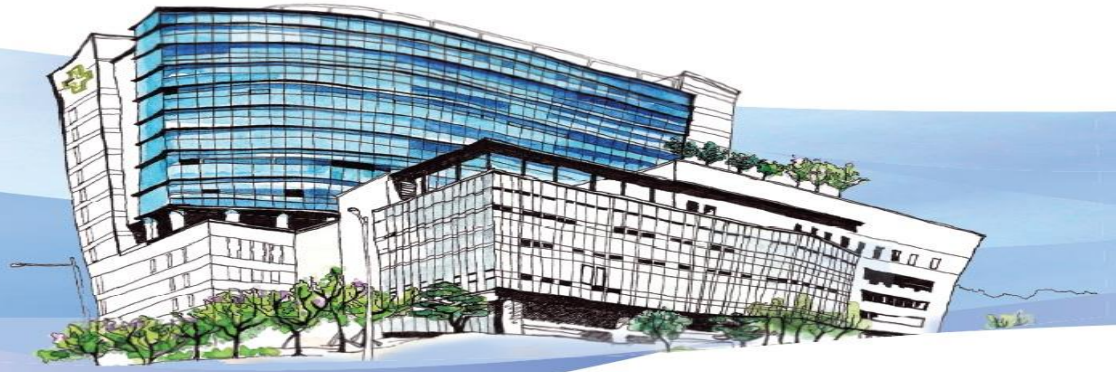


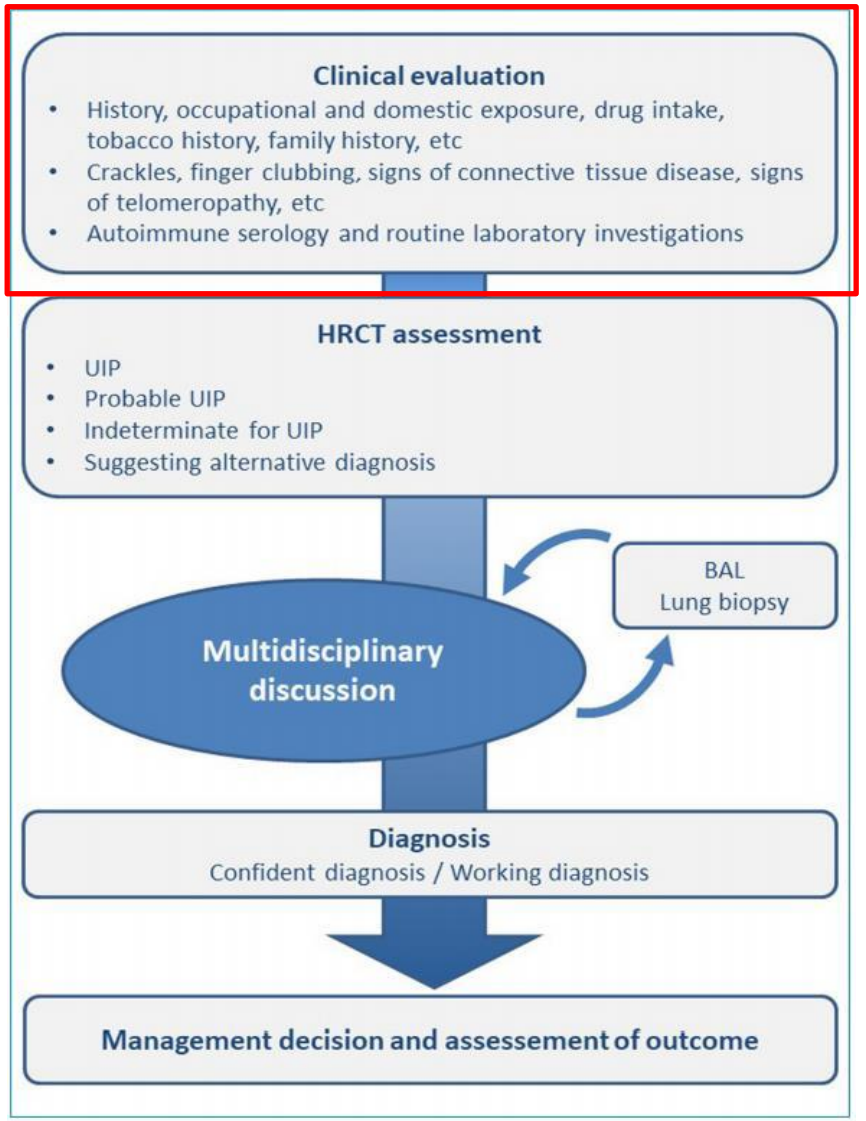
Cryobiopsy vs. Surgical Lung Biopsy for the Diagnosis of ILD

Pro

Diagnostic work-up

간질성폐질환의 원인

- Familial and occupational history
- Drug – amiodarone, MTX, leflunomide, anti-cancer drug…
- Exposure (과민성폐렴)
- Autoimmune diseases

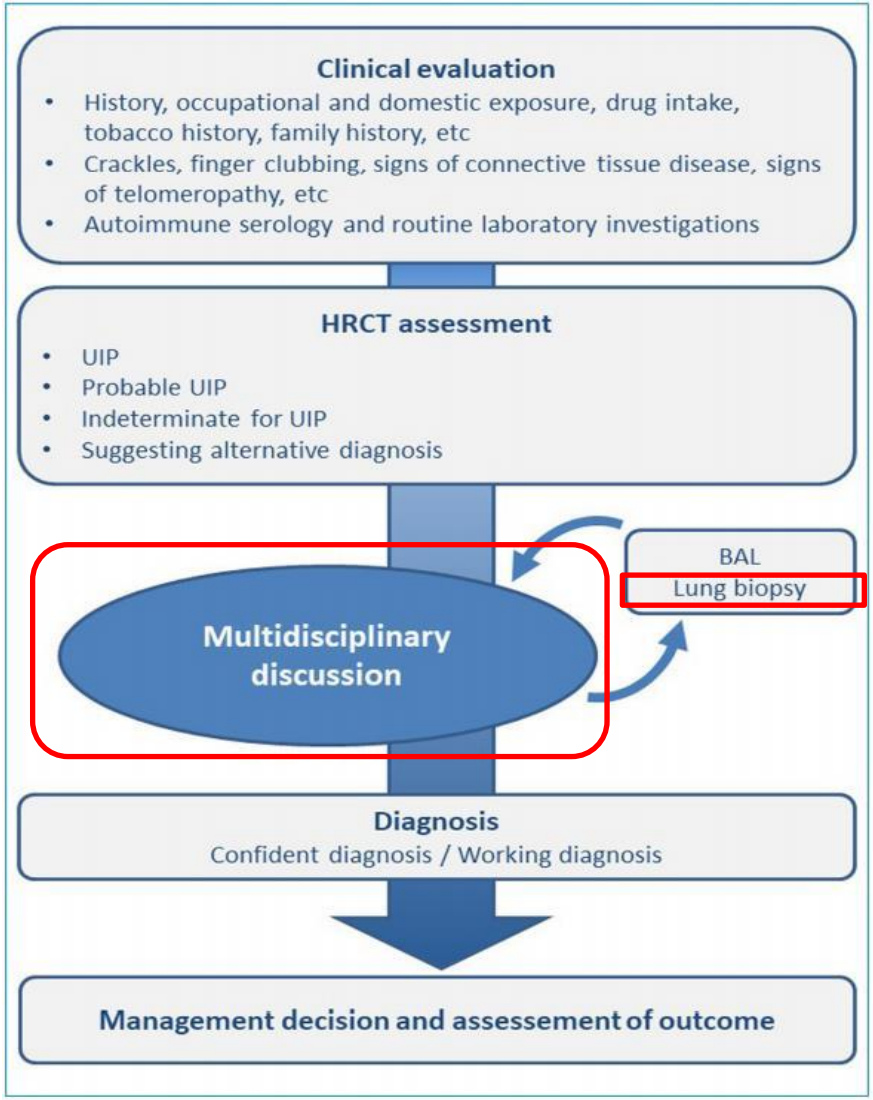


Idiopathic Interstitial Pneumonia

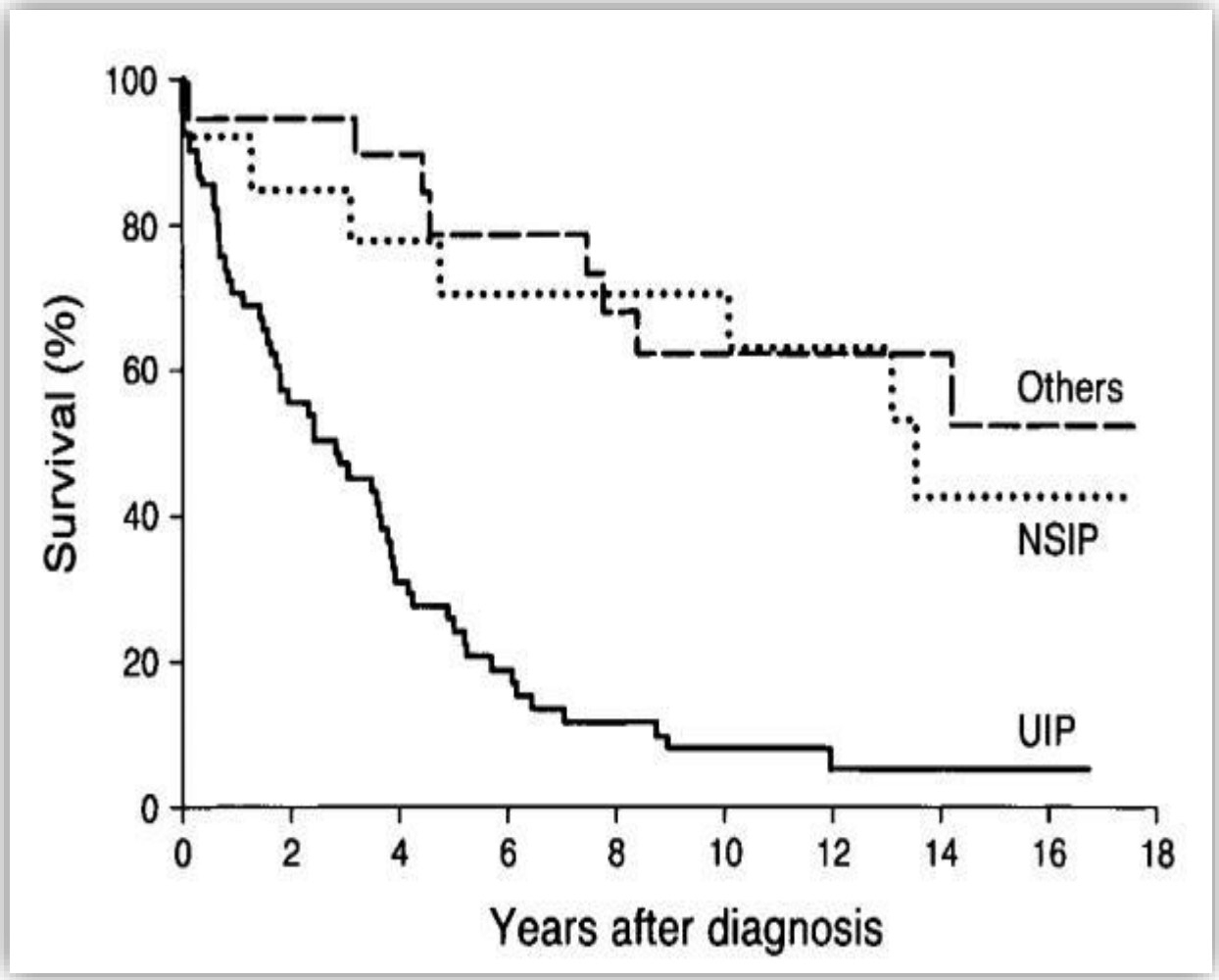
IIP

Major IIPs
- Idiopathic pulmonary fibrosis
- Idiopathic nonspecific interstitial pneumonia
- Acute interstitial pneumonia
- Desquamative interstitial pneumonia
- Respiratory bronchiolitis -interstitial lung disease
- Cryptogenic organizing pneumonia

Rare IIPs
- Idiopathic lymphoid interstitial pneumonia
- Idiopathic pleuroparen-chymal fibroelastosis
- Unclassifiable IIPs



IIP: IPF vs others



Histopathologic patterns

Diagnosis

Prognosis

Treatment

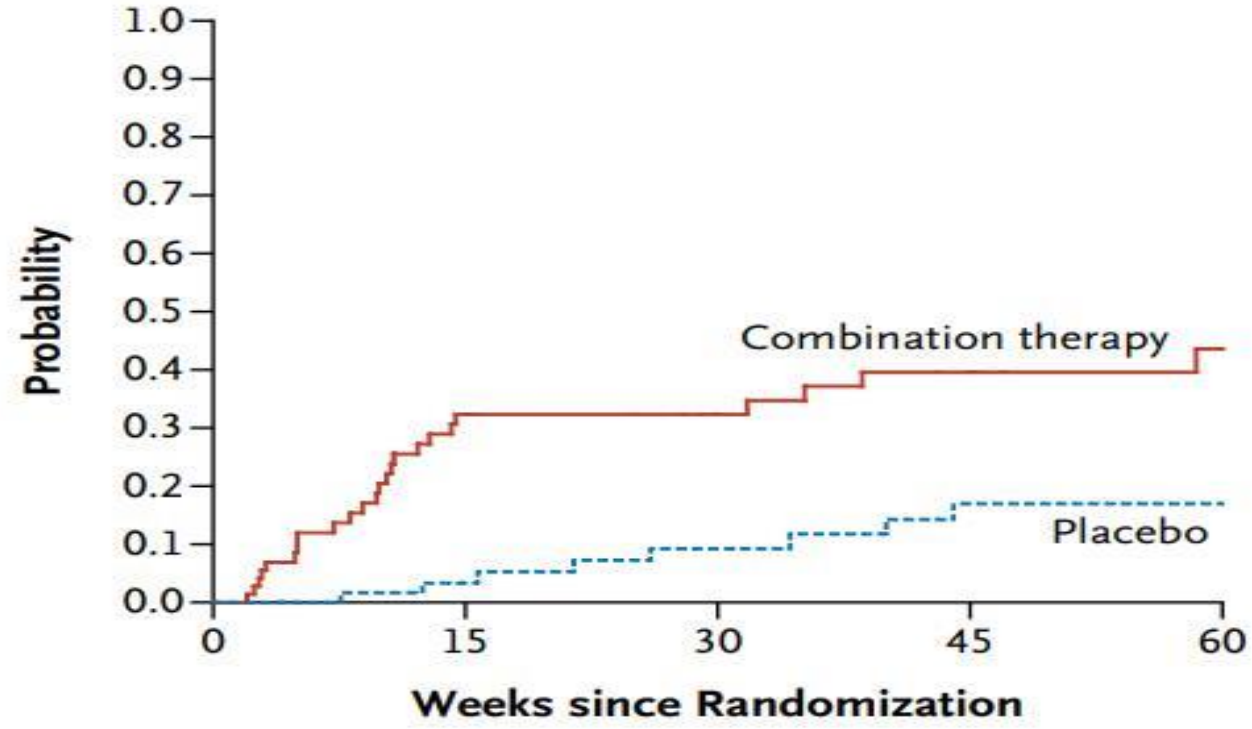
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prednisone, Azathioprine, and N-Acetylcysteine for Pulmonary Fibrosis

