

Transbronchial Lung Cryobiopsy

: The heat is on in Korea !

Contents



1

Role of histopathologic exam in ILD

2

Current evidence of TBLC (vs VATS)

3

Details of TBLC in single center experience

4

Hurdles of performing TBLC in Korea

5

Cases of TBLC

경기관지 폐냉동생검 (VOTE)



- 1. 경기관지 폐냉동생검이 간질성폐질환 환자의 진료에서 필요하다고 생각한다
- 2. 경기관지 폐냉동생검을 우리 기관에서 시행할 의향이 있다
- 3. 경기관지 폐냉동생검의 실행에 대해 궁금하고, 정보 및 경험을 공유하는 것이 필요하다고 생각한다

경기관지 폐냉동생검



평가사업단-1913

보건의료 근거창출을 선도하는 전문기관

NECA

한국보건의료연구원

수신 인제대학교 해운대백병원
(경유)

제목 '경기관지 폐냉동생검'에 대한 안전성·유효성 평가결과 통보

1. 귀 기관의 무궁한 발전을 기원합니다.
2. 관련근거
 - 가. 의료법 제53조(법률 제15540호, 2020.3.28.)
 - 나. 신의료기술평가에 관한 규칙 제4조(보건복지부령 제651호, 2019.7.4.)
 - 다. 신의료기술평가의 절차와 방법 등에 관한 규정 제6조(보건복지부고시 제2019-40호, 2019.3.15.)
 - 라. 2020년 제6차 신의료기술평가위원회 개최 결과 보고(평가사업단-1880, 2020.7.7.)
 - 마. 신의료기술평가신청서("경기관지 폐냉동생검", 접수일: 2019.12.13.)
3. 위와 관련, 귀 기관에서 신청한 「경기관지 폐냉동생검」(접수번호 2019-128호, 2019.12.13.)은 2020년 제6차 신의료기술평가위원회(2020.6.26.) 심의결과, 조직 생검이 필요한 폐질환 의심환자를 대상으로 수행 시 질환 진단에 도움을 줄 수 있는 안전성 및 유효성이 있는 기술로 심의되었음을 알려드리오니 관련 업무에 참고하시기 바랍니다.

경기관지 폐냉동생검



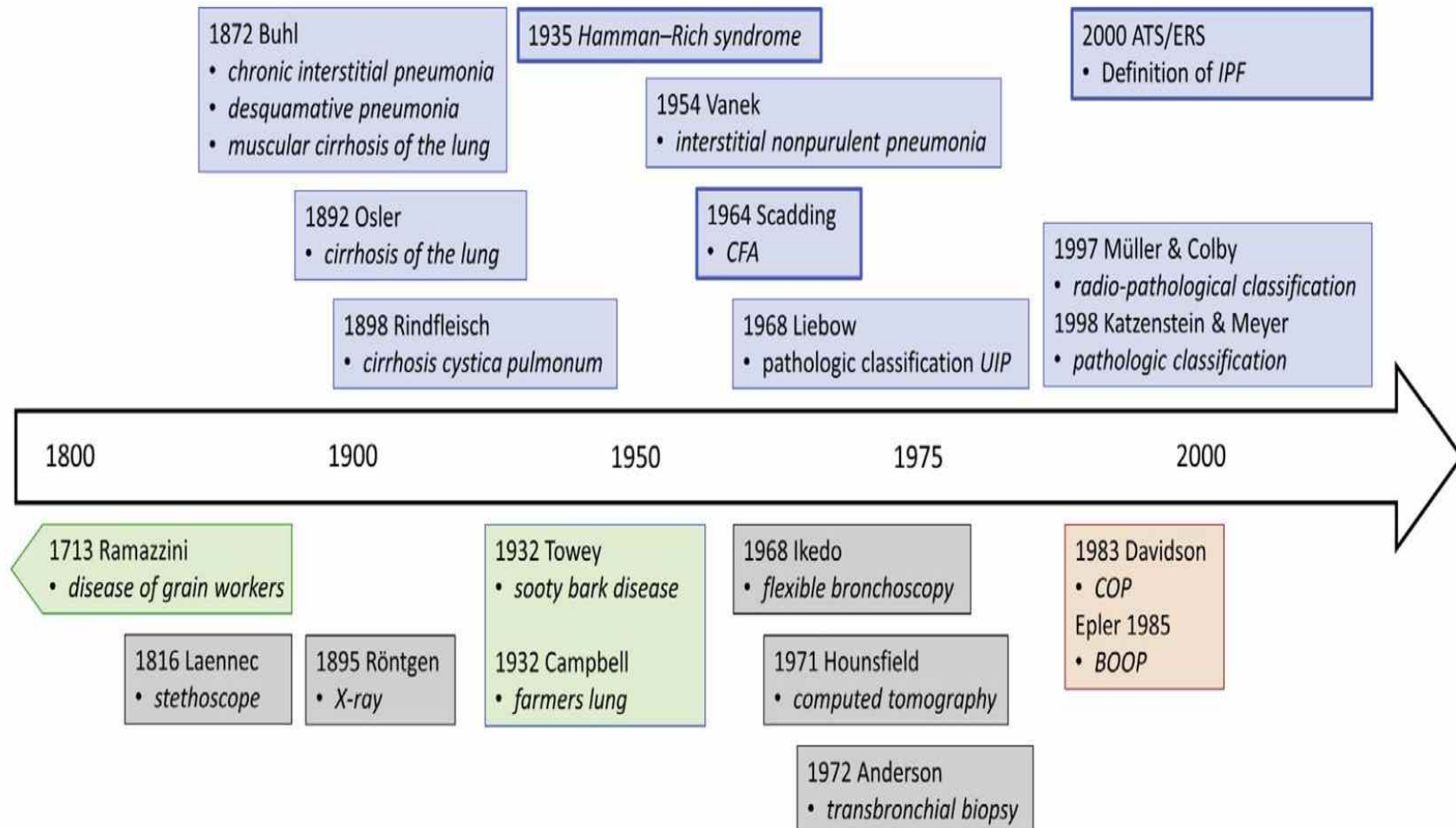
보건복지부 고시 제2022- 3호

「국민건강보험법 시행령」 제21조제2항·3항 및 「국민건강보험 요양급여의 기준에 관한 규칙」 제8조제2항부터 제5항까지, 제9조제1항, 제11조제1항, 제12조제2항 및 제13조 제1항·제3항에 의한 「건강보험 행위 급여·비급여 목록표 및 급여 상대가치점수」 (보건복지부 고시 제2021-346호, 2021.12.29.)를 다음과 같이 개정·발령합니다.

2022년 1월 7일
보건복지부장관

E7596	바. 경기관지폐냉동생검 Transbronchial Lung Cryobiopsy 주 : 사용된 일회용 냉동프로브, 지혈용 풍선카테터는 별도 산정한다.	1,766.52
-------	---	----------

Interstitial lung disease



Diagnosis of ILD



Evol

Study

Liebo

Katz

M

ATS/

C

ATS/

U

(i

However, lung sampling is often indicated and needed to help the specific cause and deferential diagnosis of the disease in hope of initiating treatment that can arrest or slow its progression

In international guideline, the committee recommended lung biopsy in some patients with probable UIP pattern on HRCT and patients with other than UIP on HRCT

Importance of lung biopsy; not MDD without histopathologic sample

VATS: gold standard

initial

a,

oid

osis;

unclassified III

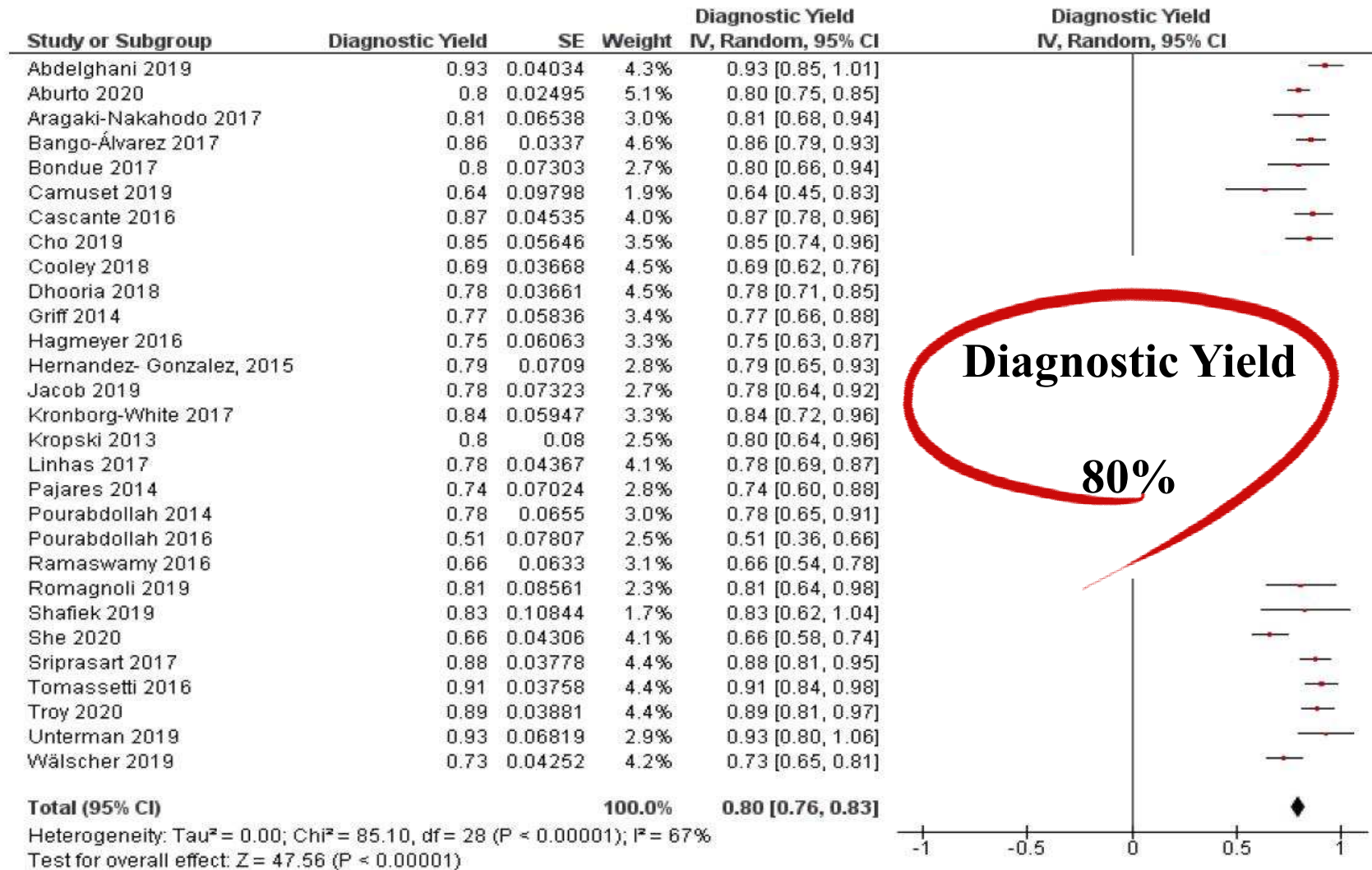
Systemic Review of TBLC (2022)



