# IPF in practice

## Personalizzare l'algoritmo terapeutico

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# Utilità e limiti della criobiopsia: l'esperienza dell'ospedale San Giuseppe

*Sergio Harari*

*U.O. di Pneumologia e Terapia Semi Intensiva UTIR*
*Servizio di Fisiopatologia Respiratoria ed Emodinamica Polmonare*
*Ospedale San Giuseppe – MultiMedica Milano*

# Utility of a lung biopsy for the diagnosis of IPF

- Clinical and radiologic data that result in a confident diagnosis by a pulmonologist or radiologist with extensive experience in the care of patients with interstitial lung diseases are sufficient to obviate the need for a lung biopsy.
- For these clinicians, the sensitivity, specificity, accuracy, and positive predictive value of a confident diagnosis are very high.
- It is important to note, however, that a confident clinical diagnosis of IPF identified only one-half of the patients who actually have this disorder.



Hunninghake GW et al. *AJRCCM* 2001; 164:193

diagnostic agreement and accuracy for IPF between expert physicians and their respective MDT meetings is similar

Walsh SL et al. Lancet Respir Med 2016; 4: 557

TABLE 5 Comparisons of weighted kappa values ($\kappa_w$) for interobserver agreement on the diagnostic likelihood of a diagnosis of idiopathic pulmonary fibrosis between various subgroups

| Group comparisons | Interobserver agreement ($\kappa_w$) | p |
|---|---|---|
| Physicians, expert panel (n=34) | 0.65 (IQR 0.53–0.72) | <0.001 |
| Remaining physician group (n=370) | 0.53 (IQR 0.41–0.63) | |
| University hospital physicians (n=288) | 0.56 (IQR 0.45–0.65) | <0.001 |
| Non-university hospital physicians (n=116) | 0.49 (IQR 0.38–0.59) | |
| MDT meeting available (n=328) | 0.56 (IQR 0.45–0.65) | <0.001 |
| No MDT meeting available (n=76) | 0.46 (IQR 0.33–0.58) | |

MDT: multidisciplinary team.

Walsh SL et al. Eur Respir J 2017

# Utility of a lung biopsy for the diagnosis of IPF

Lung biopsy may be required for diagnosis :

- when patients are cared for by less experienced clinicians
- when the diagnosis is uncertain
- when the clinical diagnosis is not IPF



Hunninghake GW et al. *AJRCCM* 2001; 164:193

# How perform a good lung biopsy?

- Selection of areas to be sampled according to HRCT
- Multiple biopsies at least from two different areas, avoiding the tip of the lobes and the lingula
- Avoid areas with honeycombing
- Deep biopsies, as far as possible without artefacts, of adequate size (> 3 cm)
- Surgical biopsies should be inflated with fixative to avoid specimen atelectasia



Hunninghake GW et al. *AJRCCM* 2001; 164:193

- VATS lung biopsy for diagnosis of ILD, is not an entirely benign procedure.
- Biopsy rarely may trigger an acute exacerbation of IPF.
- The risk of post-operative complications appears to be greatest in those dependent on oxygen and those who have pulmonary hypertension and low DLCO.
- This information may be used in weighing the risk– benefit ratio of biopsy in individual patients

Kreider et al, Ann Thorac Surg 2007; 83, 1140
Durheim et al. Ann Thorac Surg 2017; 104: 465

