서울아산병원
Asan Medical Center

Cryotherapy for Central Airway Lesions fosusing on Cryoextraction

Wonjun Ji

Department of Pulmonary and Critical Care Medicine
Asan Medical Center

Contents

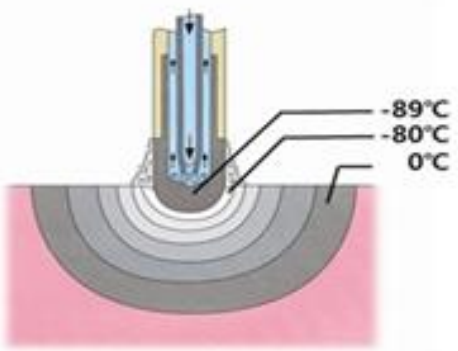
Introduction - Cryotherapy

- **Cryotherapy**

  빠른 동결 속도(faster freeze rate)와 느린 융해 속도(slower thaw rate), 동결-융해 주기(freeze-thaw cycle)의 반복을 통하여 세포를 파괴하는 기관지 내시경 치료

  - Cryotherapy: 병변에 대해 freezing/thawing cycle을 반복하여 조직 괴사를 유도

  - Cryoextraction/recannalization: cyoprobe에 냉각되어 있는 조직을 pulling out하면서 제거



- 기관지내시경 교과서, 대한결핵및호흡기학회, 2019

Introduction - Cryotherapy

- Equipment: Cryogen + Cryomachine

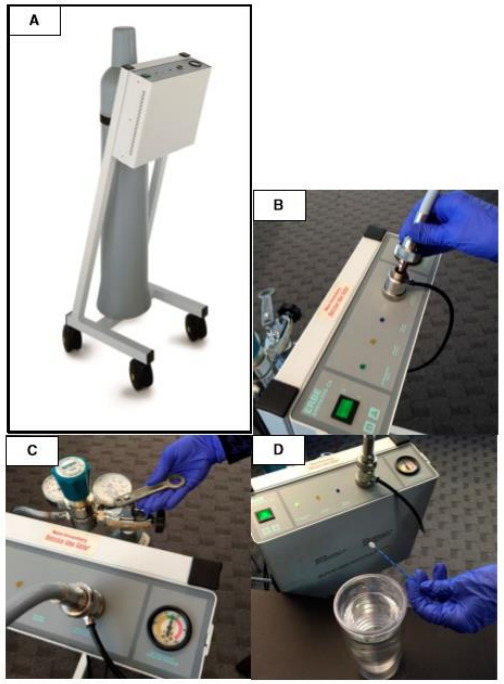
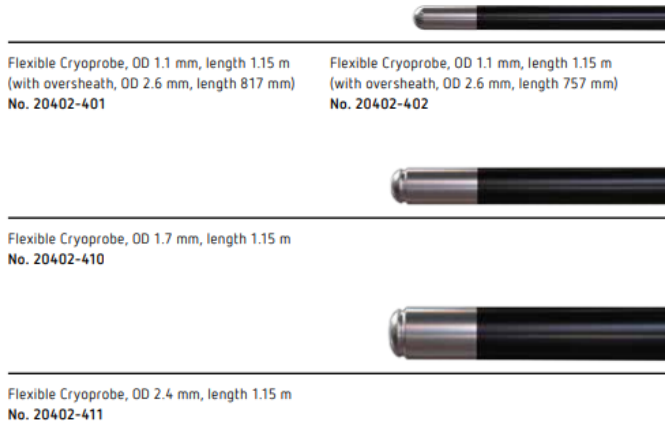


Figure 1. ERBOKRYO CA cryomachine (Erbe, Tubingen, Germany). (*A*) The cryogen is stored in the compressed tank held in the center of the machine. (*B*) The flexible cryoprobe connects the cryoprobe to the cryogen via a connection adapter. (*C*) The cylinder valve is then opened to allow the compressed gas to enter the machine via the transfer line. (*D*) The flow of cryogen is controlled using the footswitch. Depressing the pedal will allow freezing. Reprinted with permission from Erbe USA Inc.

- Ann Am Thorac Soc 2016;13(8):1405

	1세대(ERBECRYO®)	2세대 (ERBECRYO2®)
Cryogen	N_2O	CO_2
Size of Probe	1.9 / 2.4 mm	1.1 / 1.7 / 2.4 mm
Thaw rate	Slow	Fast

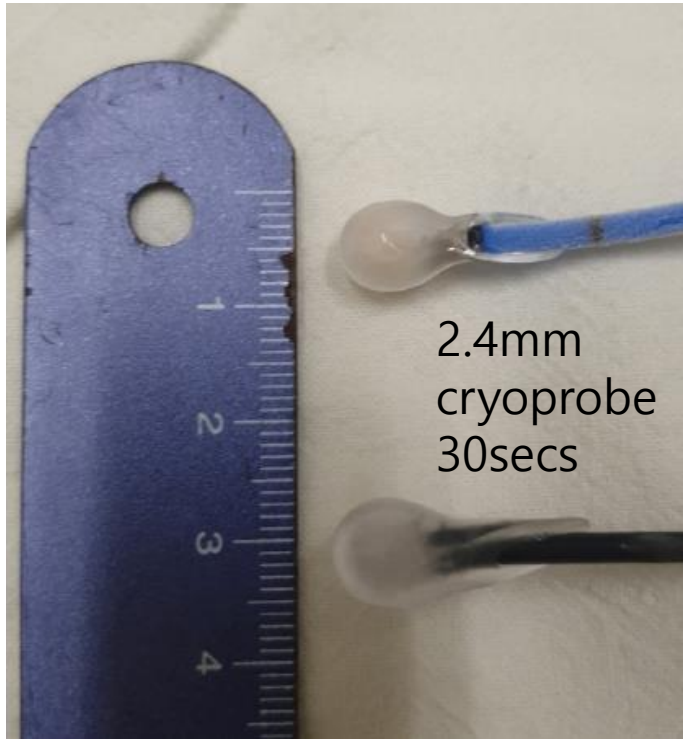


- Provided by ERBE®

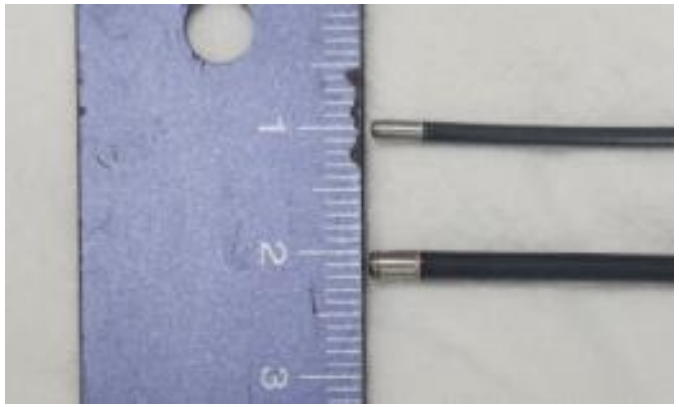
Introduction - Cryotherapy

- 일반적으로 3 mm 굵기의 cryoprobe를 사용할 경우 파괴되는 크기는 대략 직경 1 cm, 깊이는 대략 3 mm 정도로 보고됨

- 기관지내시경 교과서, 대한결핵및호흡기학회, 2019

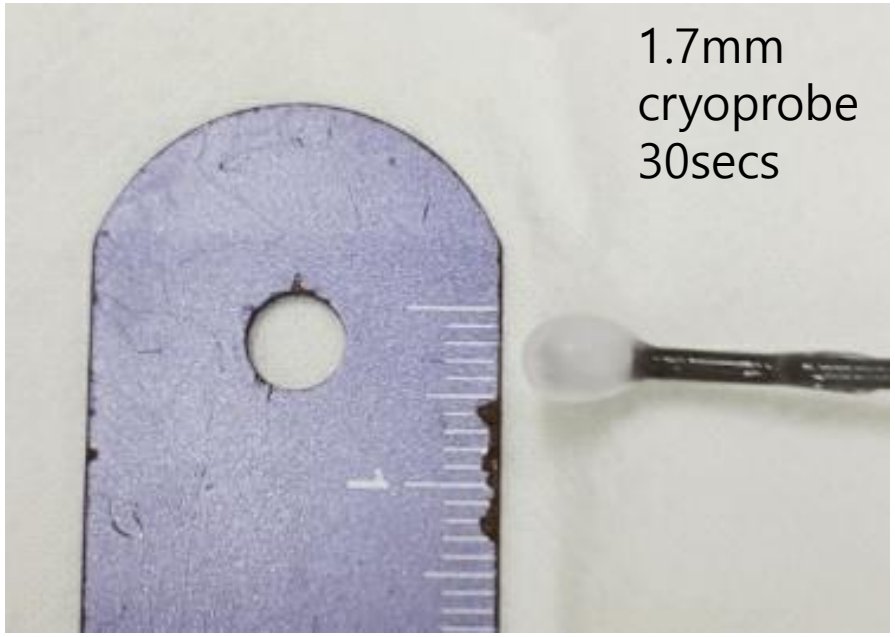


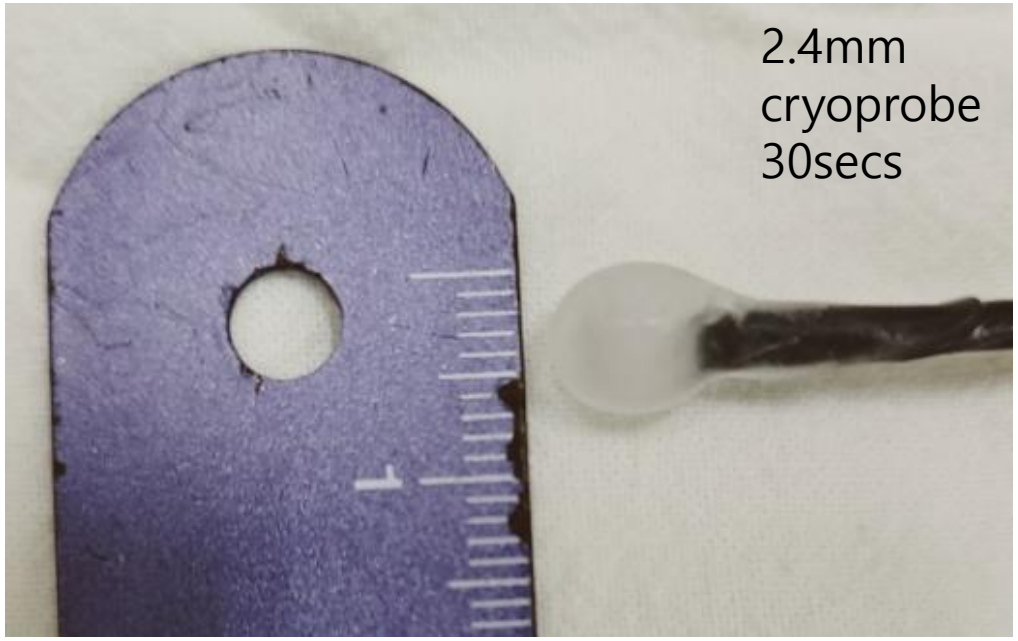
Introduction - Cryotherapy



1.7mm cryoprobe

2.4mm cryoprobe





Cryotherapy for benign central airway lesions

Cryotherapy for benign lesions

- Endobronchial foreign body removal
  - Foreign body
  - Broncholith
  - Blood clot
- Post intubation stenosis (combined with laser or alone)
- Low grade / Benign endobronchal tumor