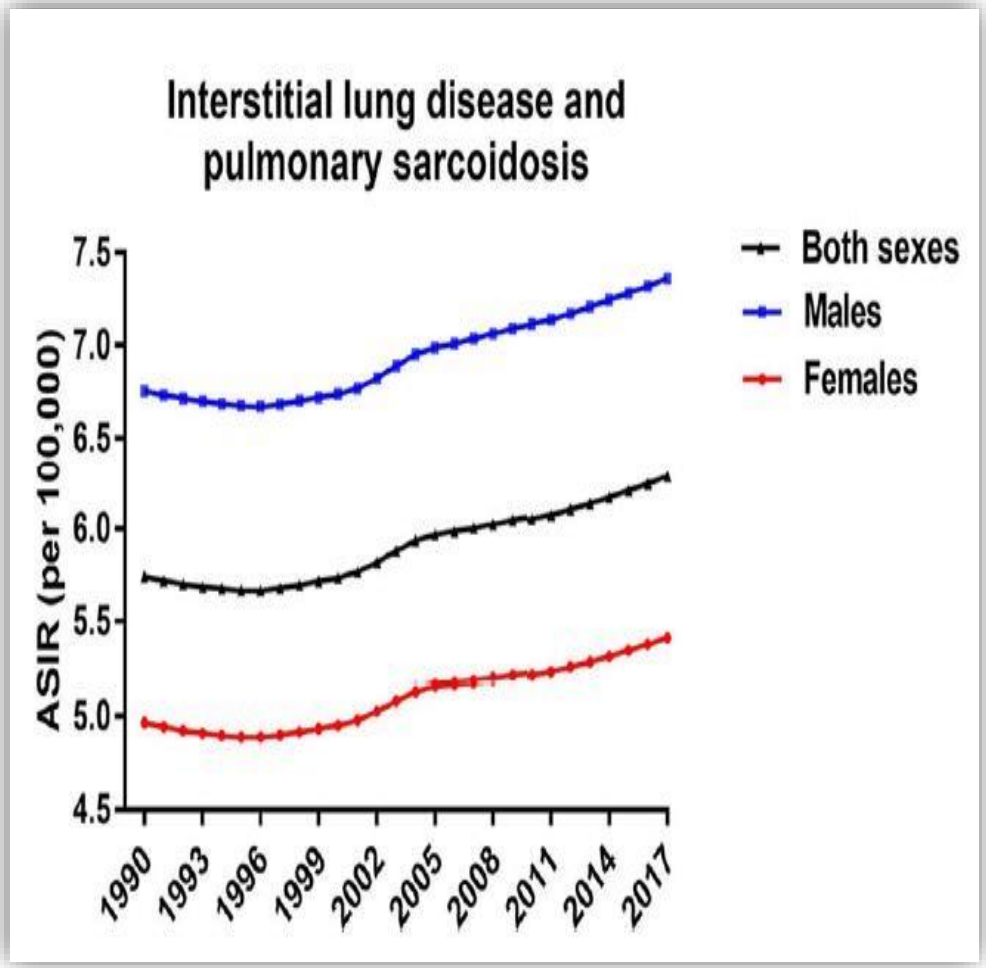
The Idiopathic Pulmonary Fibrosis Clinical Research Network*

Time to Death or Hospitalization



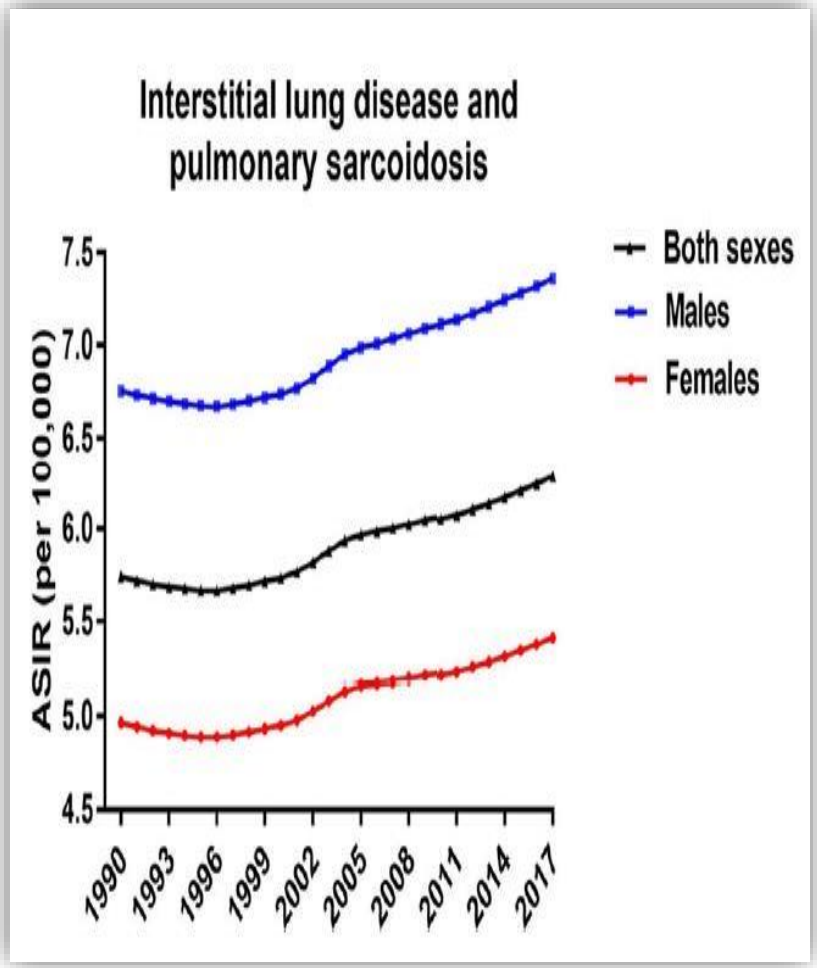
NEJM 2012;366:1968-77

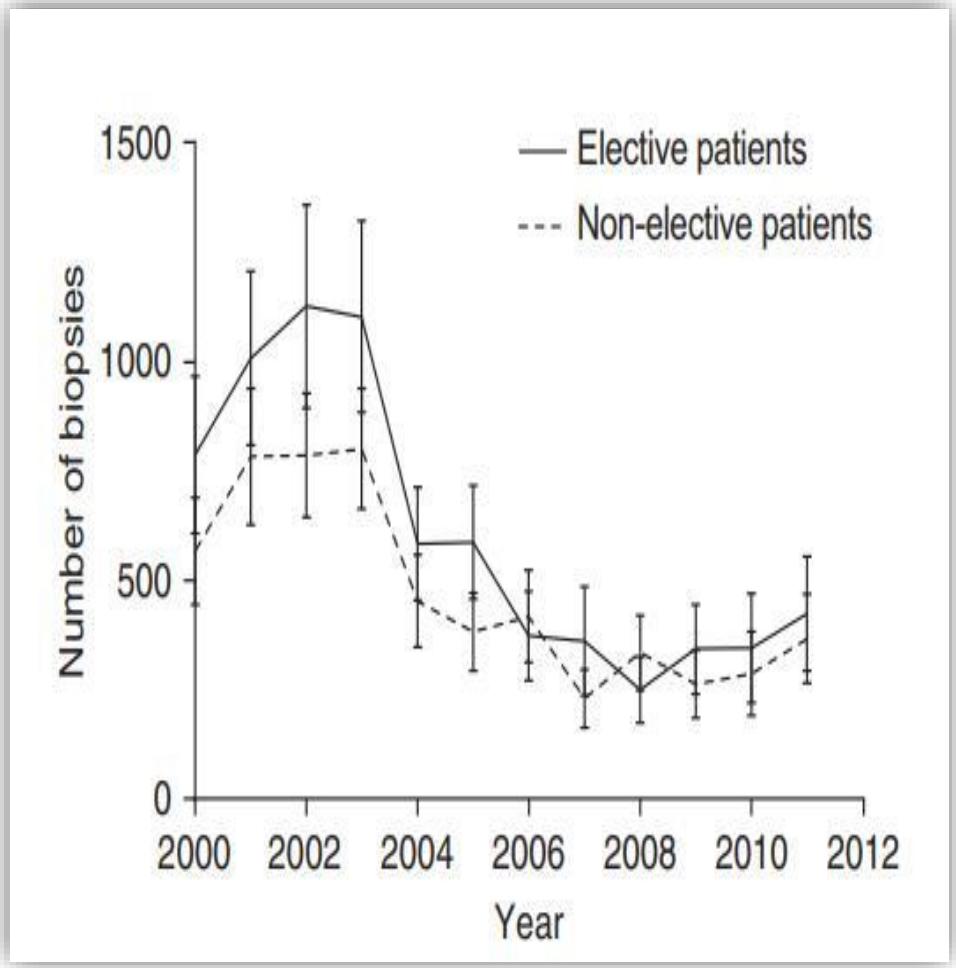
Increased incidence of ILD



Respiratory Research (2020) 21;49

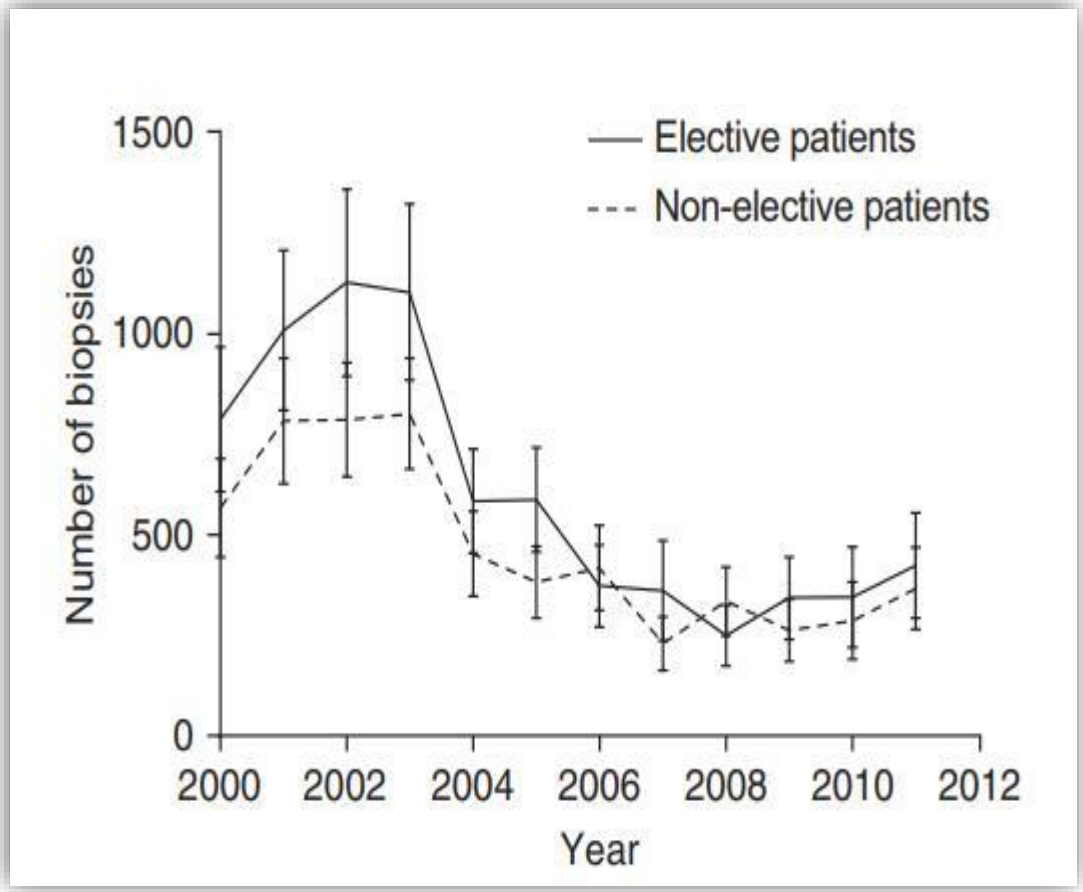
Decreased numbers of SLB in IPF





Respiratory Research (2020) 21;49

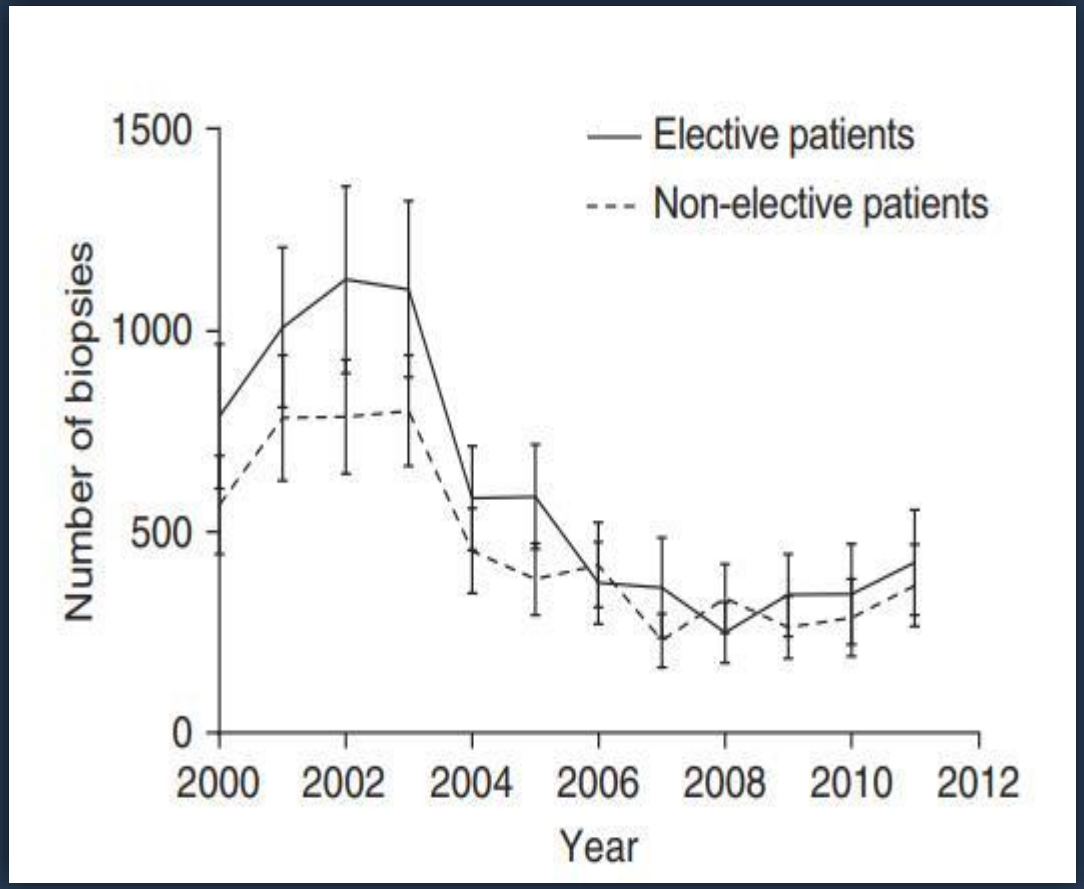
The decline in SLB for IPF



- **Recognition of the value of HRCT in diagnosis of IPF**
- **Concerns over the safety of SLB**