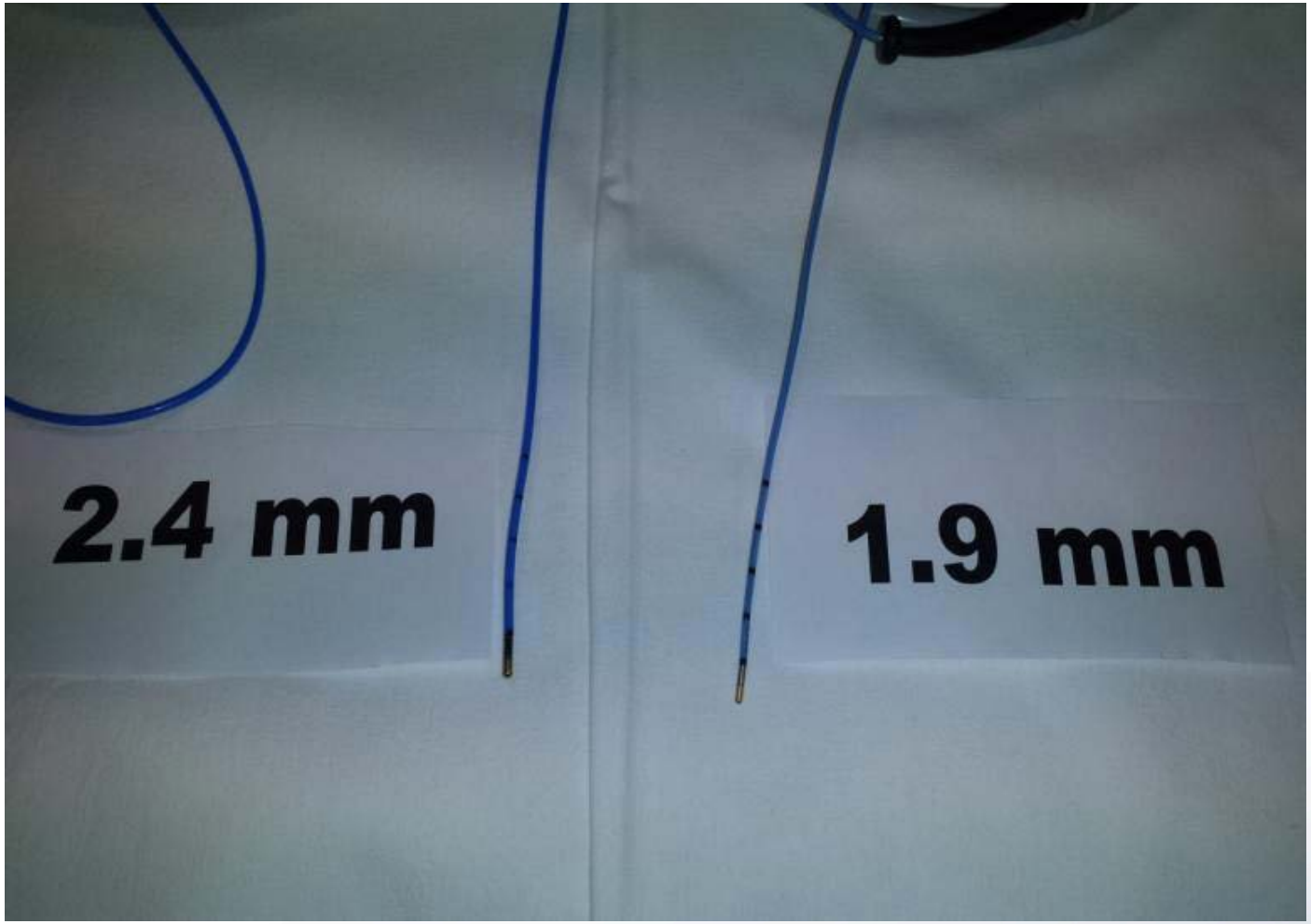
**Lung Biopsy is performed in a small number of patients**