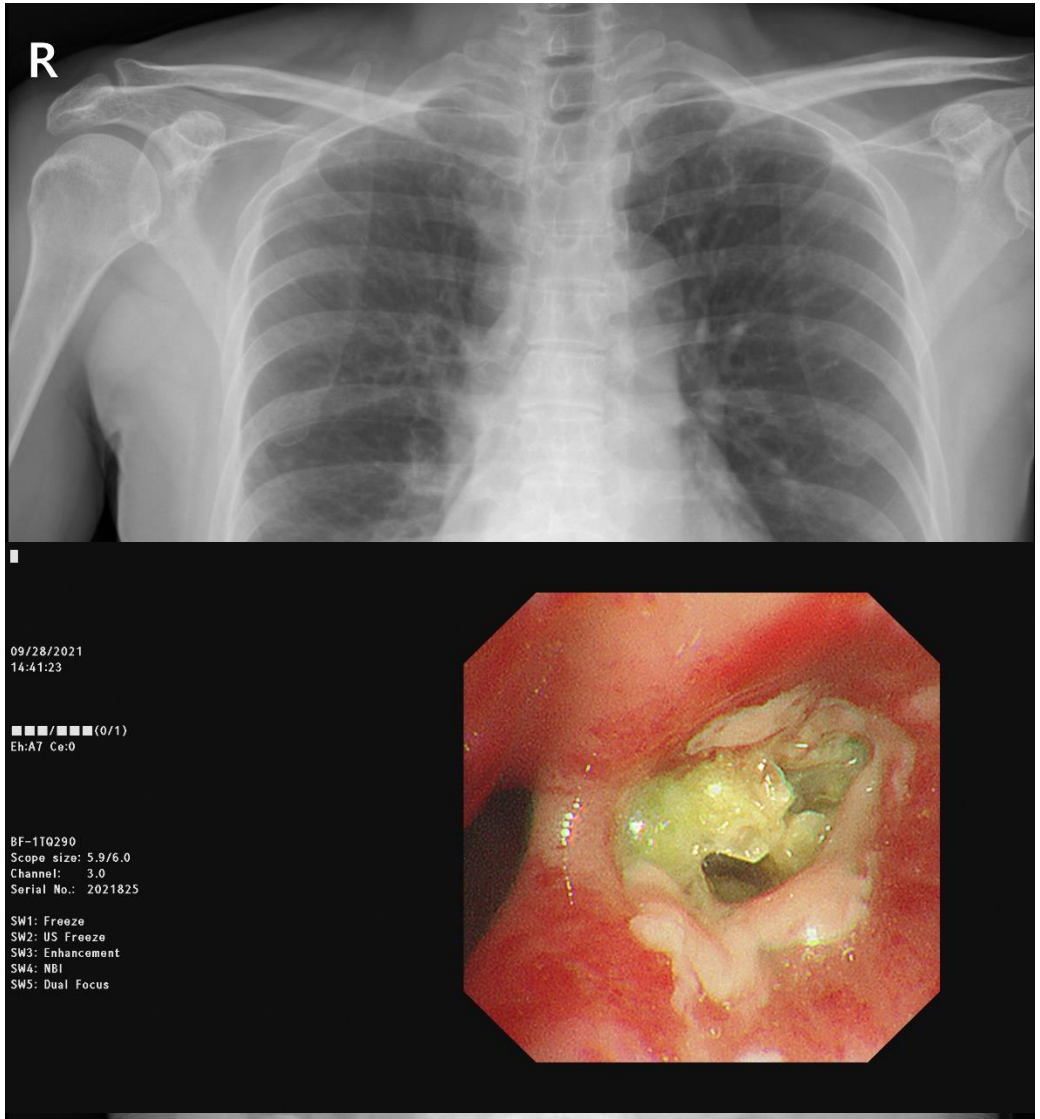
Case1 – Foreign body removal

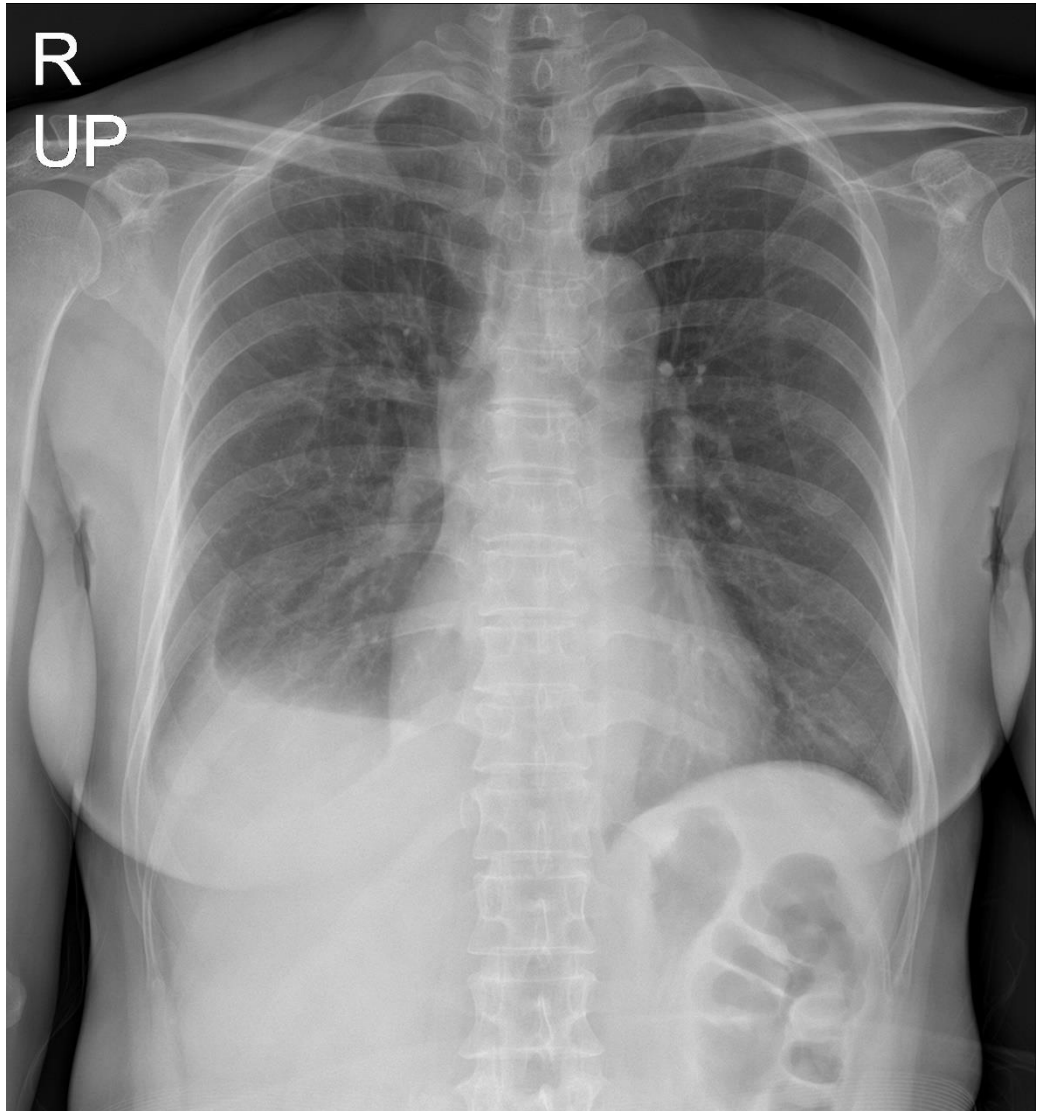
- 56/F, Foreign body aspiration (4 days ago)

•내원 4일전 삽겹살쌈 먹던 중 기도에 걸린느낌 발생 후 호흡곤란 및 기침 발현

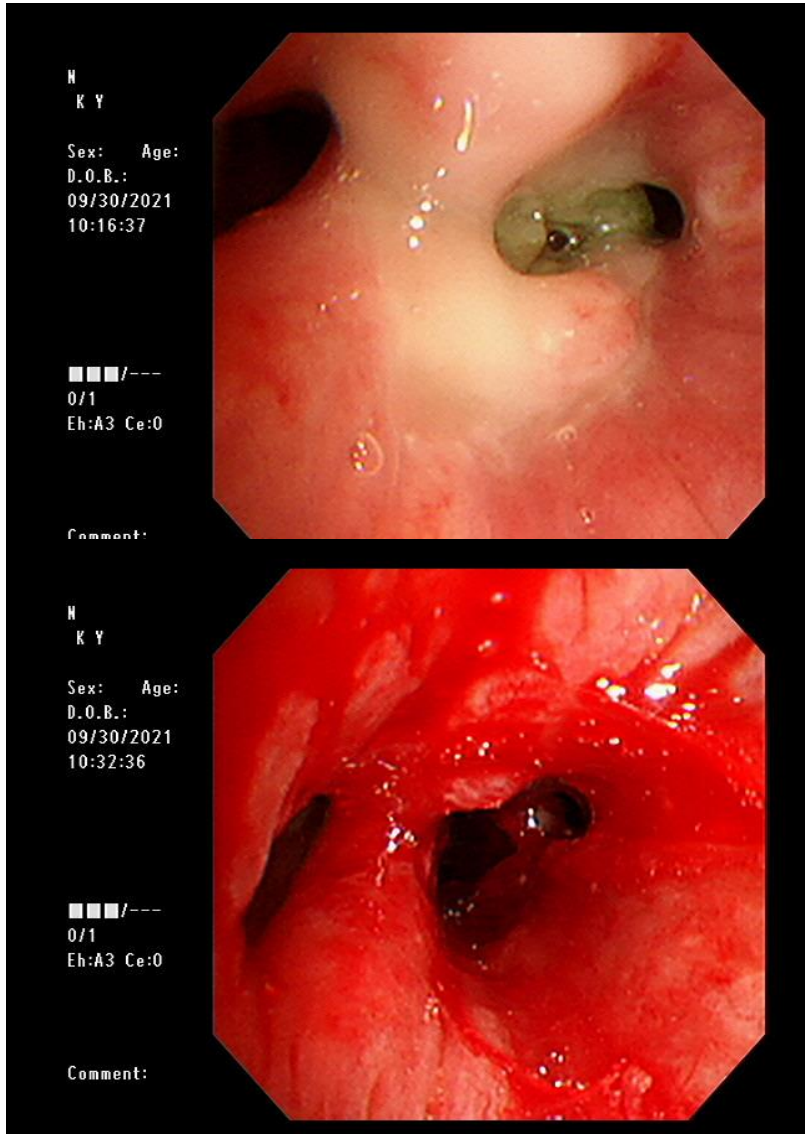
•내원 3일전 발열 동반되어 연고지 병원 방문, 기관지내시경 시도 하였으나 제거 실패 및 distal airway로 밀려들어가는 양상 및 출혈 동반되어 본원 내원

