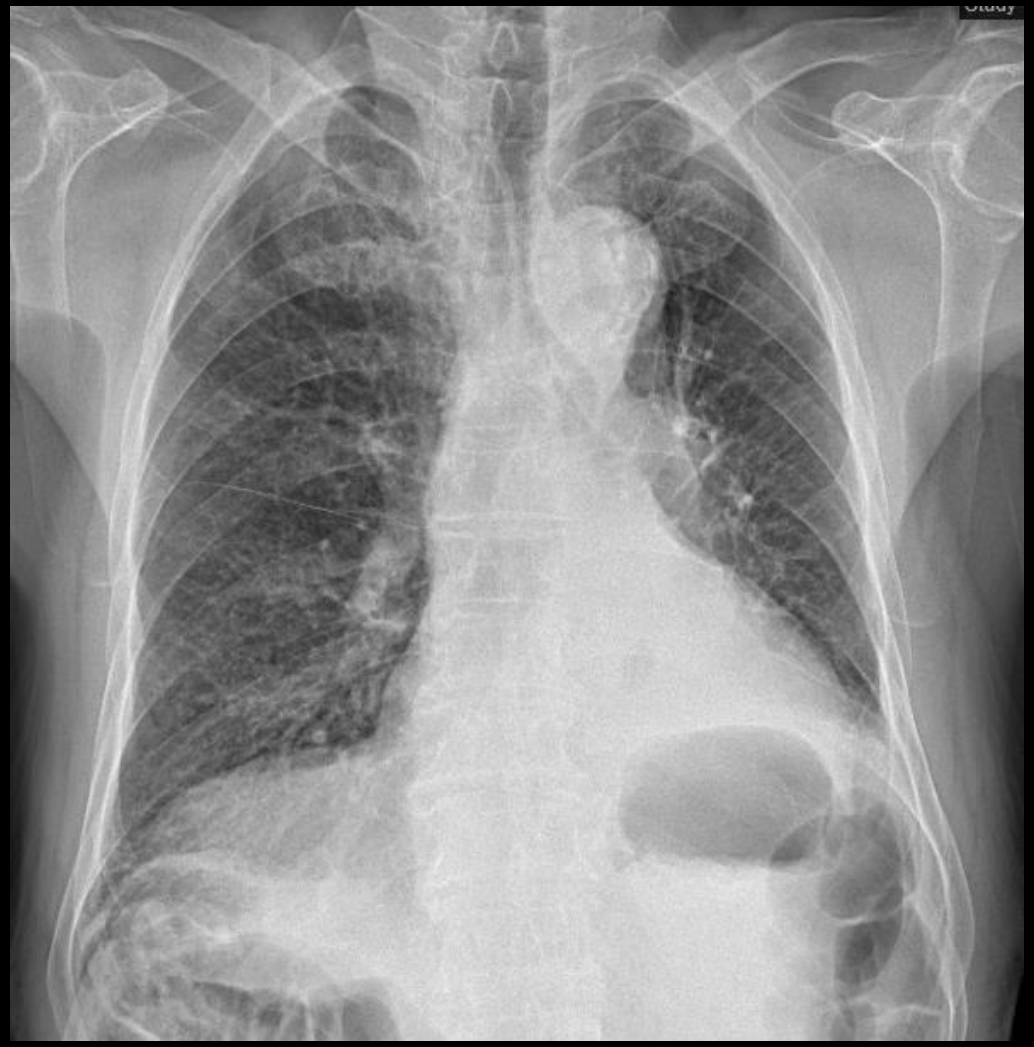


Case 2 : 86/M 1D after cryorecanalization #1

→ Room air, improved dyspnea



before



1D after

Case 2 : 86/M BFS Cryo-extraction → report

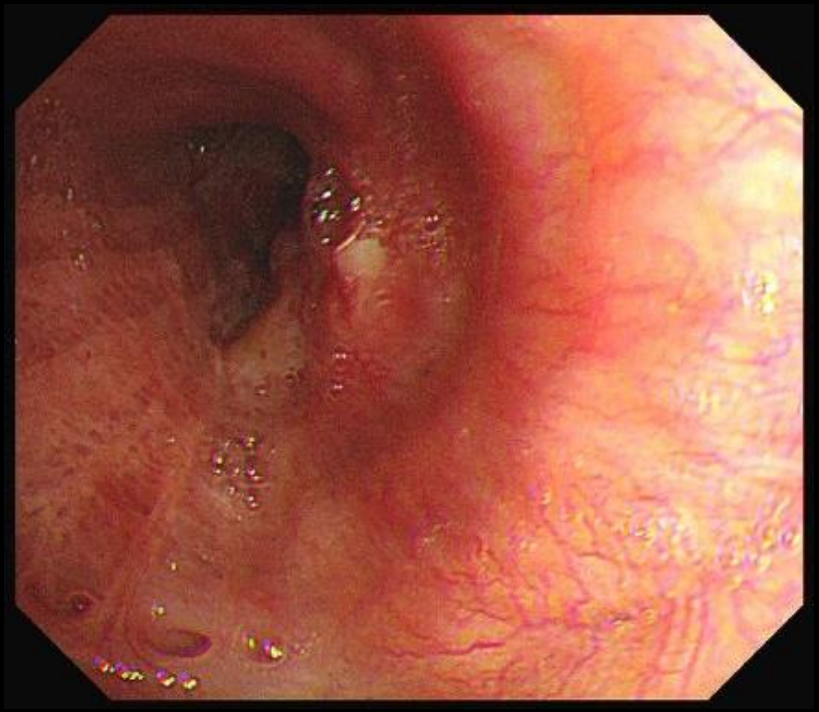
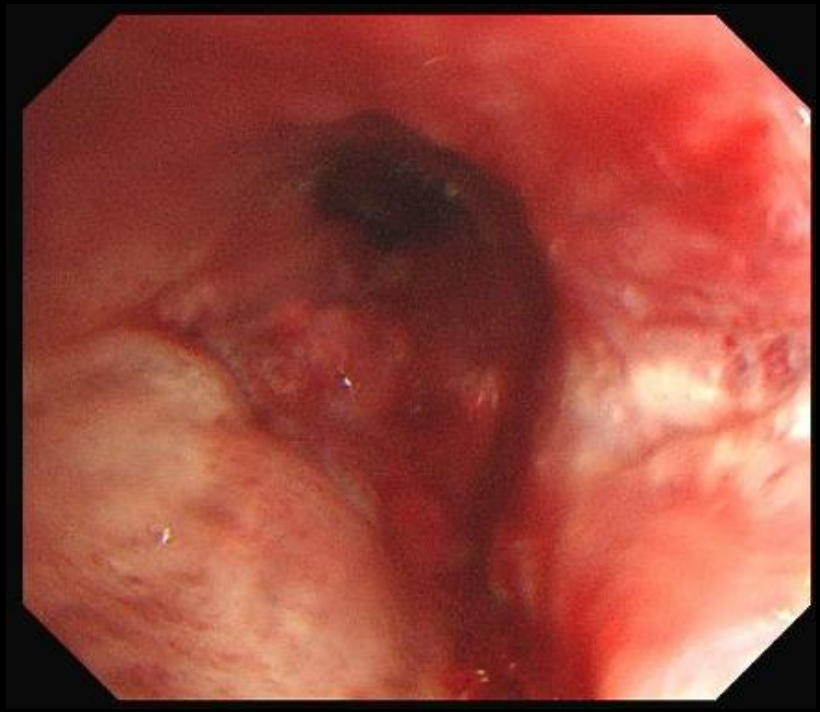
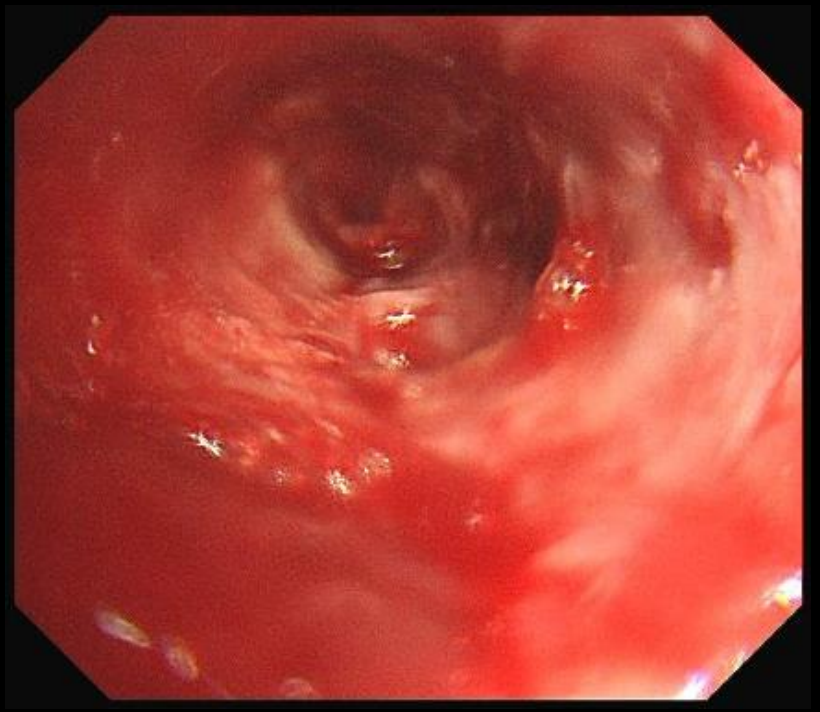
포르말린에 고정된 작은 흰색 연조직 여러 개, 1.8 x 1.5 cm임. (김연주)