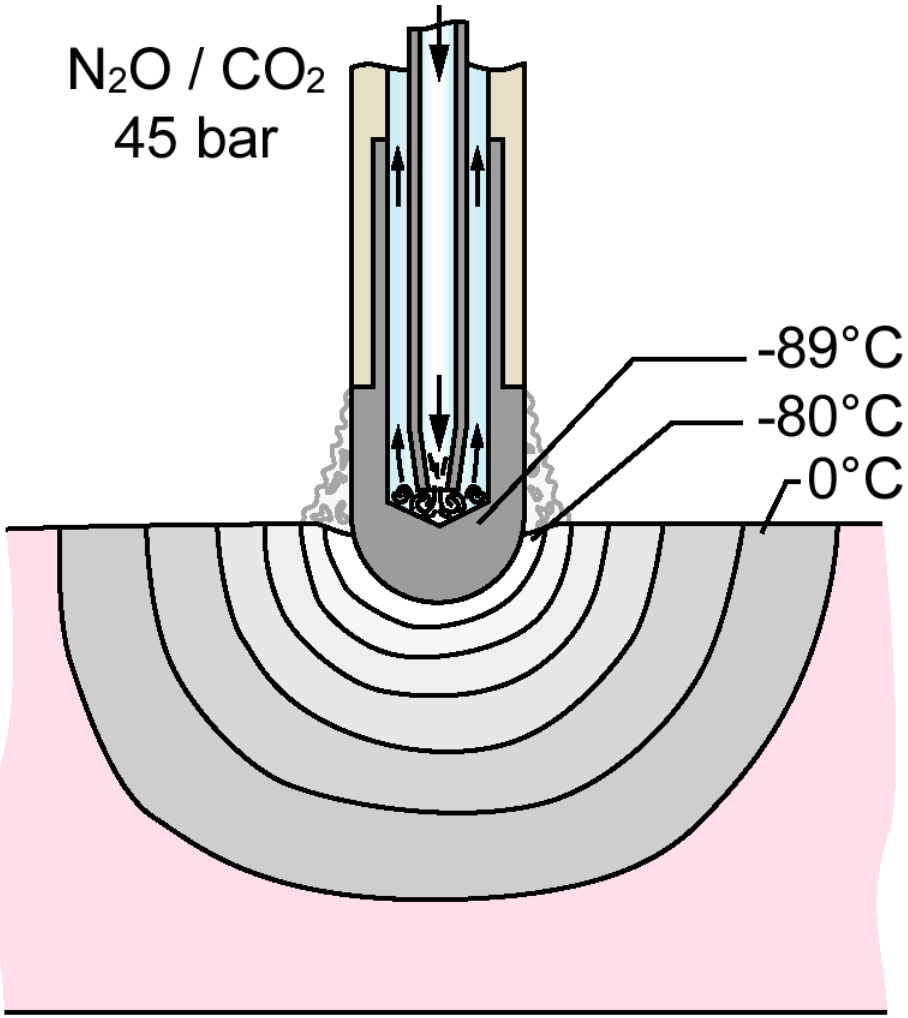
# Transbronchial cryobiopsy

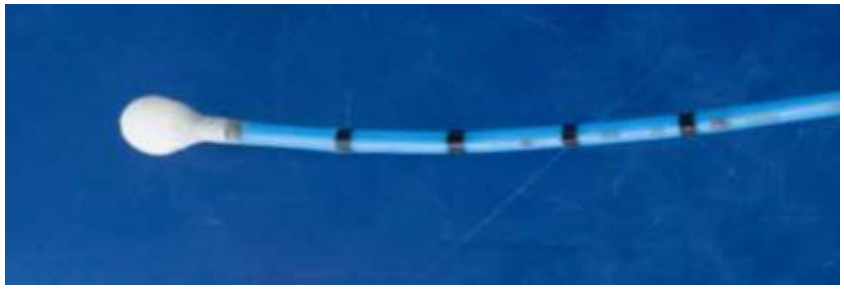
- The thecnique of CryoBx in DPLD: a call for standardization
- CryoBx: safety issue
- Diagnostic yeld and utility of Cryo for DPLDs
- Cryo: a paradigm shift in the diagnosis of DPLDs