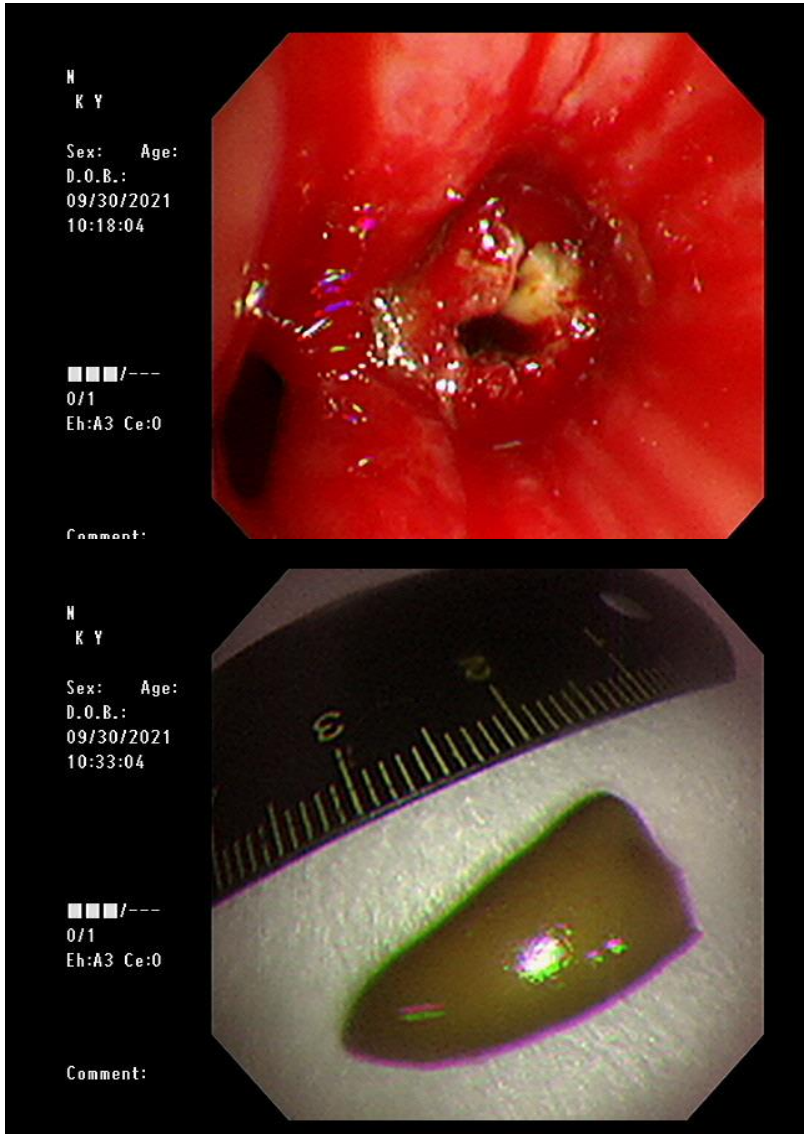
Case1 – chest PA





Case1 – Cryoextraction





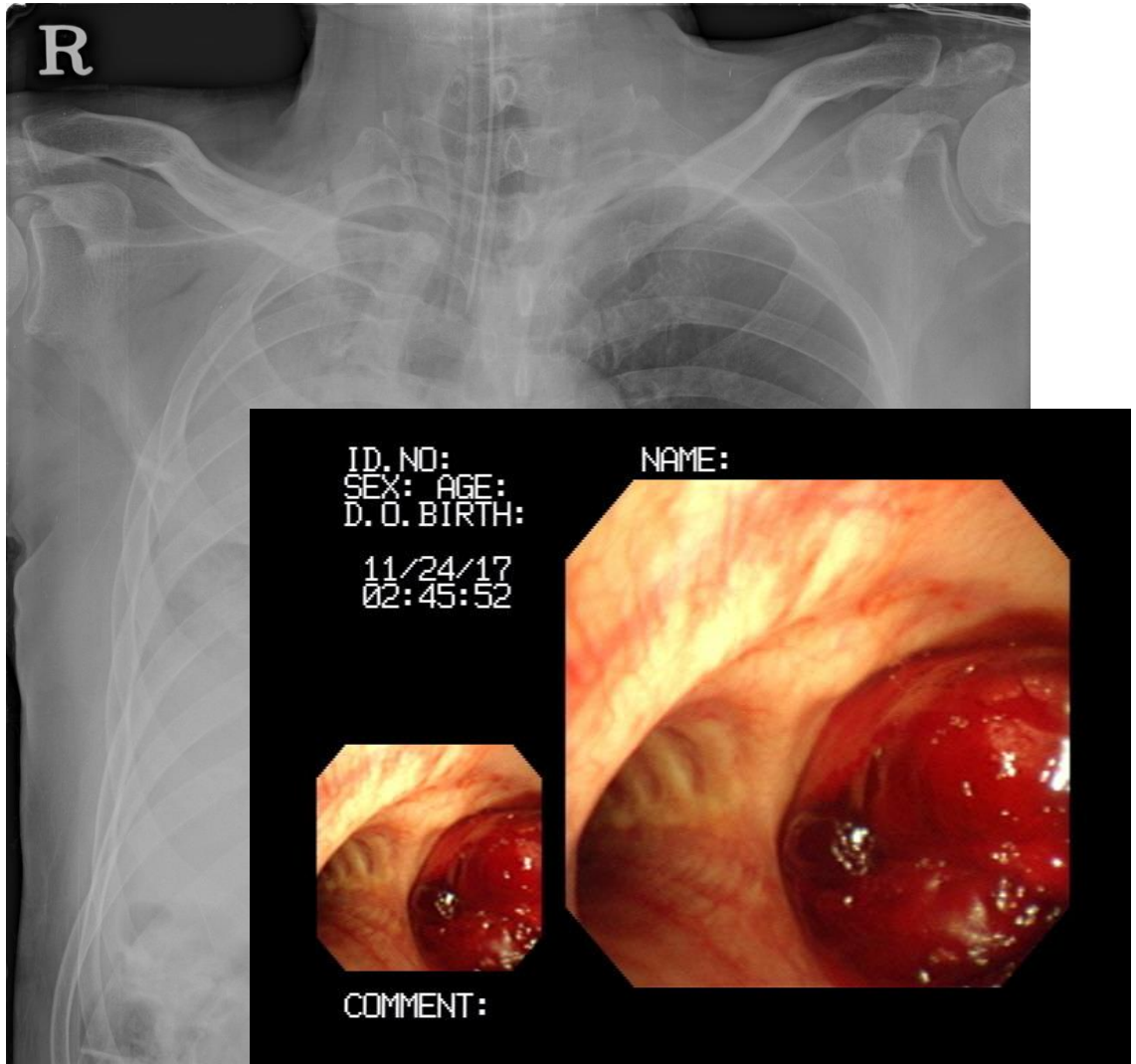
Case2 – Blood clot removal

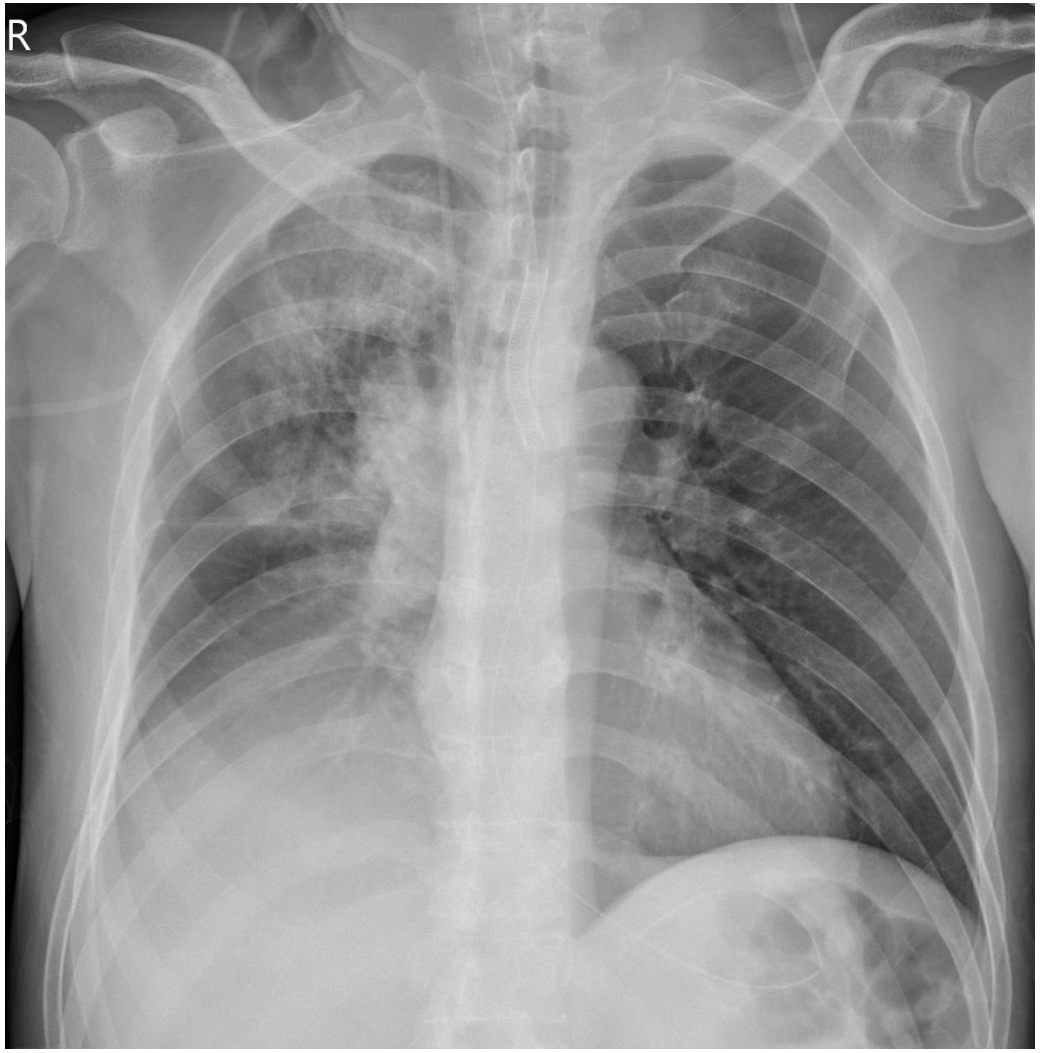
- 53/M, Hemoptysis (6 days ago)

- RCC로 97년도 Lt. radical nephrectomy 시행
- 16년 1월 RCC recur로 종양내과 추적 및 항암치료 중

- 내원 6일전부터 객혈 발생하여 악화 되는 양상으로 ER 내원
- ER 방문 후 respiratory failure로 intubation 후 ICU 입실

Case2 – Cryoextraction





Cryotherapy for benign lesions

- **Post intubation stenosis (cryotherapy alone)**

INTERNAL MEDICINE

□ CASE REPORT □

Recurred Post-intubation Tracheal Stenosis Treated with Bronchoscopic Cryotherapy

Ye-Ryung Jung, Joon Taek Jeong, Myoung Kyu Lee, Sang-Ha Kim, Suk Joong Yong, Seok Jeong Lee and Won-Yeon Lee

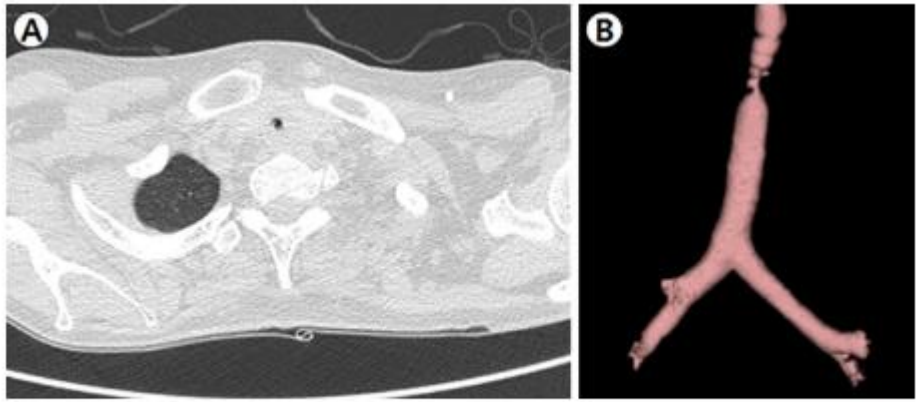
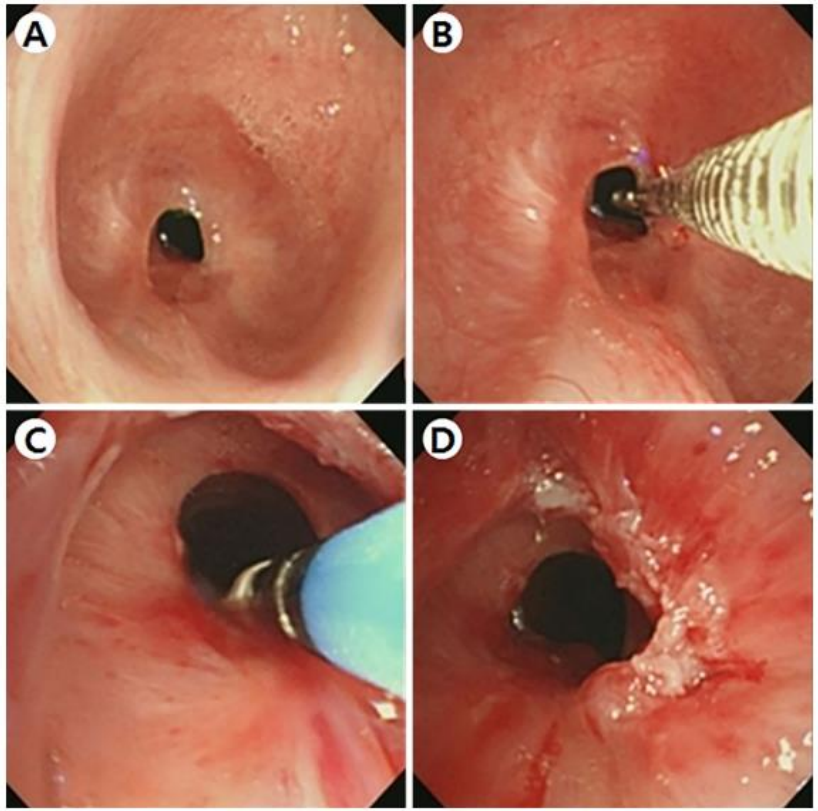


Figure 1. (A, B) Initial tracheal computed tomography shows luminal narrowing of the trachea where the narrowest diameter=3.8 mm.