Results of immunohistochemical stain;
CD56: positive, focal scattered
P40: positive
Thyroid transcription factor-1: negative
ALK(D5F3): negative

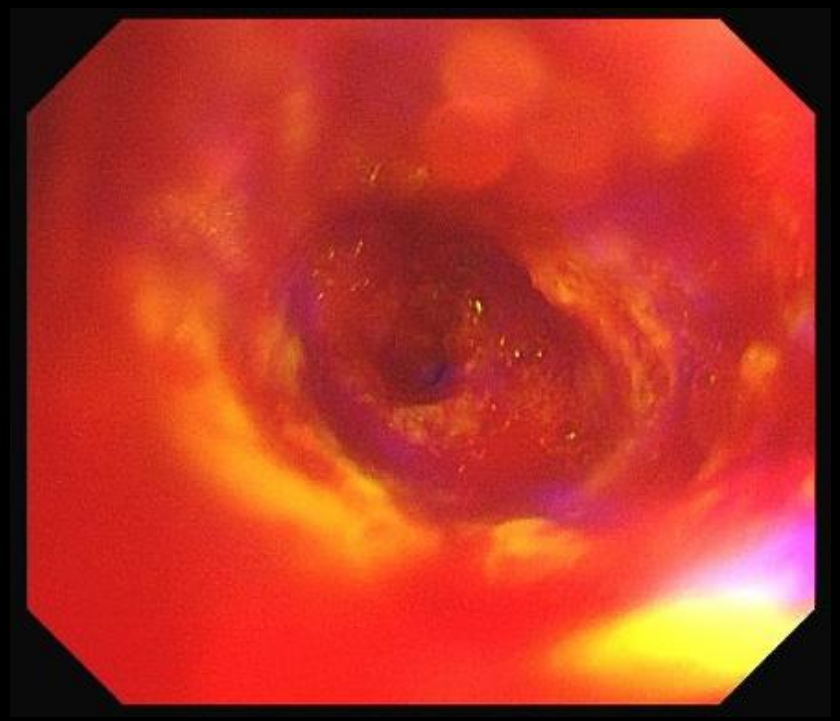
1HE)
Diagnosis: Bronchus, left main, bronchoscopic biopsy;
Non-small cell carcinoma,
favor Squamous cell carcinoma

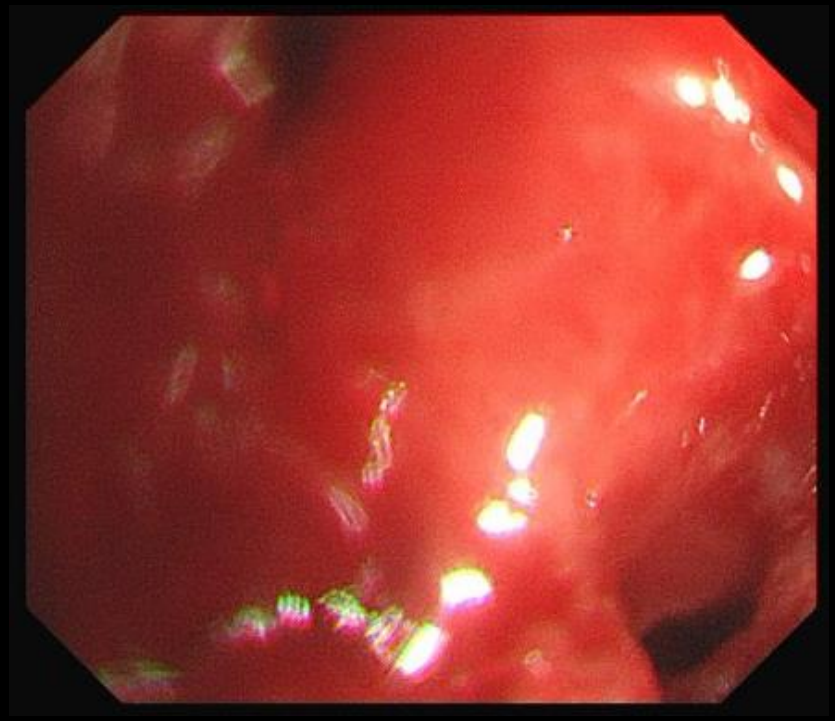
Result of PD-L1 (SP263) test;
- Expression level: <1% positive in tumor cells

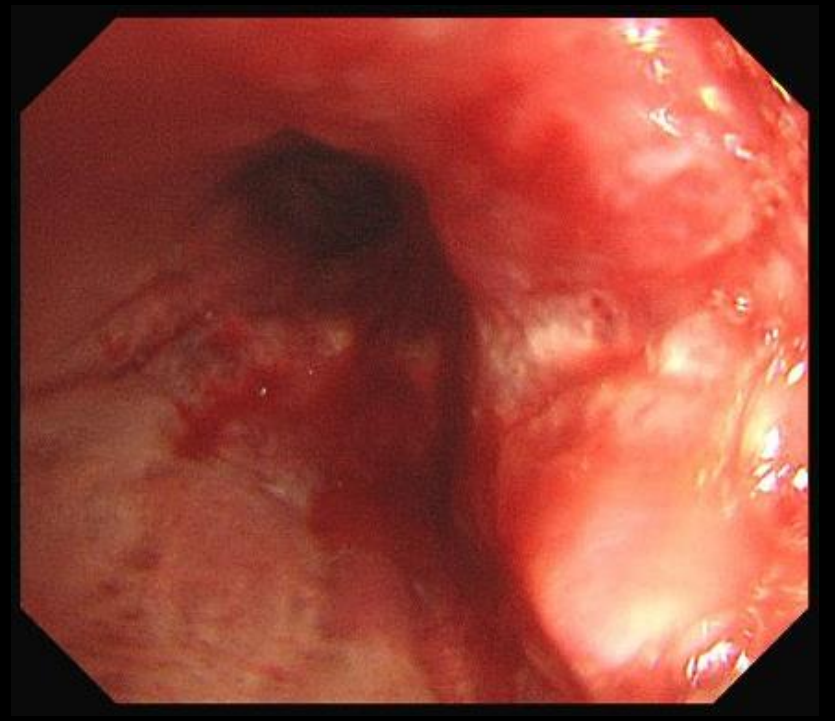
Case 2 : 86/M Cryo-extraction #2, Lt. main, after 1W