# Cryobiopsy: the equipment

# Different size of cryoprobe





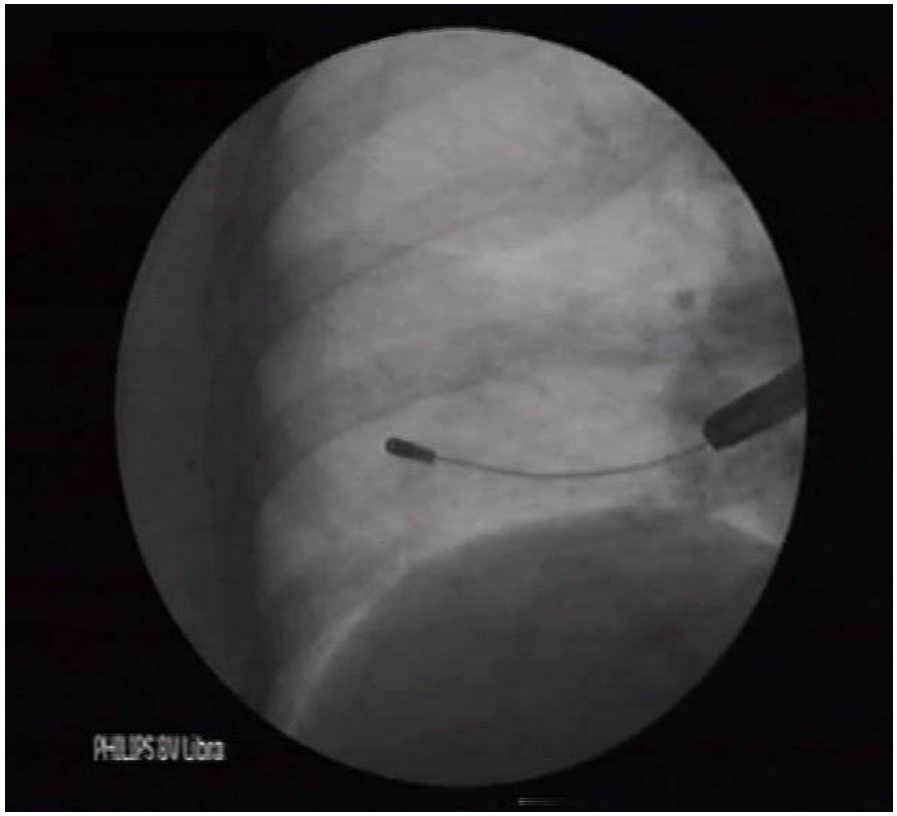



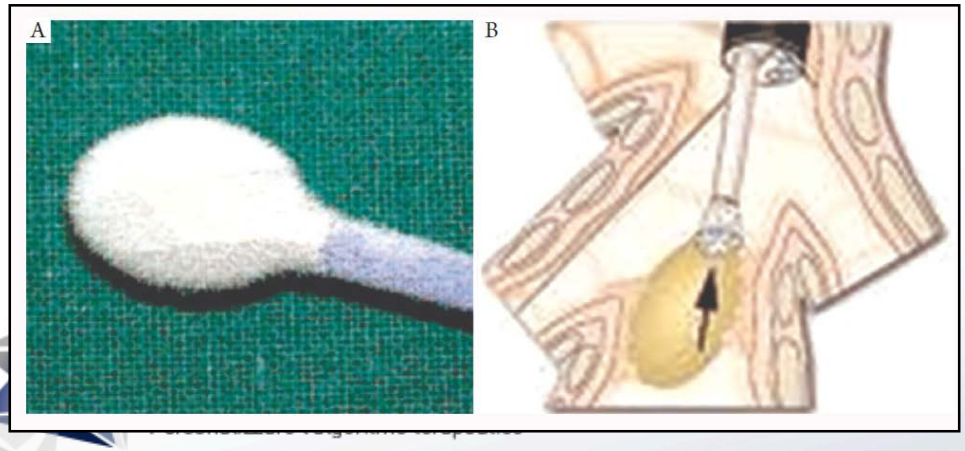
**Cryoprobe with water iceball**

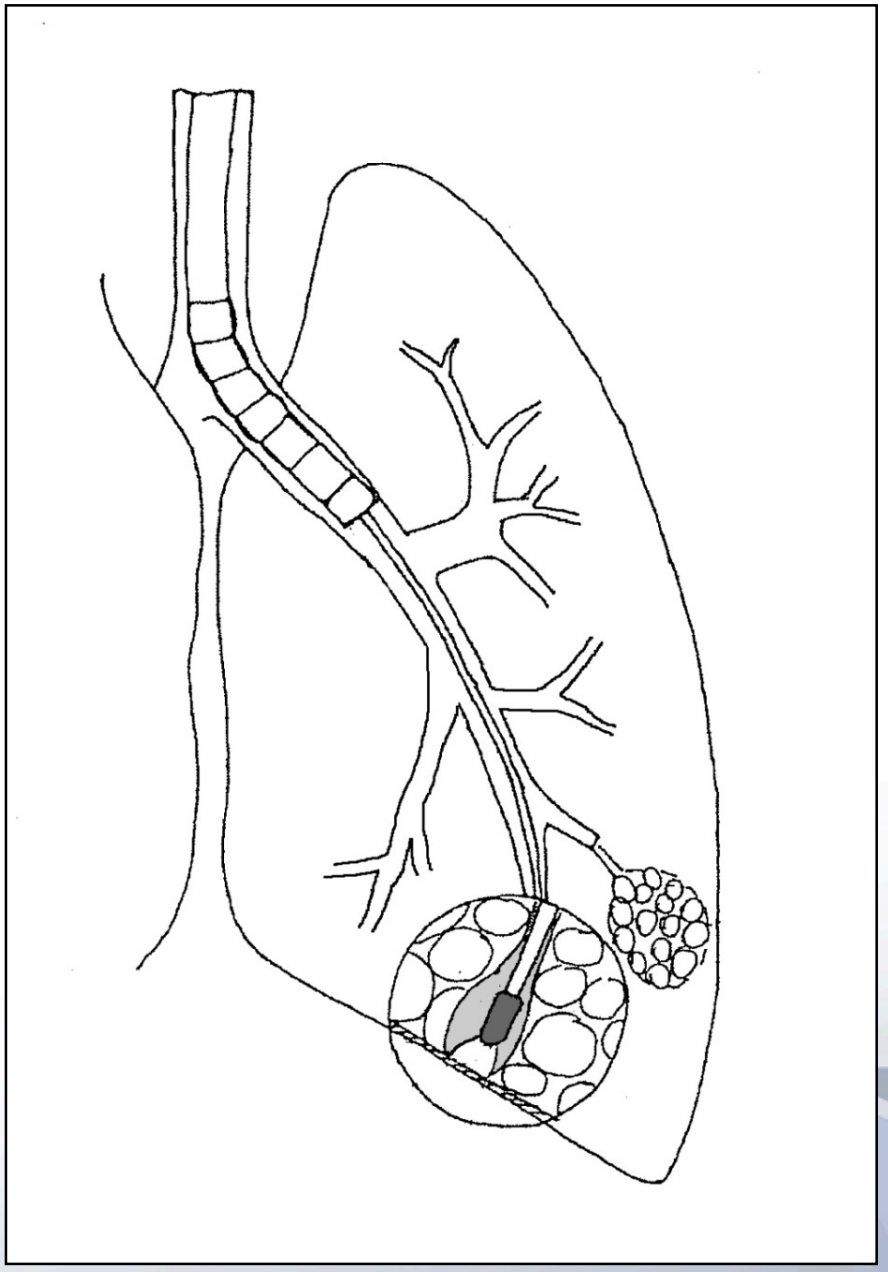
**Cryoprobe with tissue-iceball**

The gas at the tip expands due to the sudden difference in pressure **(Joule-Thomson effect), resulting in a drop in** temperature at the tip of the probe.