Author	Year	Location	Duration	Patients	Setting/Design	Cryoprobe	#Samples	Type of sedation	Fluoroscopy	Risk of bias
Abdelghani	2019	US	NA	40	Retrospective	1.9 mm	Unknown	General Anesthesia	Yes	Severe
Aburto										Severe
Aragaki-Nakahodo										Very Severe
Bango-Álvarez										None
Bondue										None
Camuset										Severe
Cascante										None
Cho										Severe
Cirak										Very Severe
Cooley										Severe
Dhooria										None
Echevarria-Uraga										Very Severe
Fruchter										Severe
Griff										Very Severe
Hagmeyer										Very Severe
Hernandez-Gonzalez										Severe
Hetzel										Very Severe
Inomata										Severe
Jacob										Very Severe
Kronborg-White	2017	Denmark	1 year	38	Retrospective	1.9 mm/2.4 mm	4	General Anesthesia	Yes	Severe

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%)

Diagnostic yield



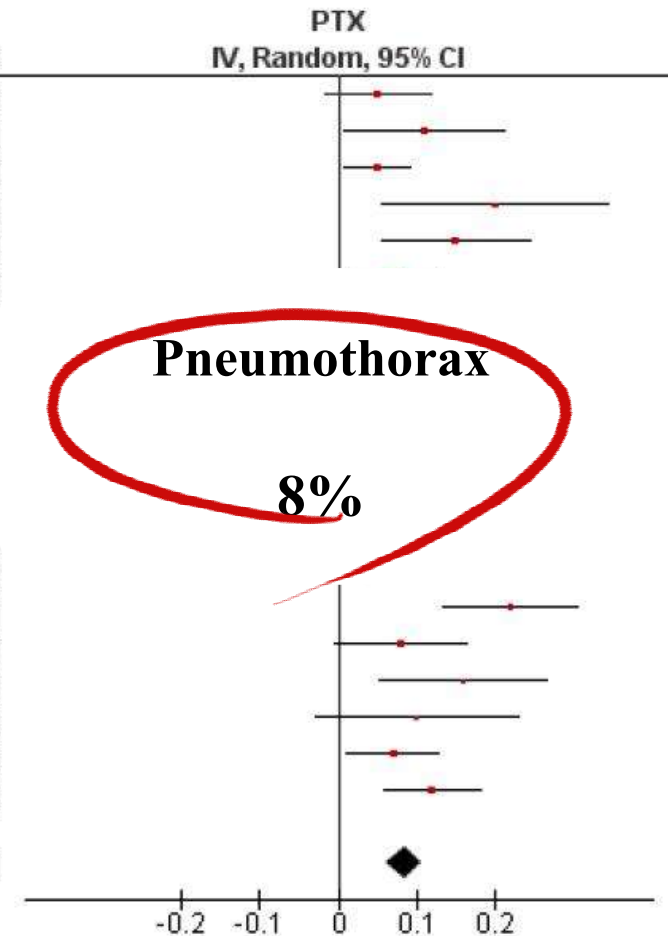
Pneumothorax



Time of chest tube drainage → similar to time after VATS

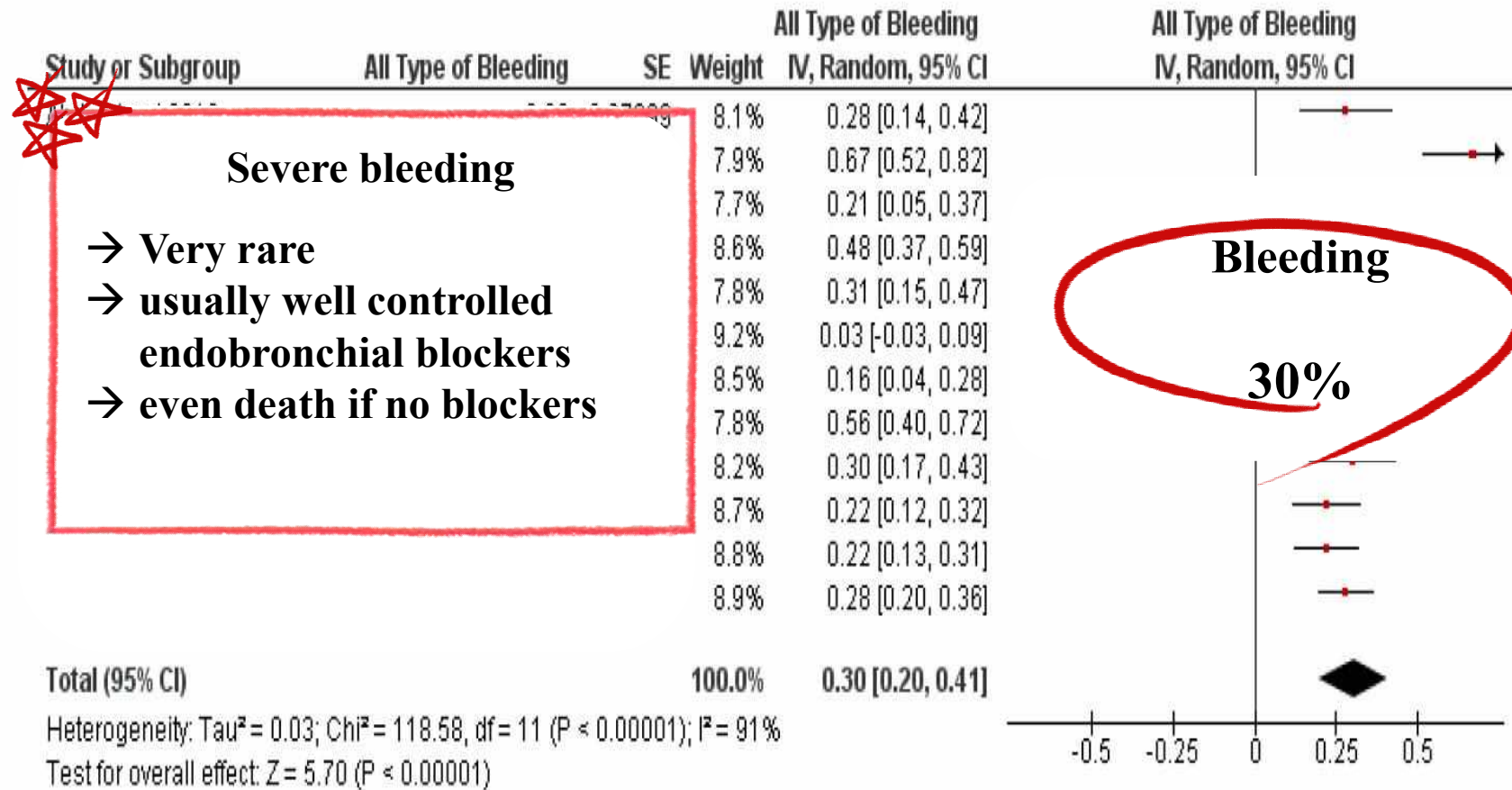
High risk
UIP histopathology
Fibrotic reticulation
Close to pleura

SE	Weight	PTX IV, Random, 95% CI
03446	5.1%	0.05 [-0.02, 0.12]
05215	3.1%	0.11 [0.01, 0.21]
02117	7.3%	0.05 [0.01, 0.09]
07303	1.9%	0.20 [0.06, 0.34]
04815	3.5%	0.15 [0.06, 0.24]
02818	6.1%	0.07 [0.01, 0.13]
02481	6.6%	0.11 [0.06, 0.16]
02766	6.2%	0.11 [0.06, 0.16]
01706	8.0%	0.03 [-0.00, 0.06]
0197	7.6%	0.03 [-0.01, 0.07]
2059	7.4%	0.08 [0.04, 0.12]
6481	2.3%	0.05 [-0.08, 0.18]
6481	2.3%	0.16 [0.03, 0.29]
1673	8.1%	0.03 [-0.00, 0.06]
4367	3.9%	0.22 [0.13, 0.31]
4344	4.0%	0.08 [-0.01, 0.17]
5465	2.9%	0.16 [0.05, 0.27]
6547	2.3%	0.10 [-0.03, 0.23]
2966	5.8%	0.07 [0.01, 0.13]
3113	5.6%	0.12 [0.06, 0.18]
100.0%		0.08 [0.06, 0.11]



Test for overall effect: $Z = 7.55$ ($P < 0.00001$)

All type of bleeding



Baseline characteristics



Characteristics	All patients (n=27)
Age, years	65.1 (63.0-71.0)
Male	20 (74.1)
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 (x10 ⁶)	1100.0 (400.0-1900.0)
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)
FEV1, % 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)

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)