- Internal Med 2016;55(22):3331

Cryotherapy for benign lesions

- **Post intubation subglottic stenosis (combined with laser)**

ORIGINAL ARTICLE WILEY

Effective treatment of post-intubation subglottic stenosis in children with holmium laser therapy and cryotherapy via flexible bronchoscopy

Anxia Jiao[1,2*] | Fang Liu[1,2*] | Andrew D. Lerner[3] | Xiaochun Rao[1,2] | Yan Guo[2,4] | Chenfang Meng[1,2] | Yuena Pan[1,2] | Gan Li[1,2] | Zheng Li[5] | Fang Wang[6] | Jing Zhao[7,8] | Yuyan Ma[1,2] | Xicheng Liu[1,2] | Xin Ni[7,8] | Kunling Shen[2,4]

- **Prospective, single center, Beijing**
- **July 2014 ~ Dec 2016**
- **Holmium laser + Cryotherapy**
- **Success rate: 93.8% (15/16)**
- **Average number of procedures: 4.88**

- Pediatr Invest 2019;3(1):9

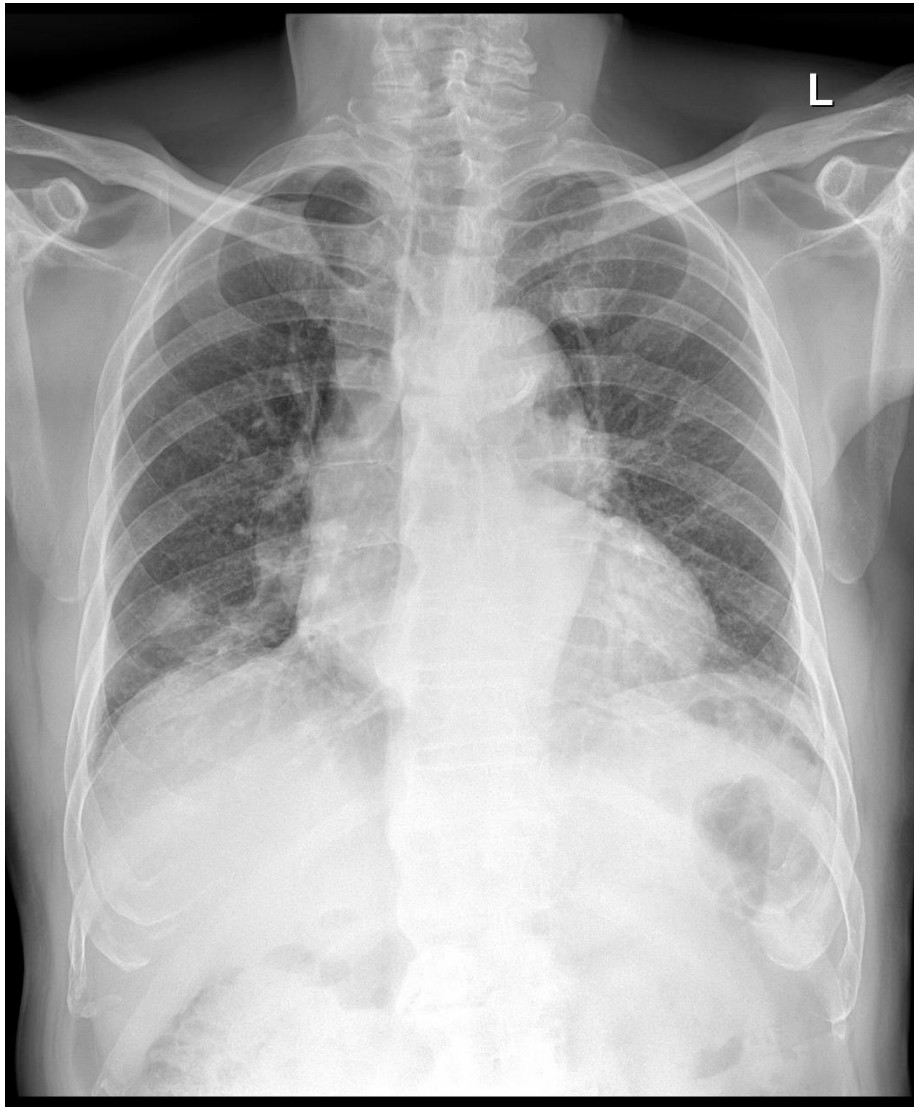
Case3 – Benign tumor

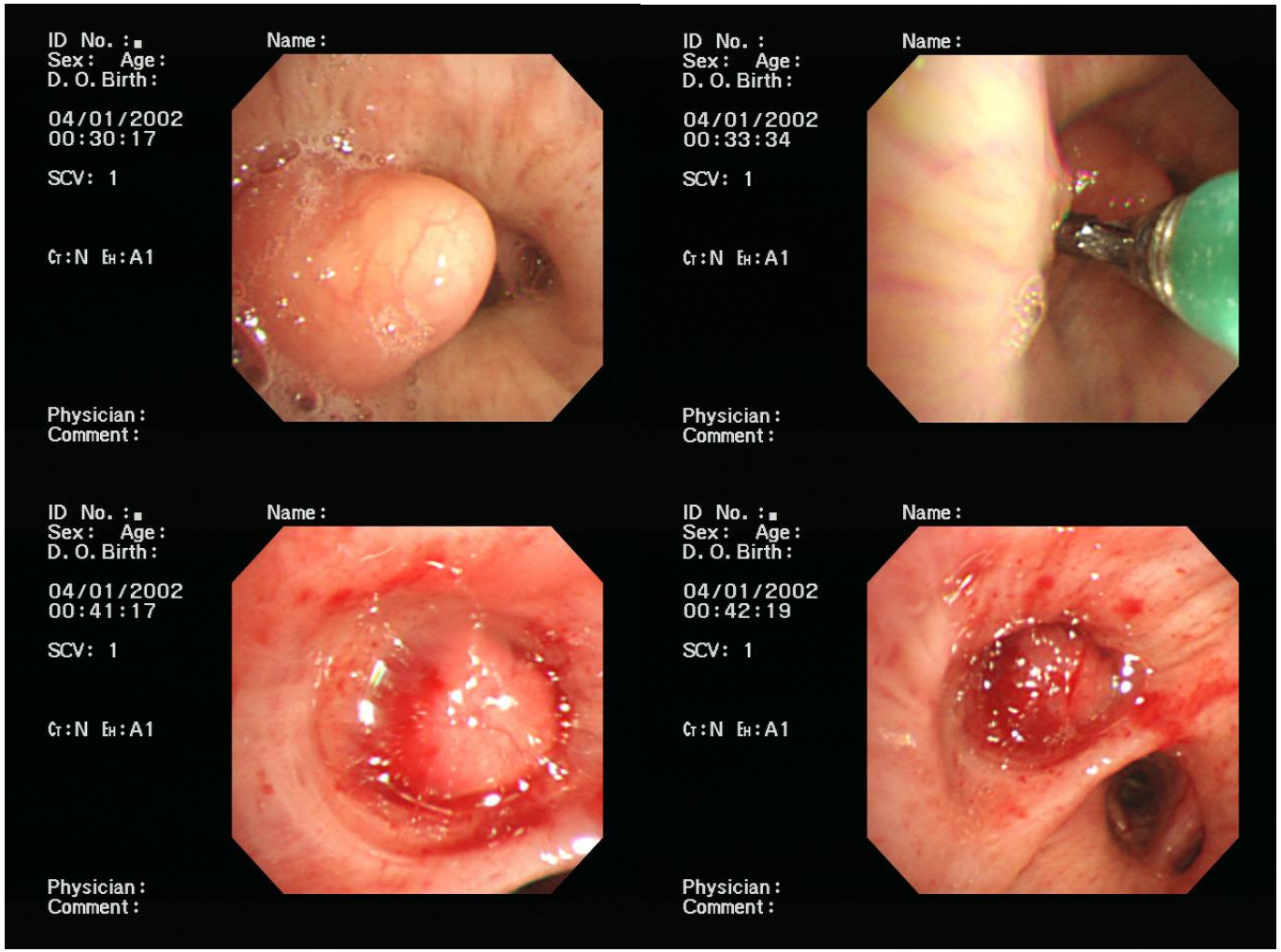
- 77/M, RML atelectasis (incidental finding)

•내원 2개월전 타원에서 수술 전 시행한 흉부 X-ray에서 이상소견으로 시행한 chest CT에서 RML endobronchial lesion 및 동반된 atelectasis 소견으로 타원에서 기관지경 검사 및 조직검사 시행 Lipoma로 진단