# Cryobiopsy: the technique



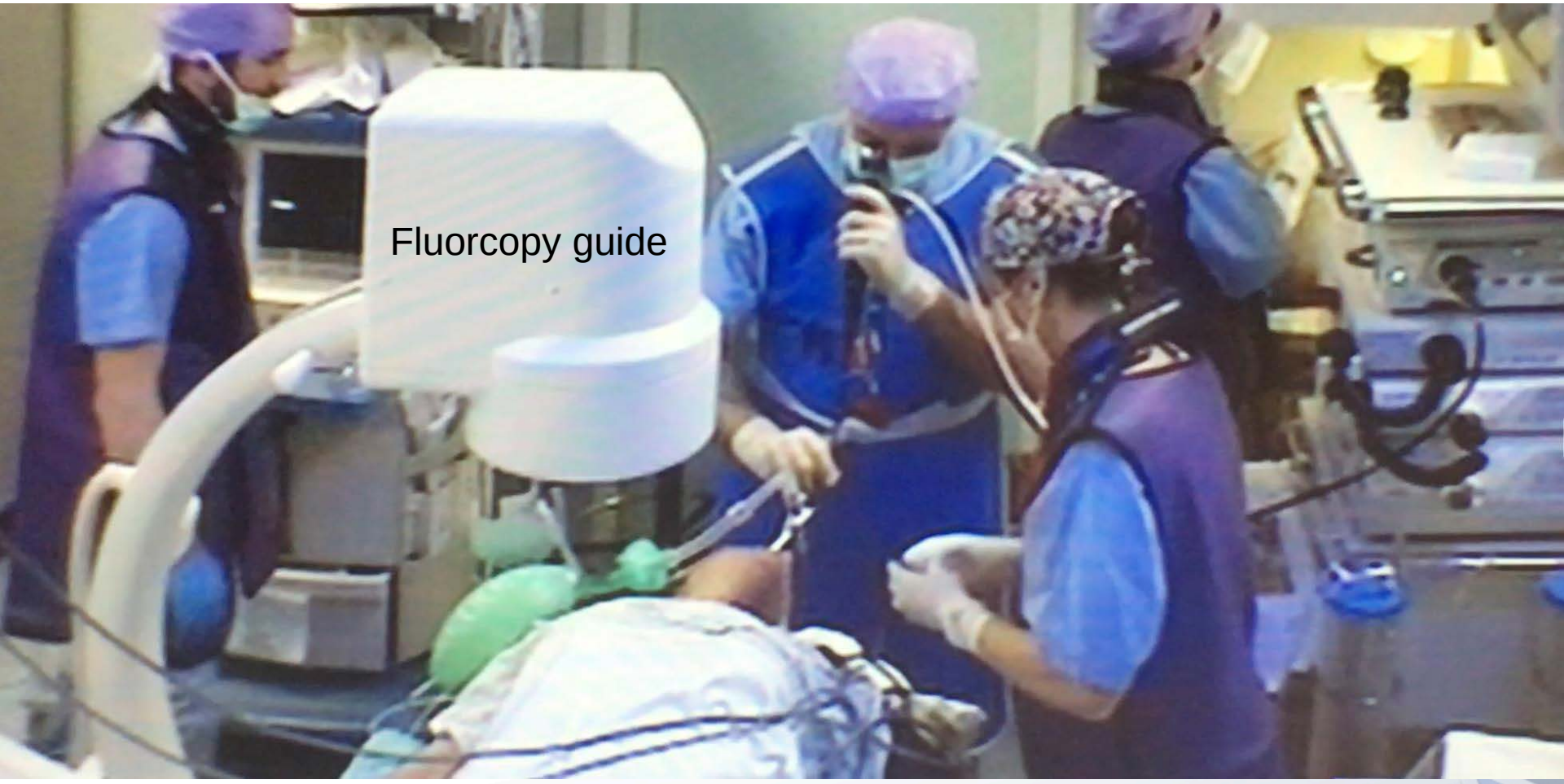



1 anesthesiologist

1 bronchoscopist

2 endoscopy nurses

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