Case 2 : 86/M Cryo-extraction #2, Lt. main, after 1W

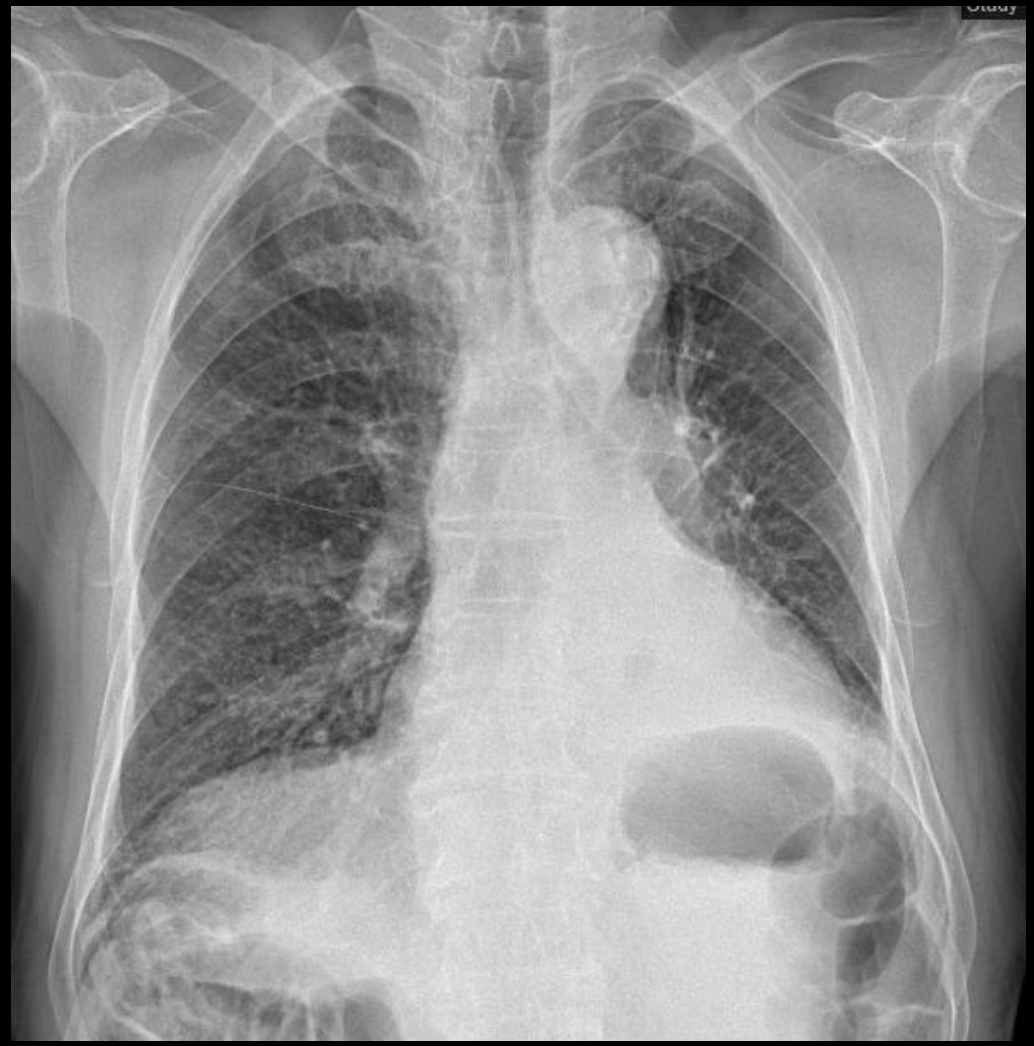




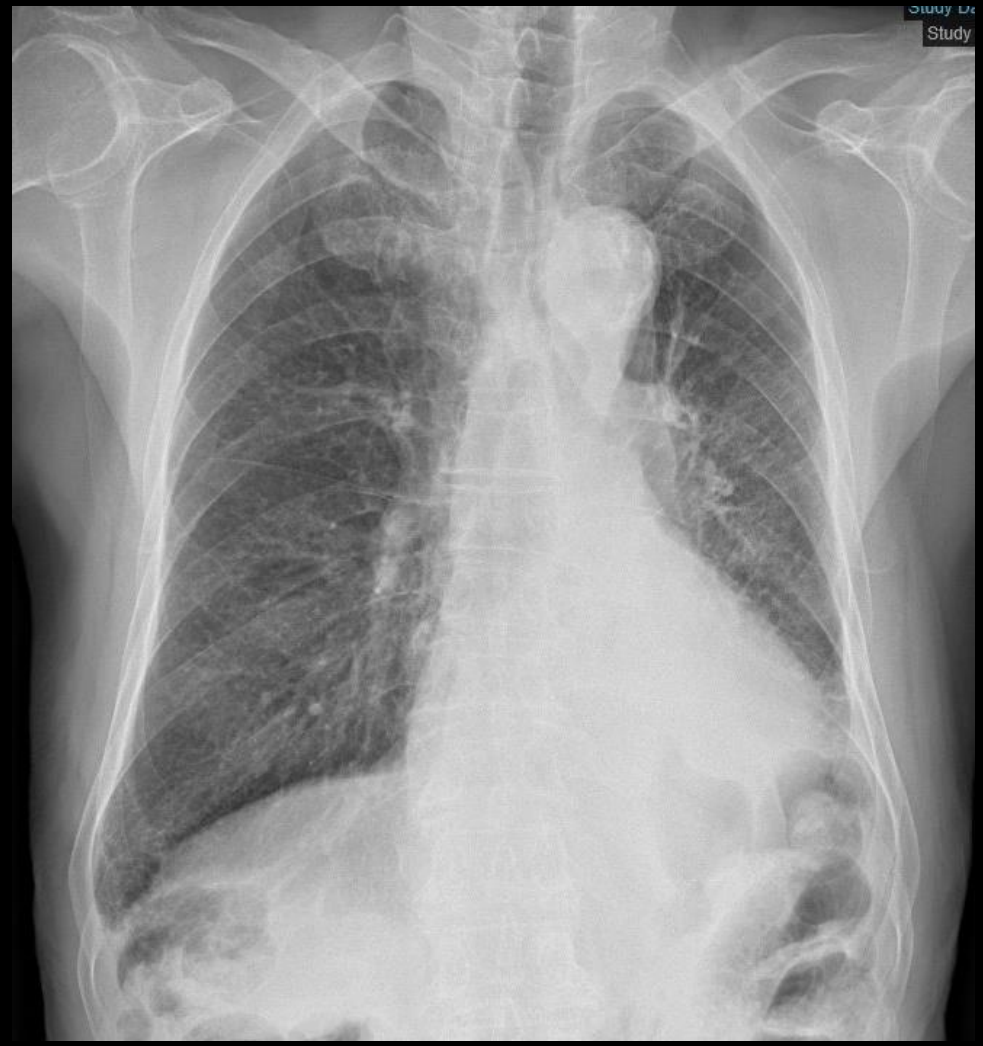


LLL (sup./basal)

Case 2 : 86/M 1D after cryorecanalization #2



before



1D after

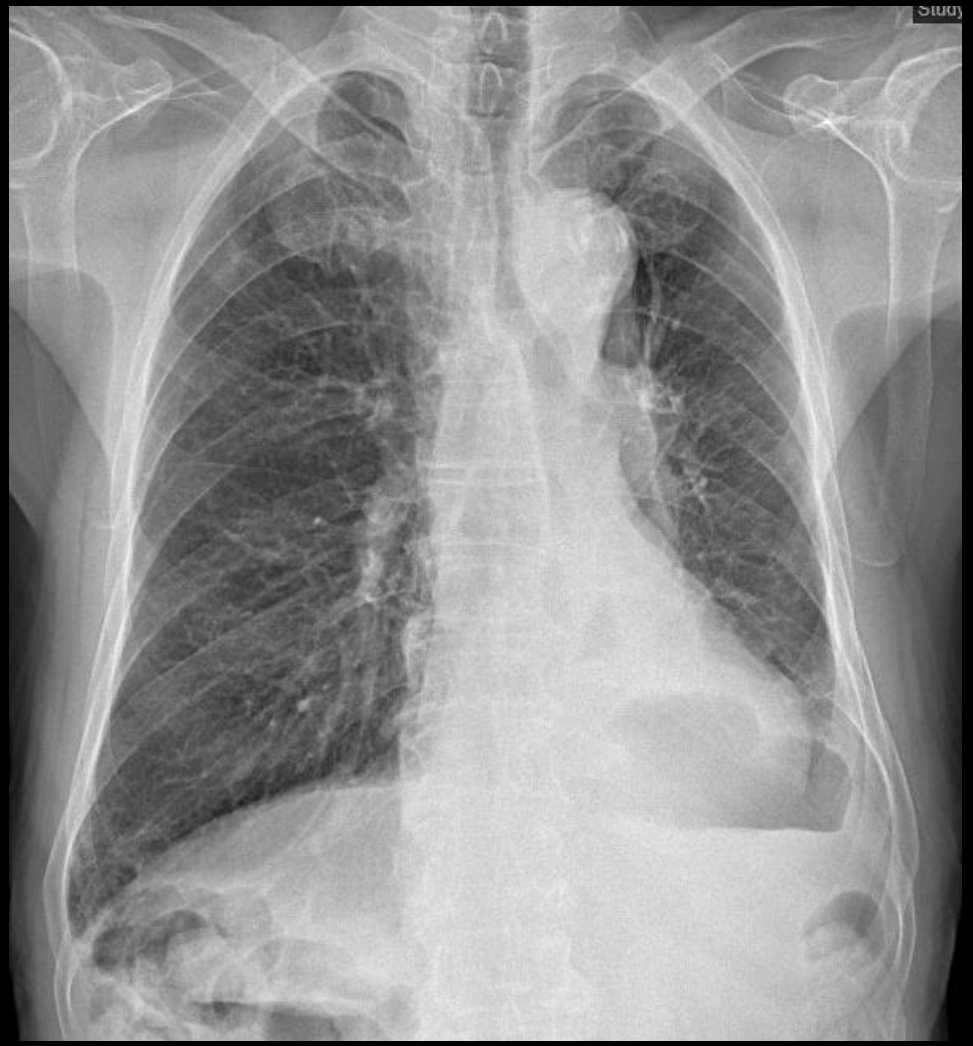
Case 2 : 86/M Multidisciplinary approach

#. NSCLC, Lt. main bronchus involvement, SqCC, cT4N2M0, stage IIIB

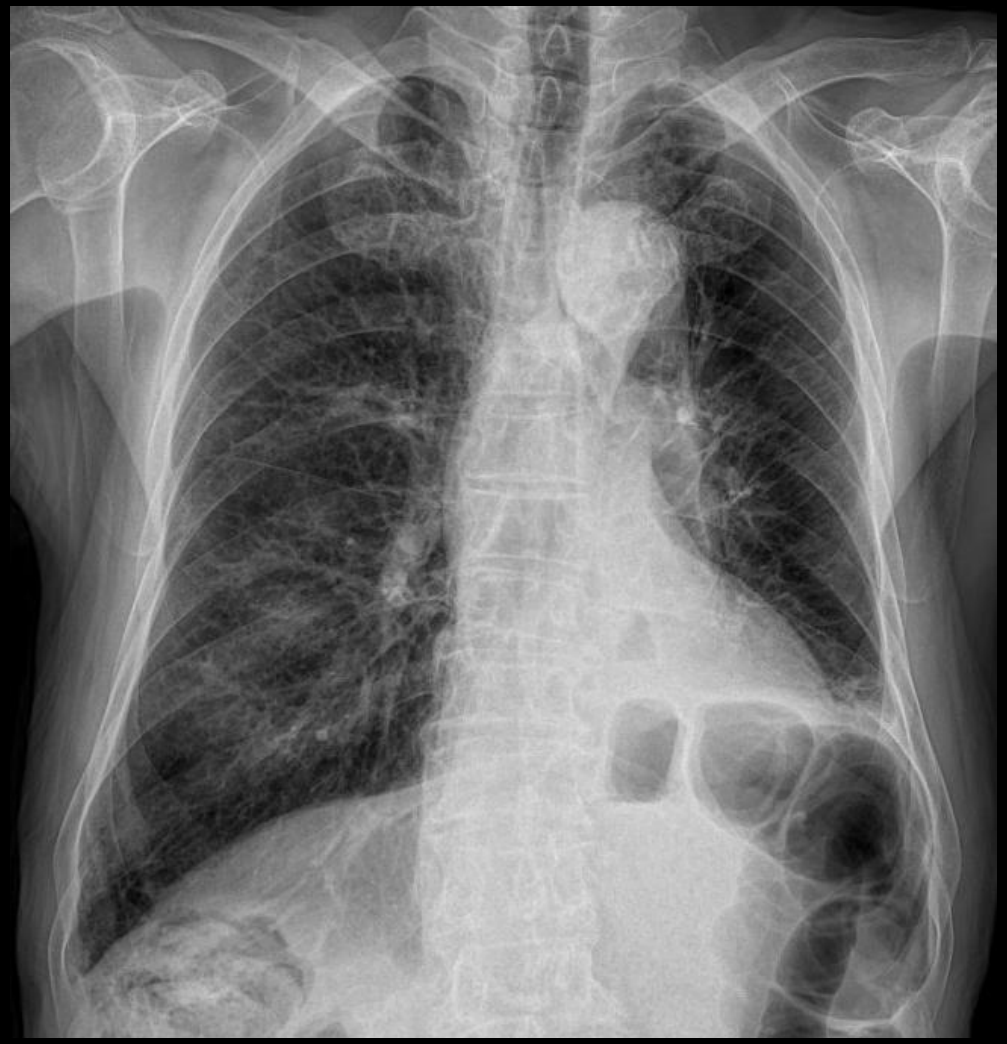
→ 고령으로 CCRT는 불가능함, 환자의 의지와 활동도에 따라 palliative thoracic RT (30Gy/10fx or 50Gy/20fx or 60Gy/30) 선량 결정