Deep sedation vs G/A

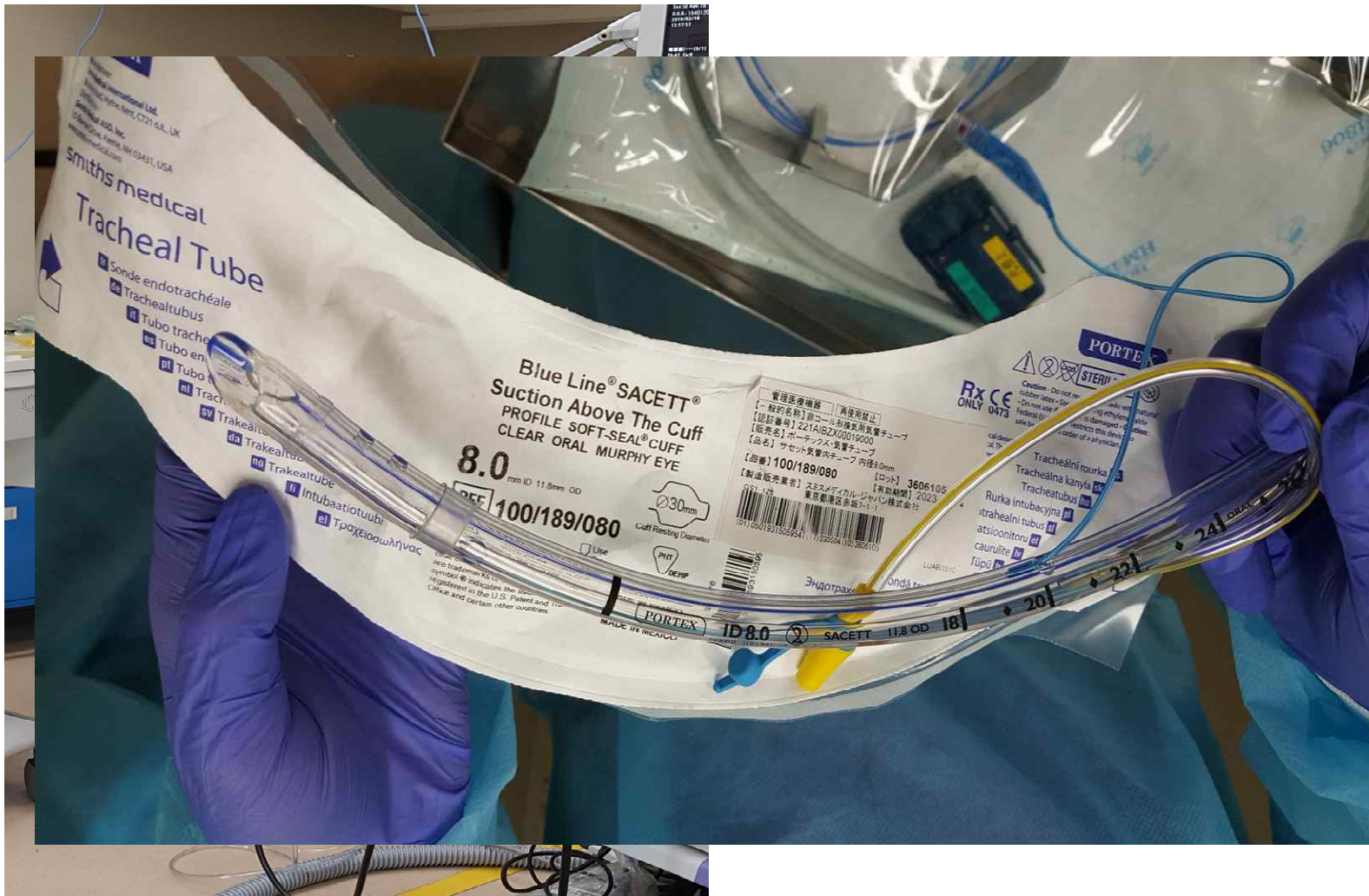


Deep sedation

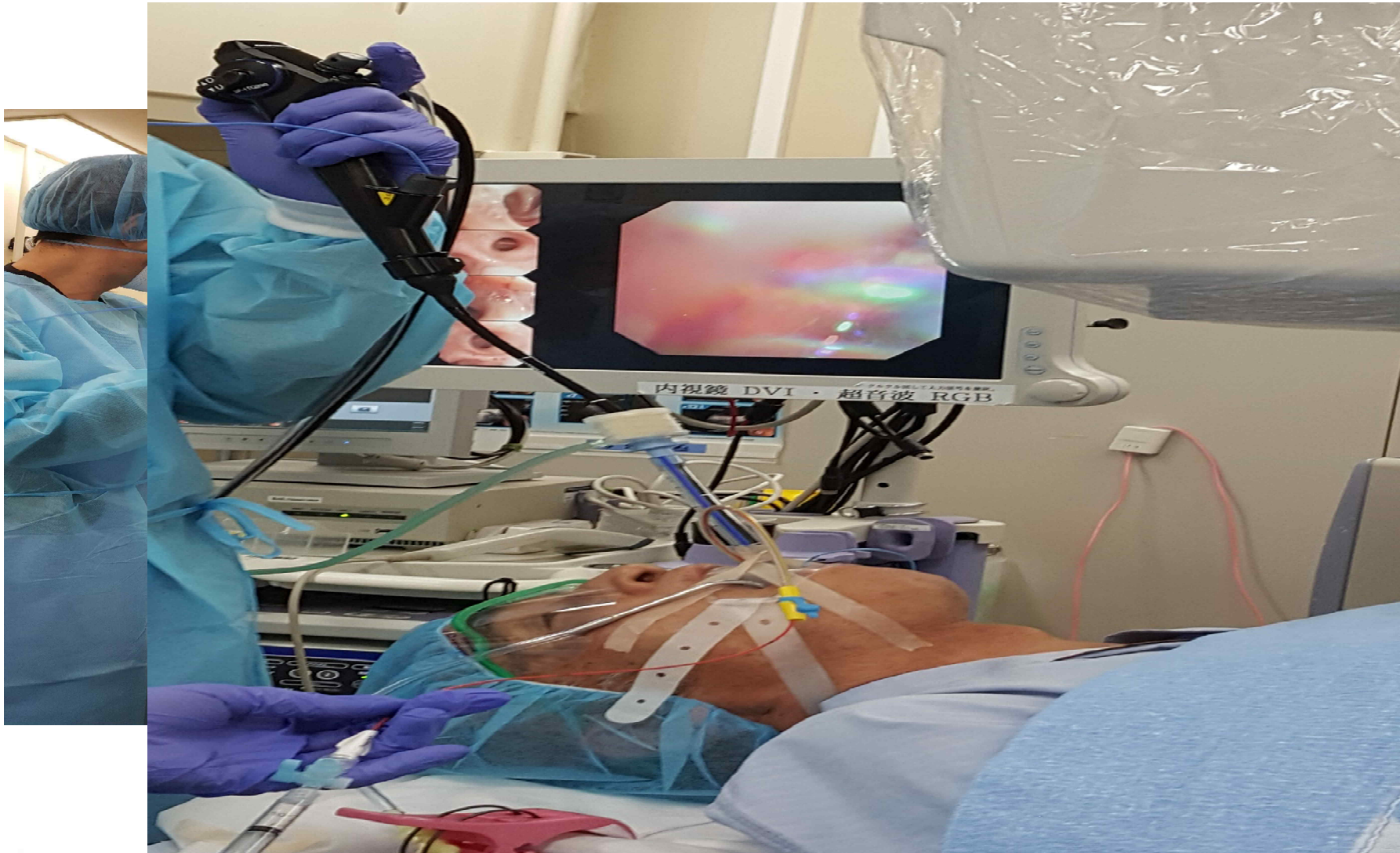
- Midazolam (2~5mg IV) + Fentanyl (50~100mcg IV) + PRN adding
- Flexible bronchoscopy room or hybrid room with fluoroscopy guidance
- E-tube + Fogarty balloon catheter
- No anesthesiologist

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

Deep sedation



Deep sedation



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)

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)
- Fluoroscopy guidance with endobronchial balloon blocker
- 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

Single center experience of TBLC in Korea



Limitations of our study (experiences)

- Lack of UIP and probable UIP (5/9)
- Diagnostic yield – no comparison (VATS) / no interdisciplinary discussion

- Similar complication profiles though small numbers of cases (or learning curve)
 - Adequate sample quality
- Additional diagnostic role of indeterminate/alternative pattern

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

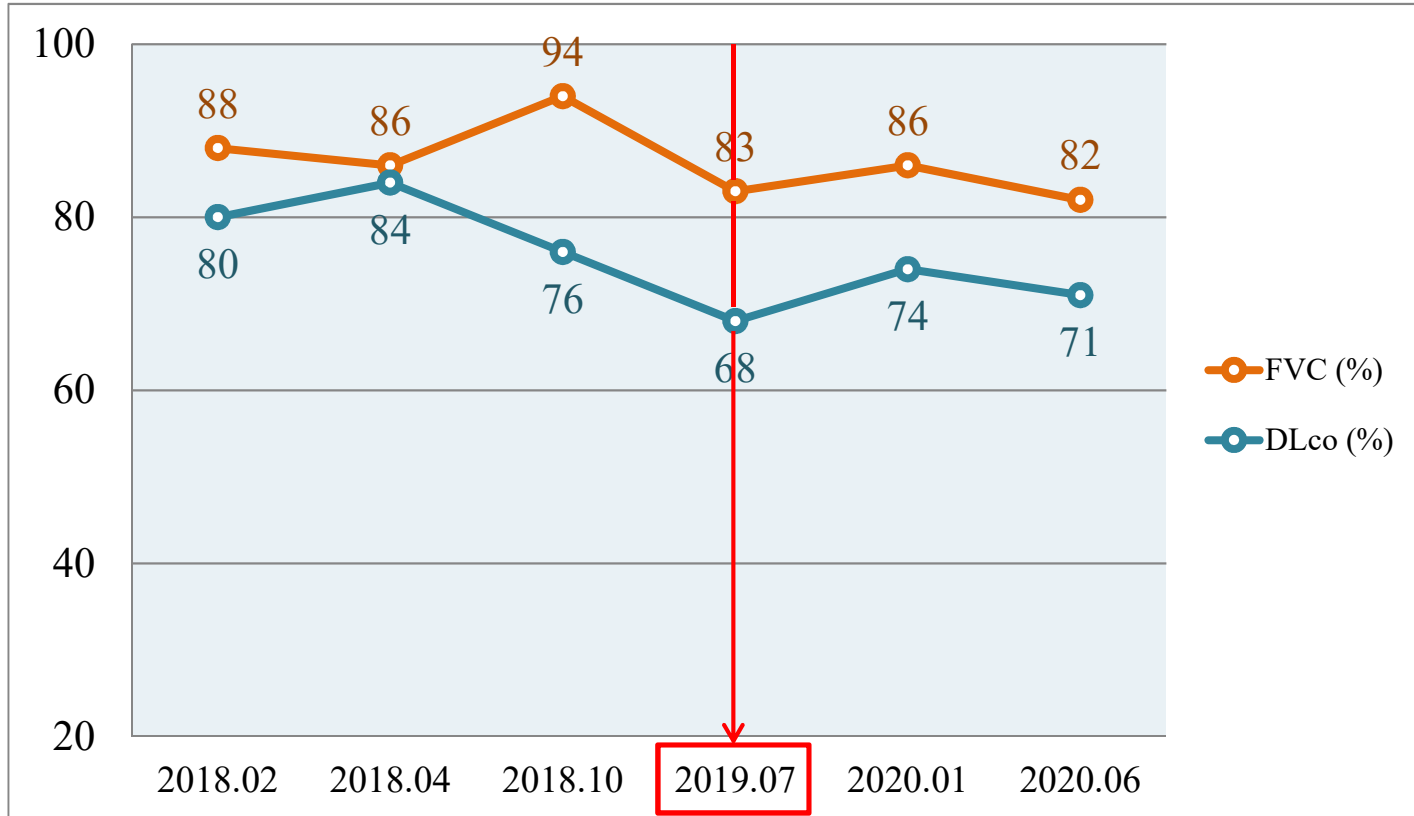
	간]					
	마취중말초산소포화도 감시	3,050	610	2,440		
	산소10L/1분당[전신마취시]	180	36	144		
	탄산가스흡수제	1,384	277	1,107		
	굴곡성기관지경 기관내삽관술[마취]	114,850	22,970	91,880		
치료재료대	Endotracheal Tube	13,990	2,798	11,192		
마취관련 비용		482,400	64,679	258,721		159,000