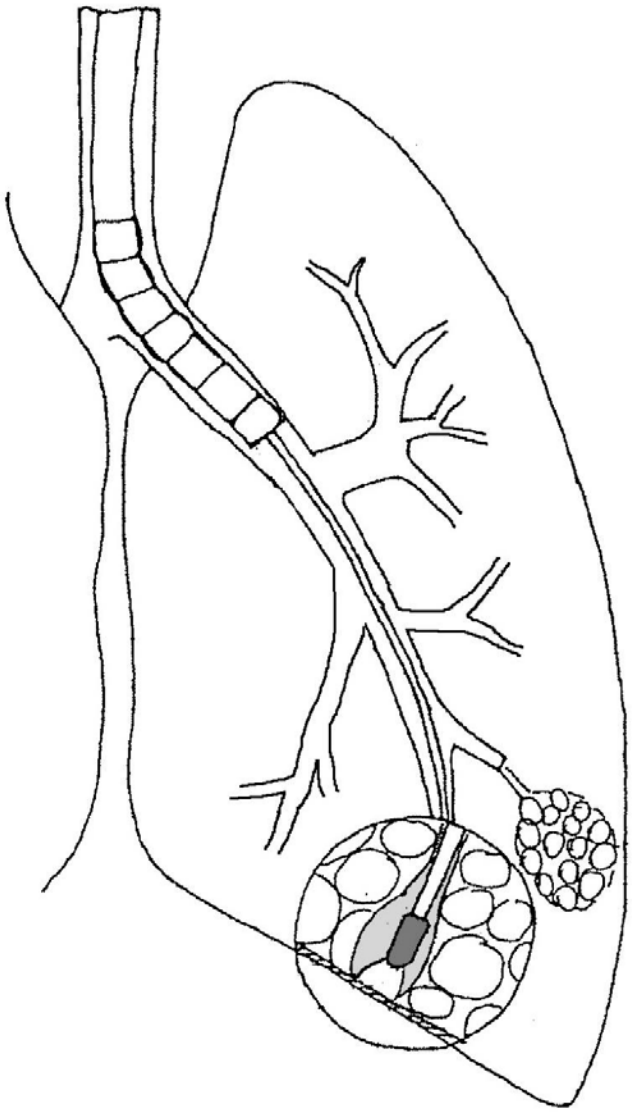
# The endoscopy room



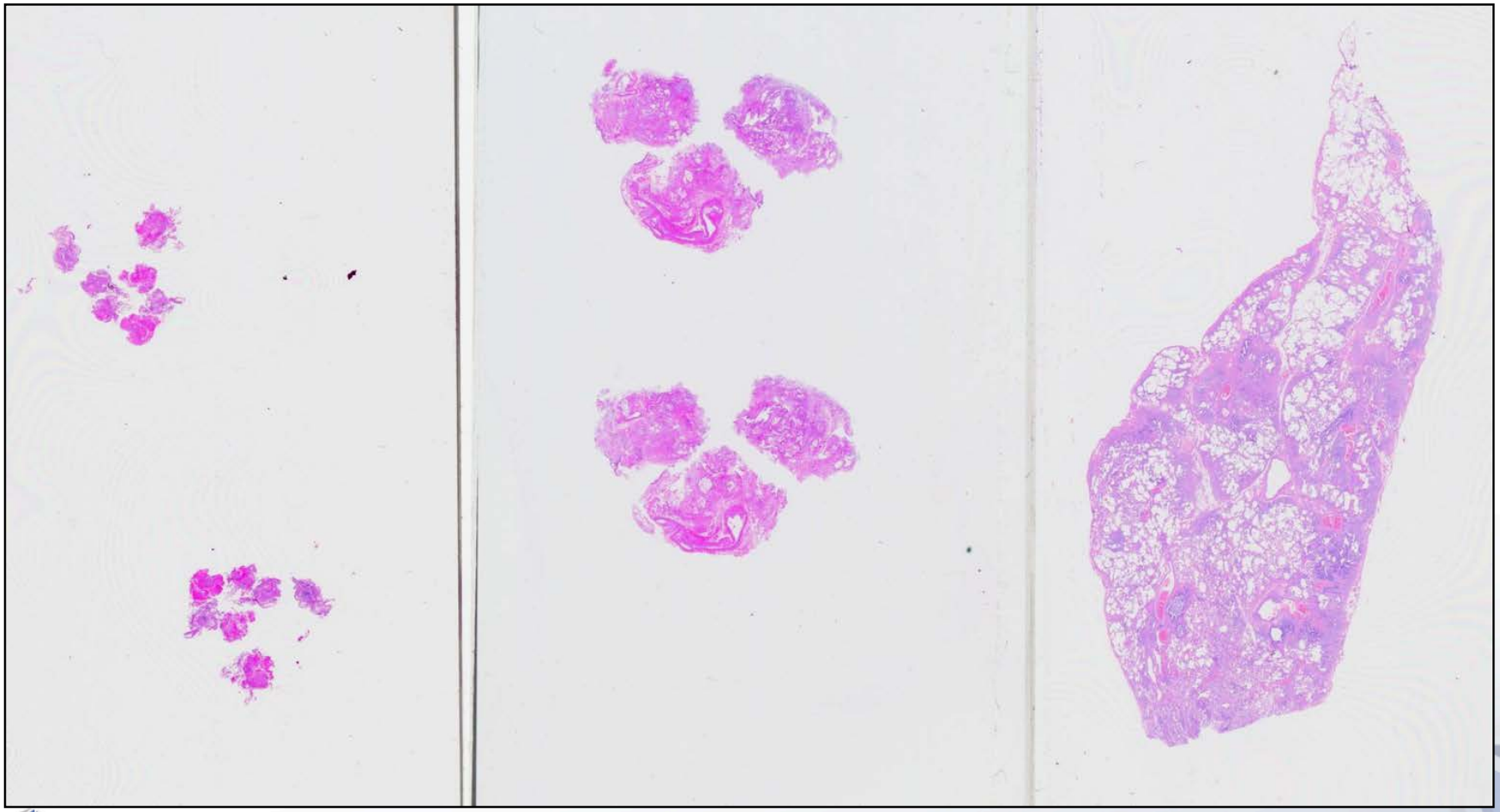
# Transbronchial cryobiopsy San Giuseppe H's recipe