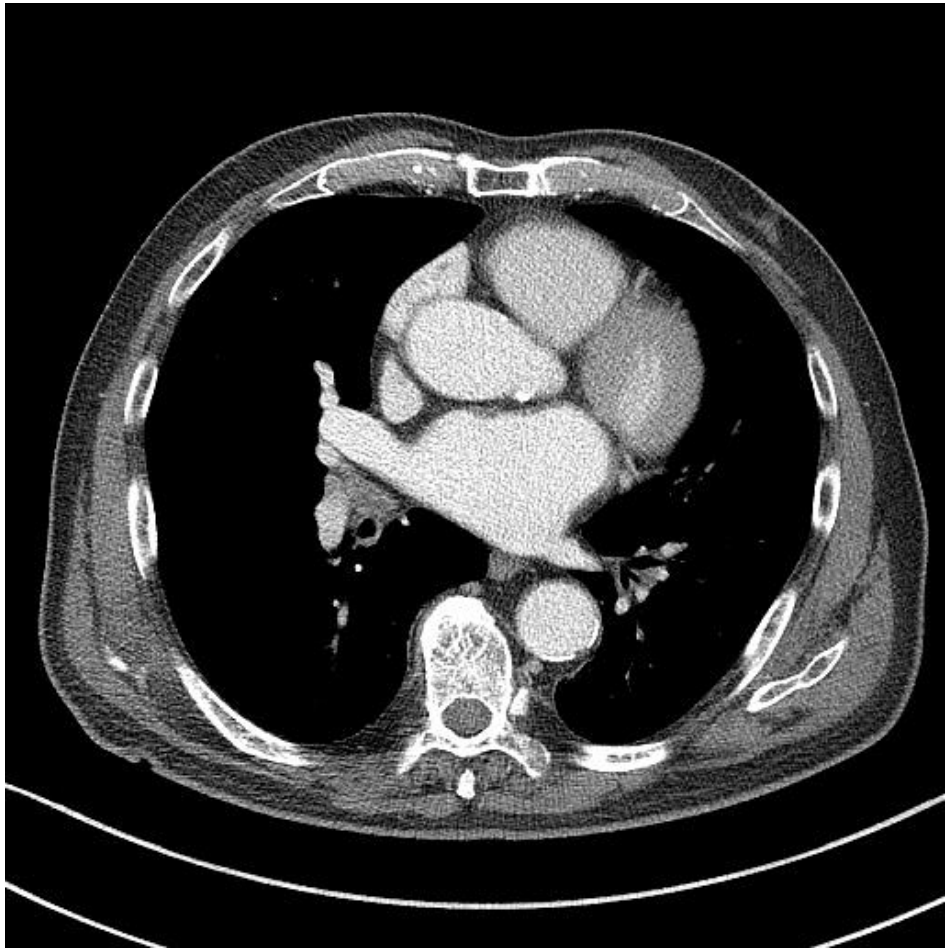
•RML endobronchial mass 제거 위하여 본원 내원함

Case3 – chest PA, outside BFS

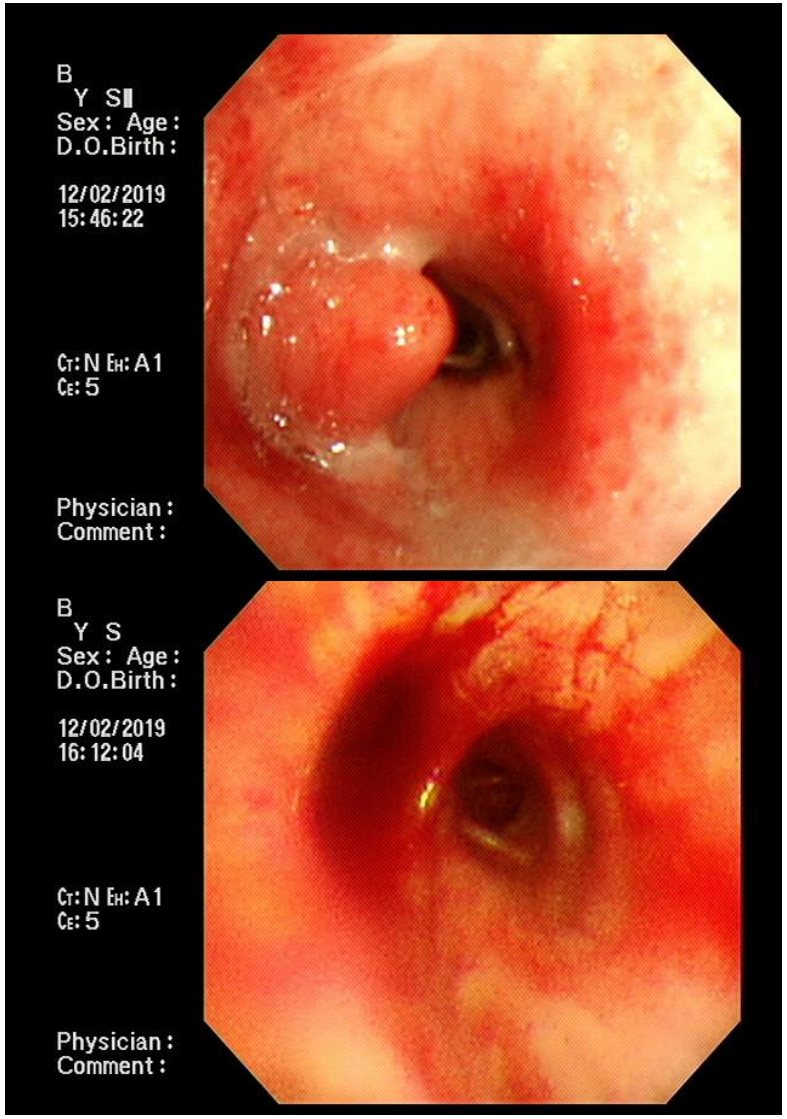


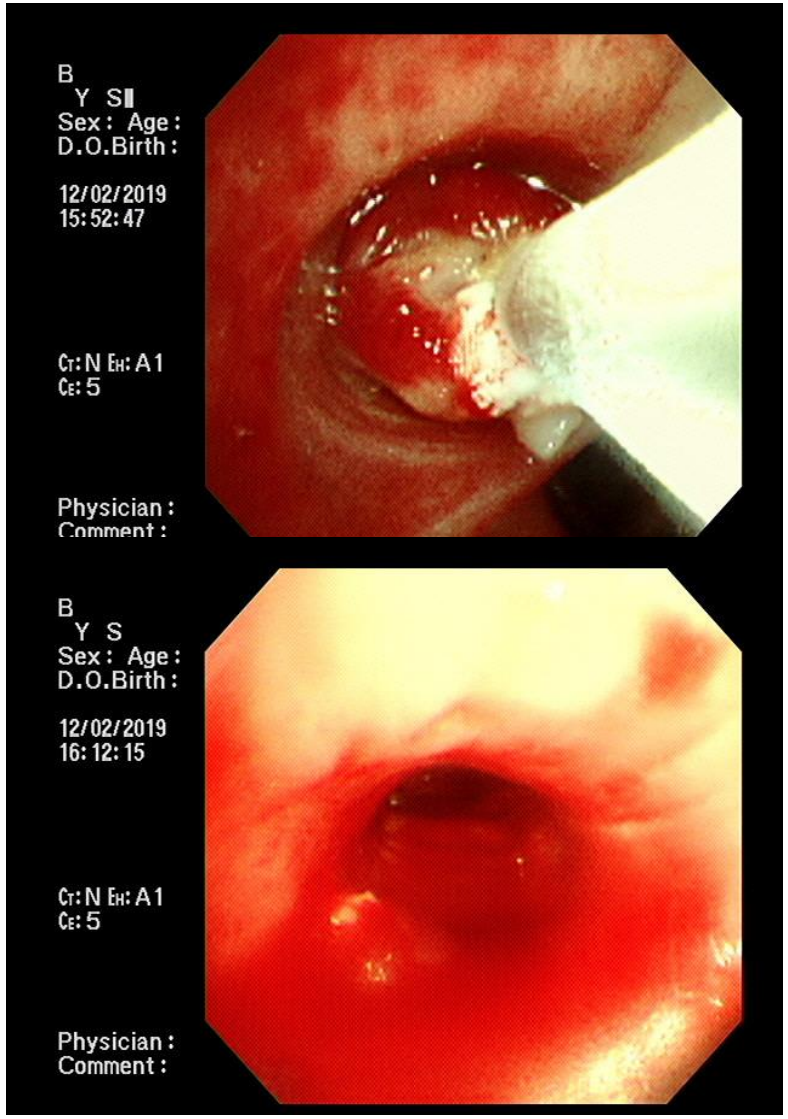


Case3 – chest CT

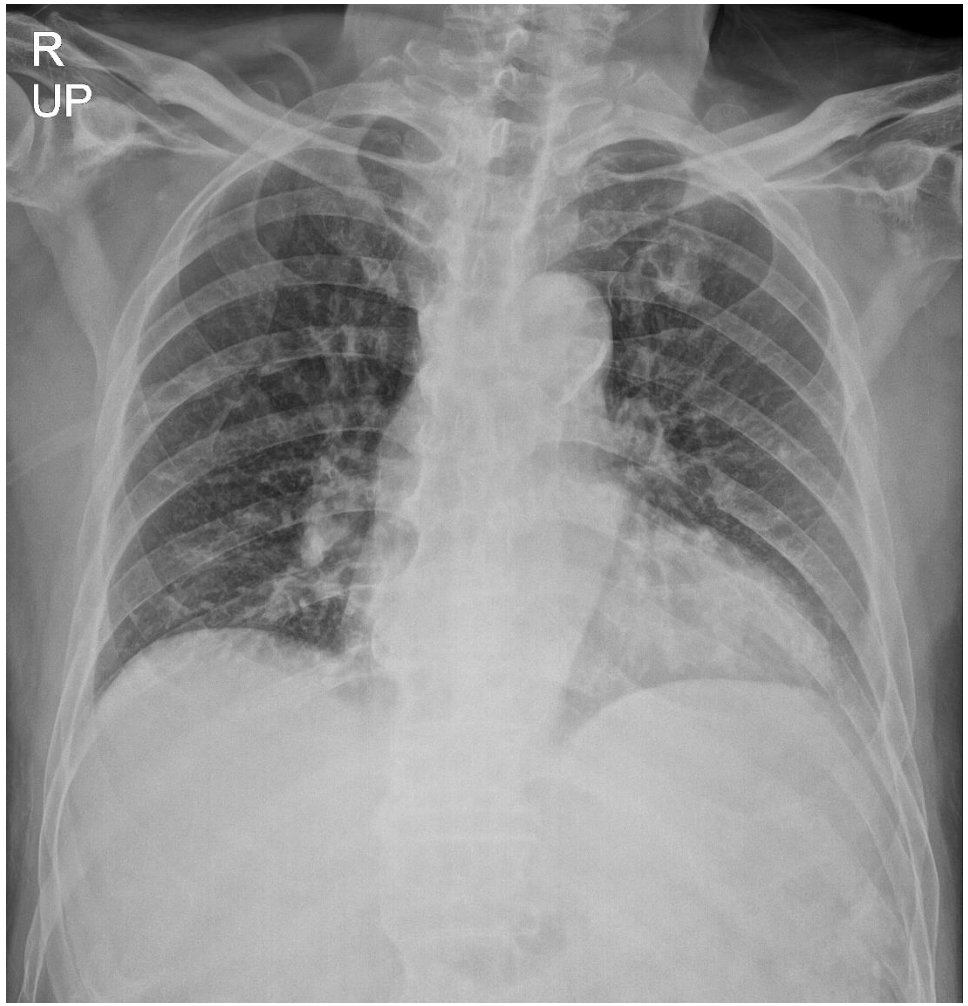


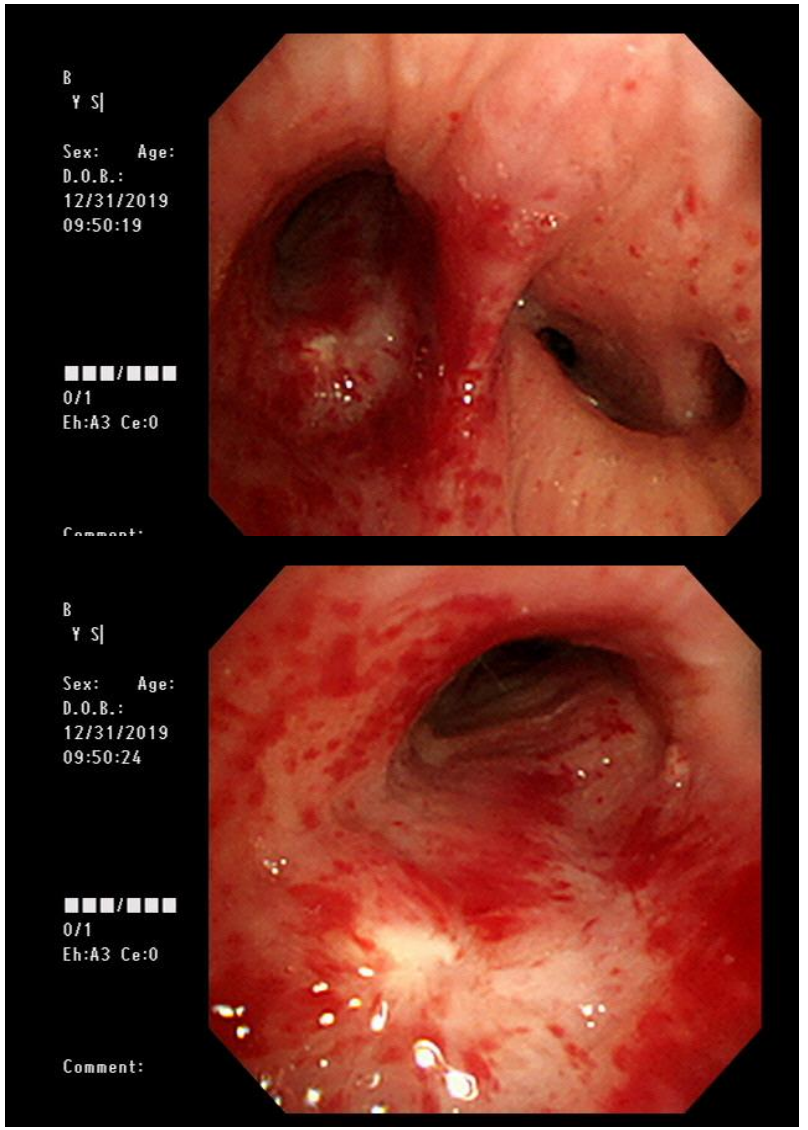
Case3 – Cryoextraction





Case3 – chest PA, f/u BFS (4 wks)





Cryotherapy in malignant Central airway lesions

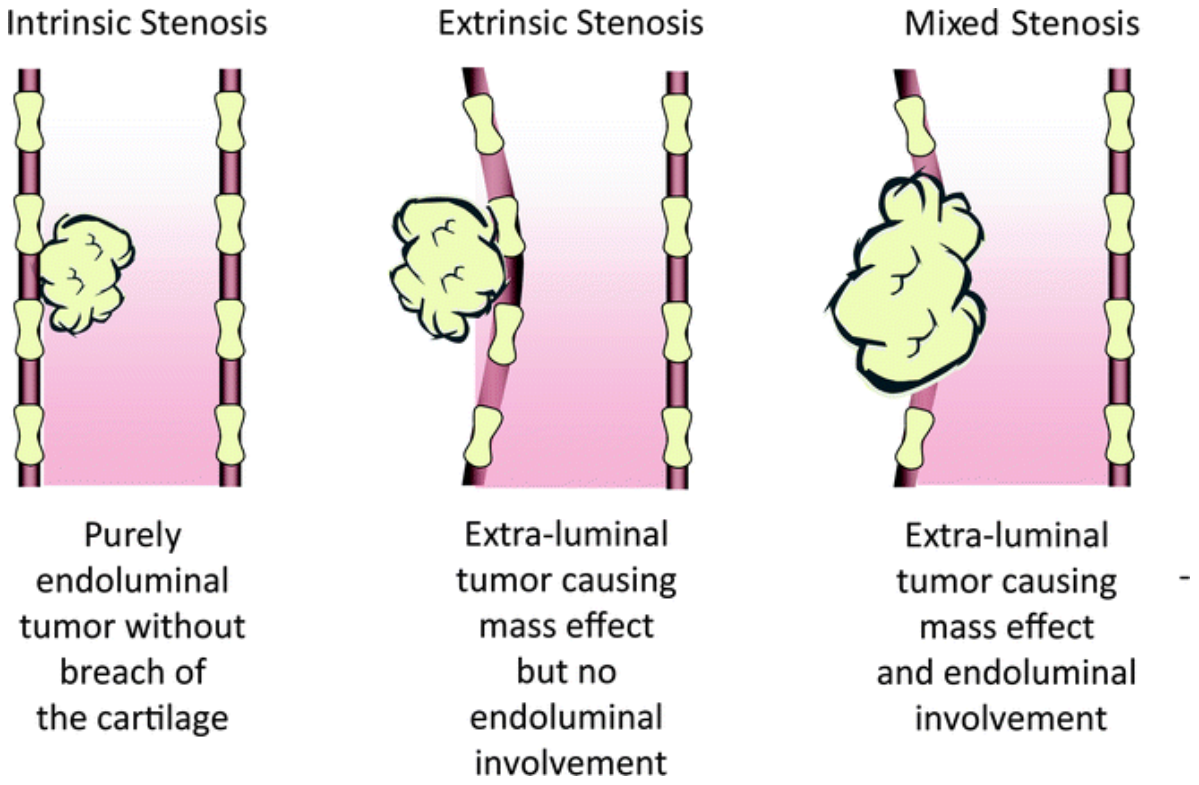
Cryotherapy in malignant lesions

- **Treatment of superficial endobronchial malignancy**
- **Palliation of central airway obstruction (CAO) in advanced malignancy**