→ 보호자분 최종적으로 방사선치료 refuse (이유: radiation esophagitis risk 및 고령으로 원하지 않으심)

Case 2 : 86/M 1M opd f/u → f/u loss



Before discharge



1M

Case 2 : 86/M 14M later

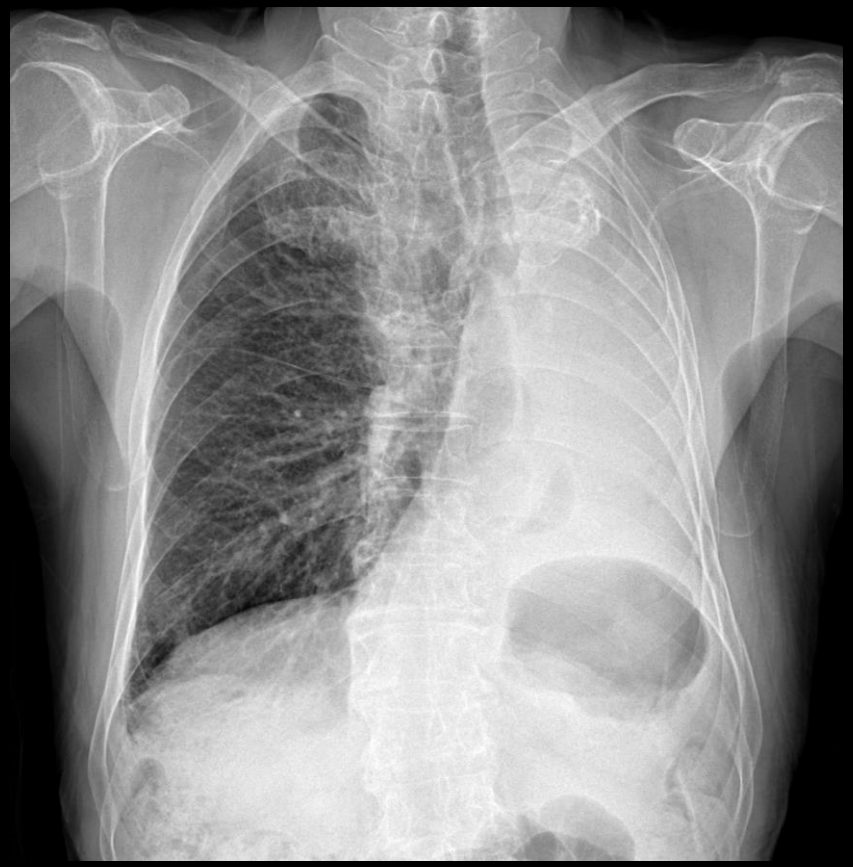
외래경과 : **내과호흡기·알레르기 (2025-02-21)**
소견 및 계획 >
소견

Lt lung total atelectasis 소견으로 cryo-recalalization 후
NSCLC (2023/12/05), sqamous cell carcinoma 진단받고
RT 권유드렸으나 refuse 하신 분

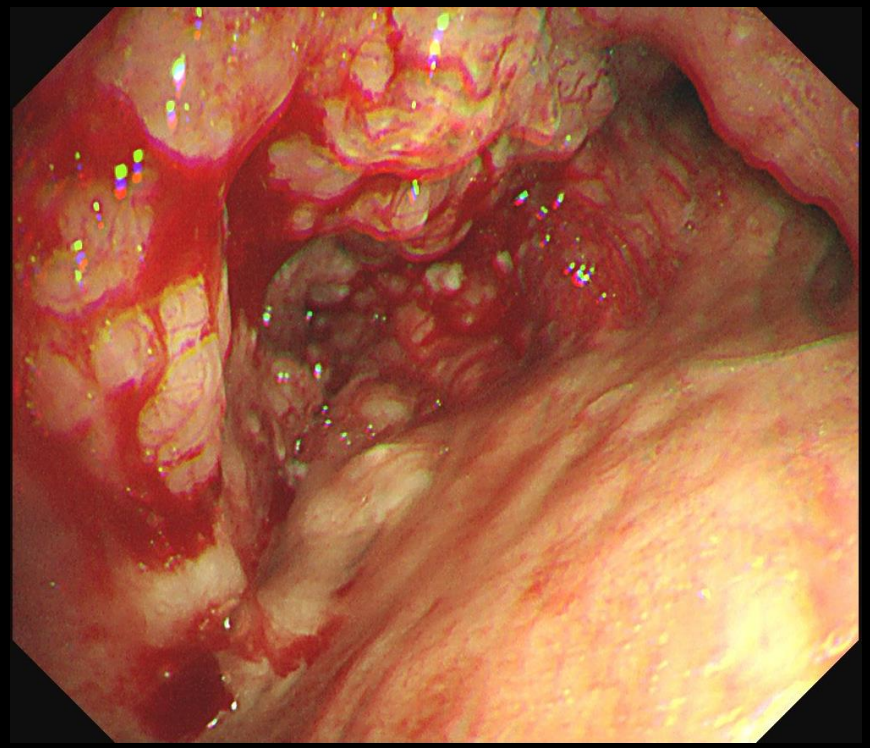
감기 및 dyspnea로 이번주 월요일 한국병원에서 CT 시행하고 약
처방 받으셨으나, dyspnea & hemoptysis 호전 없어 내원함.

지난주까지는 특별한 증상 없이 잘 계심.

Case 2 : 86/M 14M later



Case 2 : 86/M 14M later



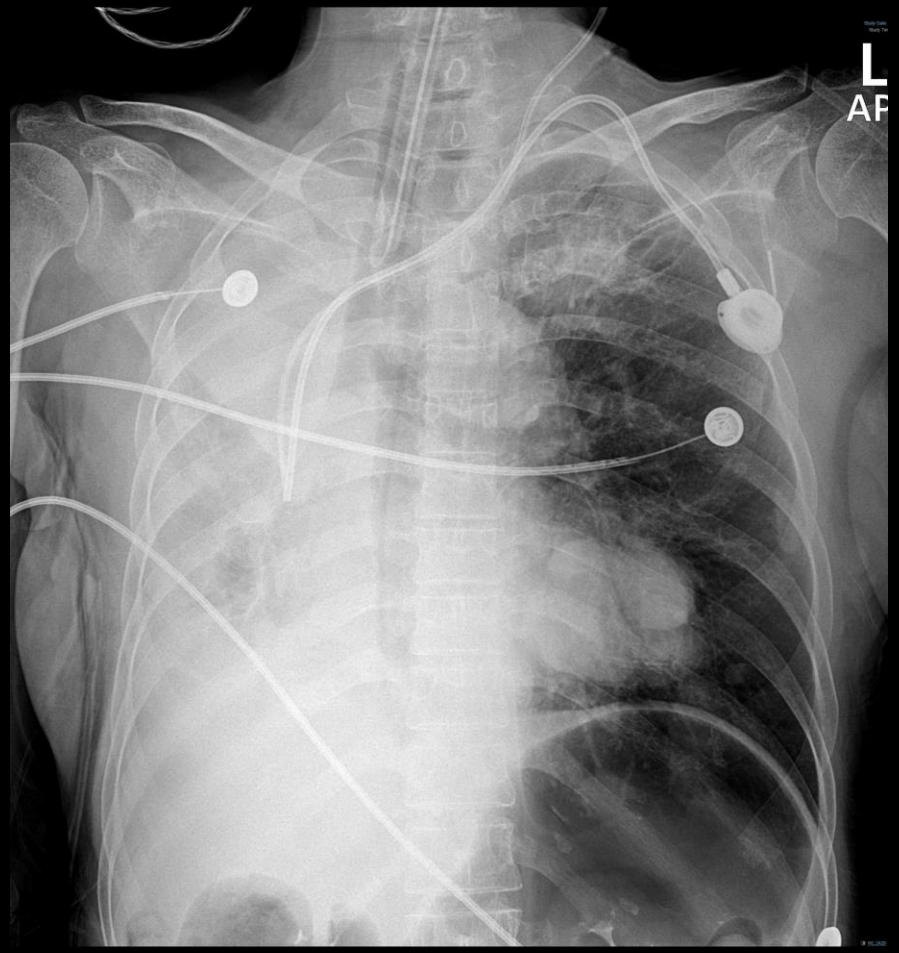
ICU 전동하고 intubation 후 cryo-recalalization 권유