CASE 1



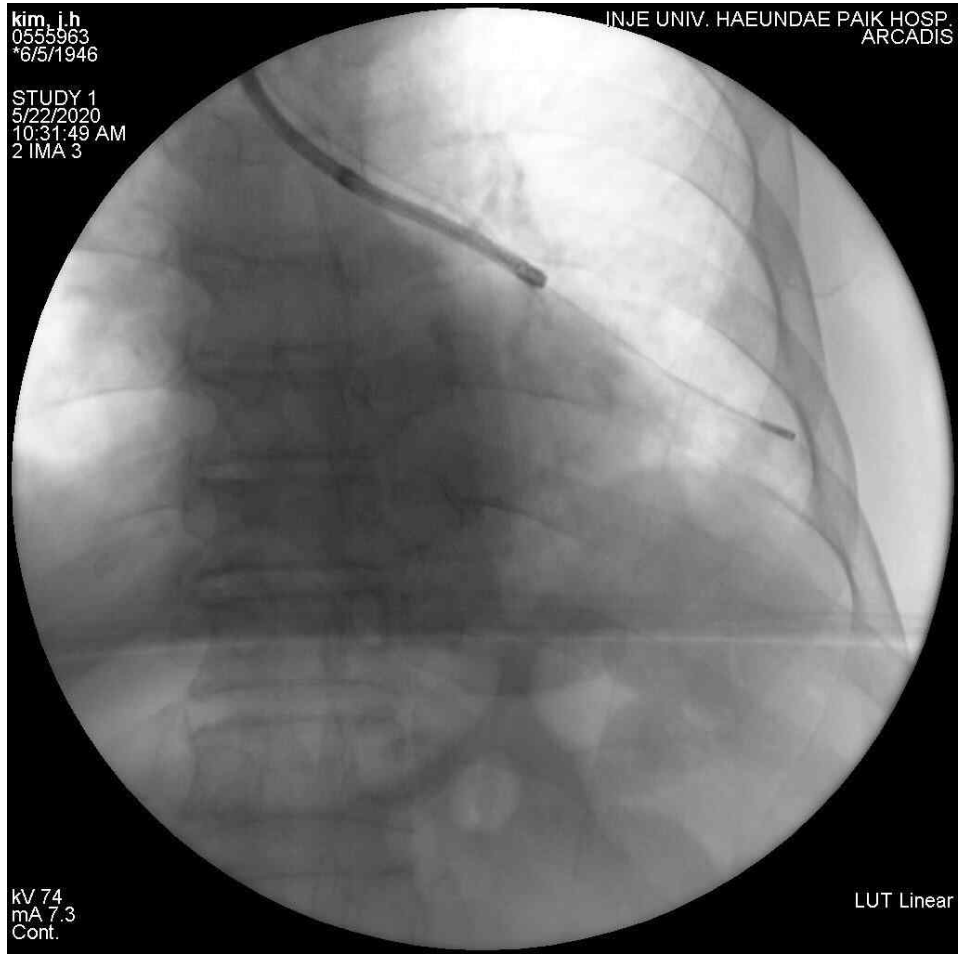
- M / 62
- C.C : Dyspnea
- PI : 42갑년의 흡연자로 3개월 전부터 숨이 차다고 병원에 왔다. 빠르게 걷거나, 계단을 오르면 숨차다고 한다. 마른 기침은 있지만, 객담은 없다고 한다.
- Current smoker, 42pyrs
- Family history (-) Social history(-)
- Gout(2009), COPD(2018) , Alcoholic liver disease, Hyperlipoproteinemia (2019)

• PFT

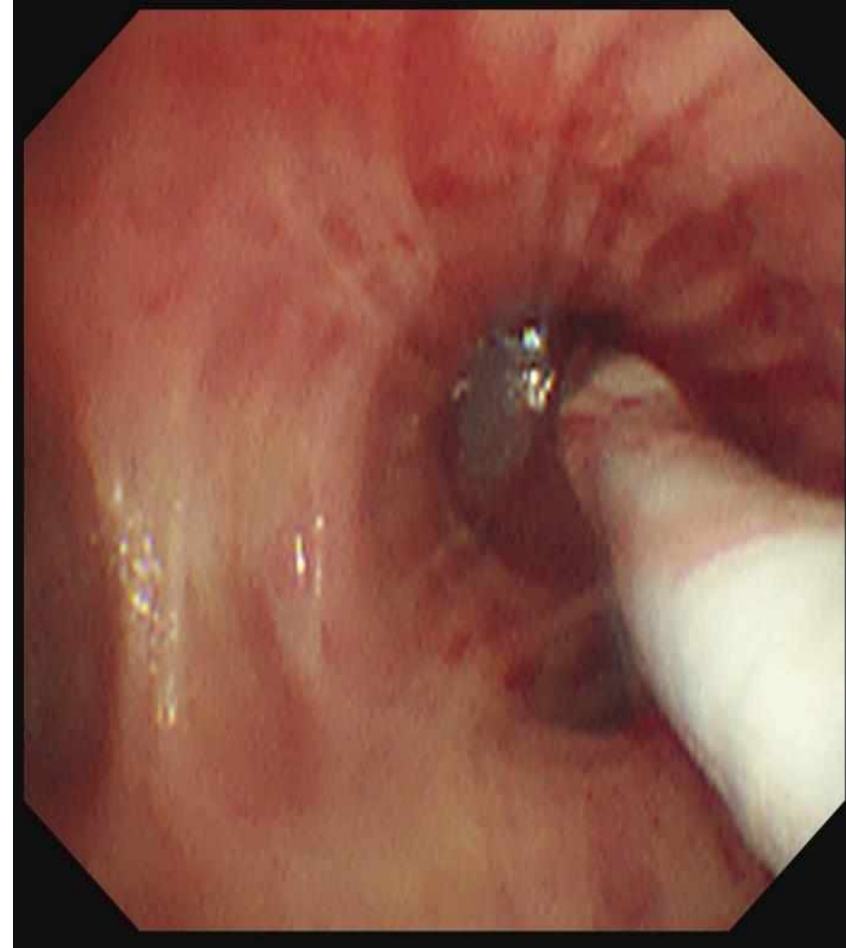


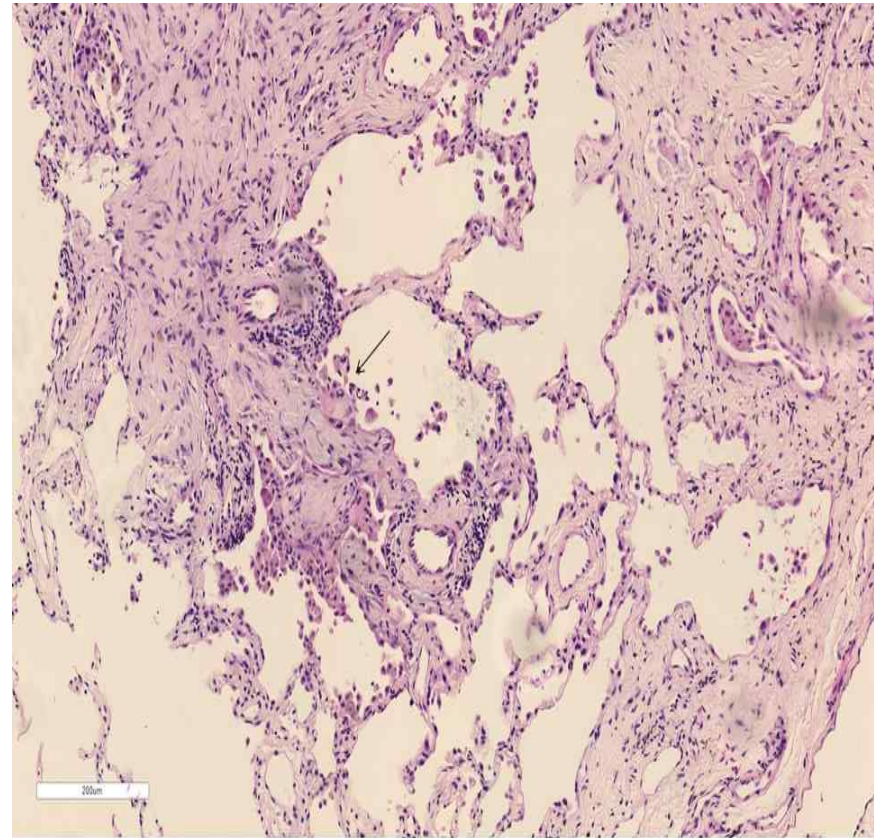
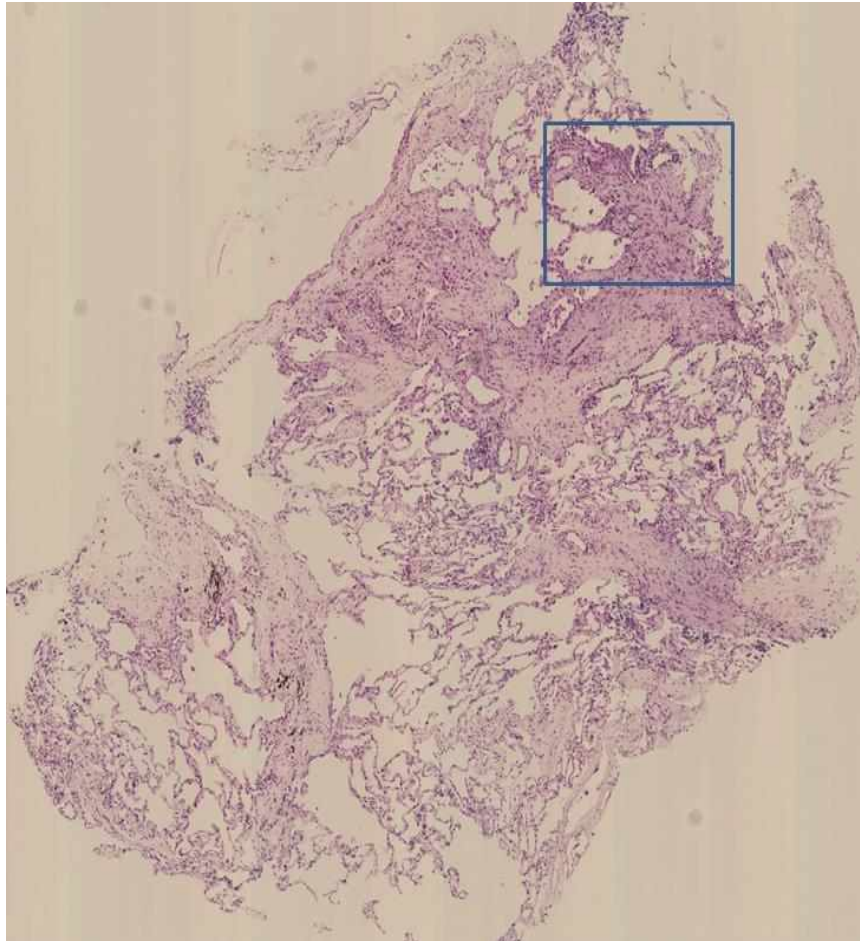
• 6MWT

	Initial SpO ₂ (%)	End SpO ₂ (%)	Distance(m)
2018.04.24	99	97	369
2019.07.23	95	97	444
2020.01.08	96	96	528
2020.06.17	99	98	540



Transbronchial lung cryobiopsy





Young mural and intra-alveolar fibrosis and slight lymphocyte infiltration Alveolar macrophages

Sample quality - A
Peri-lobular fibrosis, Fibroblastic foci
No honeycombing
Probable UIP with high confidence (A)