Classification of MCAO

- Intrinsic (endoluminal)
- Extrinsic (extraluminal)
- Mixed

→ Impact on therapeutic approach



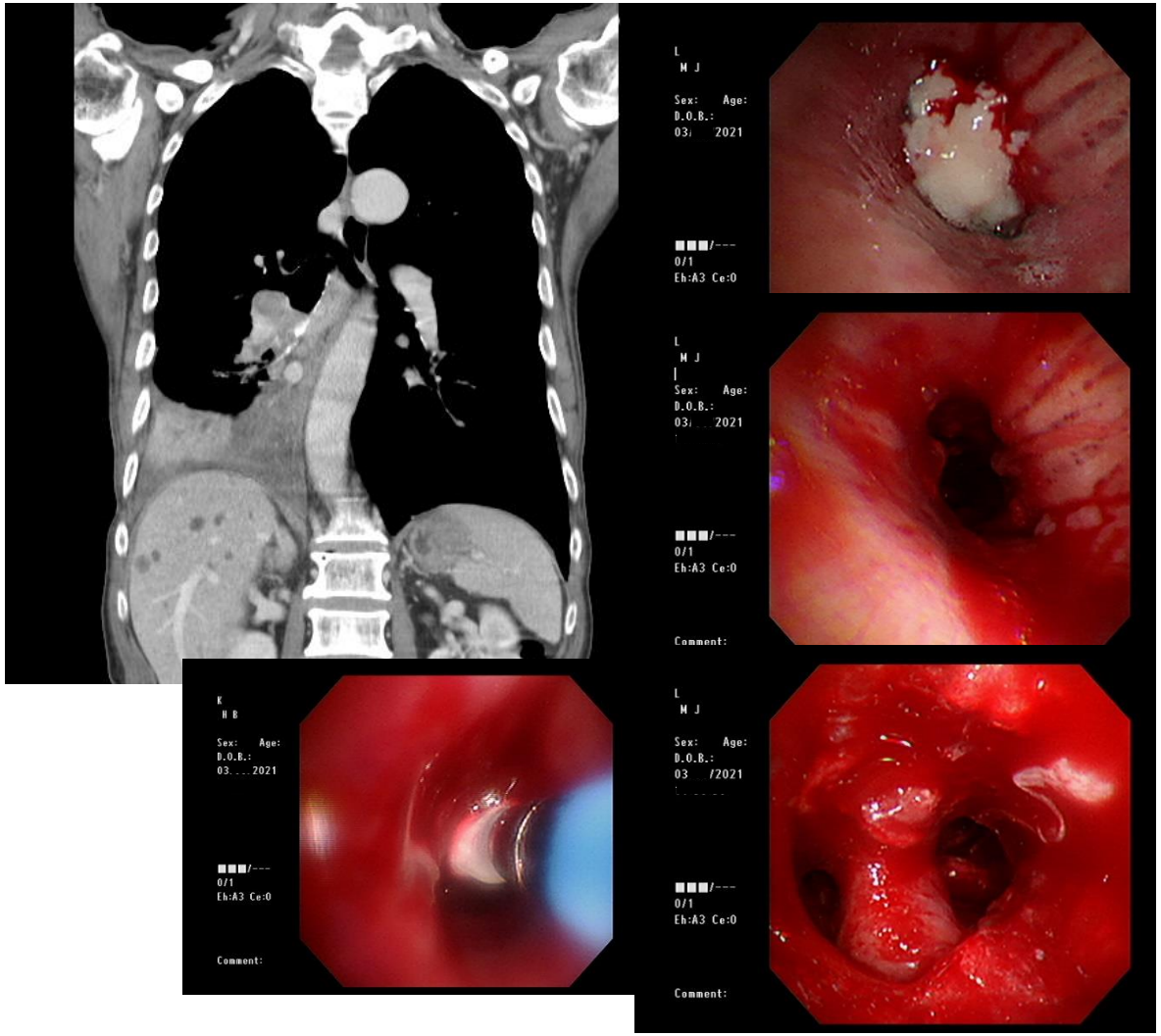
Laser & debridement	+++	-	++
Stent	±	+++	++

- A. Ernst and F.J.F. Herth (eds.), Principles and practice of interventional pulmonology. Springer 2013.

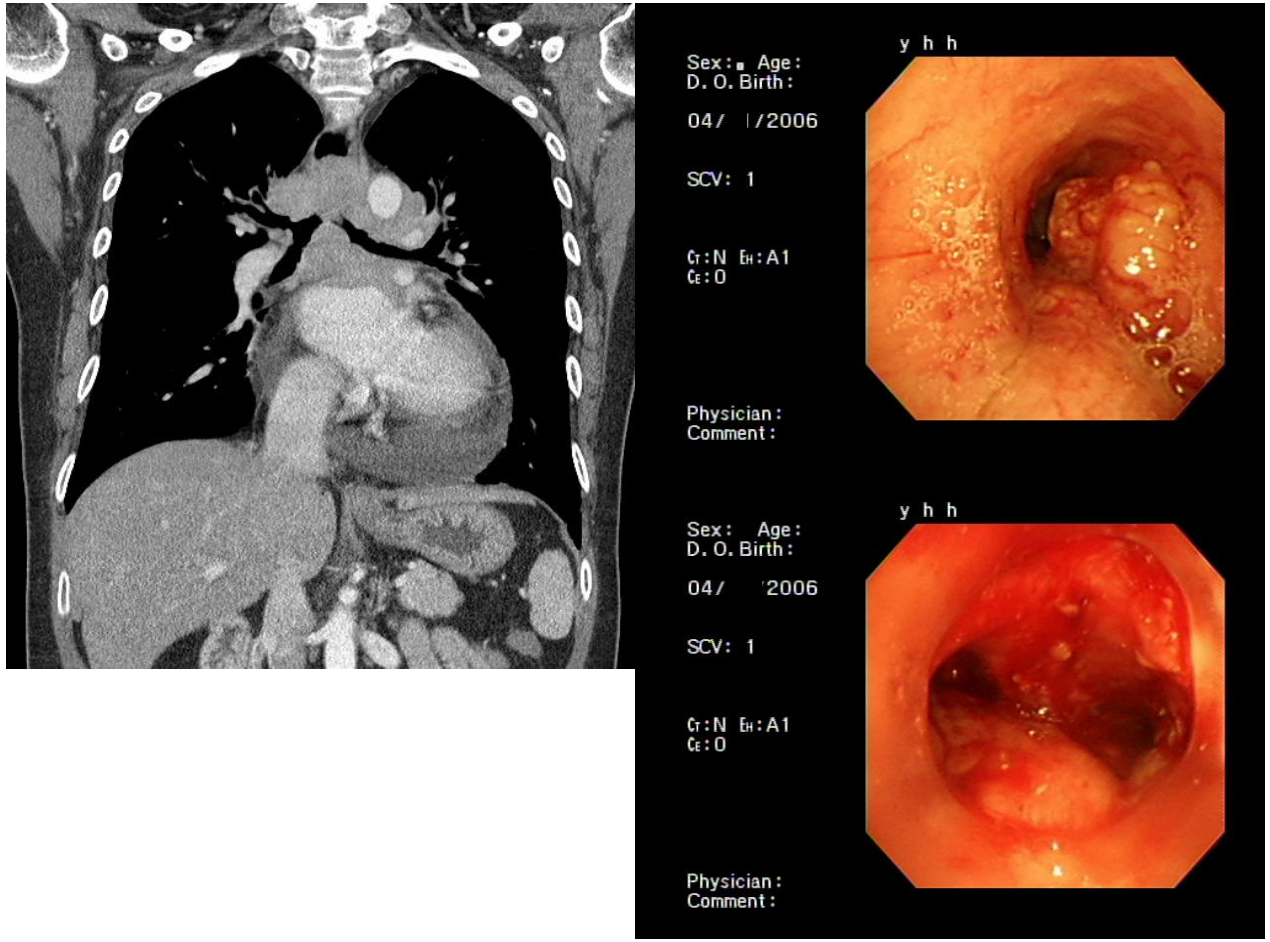
Each case on this slide is an individual case and do not fully reflect all patients' cases

AMC Cases

- Intrinsic : 70s/M NSCLC, SqCC



- Mixed : 50s/F recurred NSCLC, SqCC



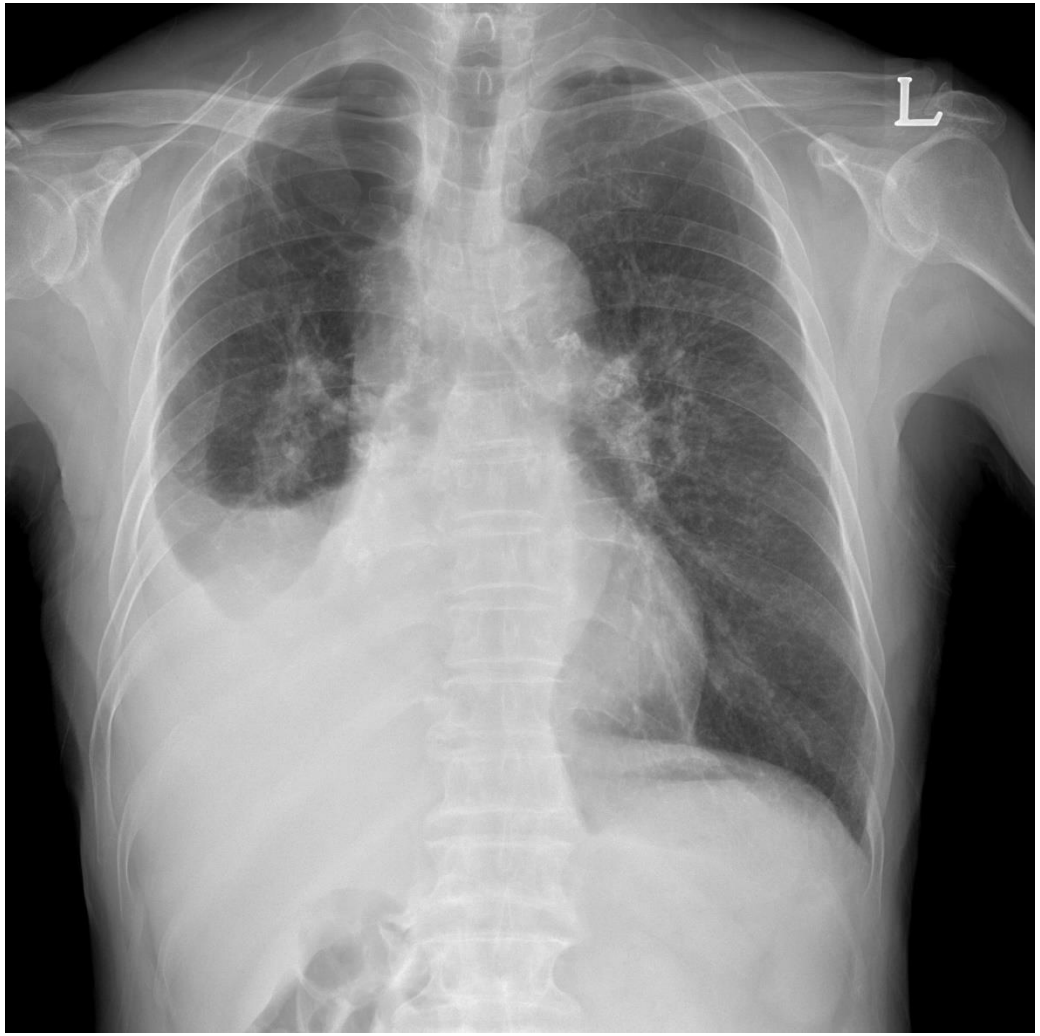
Case4 - MCAO

- 71/M, RLL atelectasis with pleural effusion

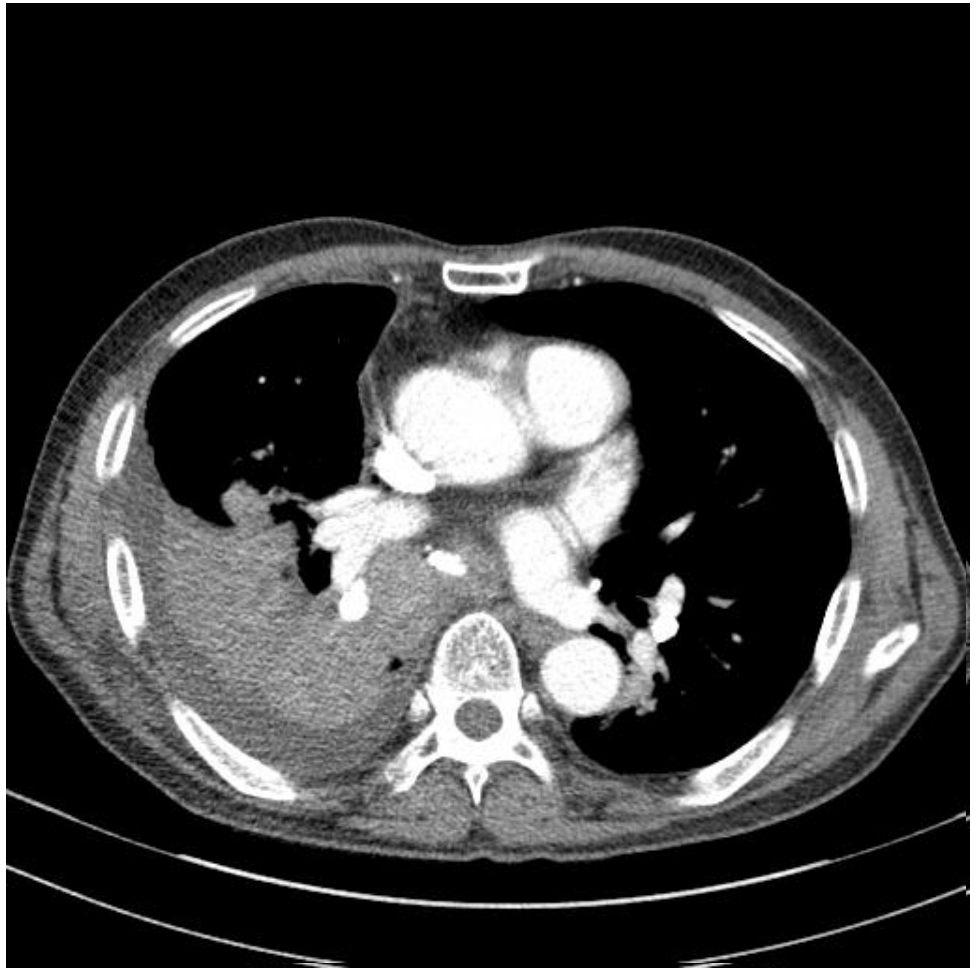
- 기저 pneumoconiosis로 연고지 병원에서 f/u 하던 분으로