AJRCCM 2016;193:1161-1167

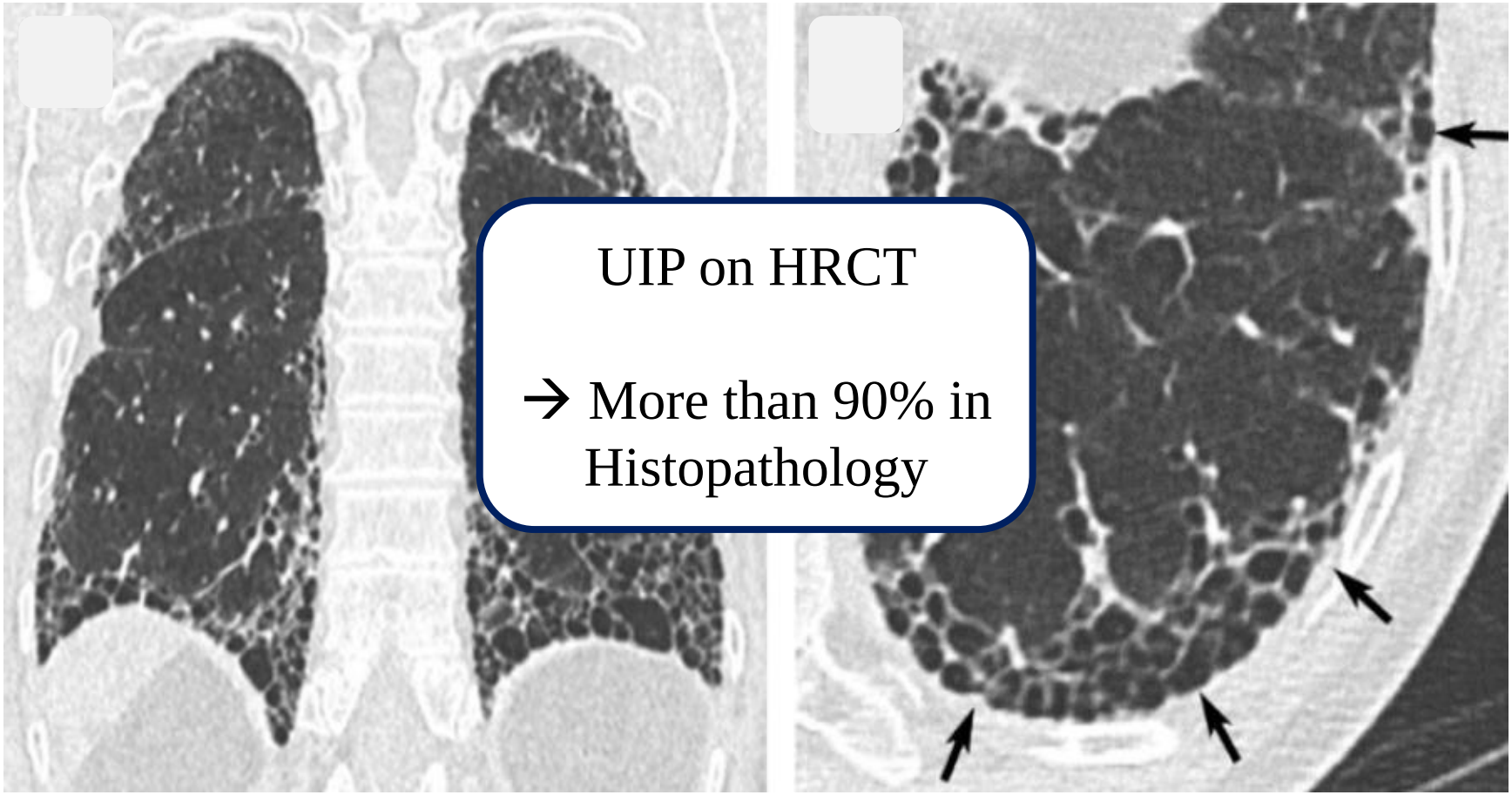
The decline in SLB for IPF



- **Recognition of the value of HRCT in diagnosis of IPF**
- Concerns over the safety of SLB

AJRCCM 2016;193:1161-1167

Role of HRCT

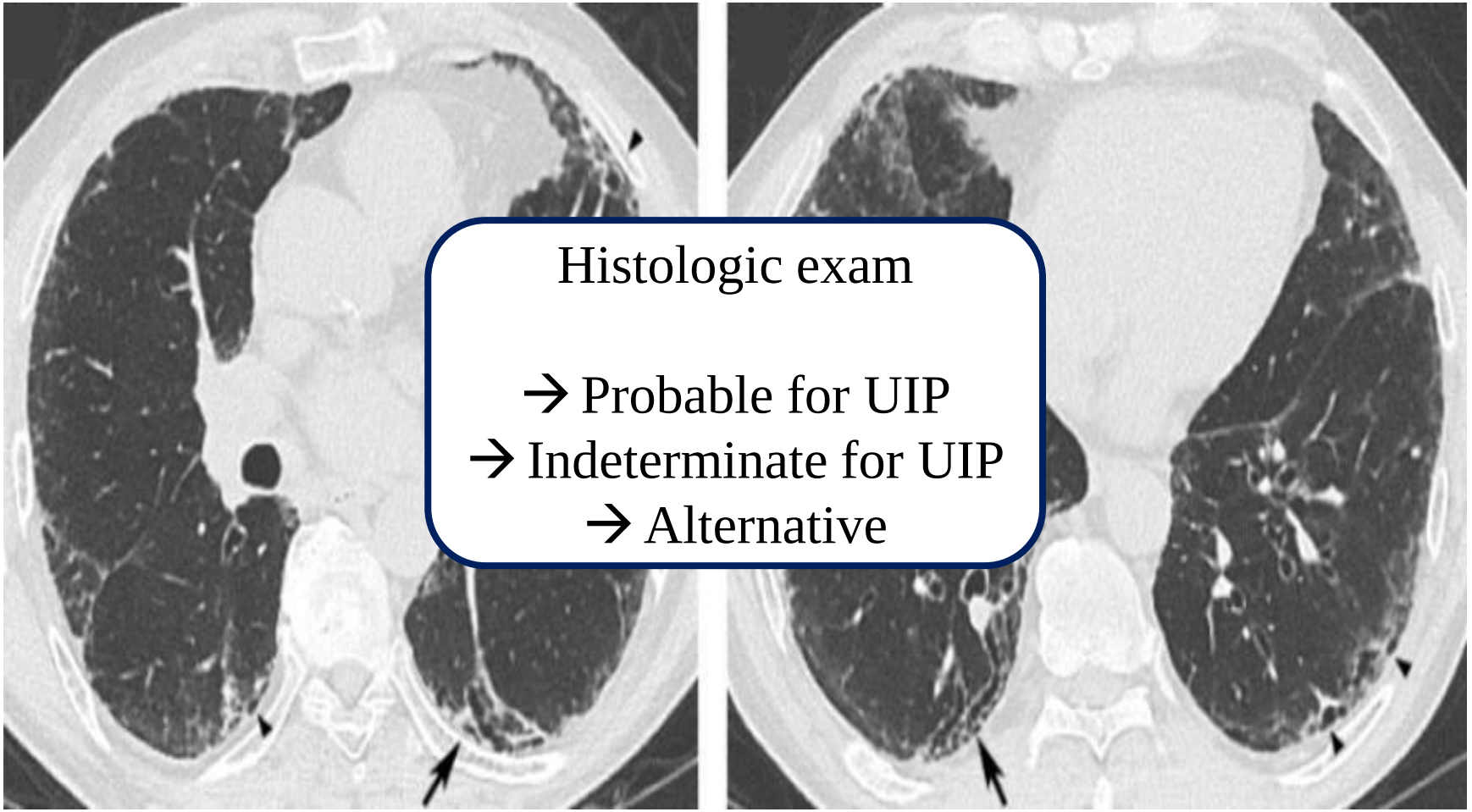


UIP on HRCT

→ More than 90% in Histopathology

AJRCCM 2018;198(5):e44-e68

Histopathologic exam

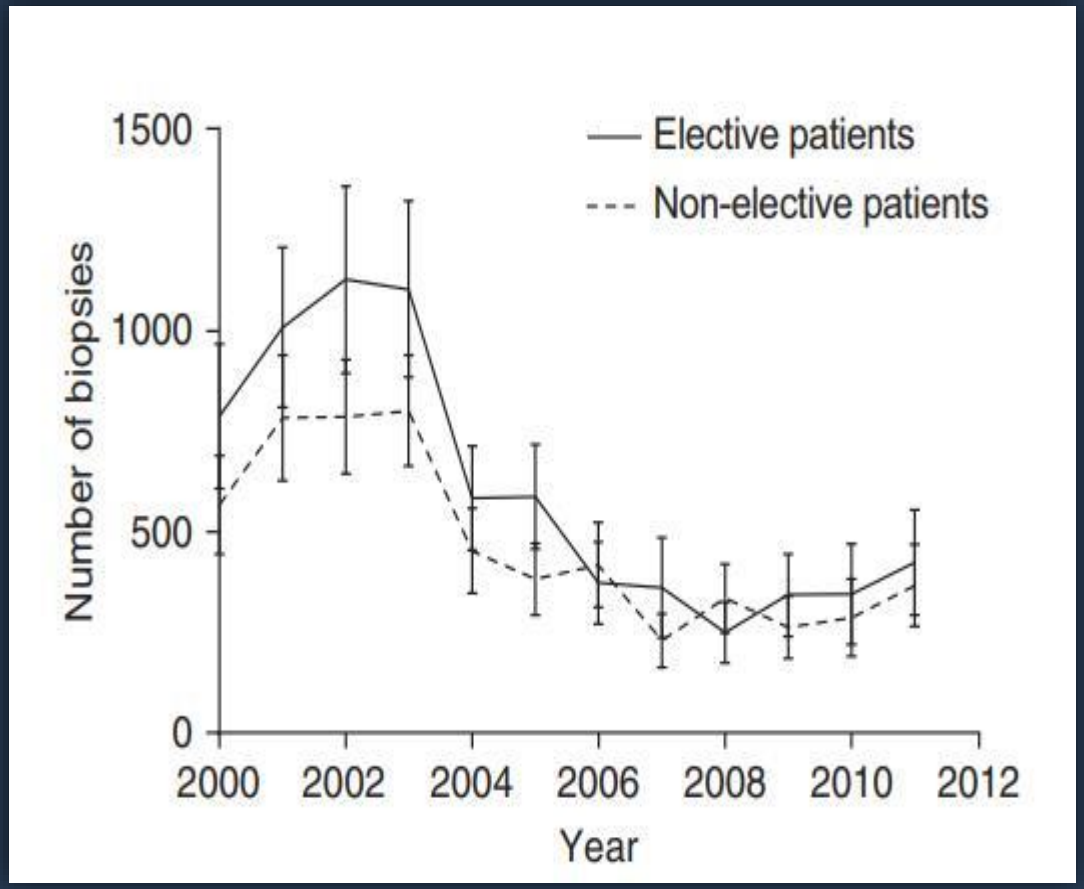


Histologic exam

→ Probable for UIP
→ Indeterminate for UIP
→ Alternative

AJRCCM 2018;198(5):e44-e68

The decline in SLB for IPF



- Recognition of the value of HRCT in diagnosis of IPF
- **Concerns over the safety of SLB**

AJRCCM 2016;193:1161-1167

Risk of mortality after surgical lung biopsy

ORIGINAL ARTICLE

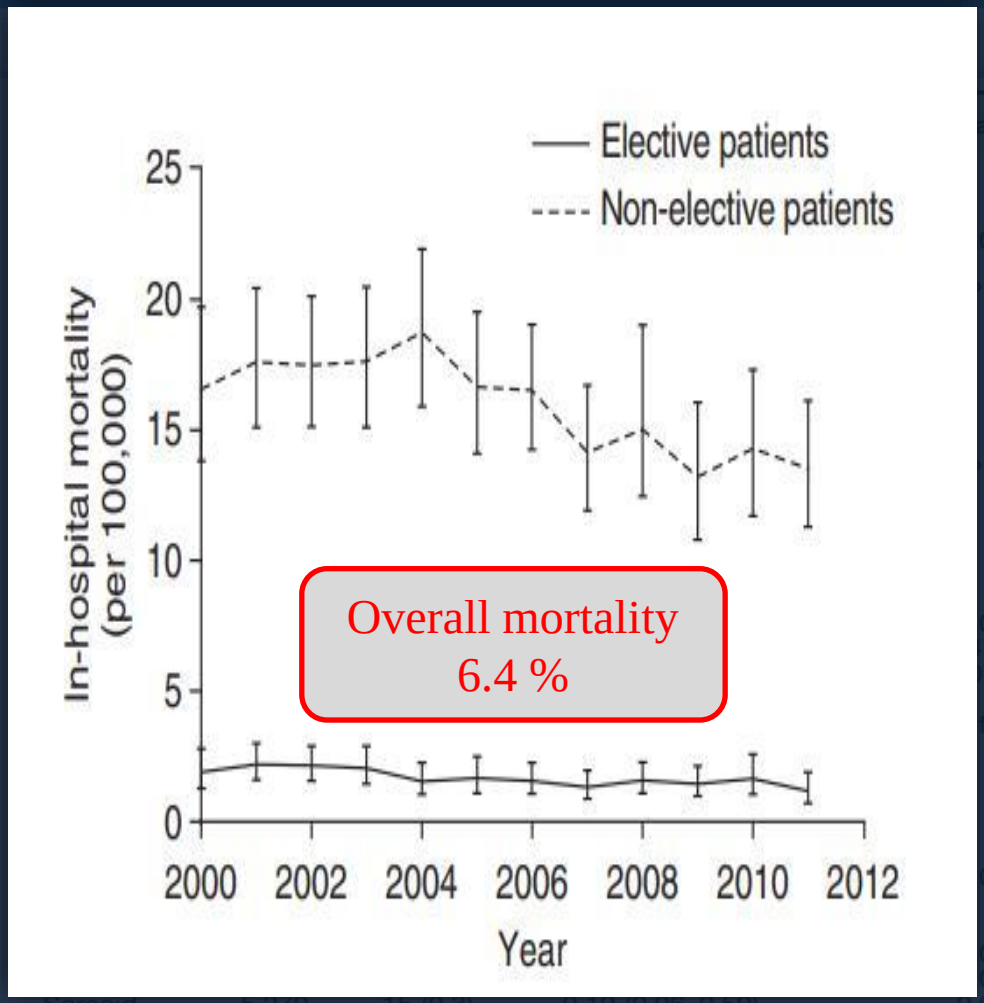
In-Hospital Mortality after Surgical Lung Biopsy for Interstitial Lung Disease in the United States

2000 to 2011

	Total Admissions (*n* = 32,022) [*Number (%)*]	Elective Admissions (*n* = 21,227) [*Number (%)*]	Nonelective Admissions (*n* = 10,310) [*Number (%)*]
Sex			
Male	15,351 (47.94)	9,942 (46.84)	5,163 (50.08)
Female	16,671 (52.06)	11,285 (53.16)	5,147 (49.92)
Age group, yr			
<45	5,192 (16.21)	3,153 (14.85)	1,958 (18.99)
45–54	6,264 (19.56)	4,229 (19.92)	1,944 (18.86)
55–64	8,093 (25.27)	5,643 (26.58)	2,331 (22.61)
65–74	8,147 (25.44)	5,623 (26.58)	2,406 (23.34)
75–84	4,037 (12.61)	2,431 (11.45)	1,535 (14.89)
>84	289 (0.90)	148 (0.70)	136 (1.32)
Level of comorbidity (updated Charlson score)			
0	13,908 (43.43)	10,627 (50.06)	3,030 (29.39)
1	10,844 (33.86)	7,158 (33.72)	3,558 (34.51)
2	3,304 (10.32)	1,728 (8.14)	1,523 (14.77)
⩾3	3,966 (12.39)	1,714 (8.07)	2,199 (21.33)

AJRCCM 2016;198:1161

Risk of mortality after surgical lung biopsy



- ✓ 12,000명, 2000~2011
- ✓ Elective → 1.7%
- ✓ Non-elective >15%
- ✓ Co-morbidity
- ✓ Age
- ✓ Male
- ✓ Open surgery
- ✓ IPF or CTD

AJRCCM 2016;198:1161

Severe complications and mortality in invasive diagnostic test

Cerebral Angiography

Complications of 19 826 Cerebral Angiography Procedures

Complication	No. of Procedures
Local	
Hematoma	828 (4.2)*
Hematoma requiring surgery	5 (0.03)
Thrombosis	9 (0.05)*
Infection	2 (0.01)*
Systemic	
Headaches	105 (0.8)†
Nausea, vomiting, transient hypotension	235 (1.2)‡
Chest pain, arrhythmia	61 (0.3)‡
Urticaria, rhinorrhea	26 (0.1)‡
Death	12 (0.06)‡
Anaphylaxis and/or circulatory collapse	5 (0.03)‡
Acute renal failure	3 (0.02)‡
Neurologic	
TIA	414 (2.09)
Reversible	71 (0.36)
Permanent	27 (0.14)
Death related to neurologic condition	10 (0.05)§
Total	522 (2.63)

Diagnostic CAG

Mortality 1% (1960s) → 0.08% (1990s)