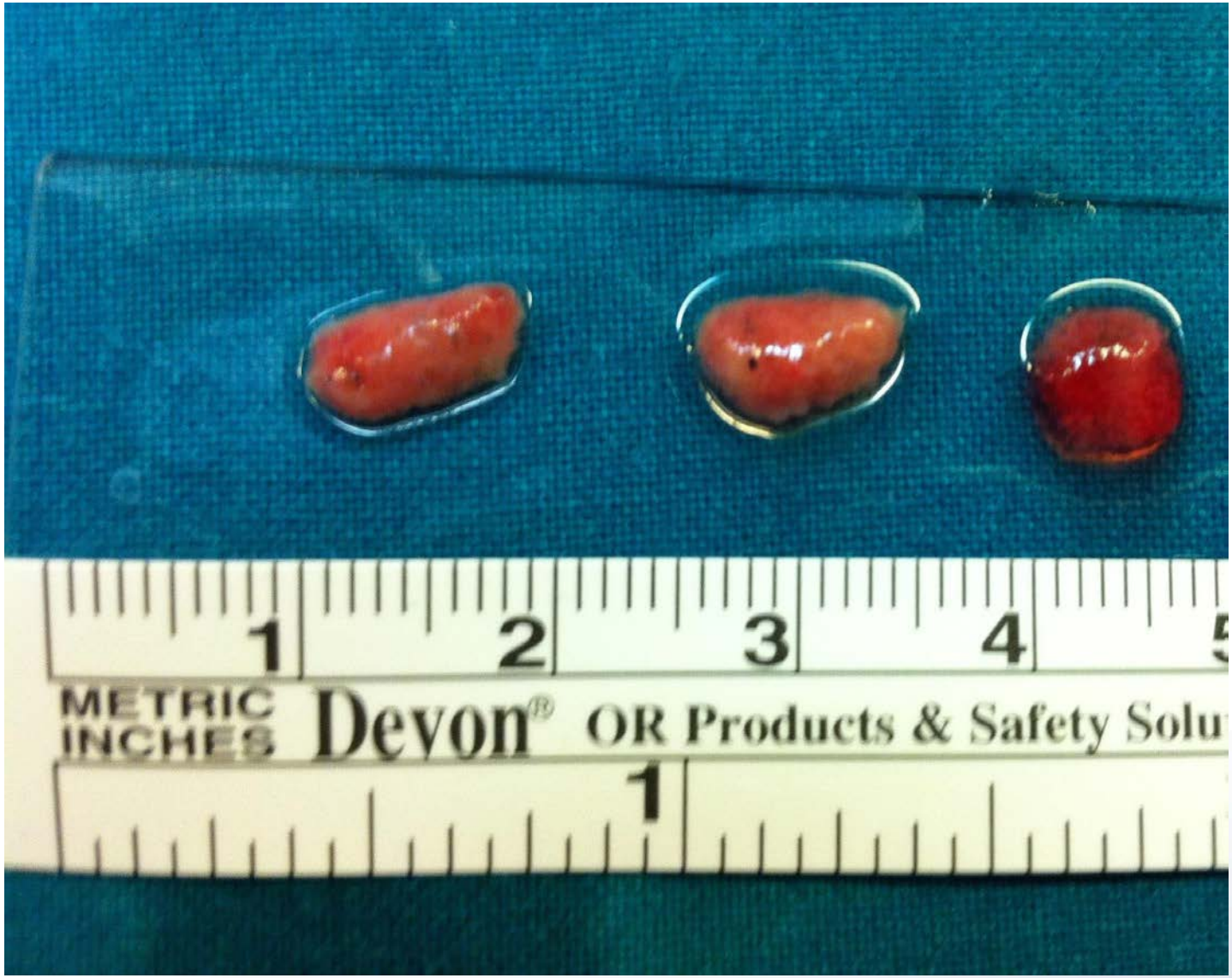
- General anesthesia
- Intubated patient
- Fiberoptic bronchoscope
- Fogarty balloon
- Fluoroscopic control
- Cryoprobe 1.9 mm
- A distance of approximately <= 10 mm from the thoracic wall
- The 1.9 probe is cooled for > 7-8'



**3-4 samples: it takes 20 minutes!**

# TBB Cryobiopsy Lung biopsy

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# Specific concerns

with regard to the rapid spread of the technique without competency and safety standards

Major reported variability in:

- Technique (intubation, sedation, b.blockers, fluoroscopy guide)
- Diagnostic yield (50-100%)
- Bleeding risk (53%-0%) and PNX risk (0-20%)