Final diagnosis by MDD



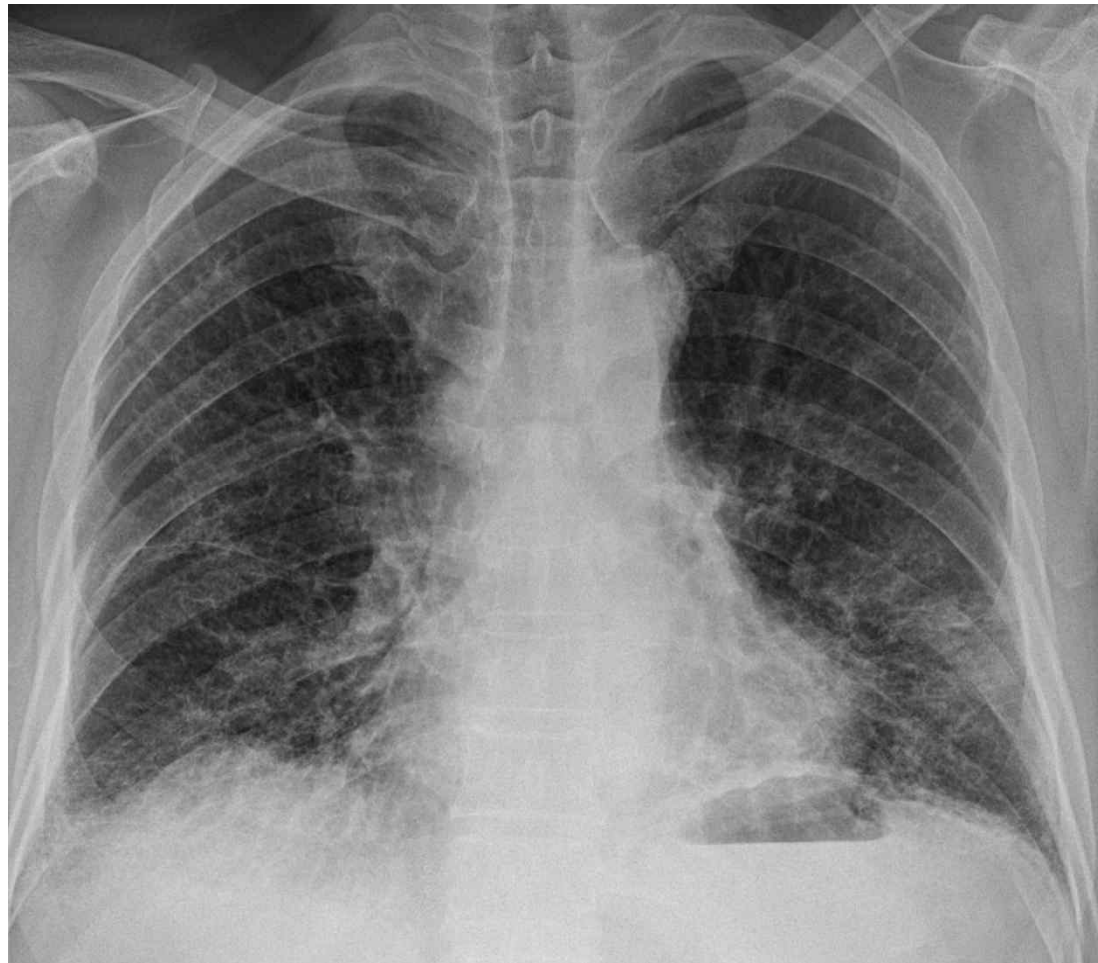
IPF suspected*		Histopathology pattern			
		UIP	Probable UIP	Indeterminate for UIP	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)**	Non-IPF dx
	Indeterminate for UIP	IPF	IPF (Likely)**	Indeterminate for IPF***	Non-IPF dx
	Alternative diagnosis	IPF (Likely)** /non-IPF dx	Non-IPF dx	Non-IPF dx	Non-IPF dx

CASE 2

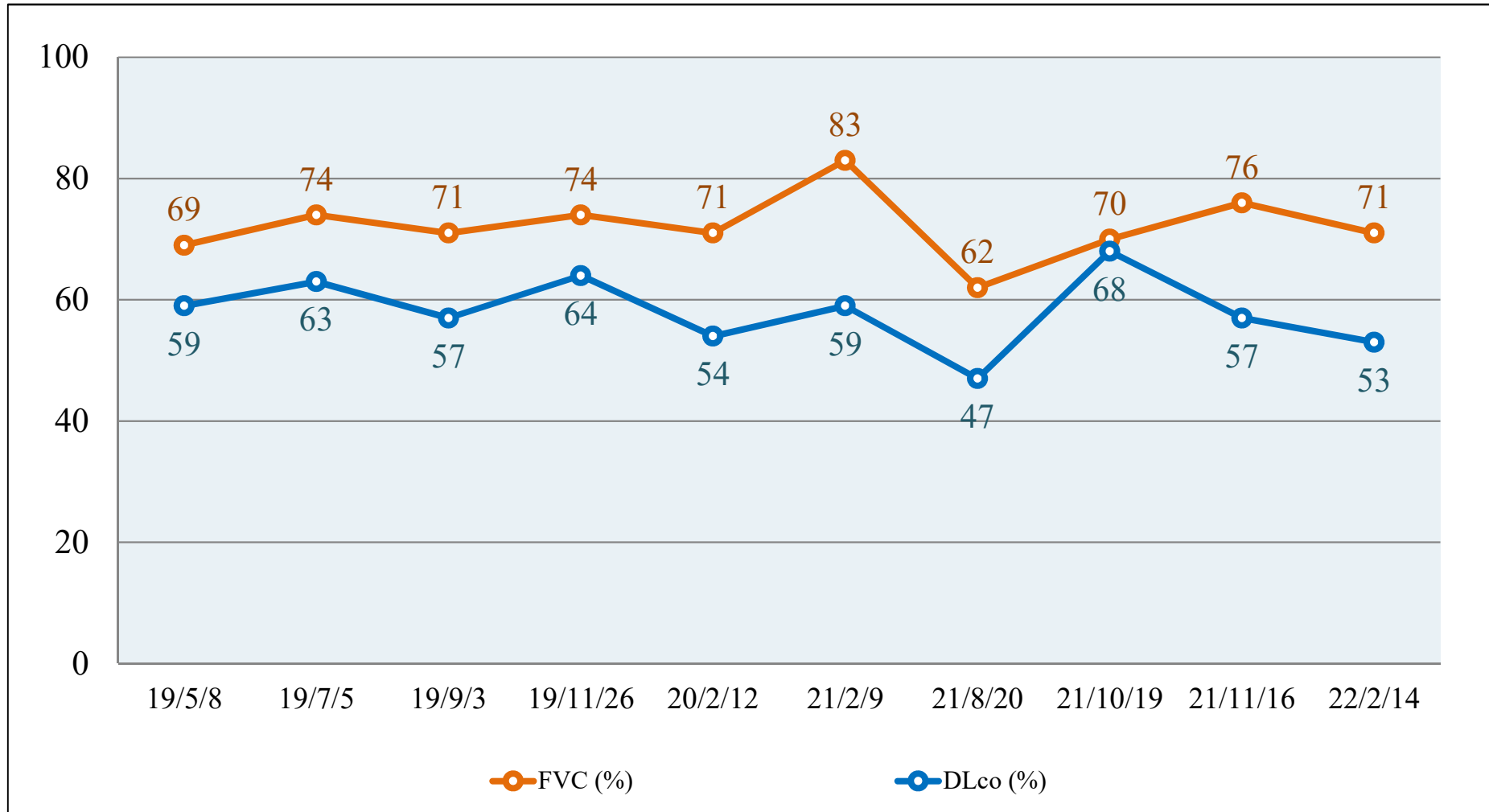


- ▶ M/58
- ▶ C.C : Dyspnea (onset: 3 years ago)
- ▶ PI : 타병원에서 IPF로 항섬유화제 치료 받고있는 환자로 secondary opinion 위해 내원함
- ▶ Arthritis (-) Raynaud (-) sicca symptom (-)
- ▶ Ex-smoker, 10pyrs 미만 (quit: 20년 전)
- ▶ DM(2017)