Reference	Patients	Incidence	CABG	MI	Death	Death,%
Bittl et al., 1993	764	3%	34.7	4.3	9	0.012
Ajluni et al., 1994	8932	0.40%	37	26	5.6	0.001
Holmes et al., 1994	2759	1.30%	36.1	16.7	4.8	0.002
Ellis., 1994	12900	0.50%	24	19	0	< 0.001
Cohen et al., 1996	2953	0.70%	41	45.5	9	0.003
Gruberg et al., 2000	30746	0.29%	39	34	10	< 0.001
Dipple., 2001	6214	0.58%	22	NA	11	0.002
Gunning et al., 2002	6245	0.80%	39	29	42	0.007
Fejka et al., 2002	25697	0.12%	39	29	42	0.002
Stankovic et al., 2004	5728	1.47%	13	27	8	0.001
Witzke et al., 2004	12658	0.30%	5	18	2.5	< 0.001
Ramana et al., 2005	4886	0.50%	0	20	8	0.002

Radiology (2007);243:3

GJHS 2012(4); 1

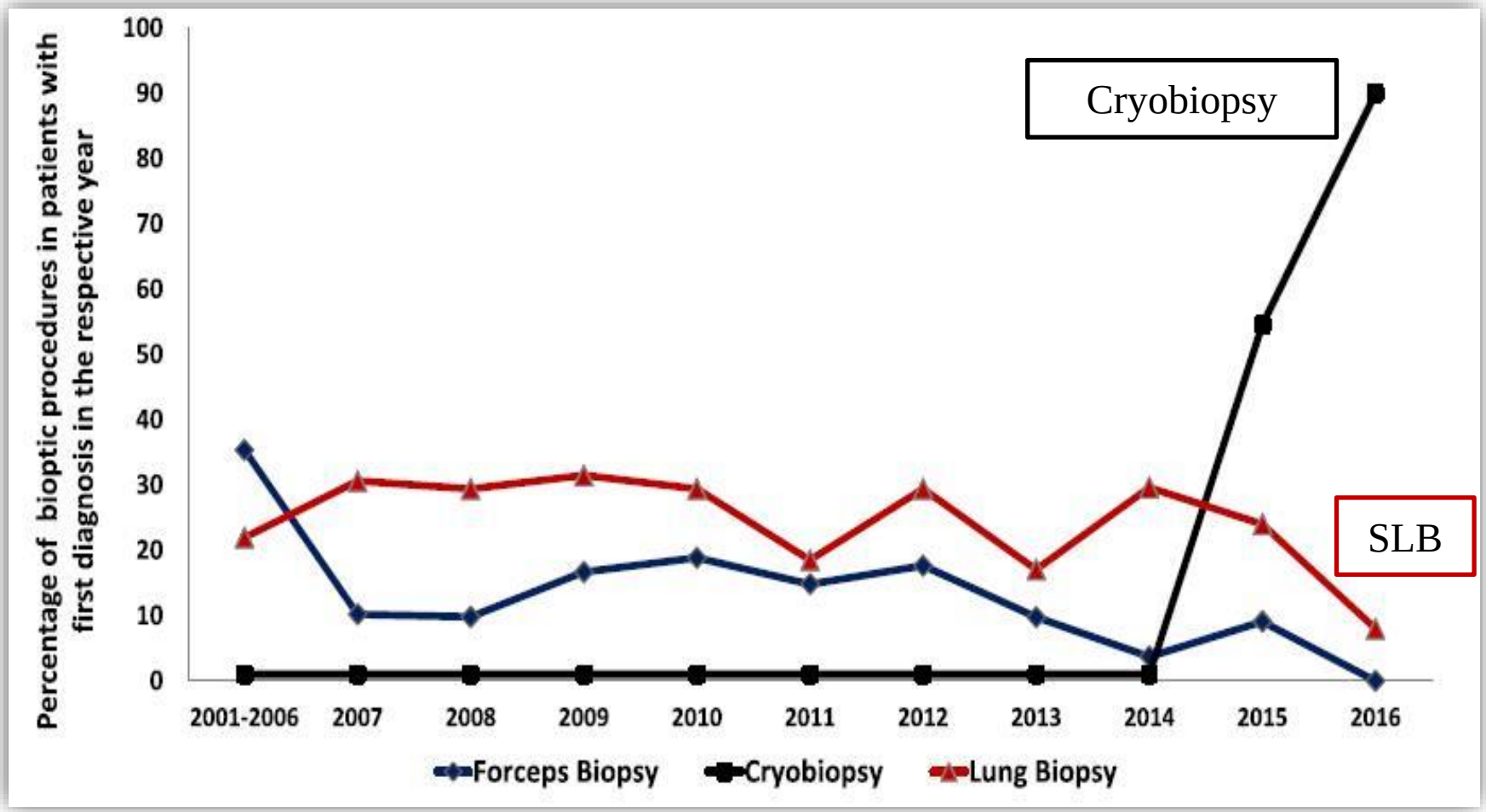
Surgical lung biopsy: VATS

- Adequate sample (100%, 2-3 different lobe)
- Diagnostic yield: 88.2%
- Mortality: 6.4 (1.5%-16.7%), procedure-related mortality (1.7%)
- AE (6.1%), bleeding (0.8%), severe bleeding (0.2%), prolonged air leak (5.9%), infection (6.5%)

- No recommendation for UIP pattern on HRCT
- Gold standard

AJRCCM 2018; 198

Procedure in IPF at the first diagnosis



Respirology Research (2018) 19:141

Indication of TBLC

- Indication of TBLC or SLB?

- IPF diagnosis

→ UIP pattern

→ Probable UIP pattern

- Benefits (diagnostic yield) vs Risks (Safety)

- No absolute contra-indication

Respiration (2018) 95:188-200

Contraindication of Cryobiopsy ?

Key Points

a. The major risks after TBCB are pneumothorax and bleeding.

b. Bleeding diathesis and anticoagulant therapy, treatment with thienopyridines or other new antiplatelet drugs and thrombocytopenia with platelets $<50 \times 10^9$ /L should be considered as contraindications.

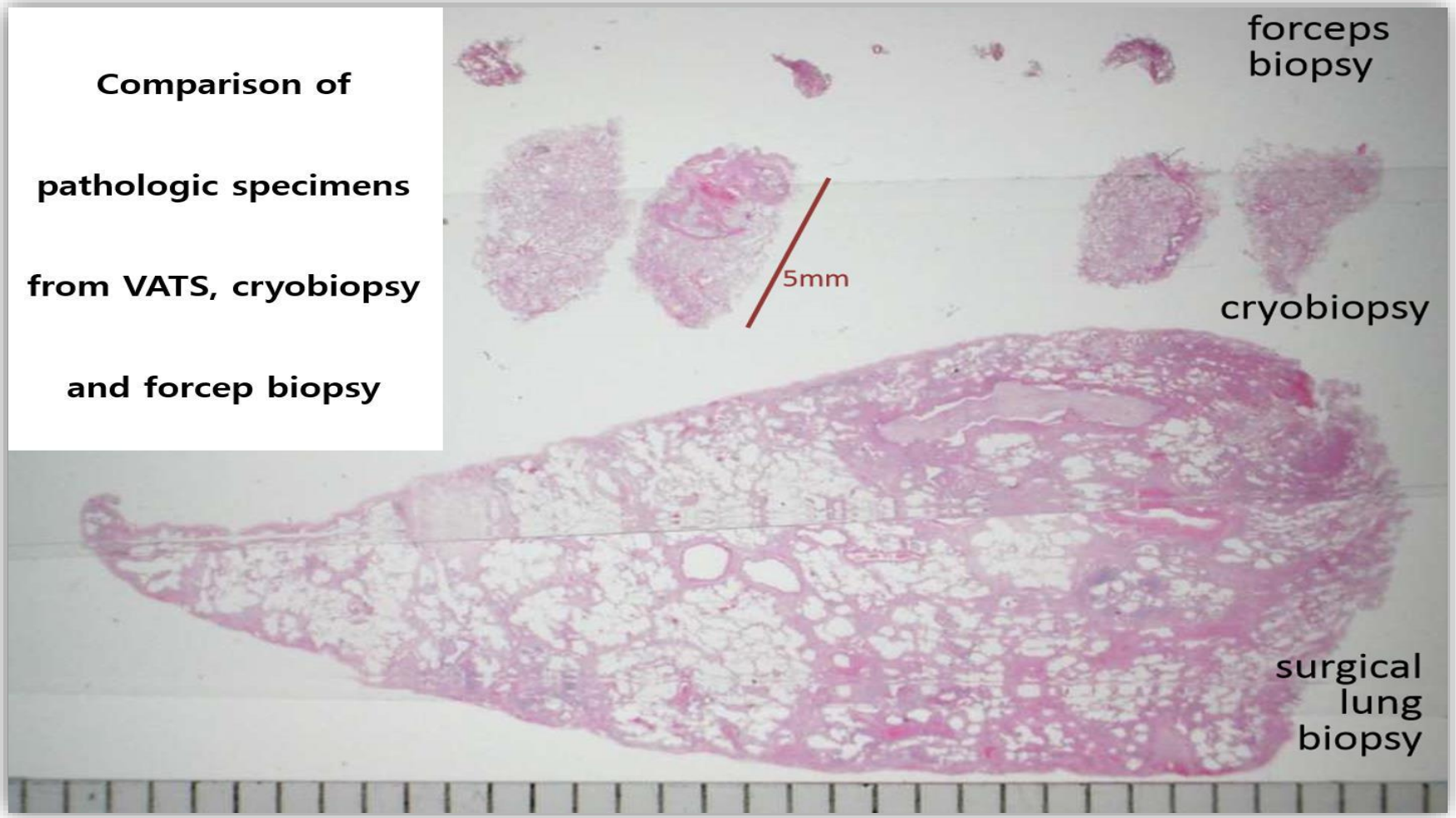
c. Pulmonary hypertension may increase the bleeding risk and is therefore considered as a relative contraindication.

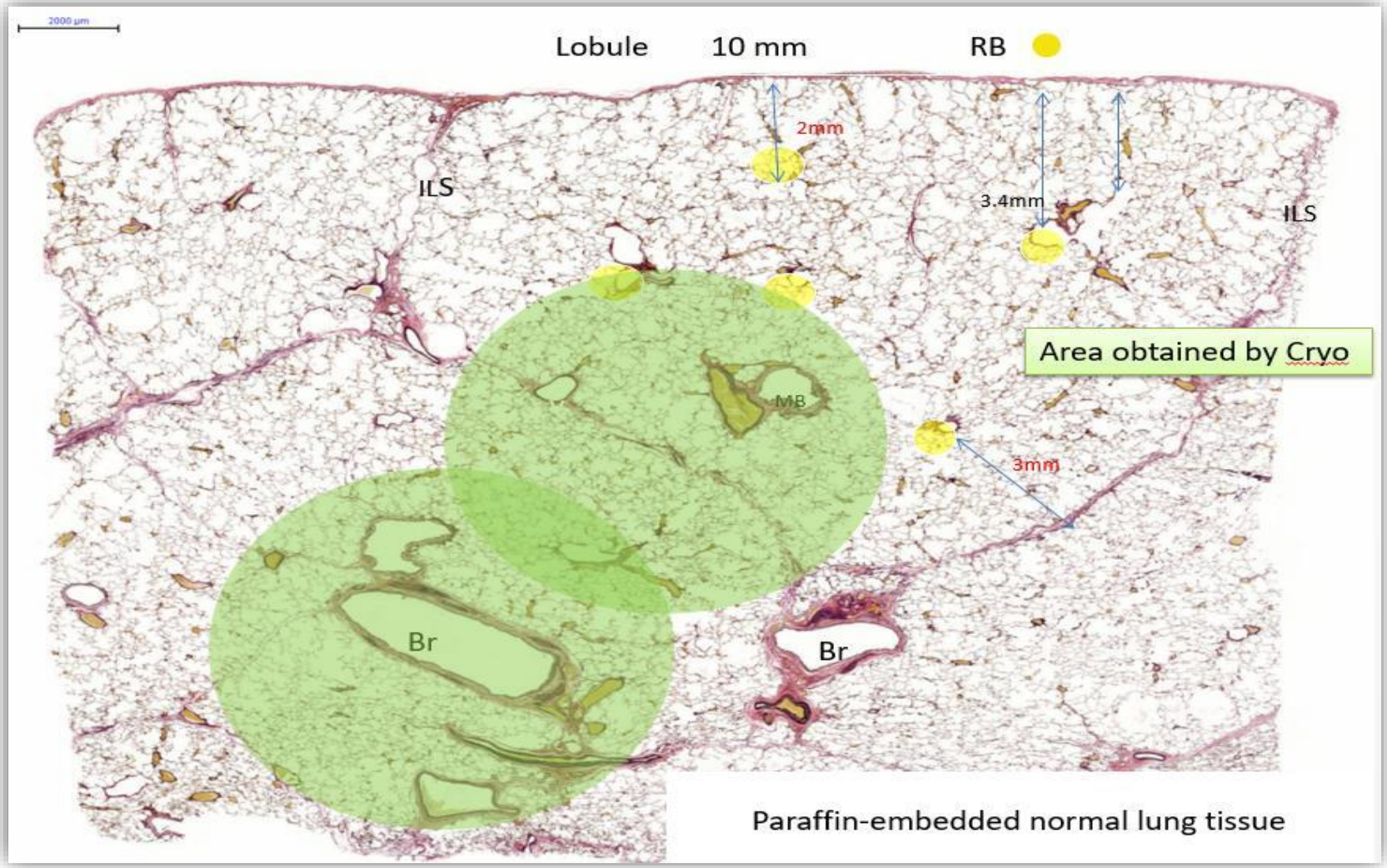
d. No age limits are suggested.

e. FVC <50% and DLCO <35% of the predicted values are regarded as relative contraindications.

Respiration (2018) 95:188-200

Transbronchial lung cryobiopsy

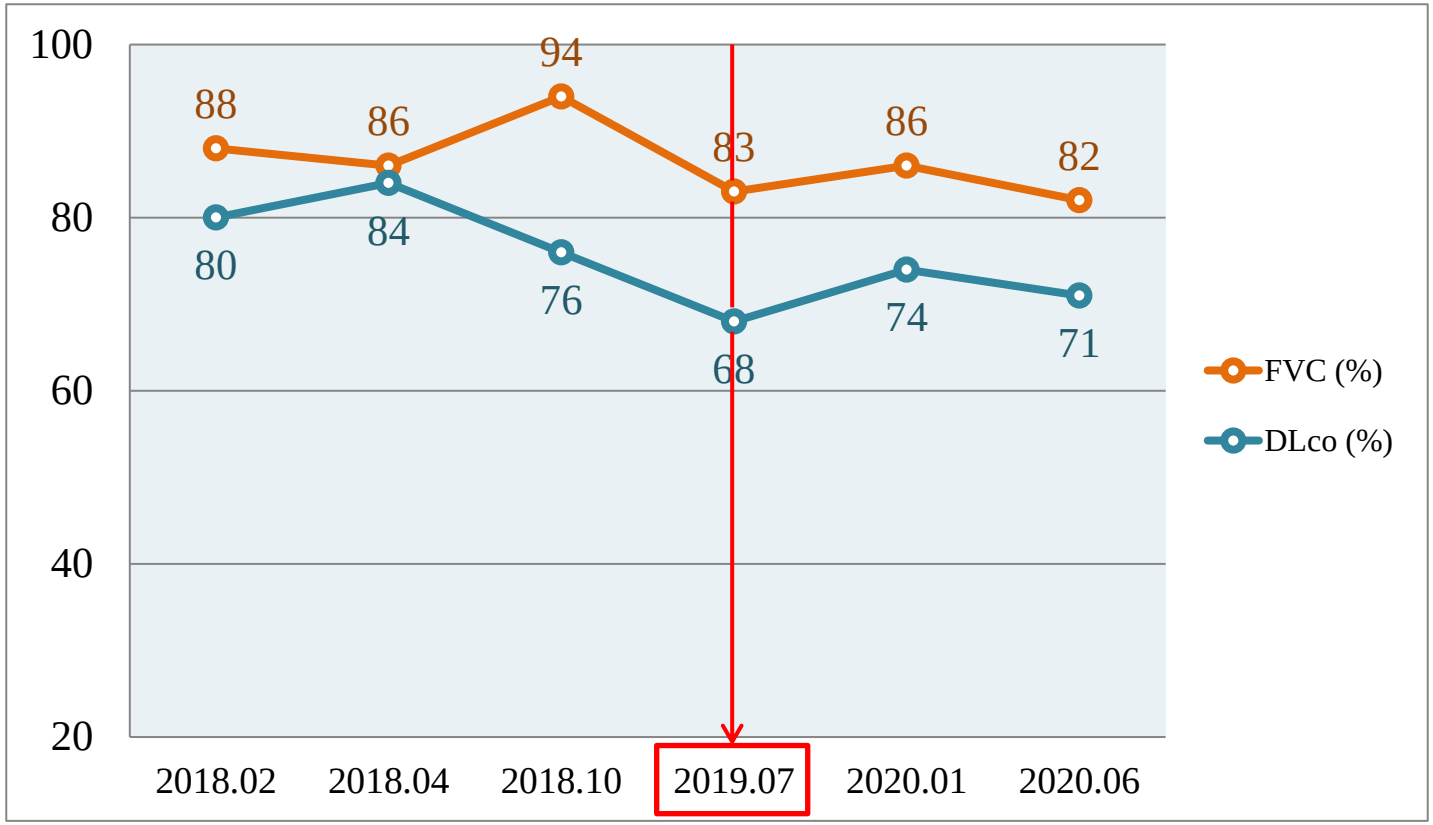



2000 μm
Lobule
10 mm
RB
2mm
3.4mm
ILS
ILS
Area obtained by Cryo
MB
3mm
Br
Br
Paraffin-embedded normal lung tissue