→ 보호자분 원하시나 환자분 강력하게 거부하시고 자의 퇴원하심

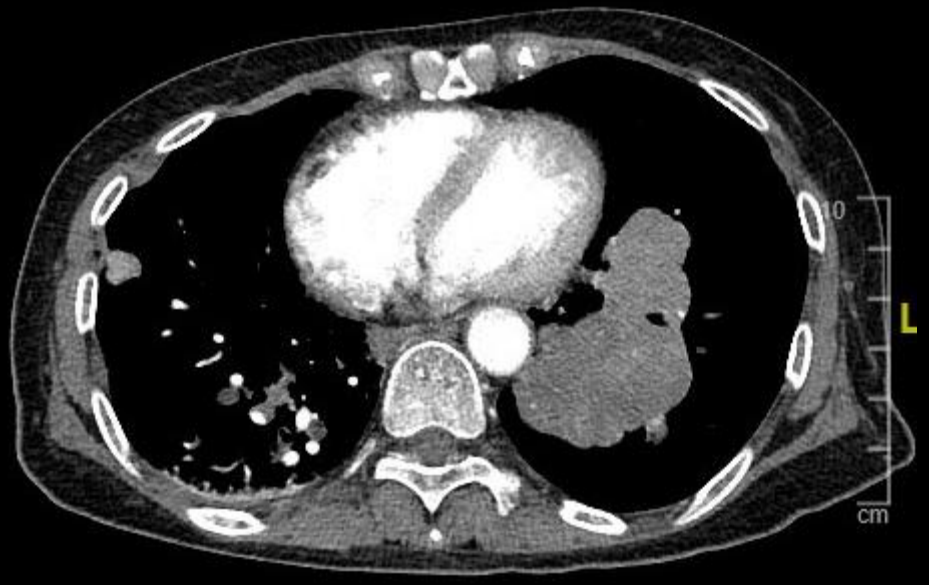
Case 3 : 68/F dyspnea

#1. Leiomyosarcoma, Lt.ovary
s/p TAH with BSO (2021.1.8): pT2bN0 (15x11cm, 30/10HPF, rectal serosa +)
s/p Adjuvant AI #6 (2021.2.16~6.3)
sequential pelvic IMRT, 50.4Gy/28fx (2021.6.28~8.3)
--> Recur (lung, Lt.ovary, p-seeding, bone)
s/p palliative RT to Lt.4th rib, 35Gy/10fx (2022.12.9~12.22)
s/p palliative AI #5 (2023.1.6~4.30) : PD
s/p Pazopanib (2023.5~2023.12): PD
s/p Gemzar/Docetaxel #4 (2023.12.29~2024.3.14): SD (slowly progression. lung)
s/p Halaven #5 (2024.5.8~8.7) : SD (mixed R) --> PD (lung)
** Halaven 1level DR since 4th cycle
s/p Nivolumab+Ipilimumab #4 (2024.9.11~11.13): PD (lung)
ON VIP #1 (2024.12.6) with neulapeg refund

최근 항암에 불응성으로 2025년 3월부터는 Hospice care 중
평소에는 일상 생활 모두 가능하고, 숨찬 증상 없으신 분
일주일 전부터 dyspnea, 내원 당일 dyspnea 급격히 악화되어 ER 내원하심
→ HFNC 적용 → intubation