Chest X-ray



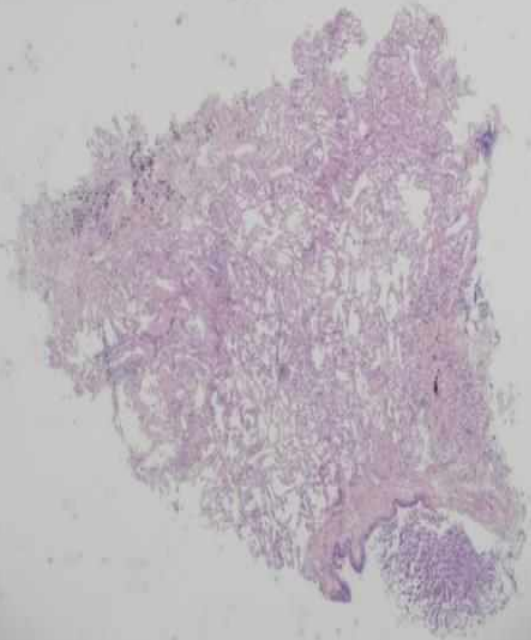
Pulmonary function test



Histopathologic analysis

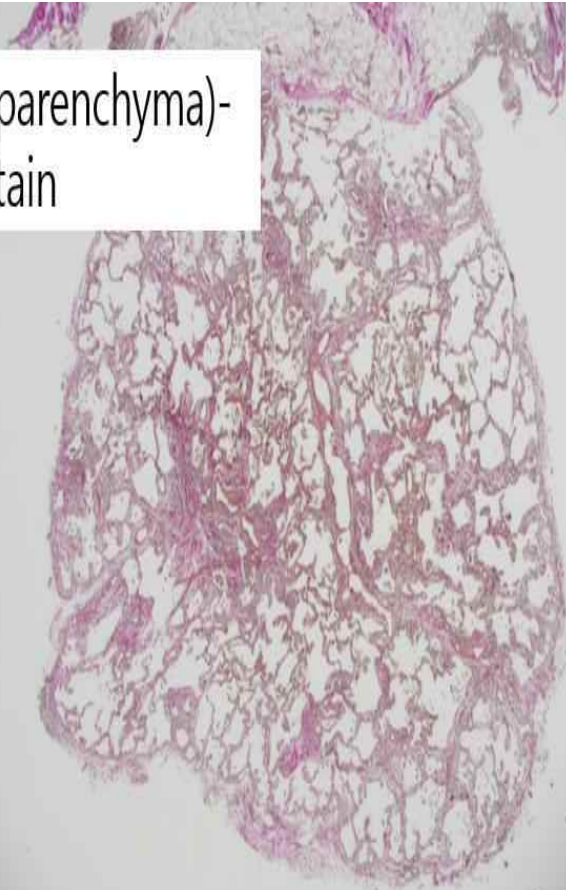


A

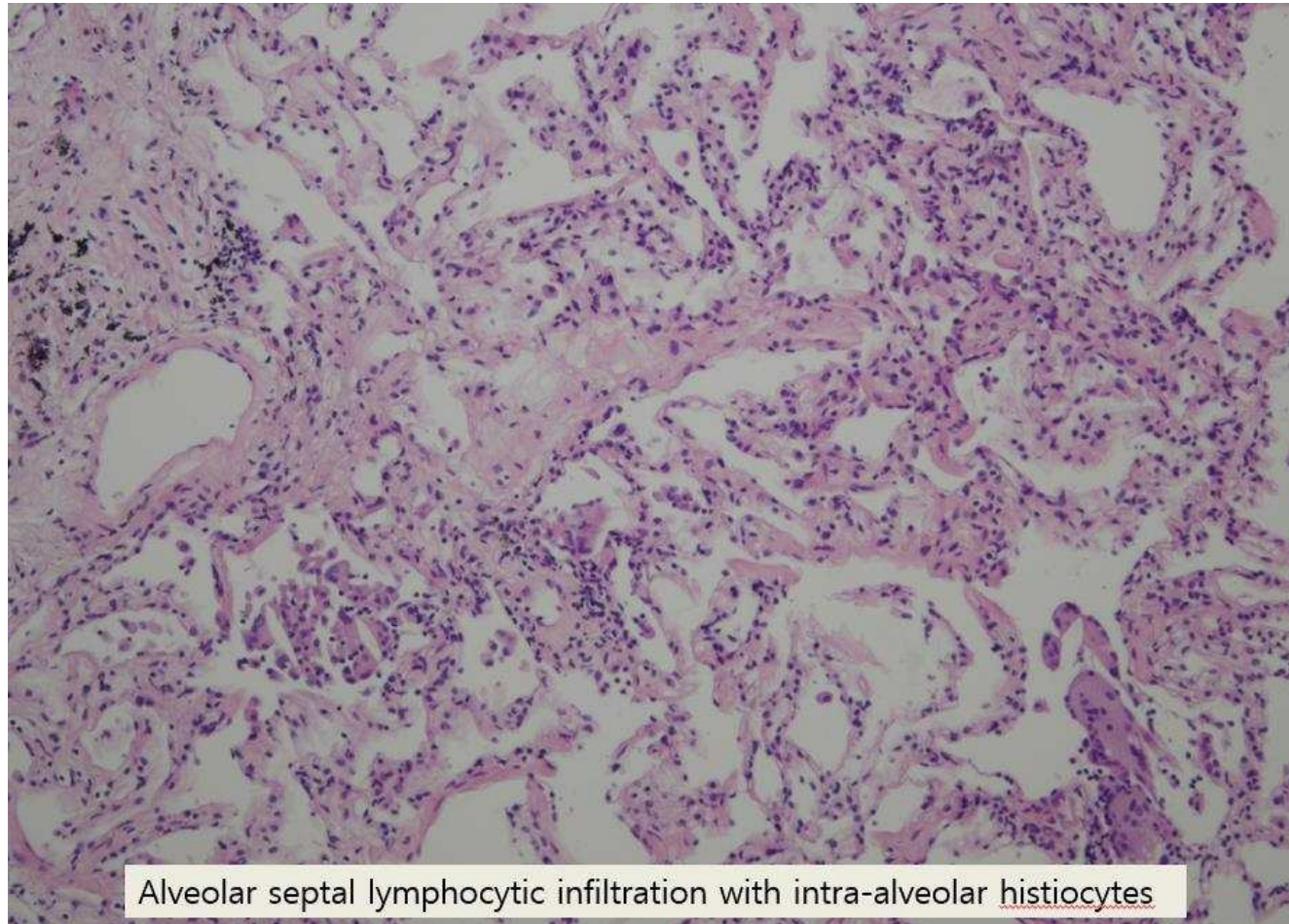


Negative for dense fibrosis, bronchiolar dilatation

B (lung parenchyma)-
elastic stain



Histopathologic analysis

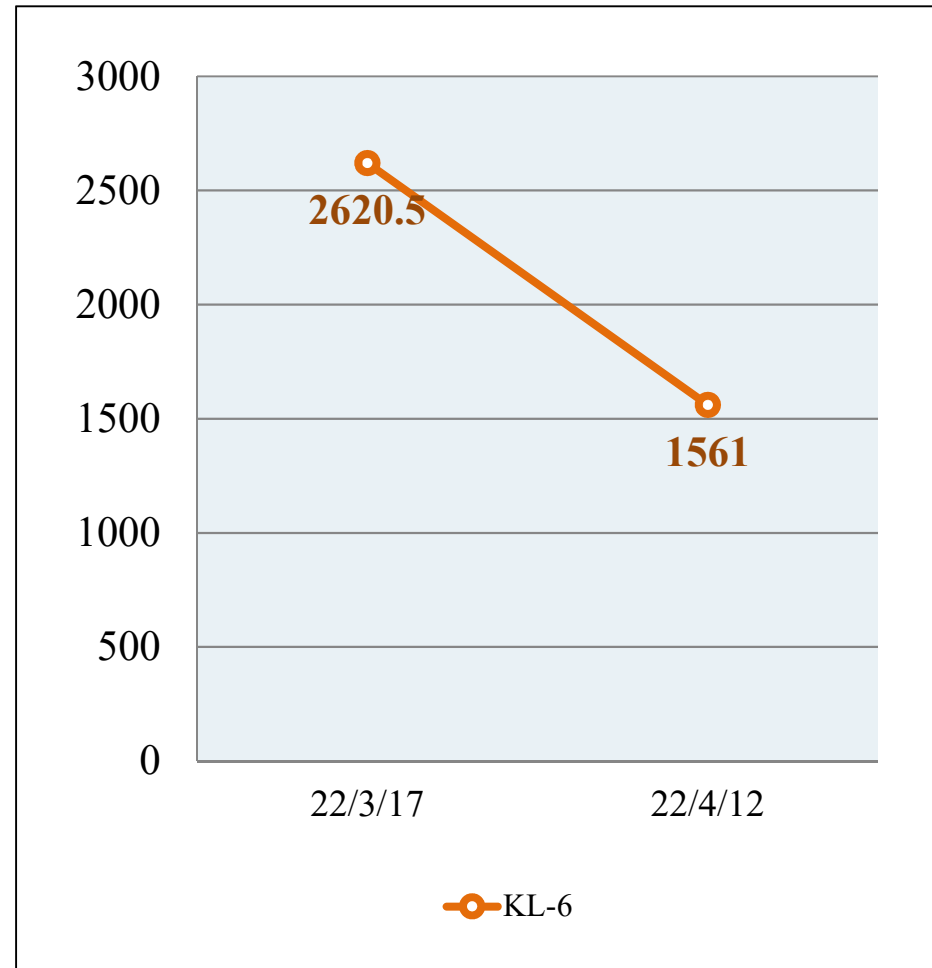


Auto-antibody & Rheumatology consultation



▶ 2022.03.17

ANA	Negative
ANCA	Negative
Anti CCP Ab	1.3
RA	< 10
KL-6	2620.5



Final diagnosis by MDD



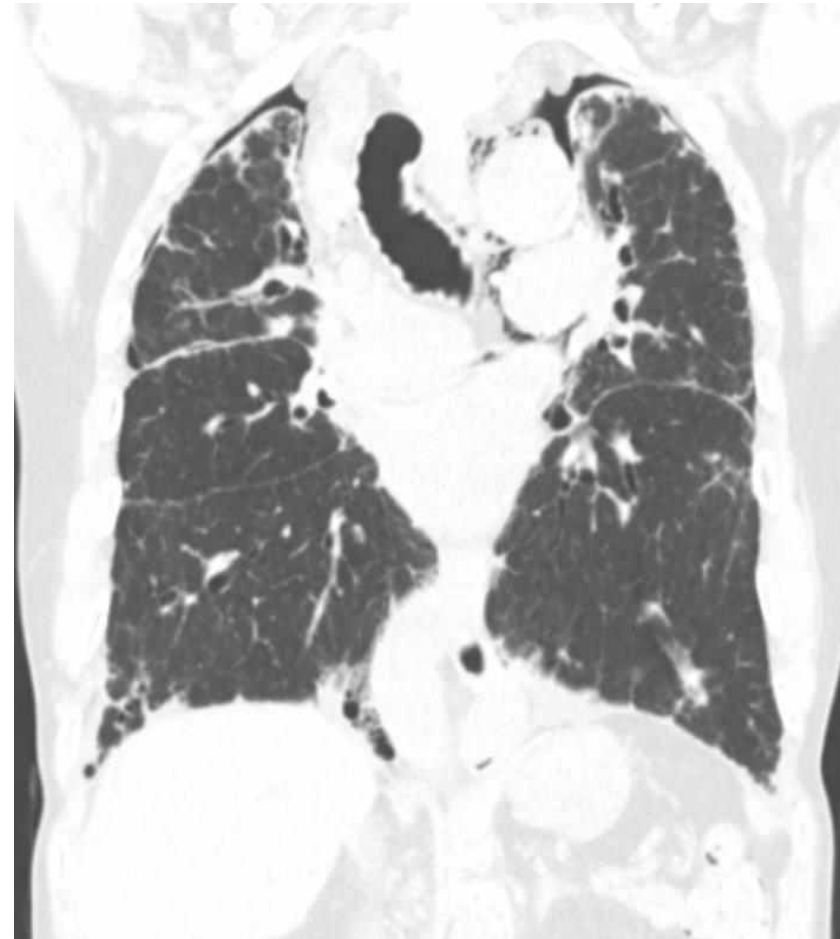
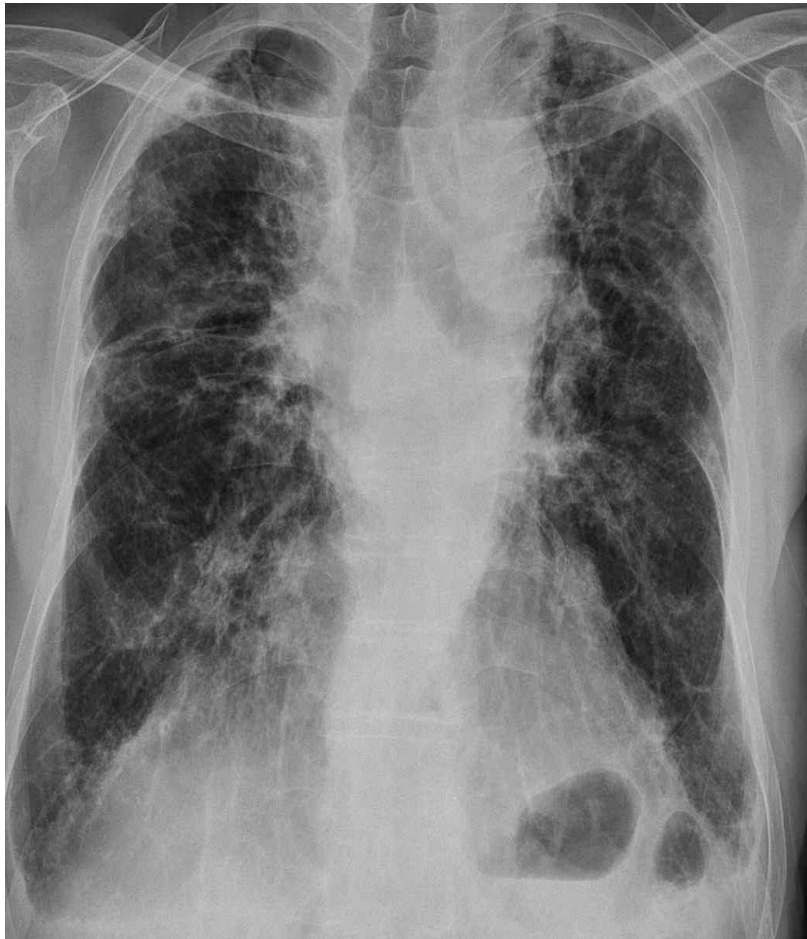
- Clinical diagnosis of other institution – IPF on pirfenidone
- Radiologic diagnosis – probable UIP vs fibrotic NSIP
- Histopathologic diagnosis – alternative (NSIP)
- Final diagnosis – NSIP (not IPF)
- Treatment: pirfenidone → corticosteroid combined with immunosuppressant agent