- 내원 1주전 시행한 chest CT에서 RBI endobronchial mass와 RML, RLL atelectasis 소견으로 F/E위해 내원함

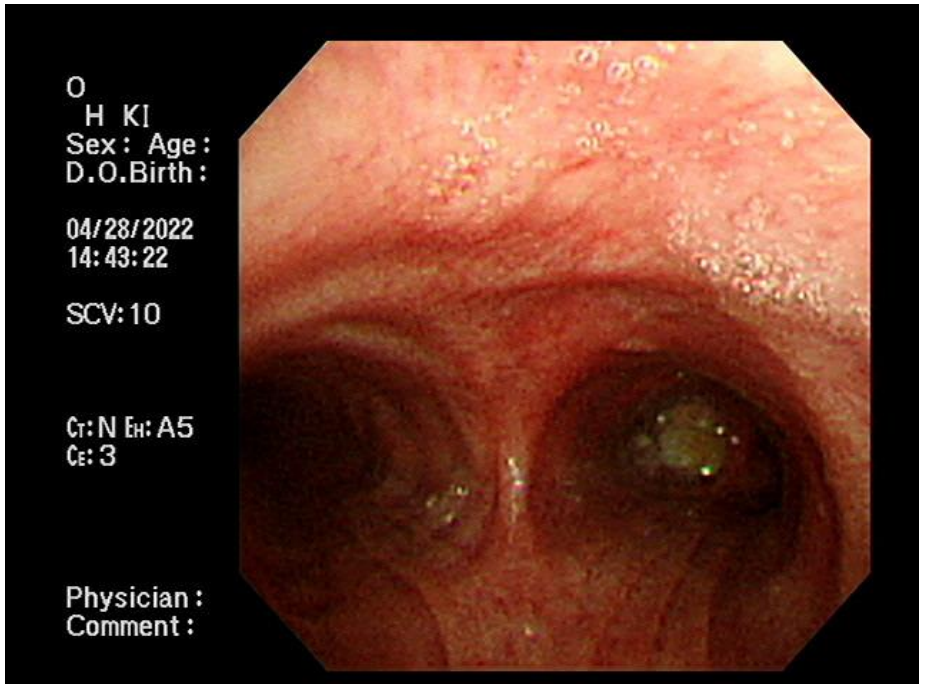
Case4 – chest PA

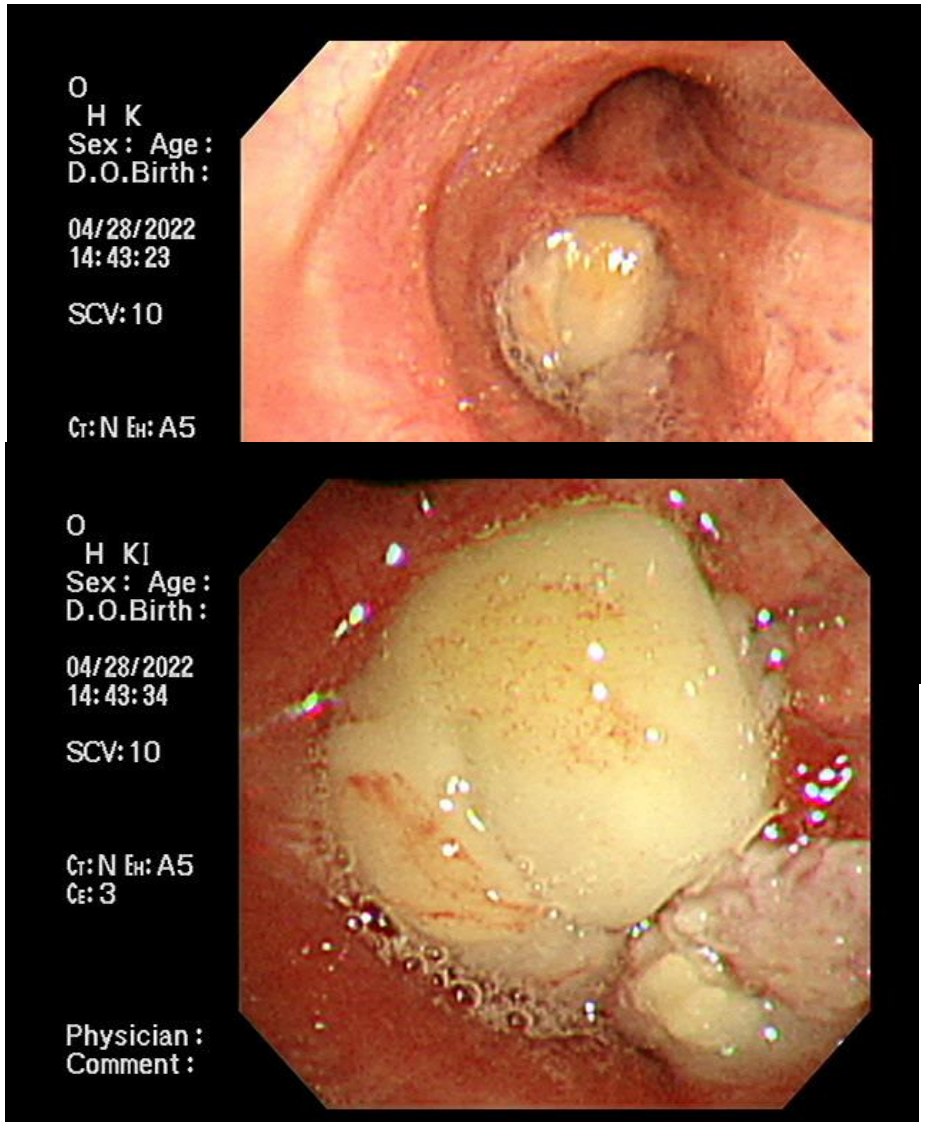


Case4 – chest CT

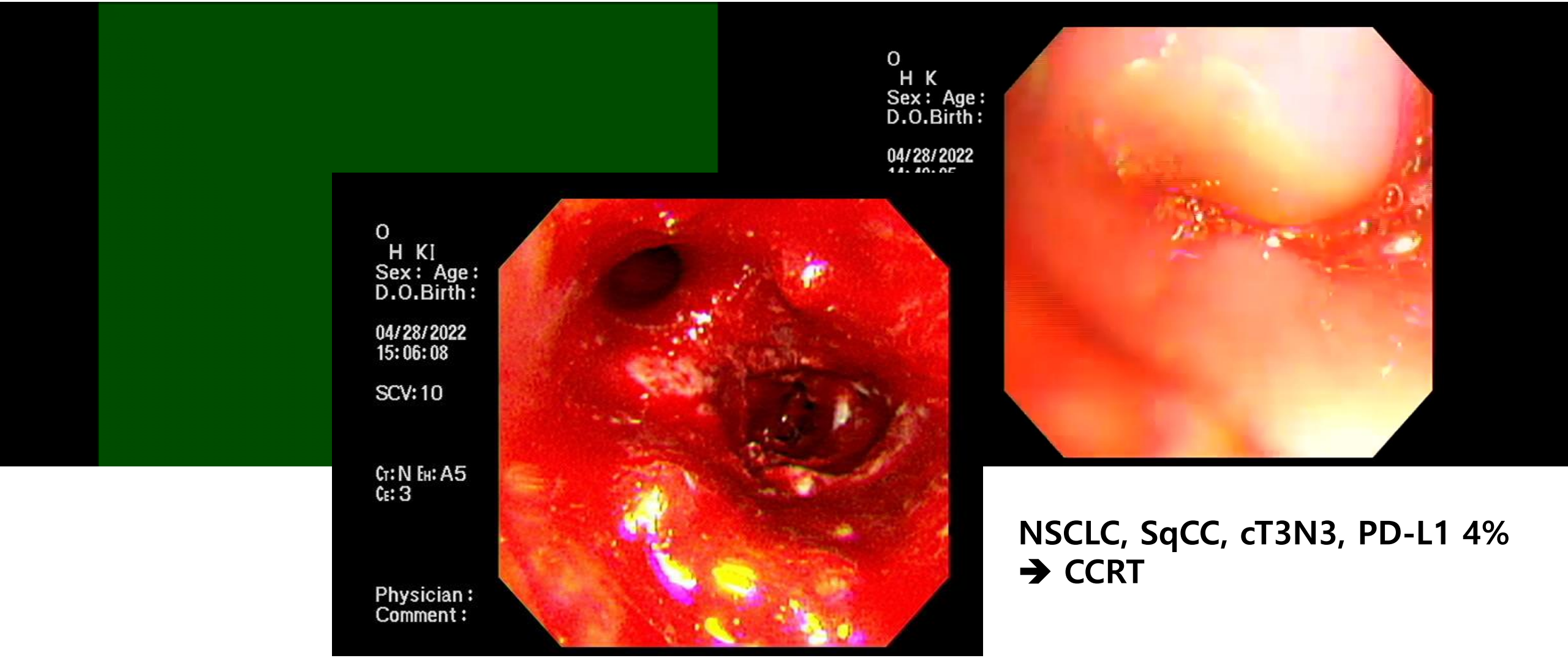


Case4 – Cryorecannalization



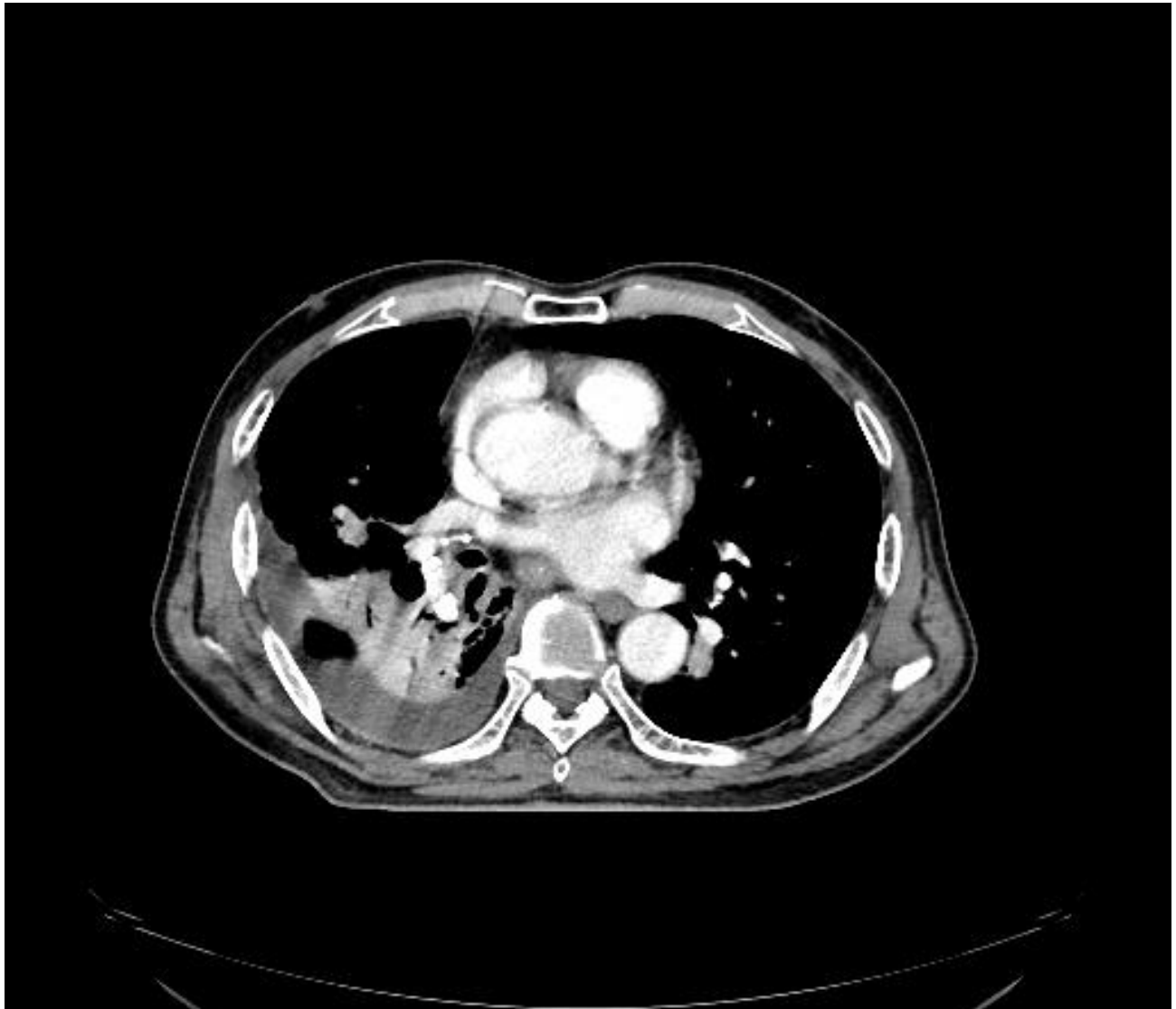


Case – cryotherapy



NSCLC, SqCC, cT3N3, PD-L1 4%
➔ CCRT

Case4 – f/u chest CT for RT



RESEARCH ARTICLE Open Access

Factors affecting survival in patients with endobronchial malignant mass after flexible Bronchoscopic cryotherapy: a cohort study

Fu-Tsai Chung[1,2,3,4*†], Chun-Liang Chou[1,2,4†], Yu-Lun Lo[2], Chih-Hsi Kuo[2], Tsai-Yu Wang[2], Chun-Hwa Wang[2], Hung-Yu Huang[1,2], Horng-Chyuan Lin[2], Chih-Hao Chang[1,2], Chung-Shu Lee[1,2], Hao-Cheng Chen[1,5] and Shu-Min Lin[2*]

- 2007-2012, Taiwan
- Retrospective cohort study
- 63 patients
- Primary lung cancer: 47
- Bleeding complication: 20.9%

Table 3 Complications and outcomes after cryotherapy ($n = 67$)

Complications	
Minor bleeding	14
Major bleeding[a]	0
Multiple procedures necessity	12
Pneumothorax[a]	0
Outcomes	
Symptoms relief	56
performance status improvement	49
Received further chemotherapy	43

[a]Those listed include complications reported from literature even without occurrence in this study

- BMC Pulmonary Medicine 2019;19:101

RESEARCH ARTICLE Open Access

Factors affecting survival in patients with endobronchial malignant mass after flexible Bronchoscopic cryotherapy: a cohort study

Fu-Tsai Chung[1,2,3,4*†], Chun-Liang Chou[1,2,4†], Yu-Lun Lo[2], Chih-Hsi Kuo[2], Tsai-Yu Wang[2], Chun-Hwa Wang[2], Hung-Yu Huang[1,2], Horng-Chyuan Lin[2], Chih-Hao Chang[1,2], Chung-Shu Lee[1,2], Hao-Cheng Chen[1,5] and Shu-Min Lin[2*]

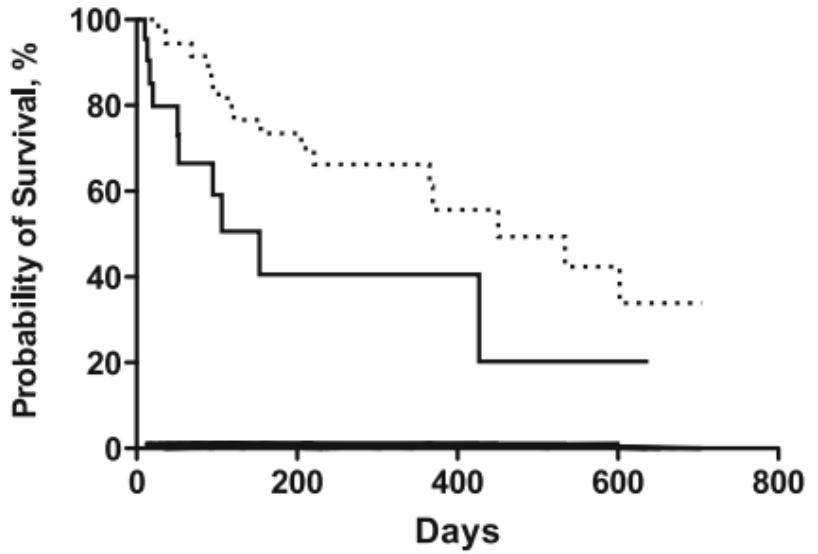


Fig. 1 Proportion of patients having received chemotherapy and cryotherapy (.....) and patients having received cryotherapy only (———) traced using the Kaplan-Meier method. Median, 472 vs. 169 days; log-rank test, $p = 0.02$; hazard ratio, 0.39; 95% confidence interval, 0.16-0.89

Table 4 Factors for survival, by multivariate analysis ($n = 67$)

	OR	95% CI	*p*
Minor bleeding	1.2	0.27–5.27	0.87
Multiple procedures necessity	0.37	0.1–1.92	0.21
Symptoms relief	1.3	0.2–11.3	0.89
Performance status improved after cryotherapy*	3.7	1.2–10.7	0.03
Ability to receive further chemotherapy after cryotherapy with improvement of performance status *	4.3	1.4–13.7	0.02

Abbreviations: *OR* odds ratio, *CI* confidential interval
*$p < 0.05$

- *BMC Pulmonary Medicine 2019;19:101*

Table 1. Cryotherapy for malignant central airway obstruction: a summary of the case series level evidence available describing the success of cryotherapy in malignant central airway obstruction

Study	Year	N	Type of Procedure	Improvement in Airway Obstruction	Safety
Mathur *et al.* (2)	1996	20	Flexible, repeat bronchoscopy 1–2 wk after probe cryotherapy	18/20 (90%), complete removal of tumor; 12/17 (71%), improved dyspnea; 5/5, improved hemoptysis	1 cardiac arrest
Walsh *et al.* (35)	1990	33	Rigid, repeat bronchoscopy 2–4 wk after probe cryotherapy	26/33 (79%), initial overall subjective improvement; 20/26 (77%), improved obstruction; 6/9 (67%), improved hemoptysis; 7/29 (24%), improvement in FEV_1 and FVC; 6/22 (27%), improvement in 6MWT*	No complications
Marasso *et al.* (38)	1993	234	Rigid, repeat bronchoscopy 6–8 d after probe cryotherapy	78/115 (68%), improved atelectasis; 58/62 (94%), improved hemoptysis; 87/107 (81%), improved dyspnea; 120/168 (71%), improved oxygenation†	Not reported
Maiwand (39)	1986	75	Rigid, repeat bronchoscopy at 2, 4, and 8 wk after probe cryotherapy	20/33 (61%), improved stridor; 23/31 (74%), improved dyspnea; 11/11, improved hemoptysis; 60/75 (80%), improved obstruction	No complications