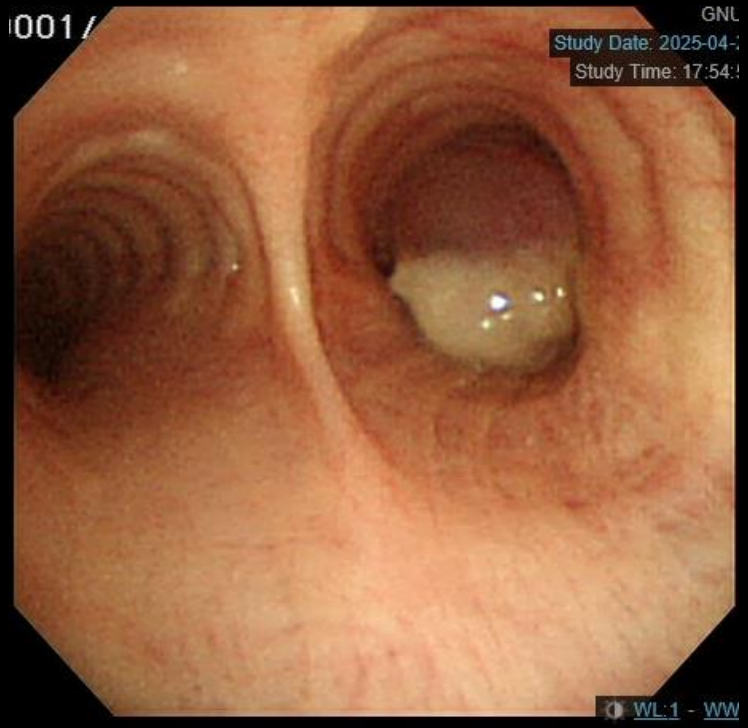


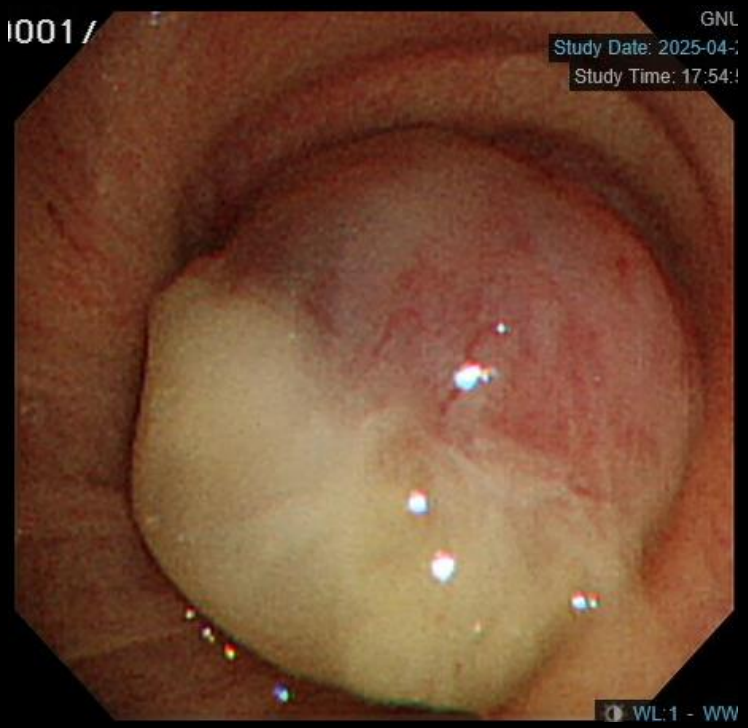
Case 3 : 68/F



MCAO in Rt. main & LLL bronchus

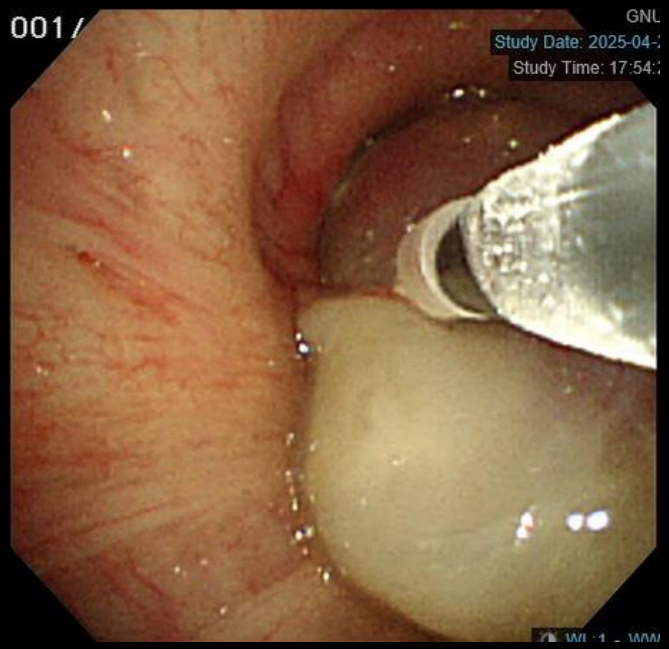
Case 3 : 68/F

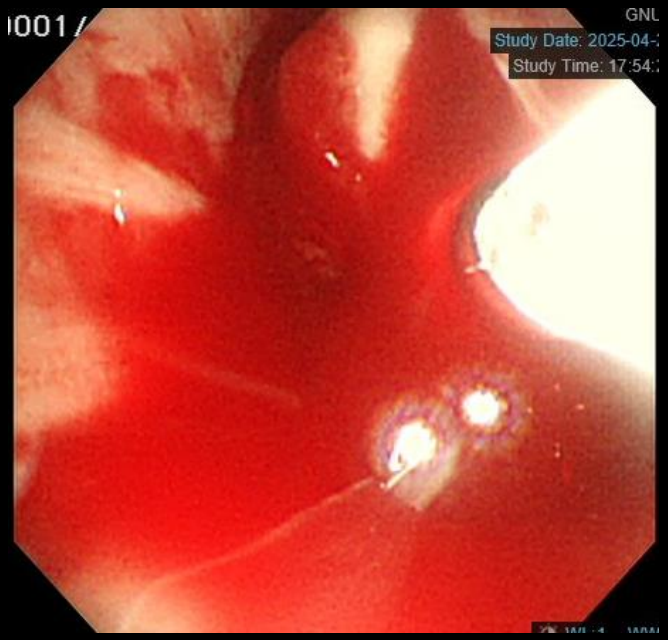


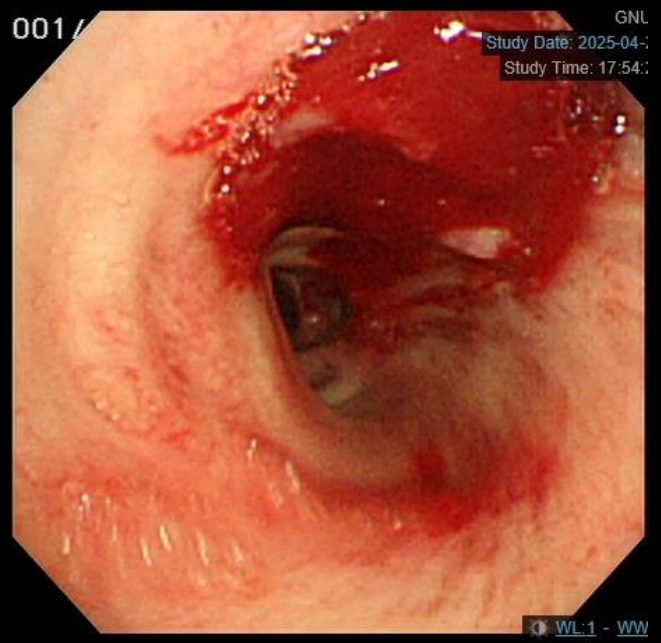


MCAO in Rt. main bronchus, endoluminal type

Case 3 : 68/F 1st Cryo-extraction

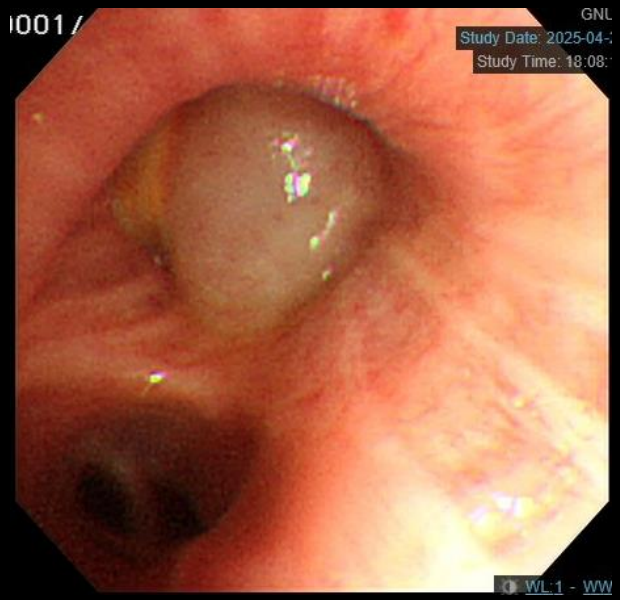


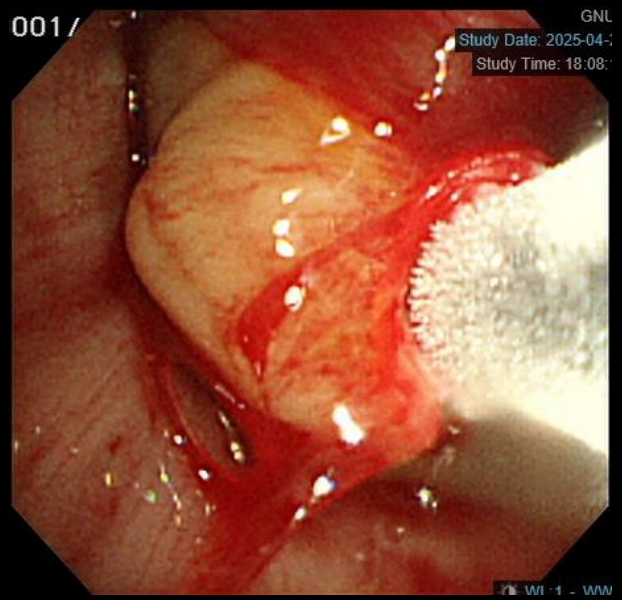


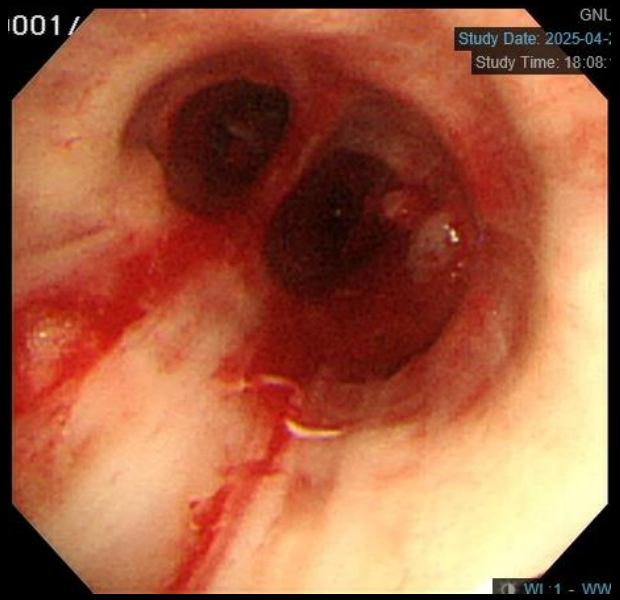


Cryo-extraction in Rt. main bronchus