CASE 3

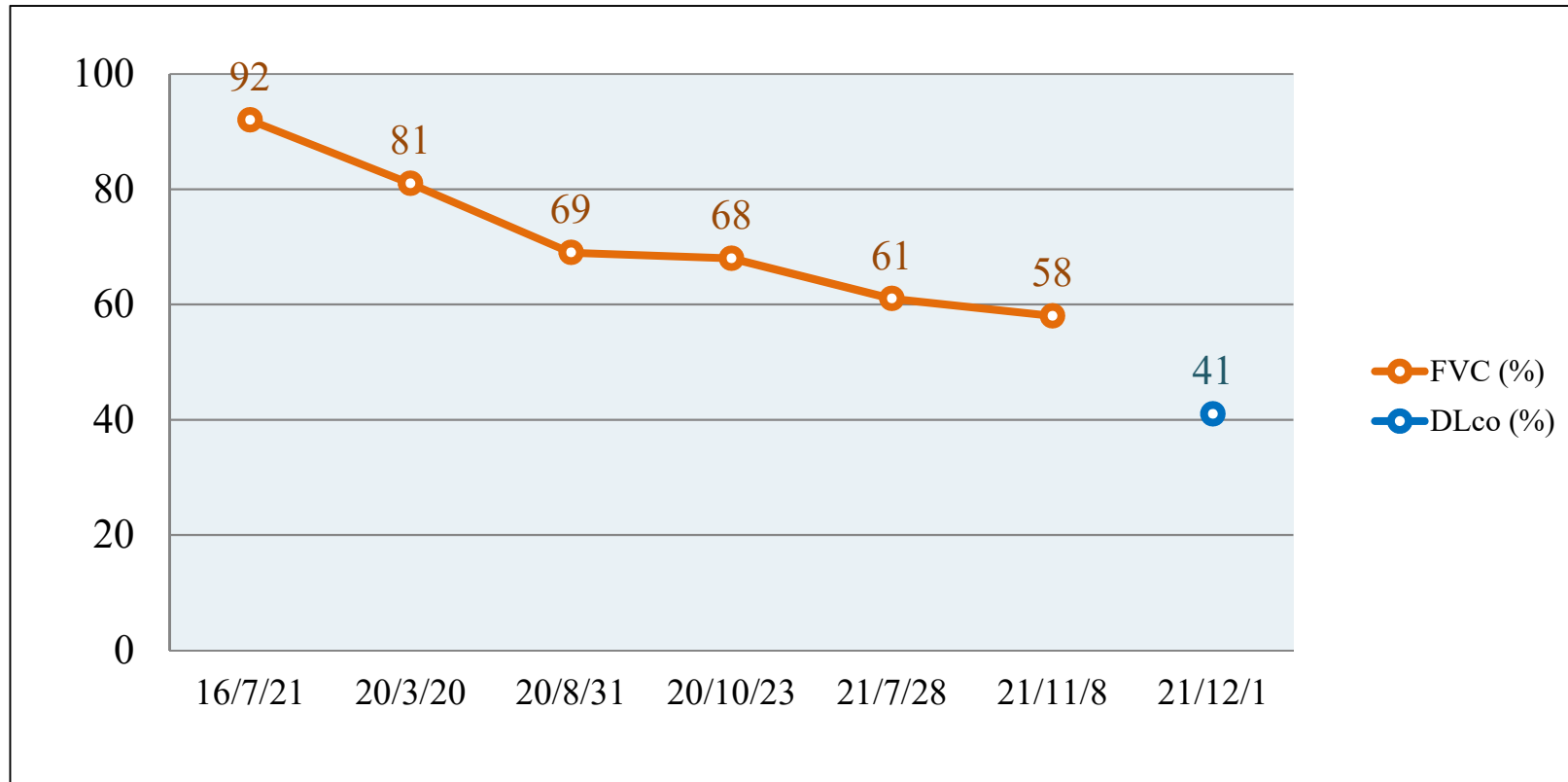


- ▶ M / 75
- ▶ C.C : Dyspnea (mMRC gr 3)
- ▶ PI : 타병원 흉부CT 이상소견으로 경과 관찰 하던 중, 악화되어 ILN 진단 위해 내원
- ▶ Arthritis (-) Raynaud (-) sicca symptom (-)
- ▶ Ex-smoker, 10pyrs
- ▶ Family history (-) Social history (-)
- ▶ MI(2017)

Radiologic findings

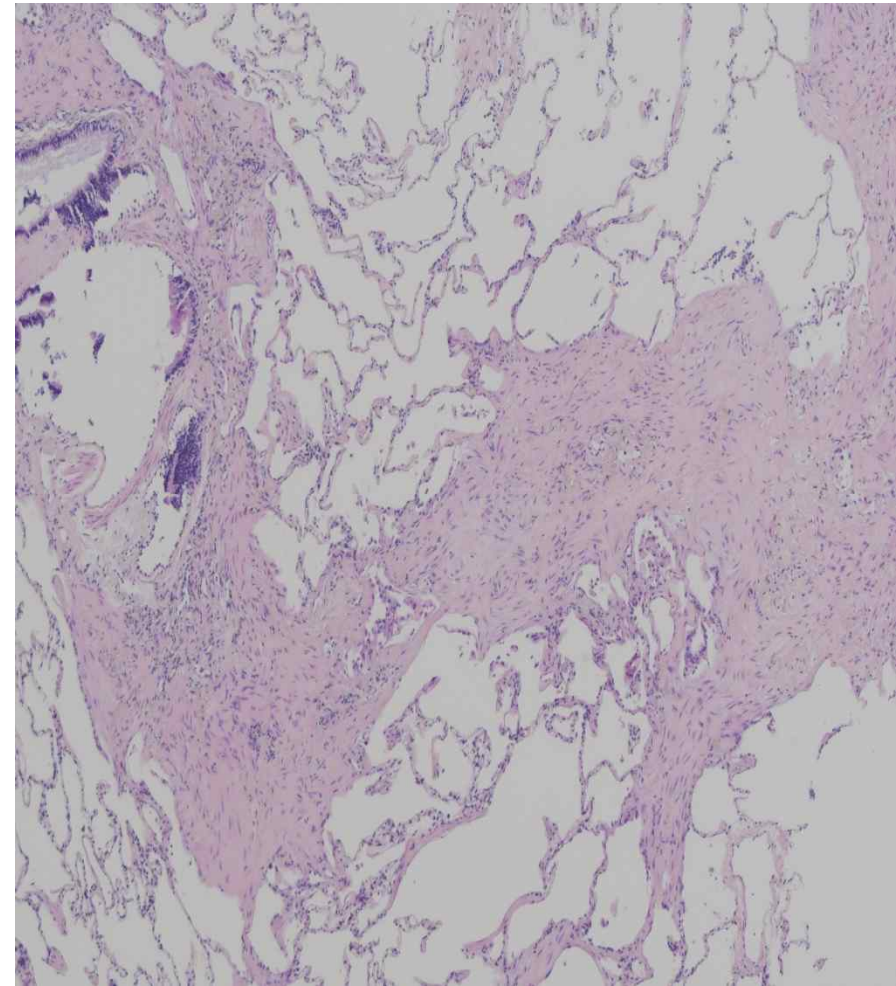
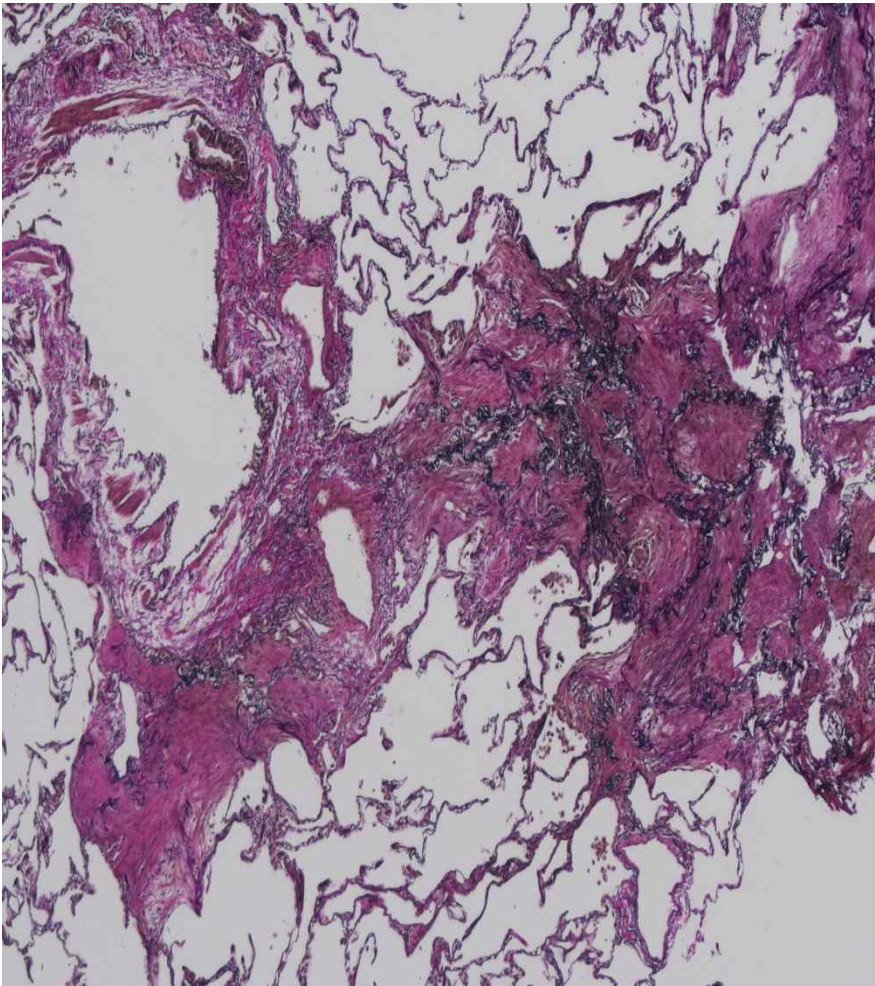


Pulmonary function test



6MWT	Initial SpO ₂ (%)	lowest SpO ₂ (%)	Distance(m)
2021-12-01	94	84	555

Histopathologic analysis



Histopathologic analysis



TBLC 2021.12.03

Lung, A, B8a, right

Intra-alveolar fibrosis with alveolar septal elastosis,
consistent with pleuroparenchymal fibroelastosis