Maiwand (40)	1999	153	Rigid, repeat bronchoscopy 2 wk after probe cryotherapy	85/133 (64%), improved dyspnea; 82/120 (68%), improved cough; 51/55 (93%), improved hemoptysis; average increase in FEV_1,110 ml‡; average increase in FVC, 90 ml‡	3/153 (2%), bleeding; 1/153 (0.7%), pneumothorax
Maiwand *et al.* (41)	2004	476	Rigid, repeat bronchoscopy 2 wk after probe cryotherapy	301/436 (69%), improved cough; 278/469 (59%), improved dyspnea; 138/180 (76%), improved hemoptysis; average increase in FEV_1, 90 ml‡; average increase in FVC, 130 ml‡; improvement in mean Karnofsky score	0.7%, bleeding; 0.1%, pneumothorax; 0.9%, respiratory distress§
Hetzel *et al.* (19)	2004	60	Flexible, single session of cryorecanalization	50/60 (83%), complete or partial resolution of obstruction (37/60 complete resolution)	No major complications; 6/60 (10%), bleeding treated with APC
Schumann *et al.* (22)	2010	225	Flexible, 193/225, rigid, 31/225, single session of cryorecanalization	205/225 (91%), improvement in condition‖ and/or ability to clear secretions	No major complications; 28/225 (12%), mild or moderate bleeding¶
Inaty *et al.* (42)	2016	88	Rigid, cryorecanalization with concomitant procedures	83/88 (94%), complete or partial resolution of obstruction after first procedure	Case series included 68 cases of benign airway obstruction; 6/156 (total cohort) with moderate bleeding controlled with APC and/or electrocautery

- Ann Am Thorac Soc 2016;13(8):1405

Cryotherapy in malignant lesions

- Complication rate: 0~50%

Table 2. Complications of endoscopic cryotherapy

Year	Author	Occurrence		Complications	Treatment
2008	Jung et al. [13]	2/4	50%	al emphysema, hemoptysis	Controlled by conservative management
2007	Beeson [14]			age	Controlled by conservative management
2006	Berotoletti et al. [15]	2/18	11.1%	age, subcutaneous emphysema	Controlled by conservative management
2005	Asimakopoulos et al. [9]	35/329	10.6%	age, atrial fibrillation, dyspnea	Controlled by conservative management
2004	Hetzel et al. [16]	10/60	16.7%	age	Controlled by hemostasis with plasma beamer
2004	Maiwand et al. [17]	49/521	9.4%	sis, atrial fibrillation, dyspnea	Transient and n
2001	Deygas et al. [18]	0/35			
2001	Noppen et al. [19]	0/12			
1999	Maiwand [10]	11/153	7.2%	age, pneumothorax, anesthesia tion	Controlled by c
1990	Walsh et al. [22]	0/33			
1986	Homasson et al. [23]	2/27	7.4%	r	Transient
1986	Maiwand [24]	0/75			

Table 3. 30-day mortality after endoscopic cryotherapy

Year	Author	Occurrence (%)
2005	Asimakopoulos et al. [9]	9/32 (2.4)
2004	Maiwand et al. [17]	7/512 (1.2)
1999	Maiwand [10]	0/153 (0.0)
1986	Homasson et al. [23]	1/27 (3.7)
1981	Sanderson et al. [25]	2/28 (7.1)

- Korean J Intern Med 2011;26(2):137

Cryotherapy in South Korea

- 2022월 2월 1일 Cryobiopsy 급여 고시 (보건복지부 고시 제2022-3호)

제1편 제2부 제2장 제4절 내시경, 천자 및 생검료 나-759 기관지경검사란을 다음과 같이 한다.

분류번호	코드	분 류	점 수
		제4절 내시경, 천자 및 생검료	
		[내시경]	
나-759		기관지경검사 Bronchoscopy	
		주 : 1. 「나」, 「다」, 「라」, 「마」, 「바」를 실시한 경우에는 1회에 한해서 「가」를 별도 산정한다.	
	E7594	2. 「다」, 「라」, 「바」를 실시하기 위해 전자기유도기법을 시행할 경우 985.17점을 별도 산정하며, 「선별급여 지정 및 실시 등에 관한 기준」 별표 2에 따른 요양급여를 적용한다.	
		3. 「마」는 전자기유도기법으로 시행할 경우에 한하여 산정하며, 「선별급여 지정 및 실시 등에 관한 기준」 별표 2에 따른 요양급여를 적용한다.	
		4. 전자기유도기법시 사용된 일회용 내시경 캐뉼러는 별도 산정한다.	
	E7590	가. 기본기관지경검사 Diagnostic Bronchoscopy	1,293.72
	E7591	나. 기관지폐포세척술 Bronchoalveolar Lavage	456.48
	E7592	다. 경기관지침흡인술 Transbronchial Needle Aspiration	822.46
	E7593	라. 경기관지폐생검 Transbronchial Lung Biopsy	947.16
	E7595	마. 경기관지위치표식술 Transbronchial Localization	1,453.08
	E7596	바. 경기관지폐냉동생검 Transbronchial Lung Cryobiopsy	1,766.52
		주 : 사용된 일회용 냉동프로브, 지혈용 풍선카테터는 별도 산정한다.	

Summary

- **Bronchoscopic cryotherapy is an efficient and relatively safe interventional procedure for patients with benign and malignant central airway diseases.**
- **It is necessary to select appropriate patients in consideration of the predicted effect and complication risk.**

Thank you for your attention

서울아산병원
Asan Medical Center