Case 3 : 68/F 1st Cryo-extraction

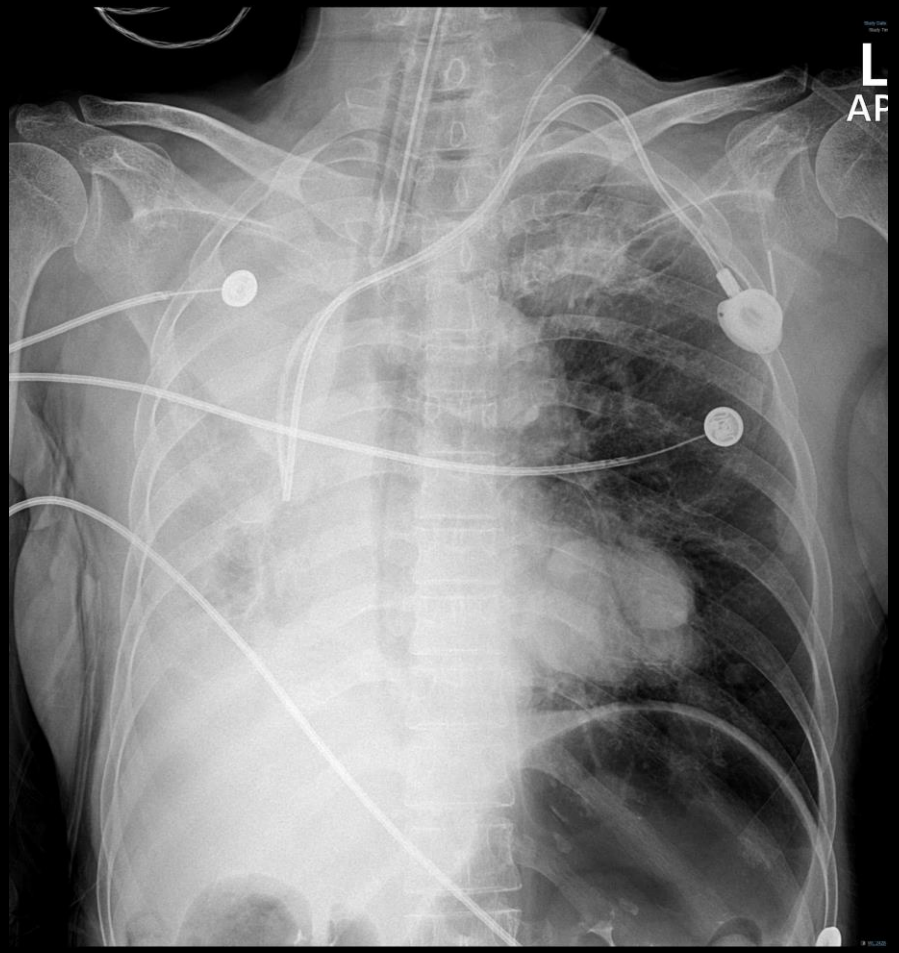


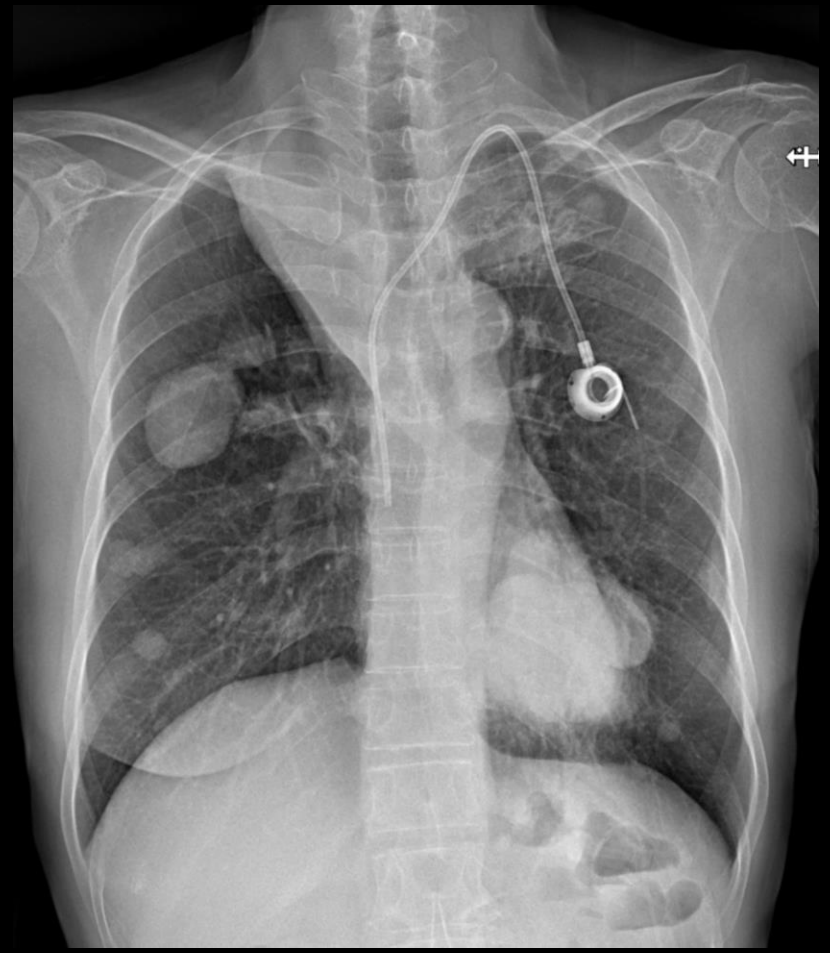




Cryo-extraction in LLL basal trunk

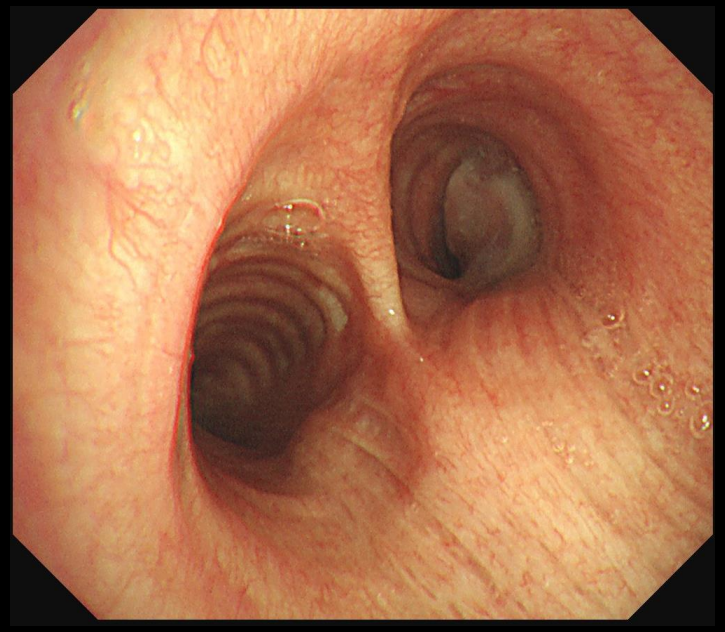
Case 3 : 68/F

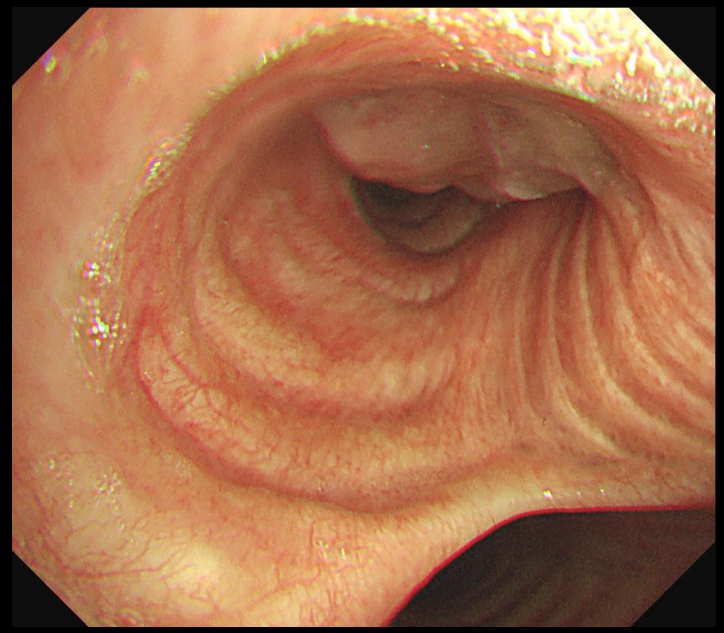




Room air, DOE (-), 걸어서 퇴원하심

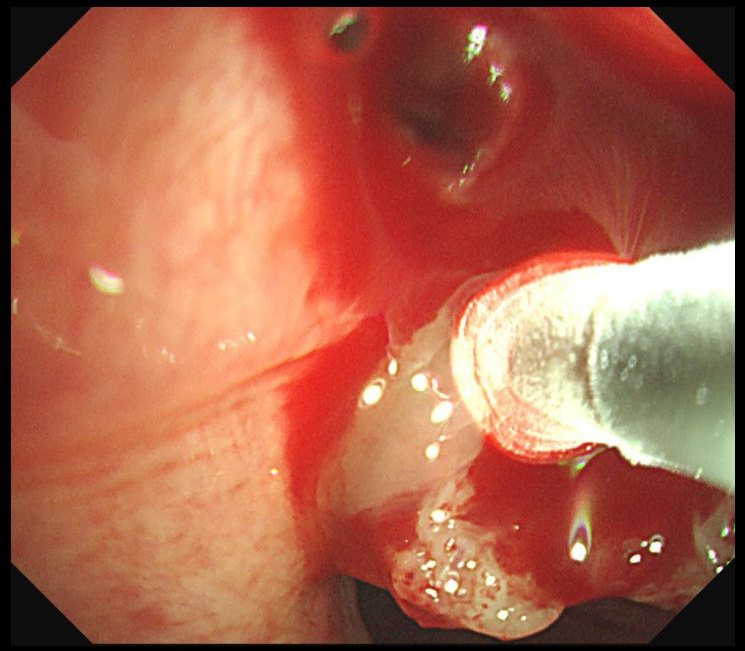
Case 3 : 68/F 1M later

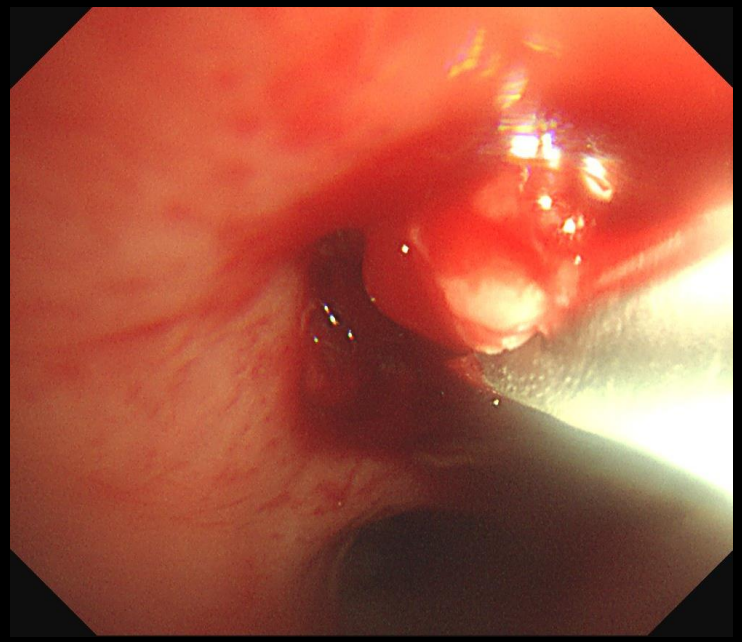


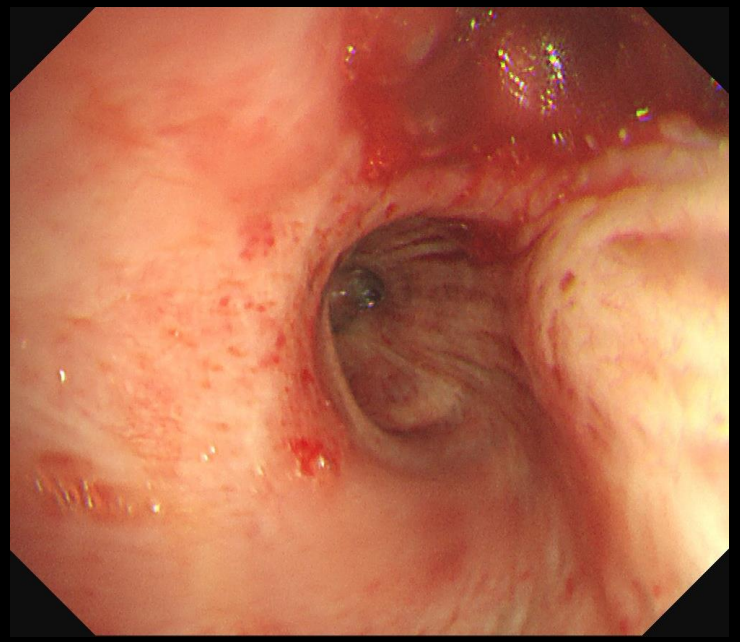


1달 뒤 : dyspnea (-), 80% 정도의 re-obstruction in Rt. main bronchus

Case 3 : 68/F　1M later