Lung, B, B9a, right

Intra-alveolar fibrosis with equivocal septal elastosis

Lung, C, B9b, right

1. Mainly peribronchial tissue
2. Small amount of lung parenchyma showing perilobular fibrosis

Final diagnosis by MDD

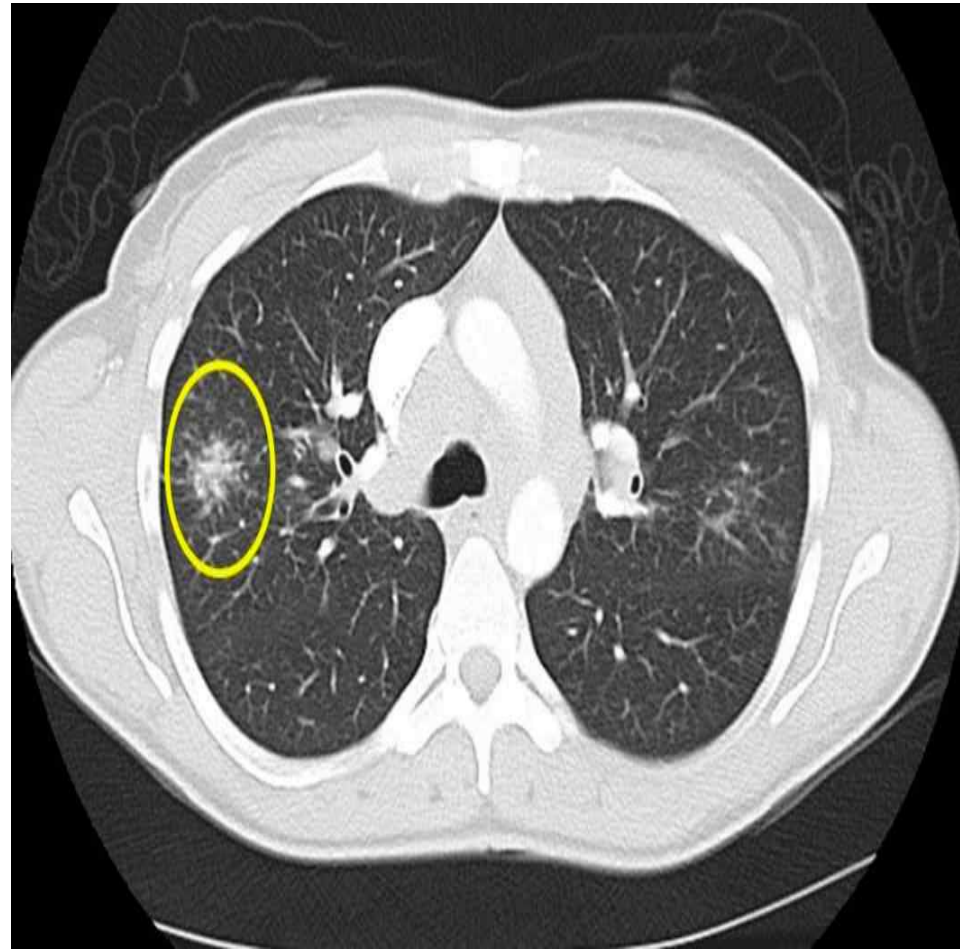


- Clinical diagnosis – PPFE (rapid progression)
- The reason of pathologic exam – evaluation of lower lung pattern for considering use of antifibrotic agent
- Histopathologic analysis – PPFE
- Final diagnosis – PPFE c lower lung involvement (PPFE pattern)

Radial endobronchial ultrasonography combined with TBLC in ILD

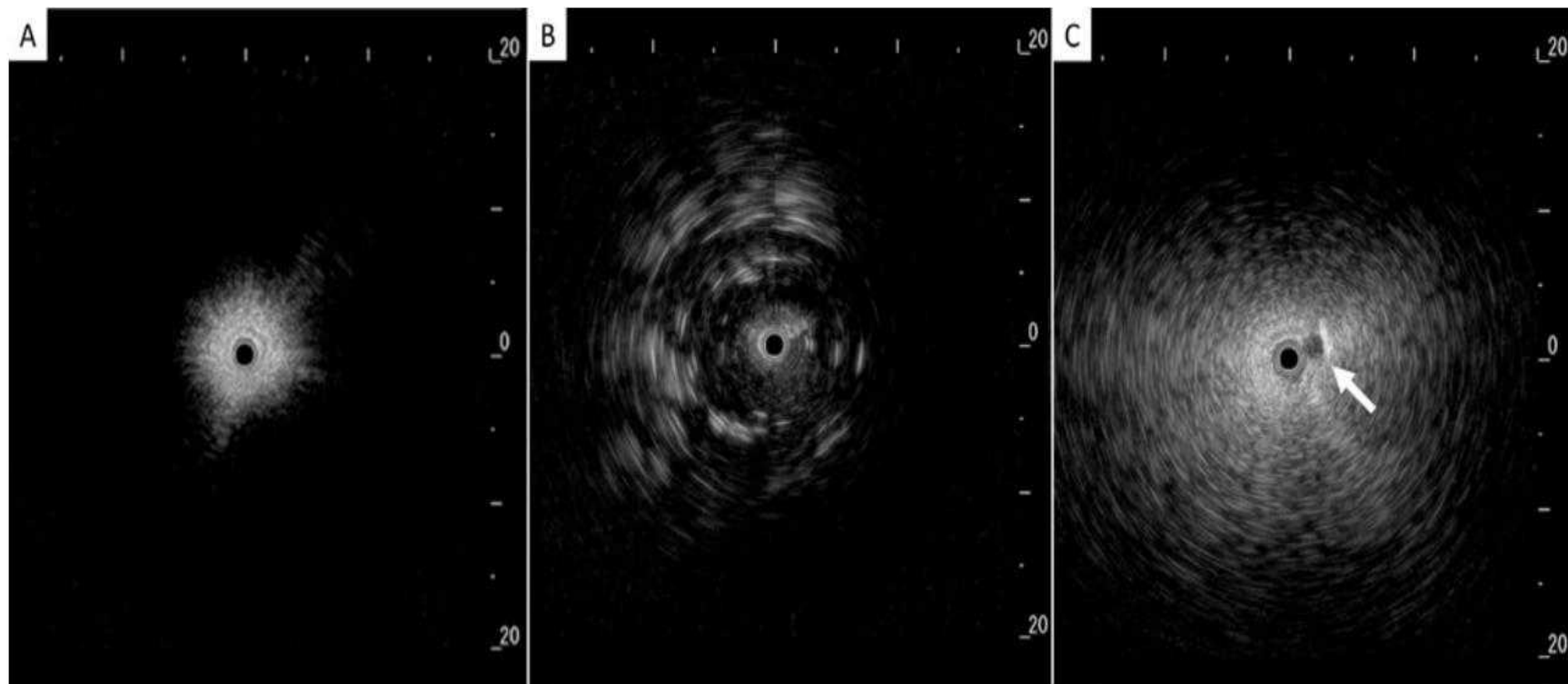


Eosinophilic pneumonia



Sarcoidosis

Radial endobronchial ultrasonography combined with TBLC in ILD

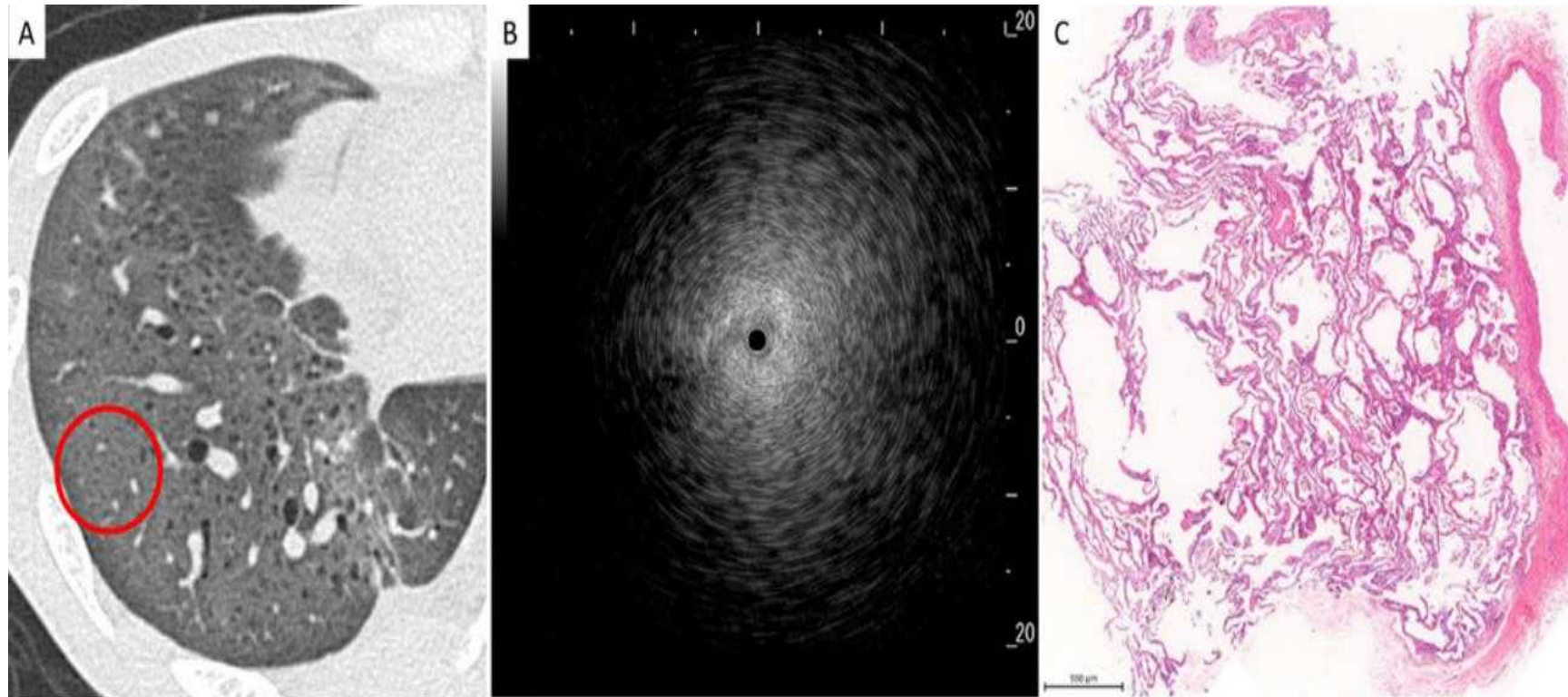


Normal lung

Dense sign

Blizzard sign

Radial endobronchial ultrasonography combined with TBLC in ILD



Blizzard sign with a whitish acoustic shadow of air-containing lung tissue

TBLC: The heat is on in Korea ???



- Surgical lung biopsy in Korean patient with IPF

~ 2012	31.9%
2012 ~ 2015	20.5%
2016 ~	15.3%

- The proportion of surgical lung biopsy in other study
- Role of HRCT
- Low rate of surgical lung biopsy in Korea (HP?)

TBLC: The heat is on 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)

Summary



- TBLC: The heat is on in Korea !!!
- TBLC: The heat is on in Korea ???
- TBLC methods
- Hurdles in Korea
- Undiagnosed ILD by TBLC → VATS or TBLC again ?
- Training and Experienced center
- **Safety \geq Diagnostic yield**

감사합니다