CASE

- 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), Alcholic liver disease, Hyperlipoproteinemia (2019)

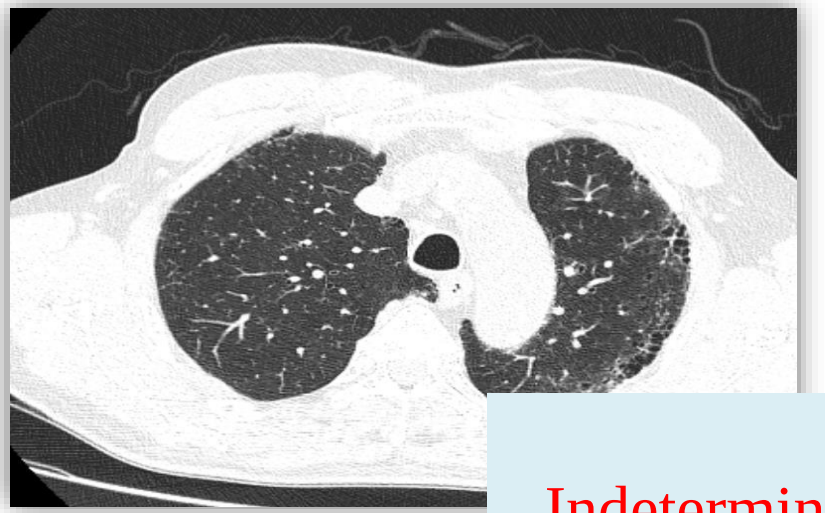
• **PFT**

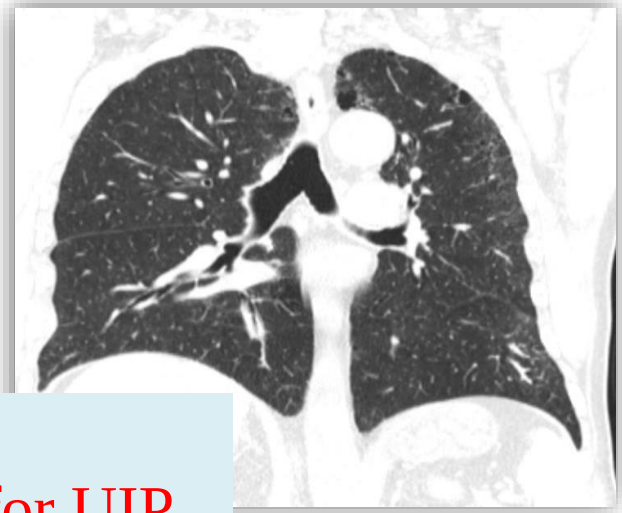


• **6MWT**

	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

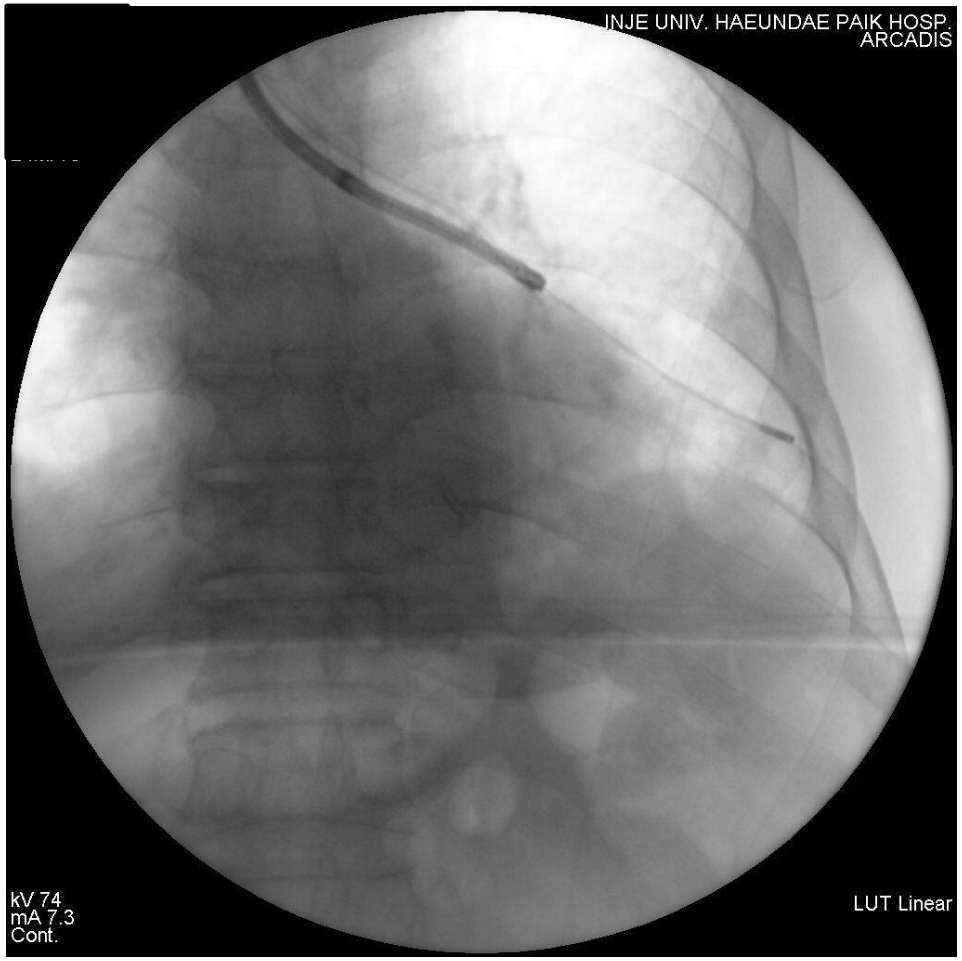
HRCT

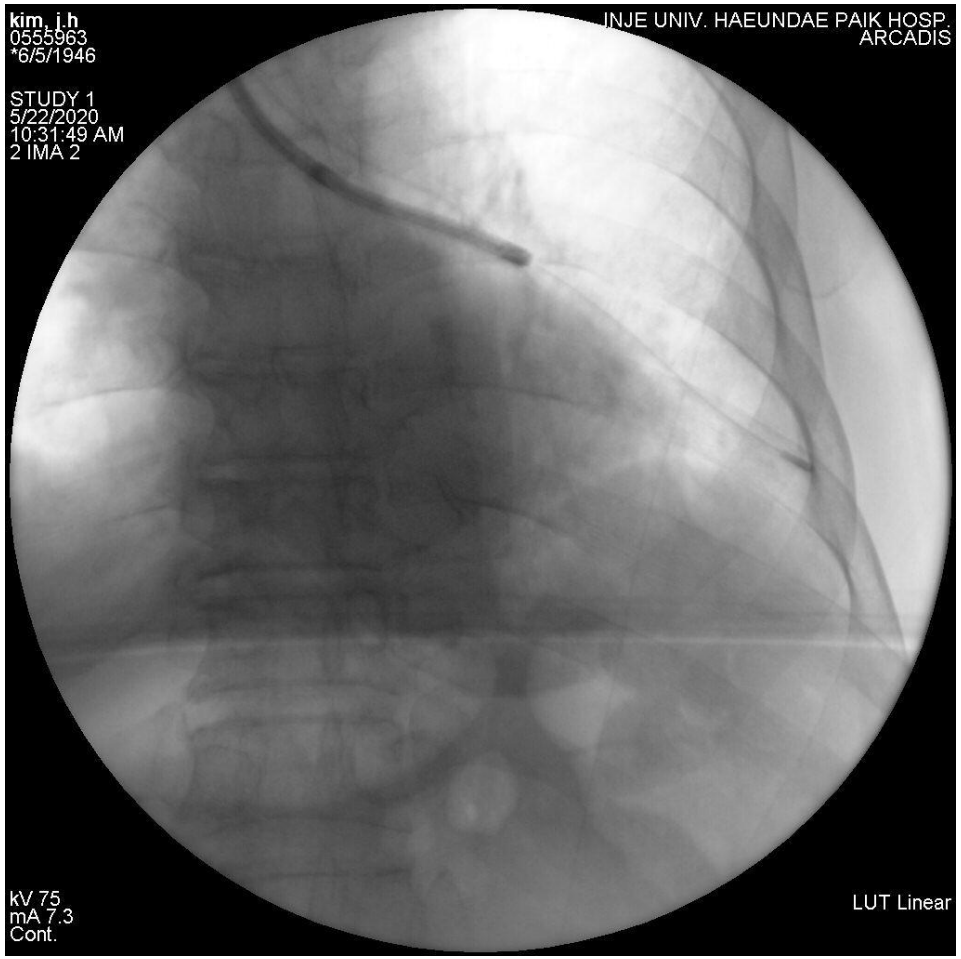


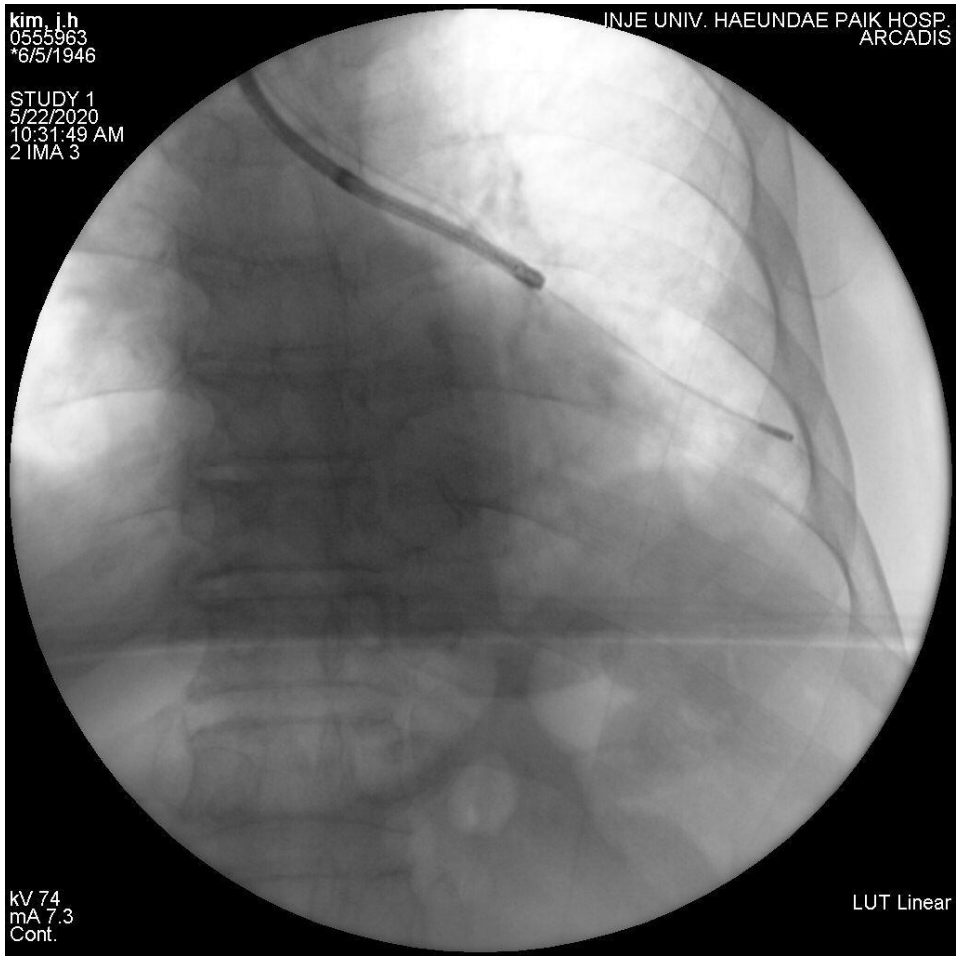


Indeterminate for UIP

Transbronchial lung cryobiopsy




kim, j.h
0555963
*6/5/1946
STUDY 1
5/22/2020
10:31:49 AM
2 IMA 2
INJE UNIV. HAEUNDAE PAIK HOSP.
ARCADIS
kV 75
mA 7.3
Cont.
LUT Linear