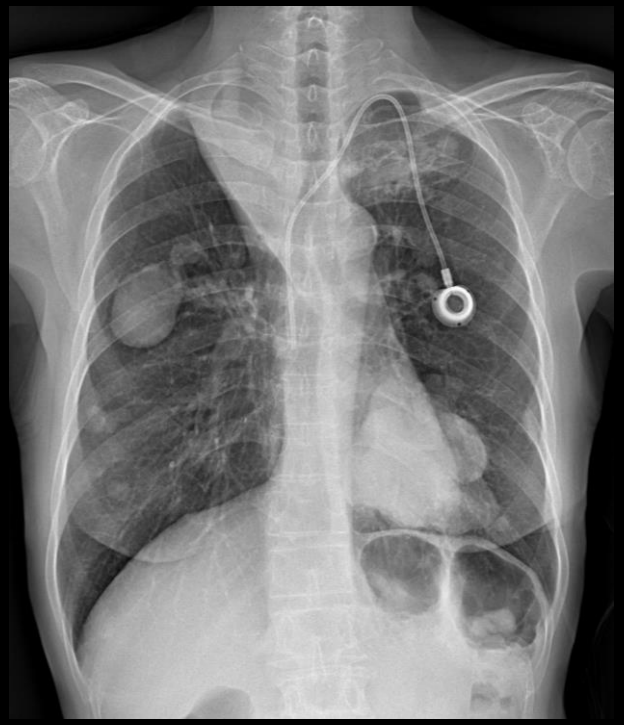




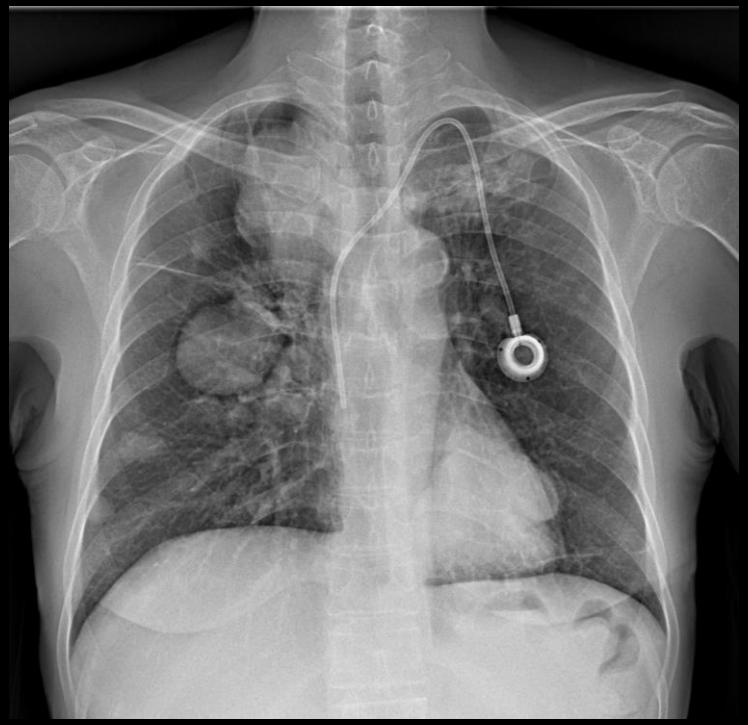
Cryo-extraction in Rt. main bronchus

→ Palliative RT to Rt.main bronchus lesion, 30Gy/10fx (2025.5.14-5.27)

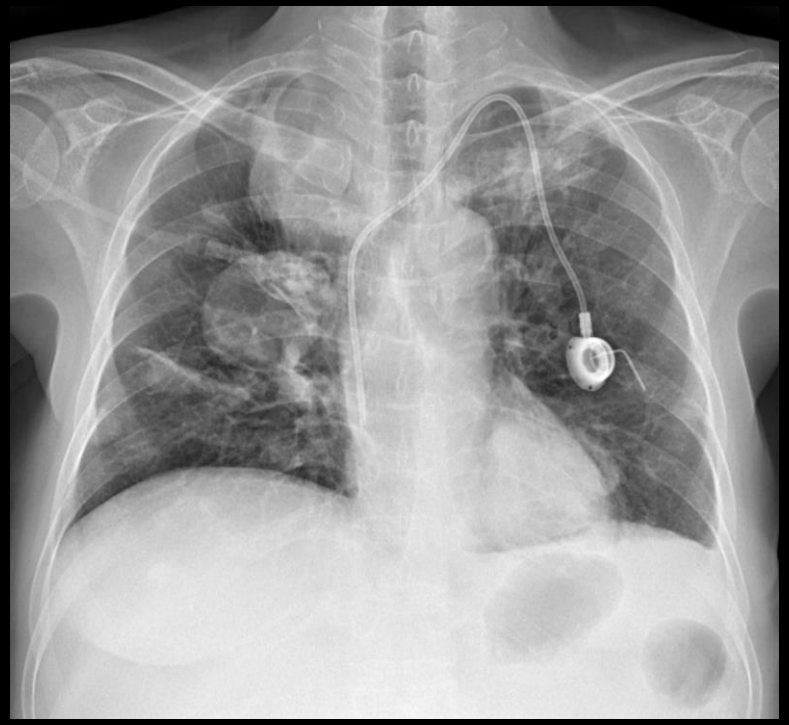
Case 3 : 68/F



#3 Cryo-extraction
2M later



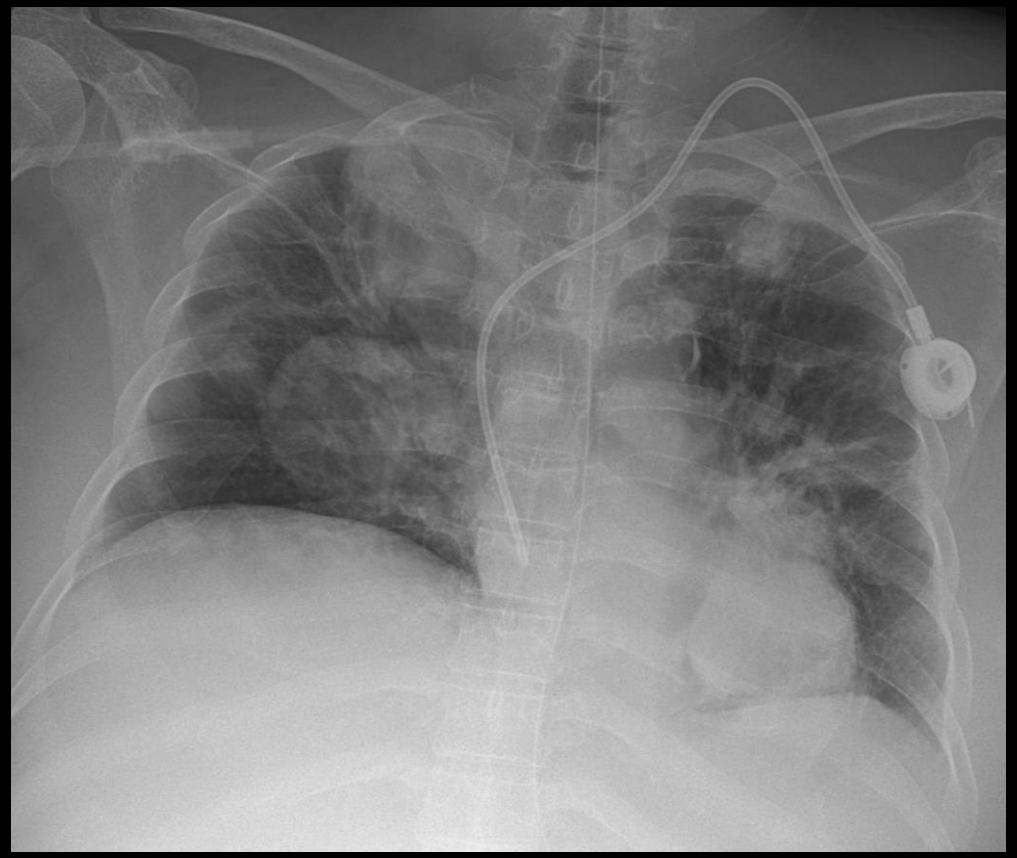
#4 Cryo-extraction
3M later



#5 Cryo-extraction
4M later

Lung & liver metastasis with ascites → rapid progression

Case 3 : 68/F



5M later → expired d/t hepatic failure

Thank You

Questions & Discussion