kim, j.h
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*6/5/1946
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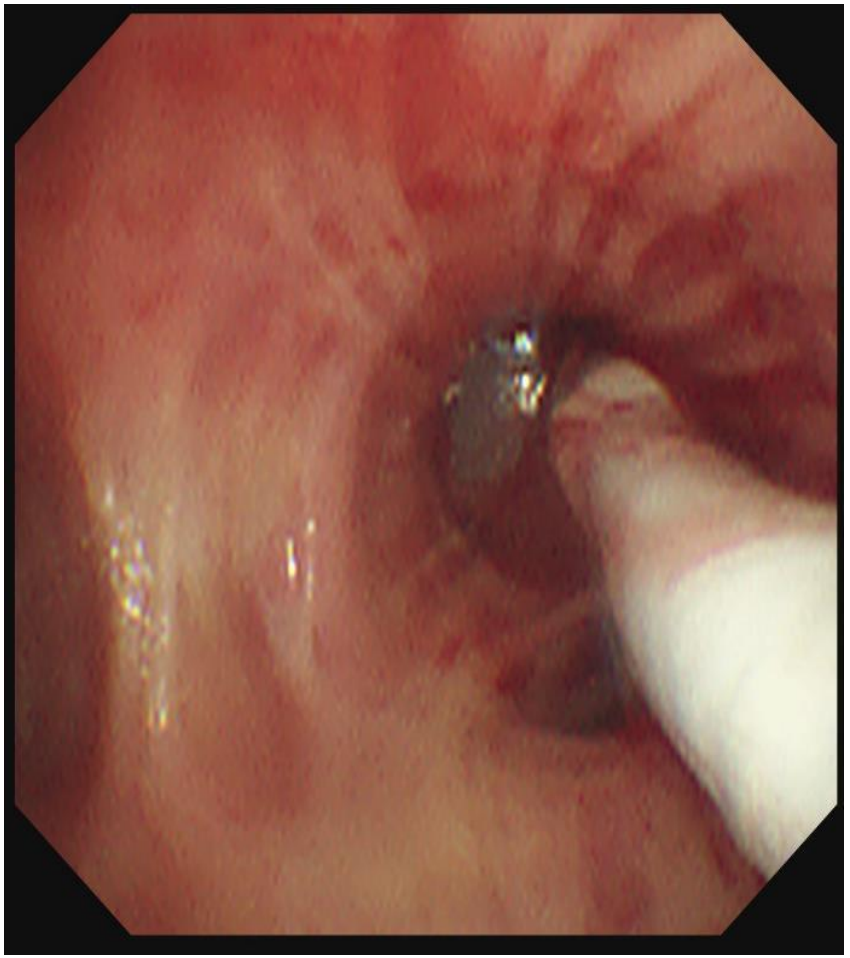
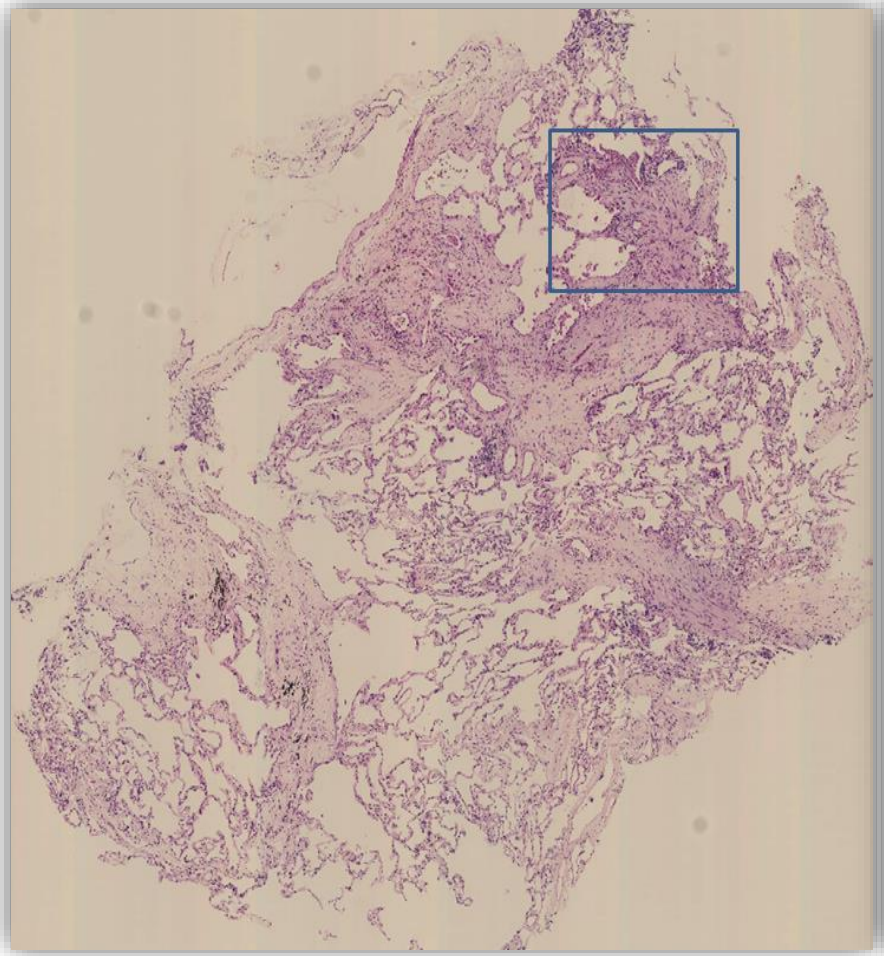
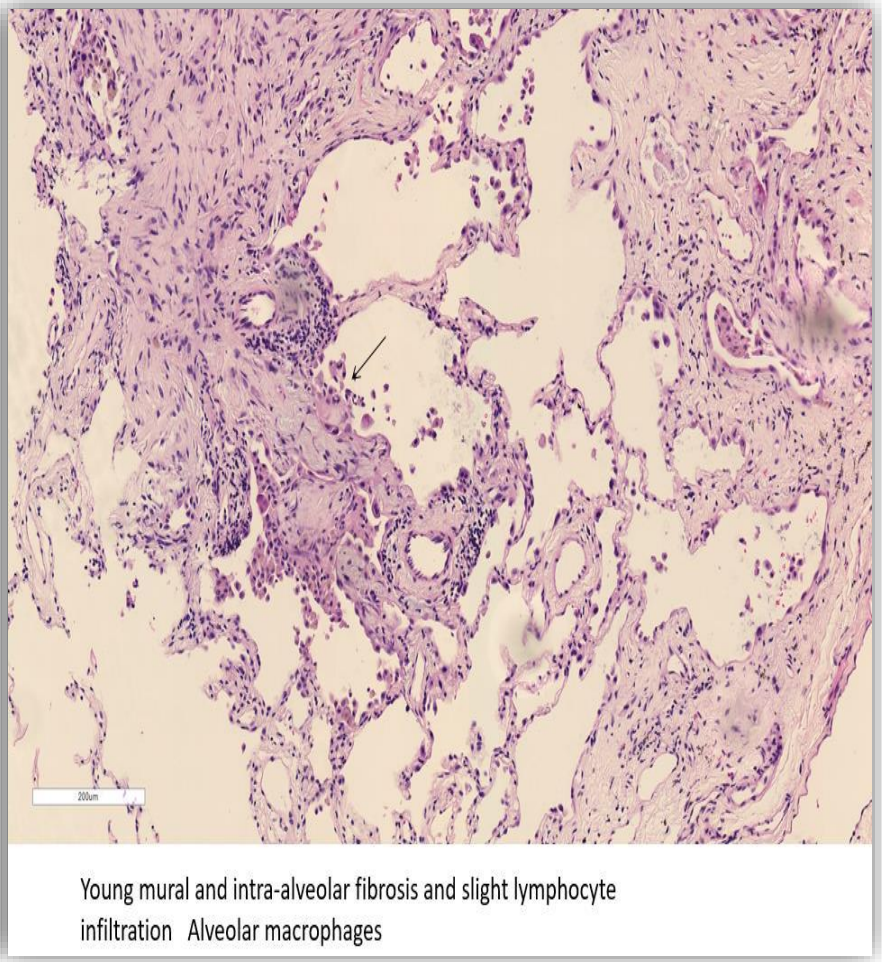
5/22/2020
10:31:49 AM
2 IMA 3
INJE UNIV. HAEUNDAE PAIK HOSP.
ARCADIS
kV 74
mA 7.3
Cont.
LUT Linear

Transbronchial lung cryobiopsy







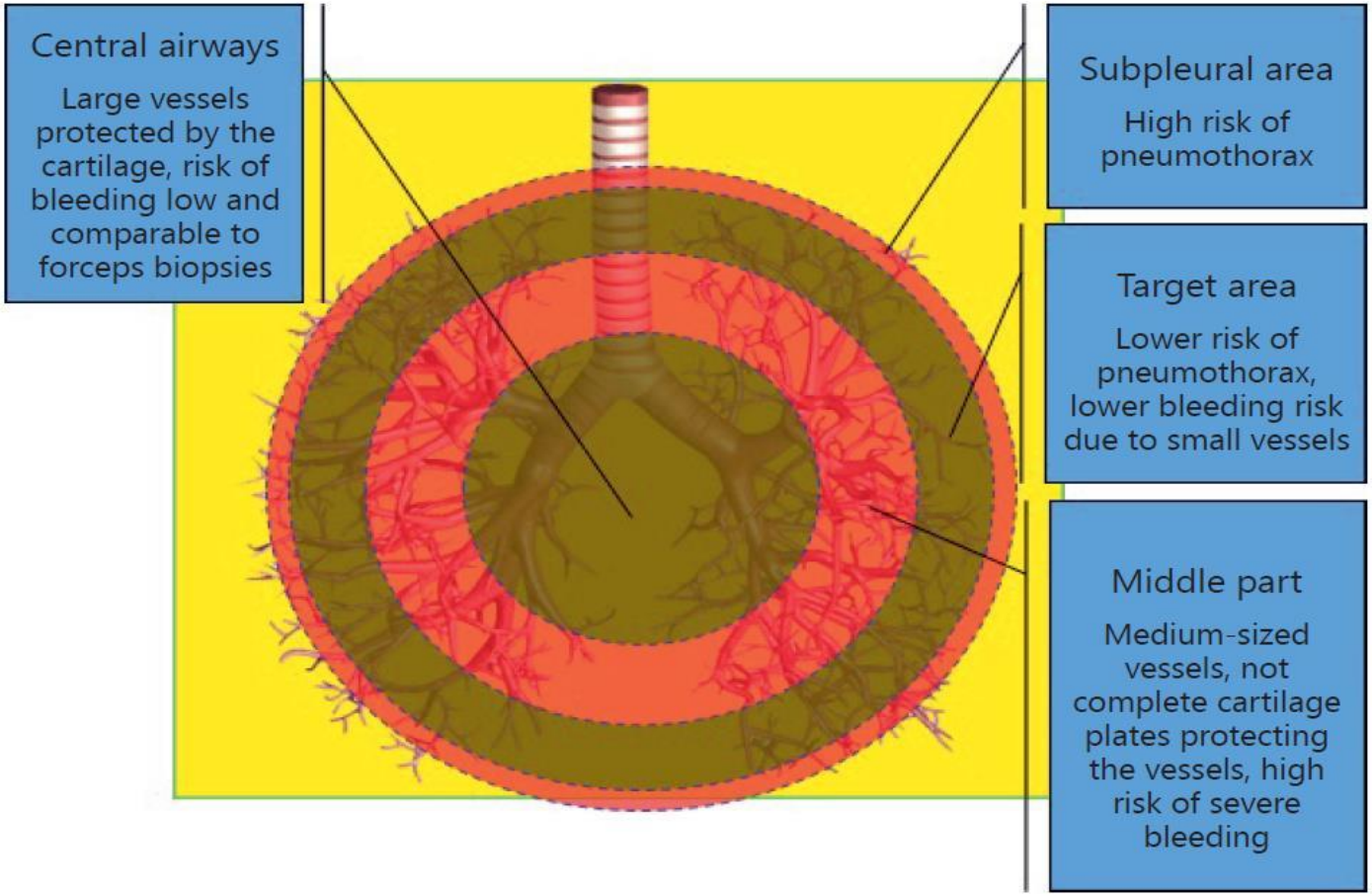
Young mural and intra-alveolar fibrosis and slight lymphocyte infiltration Alveolar macrophages

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

Final diagnosis by MDD

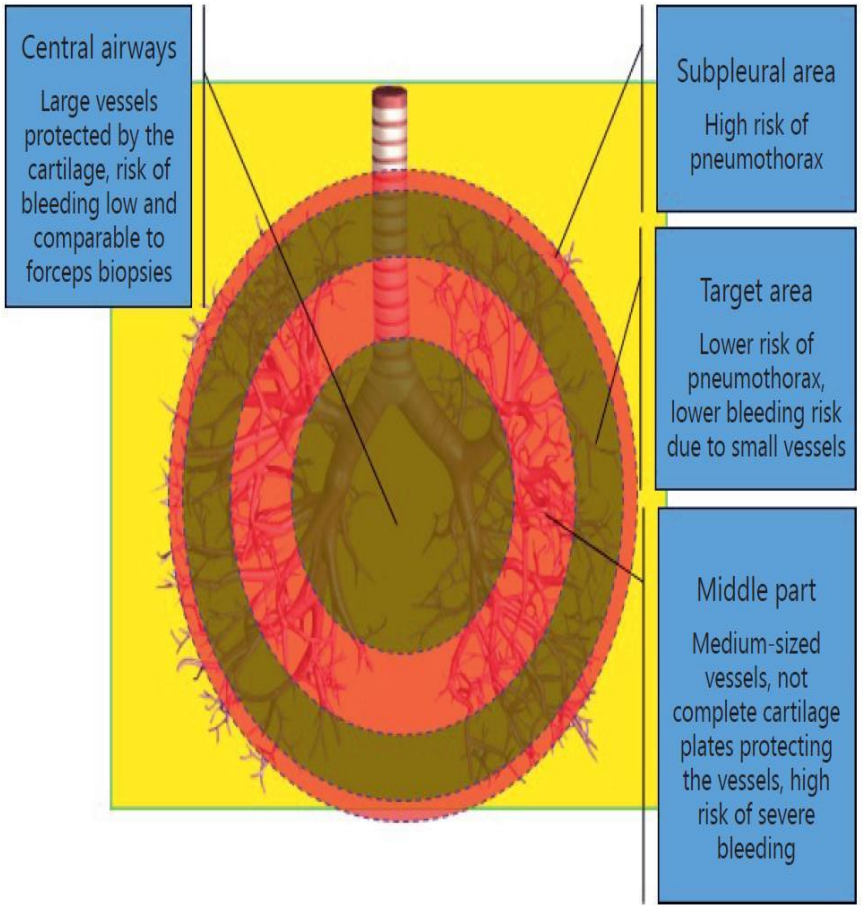
IPF suspected*		Histopathology pattern			
		UIP	Probable UIP	Indeterminate for UIP	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)**	Non-IPF dx
	Indeterminate for UIP	IPF	IPF (Likely)**	Indeterminate for IPF***	Non-IPF dx
	Alternative diagnosis	IPF (Likely)**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

Target location of cryobiopsy



Respiration (2018);95:188-200

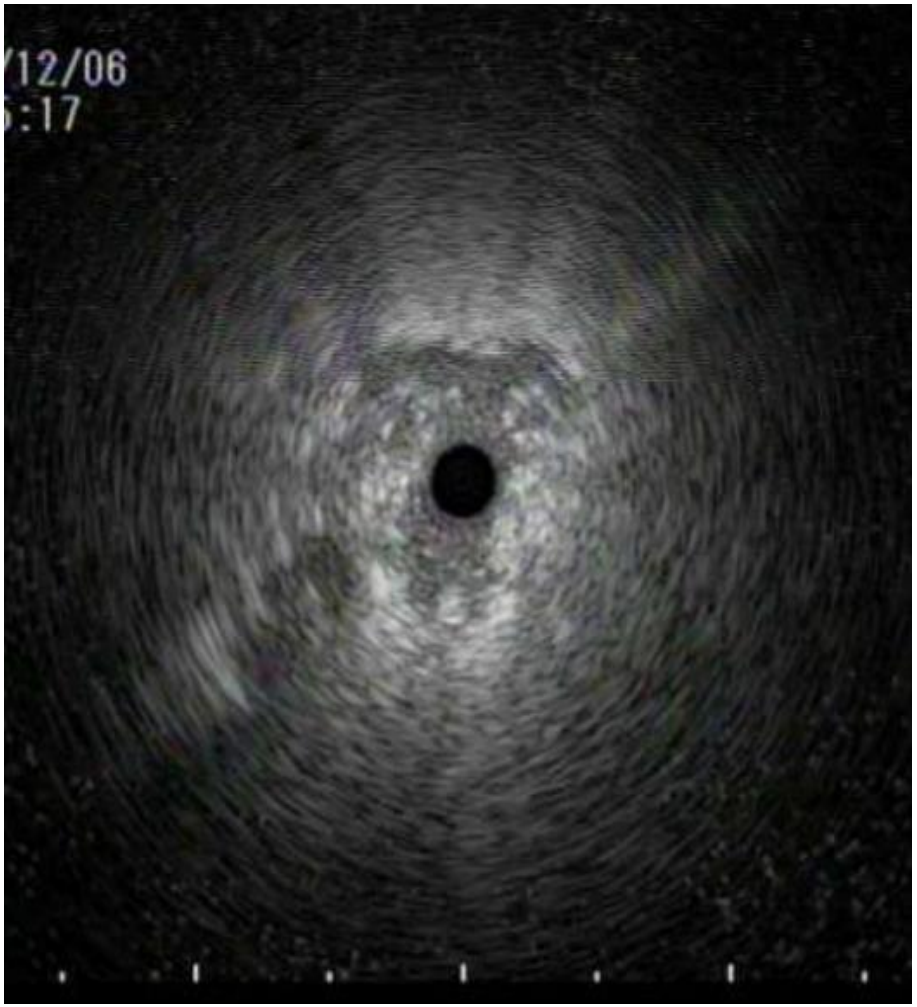
Target location of cryobiopsy



Respiration (2018);95:188-200

Cryobiopsy with radial endobronchial ultrasound

Cryobiopsy with radial endobronchial ultrasound



Characteristics of good diagnostic test

Minimally invasive

Diagnostic yield

Inexpensive

Safety

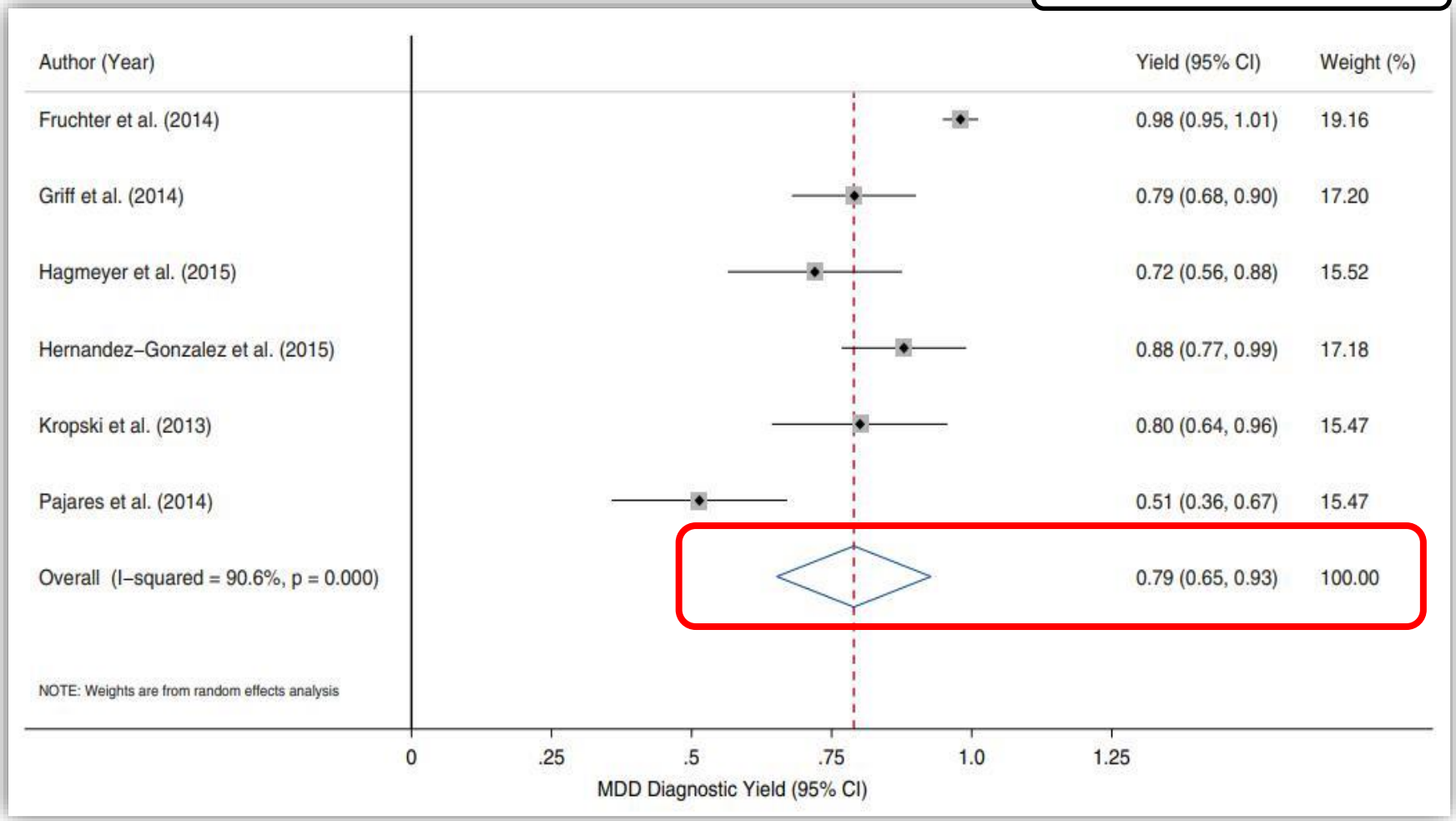
Large biopsy specimens

Multiple sites for spatial heterogeneity

Minimal crush artifact

Diagnostic yield of TBLC

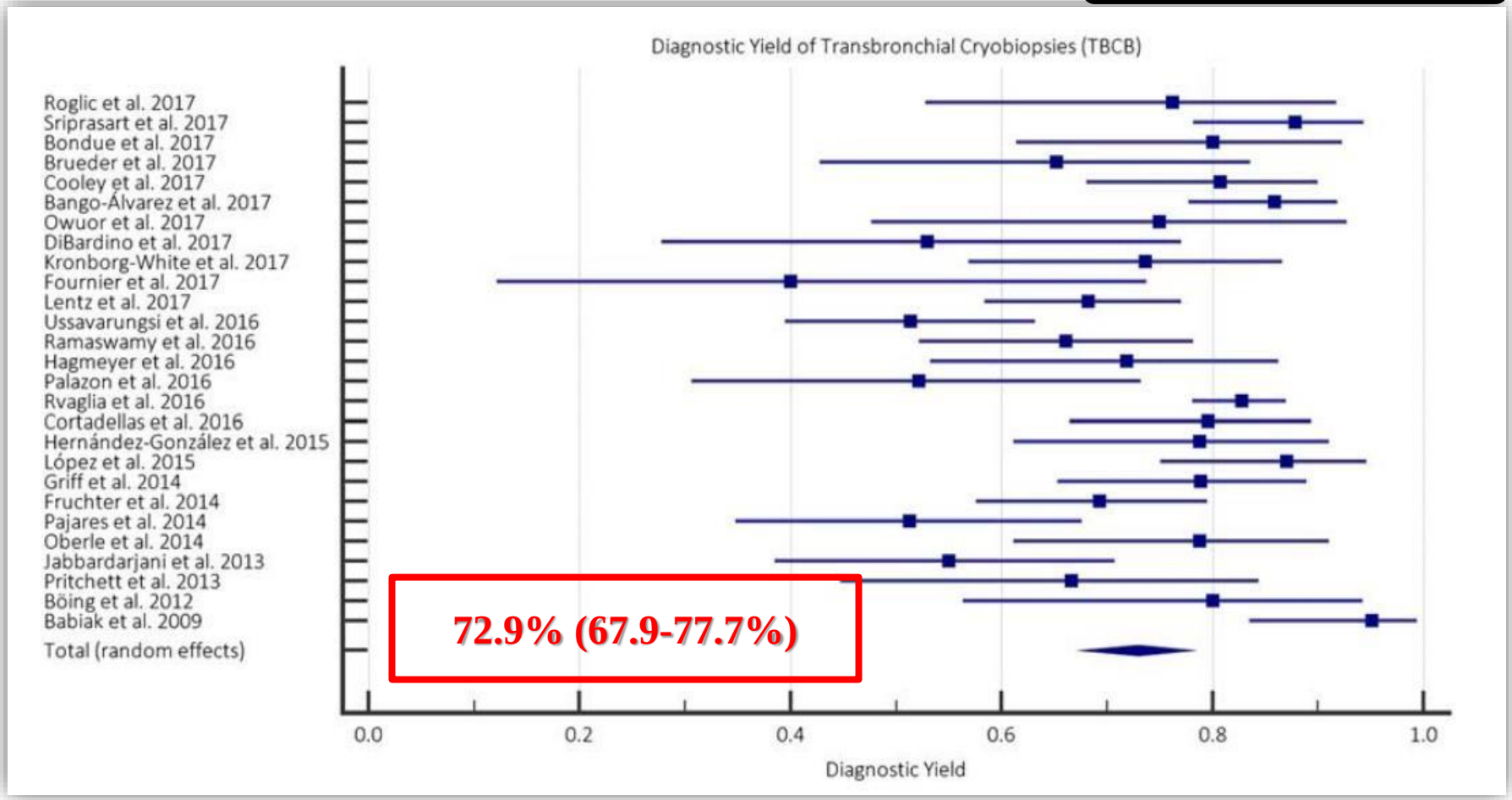
11 studies, 731 TBLC



AnnalsATS 2016; 13(10):1828-1838

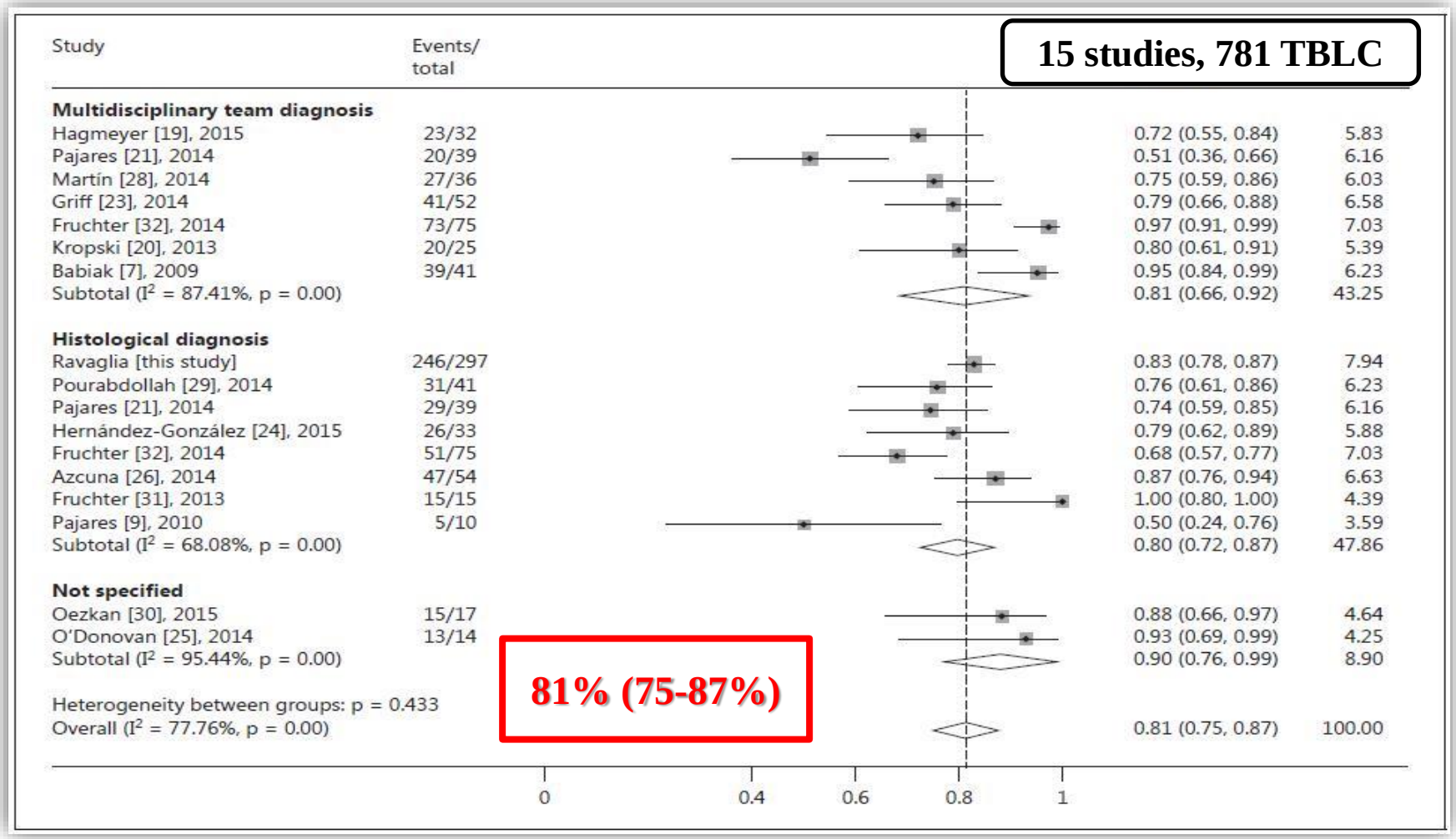
Diagnostic yield of TBLC

27 studies, 1443 TBLC



J Bronchial Intervent Pulmonol 2019;26(1)

Diagnostic yield of TBLC



Respiration 2016;91:215-227

COLDICE study

MDD

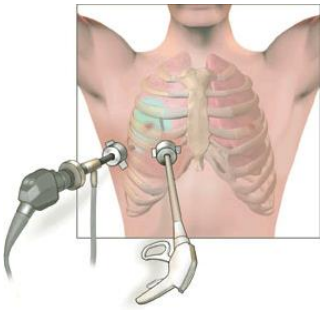
- ILD 진단 조직검사 필요

TBLC

- 최소 2곳 검체

VATS

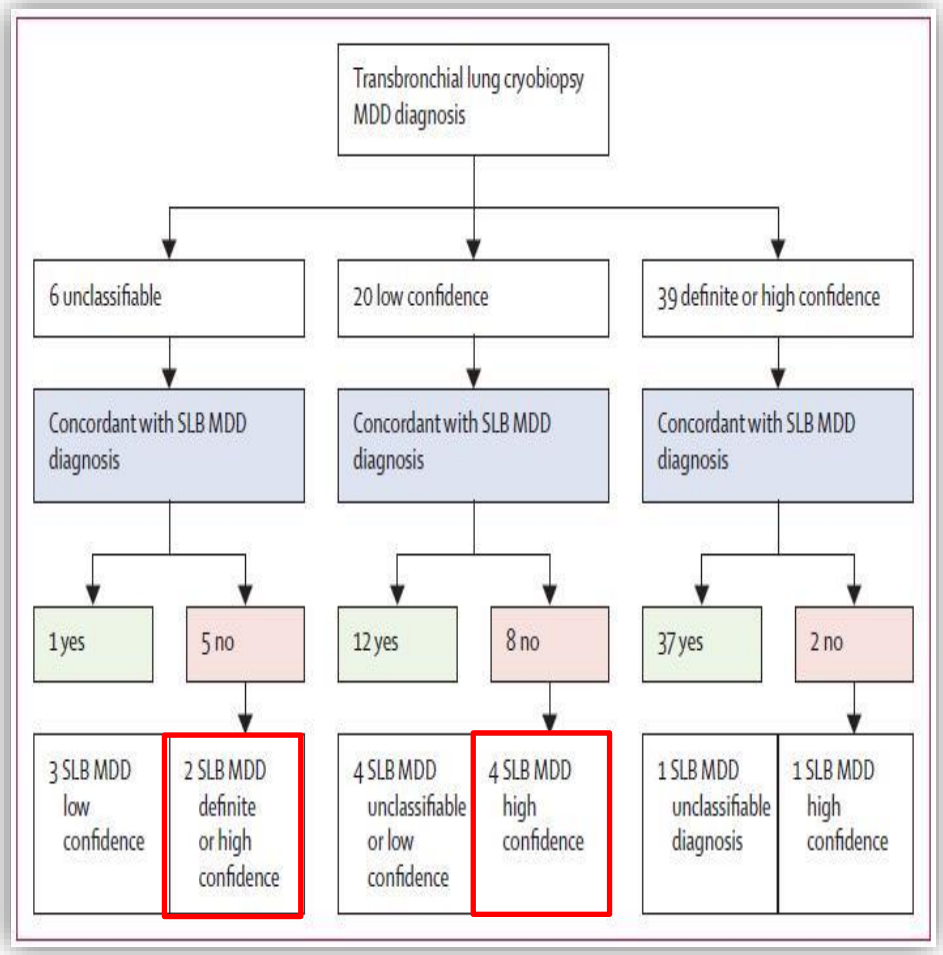
- VATS 시행



MDD

- 영상의학과, 병리과, 호흡기내과 MDD 진단

Diagnostic accuracy of transbronchial lung cryobiopsy for interstitial lung disease diagnosis (COLDICE): a prospective, comparative study



Mean tissue 7.1 mm
SLB – mean 46.4mm, hospital length median 4

- Primary outcome

1) Histopathological assessment, agreement between TBLC and SLB: 70.8% with k of 0.70

2) MDD diagnosis, agreement 76.9% with k of 0.62

- In high confidence or definite final MDD: 39 (60%) of TBLC and 48 (74%) of SLB
- In high confidence or definite final MDD, concordance was 37 (95%) of 39 TBLC

Lancet Respir Med 2019

Diagnostic accuracy of transbronchial lung cryobiopsy for interstitial lung disease diagnosis (COLDICE): a prospective, comparative study

- ✓ Good agreement of pathology and MDD diagnosis between TBLC and SLB in same patients, especially high confidence of TBLC
- ✓ Clinical utility for interstitial lung disease within MDD
- ✓ Experienced proceduralist (intervention specialist)

- ✓ Not enough data for complications of TBLC (study design and patient selection for SLB)
- ✓ Probable UIP more common in TBLC than SLB
- ✓ Low diagnostic yield for specific diagnosis other than UIP

Safety of TBLC

- Mortality rate (TBLC vs VATS: 1/297 [0.3%] vs 4/150 [2.7%], p = 0.045)
- Severe bleeding [hemodynamic or respiratory instability, tamponade or surgical interventions, transfusion or ICU care]

  → 0% - 6.3% (median: 1.1%)
- Moderate bleeding [bleeding controlled by endobronchial blocker]

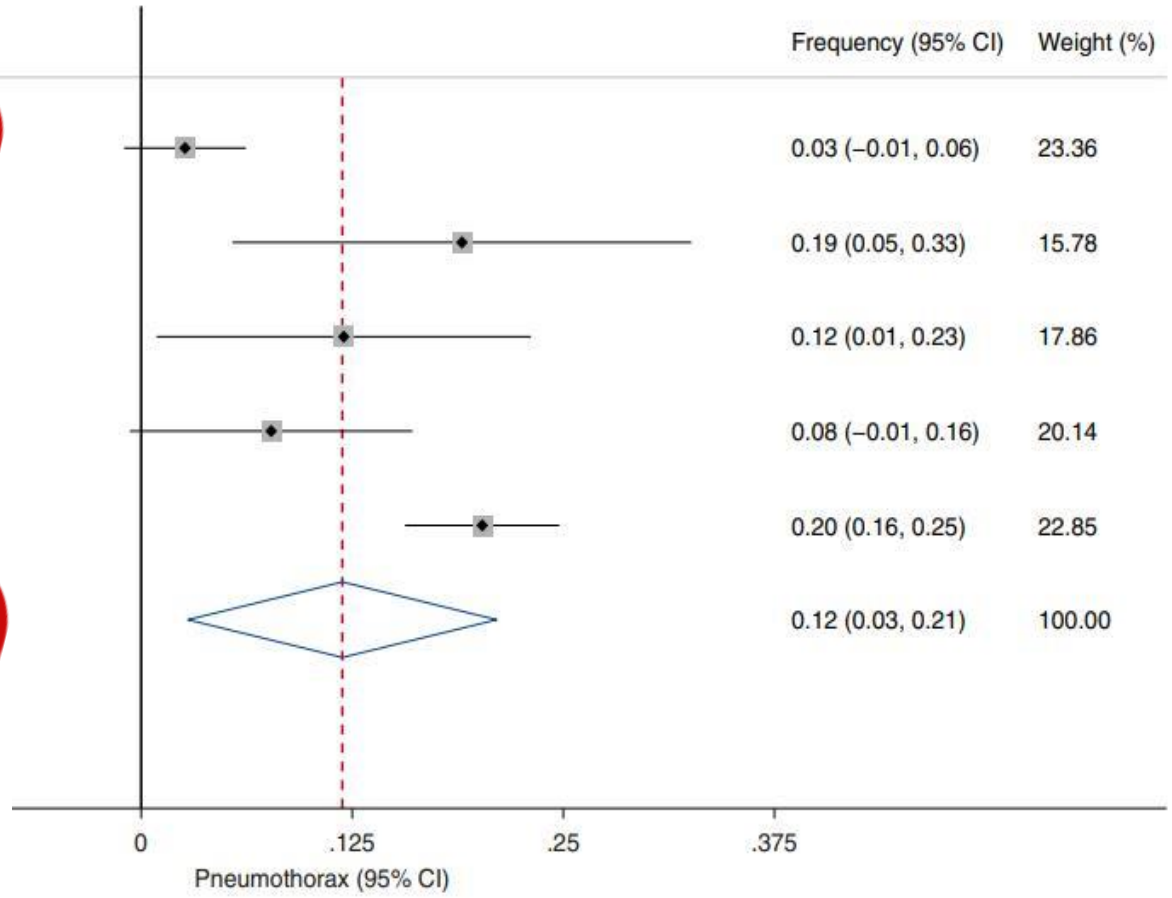
  → 1.8% - 47%
- Acute exacerbation rate (TBLC vs SLB: 1/297 [0.3%] vs 5/150 [3.3%], relative risk of 0.10 [95% CI, .012-0.85])
- Hospitalization time (TBLC vs SLB: 2.6 days vs 6.1 days, p < 0.0001)
- Pneumothorax rate: 1.4% - 20.2% (median: 9.5%) vs 100% in SLB
- **Lower rate of mortality and acute exacerbation in favor of TBLC compared with SLB**

Respiration 2016;91:215-227

Time of chest tube drainage → similar to time after VATS

High risk

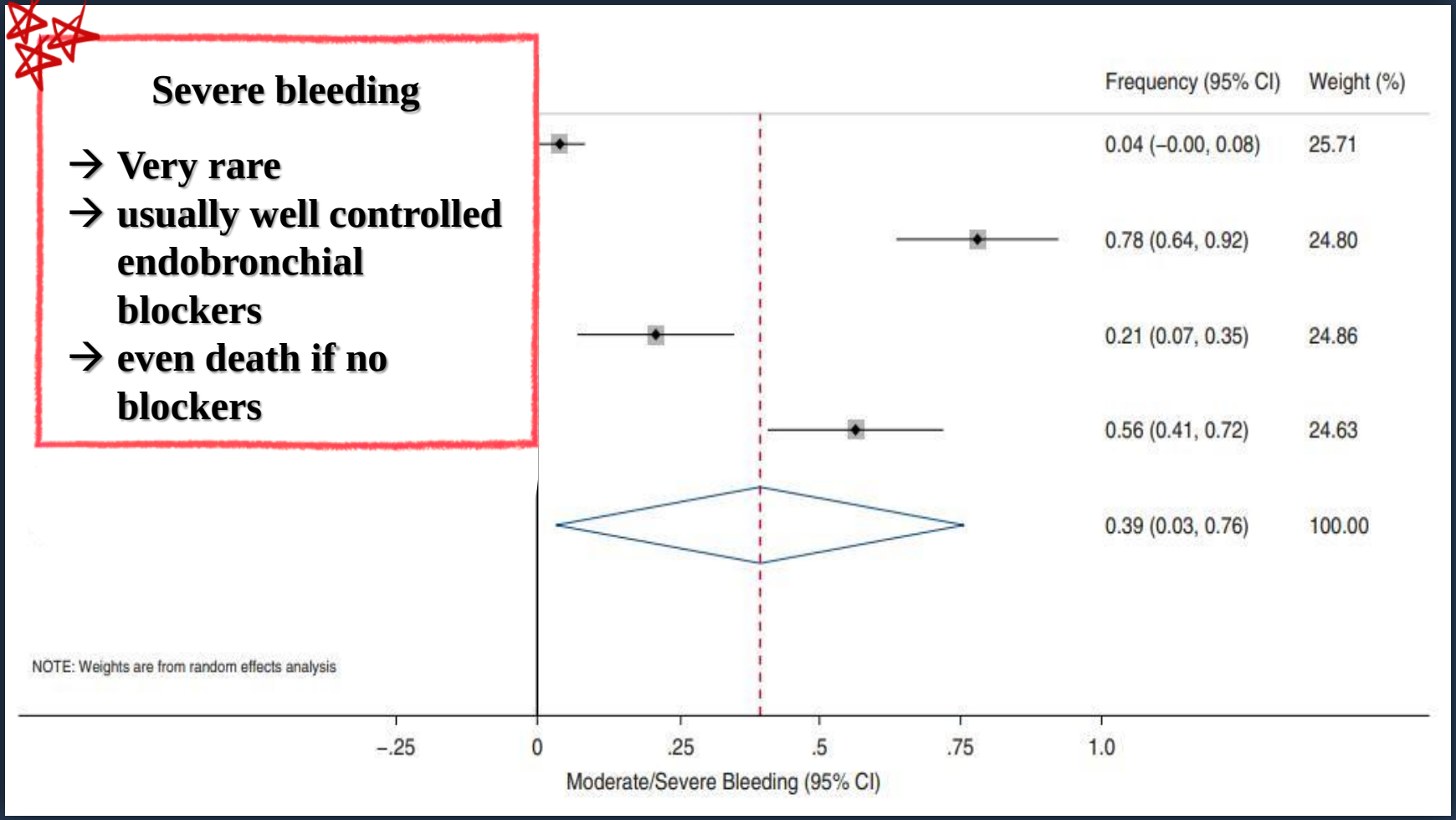
UIP histopathology
Fibrotic reticulation
Close to pleura



AnnalsATS 2016; 13(10):1828-1838

Severe bleeding

- → Very rare
- → usually well controlled endobronchial blockers
- → even death if no blockers



AnnalsATS 2016; 13(10):1828-1838

TBLC vs SLB in guidelines

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

AJRCCM 2018; 198

[Thoracic Oncology Guidelines and Consensus Statements]

CHEST

Transbronchial Cryobiopsy for the Diagnosis of Interstitial Lung Diseases

CHEST Guideline and Expert Panel Report

Check for updates

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

  (Weak Recommendation, Very Low-Quality Evidence)

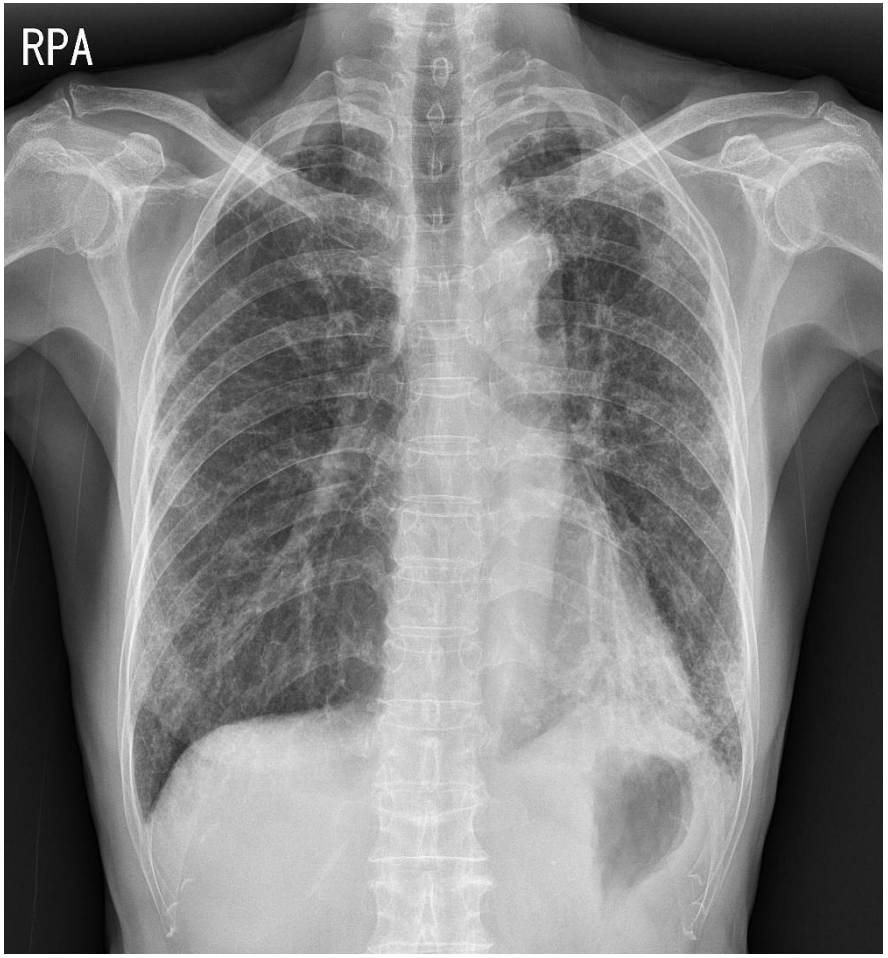
- The choice between **TBC** and surgical lung biopsy **(SLB)** should be based on **local availability** and **expertise**, **benefit-risk assessments**, and **patient preference following informed consent.**

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

Cons

- Diagnostic yield(-) → SLB or not ?
- Availability
- Cryobiopsy team
- Cost benefit
- Profitability
- Expertise (pulmonologist and pathologist)

Case



F/68
mMRC gr 2

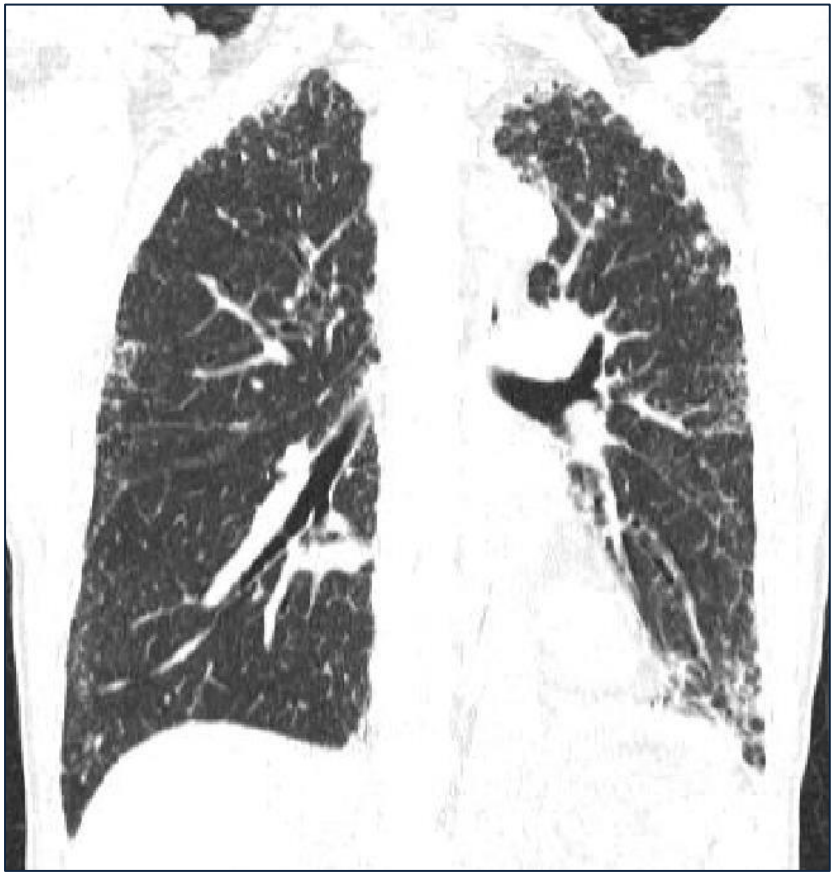
- PFT

Ratio	88 %
FVC	53 %
FEV1, predicted	59%
DLco, corrected	54 %

- 6MWT

	Baseline	End of test
Heart rate	89	117
Dyspnea(Borg scale)	1	3
Fatigue(Borg scale)	0	0
SpO2	96	84
Total distance walked in 6 minutes: 309m		

Case



Upper lung pre-dominant
or
Upper lung and lower lung co-involvement

경기관지 폐냉동생검

평가사업단-1913

보건의료 근거창출을 선도하는 전문기관

NECA 한 국 보 건 의 료 연 구 원

수 신 인제대학교 해운대백병원
(경유)
제 목 '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.

Ideal diagnostic tool for ILD

• Minimally invasive	**TBLC > VATS**
• Large biopsy specimens	**TBLC < VATS**
• Multiple sites for spatial heterogeneity	**TBLC ~ VATS**
• Diagnostic yield	**TBLC < VATS**
• Inexpensive	**TBLC ~ VATS**
• Minimal crush artifact	**TBLC ~ VATS**
• Safety compared to SLB	**TBLC > VATS**

Summary

- Diagnostic yield (MDD > Histopathologic)
- Safety
- Indication
- Hurdles in Korea
- Experienced center

  (interventional bronchoscopist and pathologist)
- Safety >>> Diagnostic yield

감사합니다