# It’s not a banal technique!

- intubated patients under deep sedation or general anesthesia.
- Fogarty ballon or an endobronchial blocker have to be used prophylactically
- fluoroscopic guidance always
- interventional pulmonologists trained at a center with experience in TBCs.
- full anesthesia support, emergency procedures with possibility to escalate care (management of massive hemoptysis and tension pneumothorax after or during the bronch), eventual admission to ICU

# TBLC: where?

- 1 cm or even < from the pleura
- More affected zones (assessed by HRCT)

# Transbronchial cryobiopsy

- The thecnique of CryoBx in DPLD: a call for standardization
- CryoBx: safety issue
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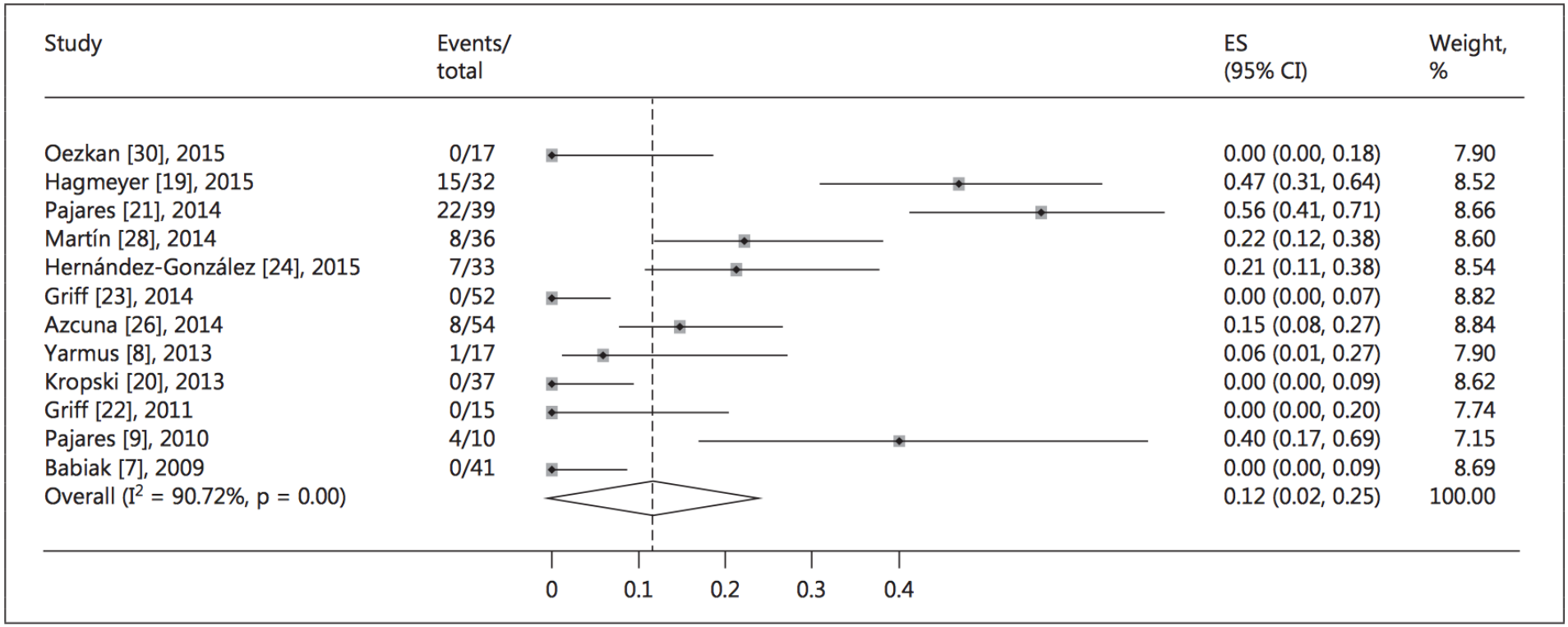
# Risk of moderate bleeding




The **overall pooled probability of developing a moderate bleeding,** as derived from 12 studies including 383 patients, was **0.12** (95% CI 0.02–0.25)



Ravaglia C et al, Respiration 2016

# PNX is the most frequent procedure related event

CRYO, N=297

- Pneumothorax, 20% (N=60)

->Chest drainage 15% (46/297), 76%(46/60)

VATS, N=150

- Pneumothorax is part of the procedure,

-> 100% chest drainage



Ravaglia C et al, Respiration 2016

# Cryo has significantly less complications, shorter hospitalization and lower costs compared to VATS

**All adverse events, excluding PNX:**

- Cryo 6/297 **0.2%**
- VATS 20/150 **13%**

P<0.0001

Median time of **Hospitalization, days:**

- Cryo **2.6 (0-17)**
- VATS **6.1 (3-48)**

P<0.0001



Ravaglia C et al, Respiration 2016

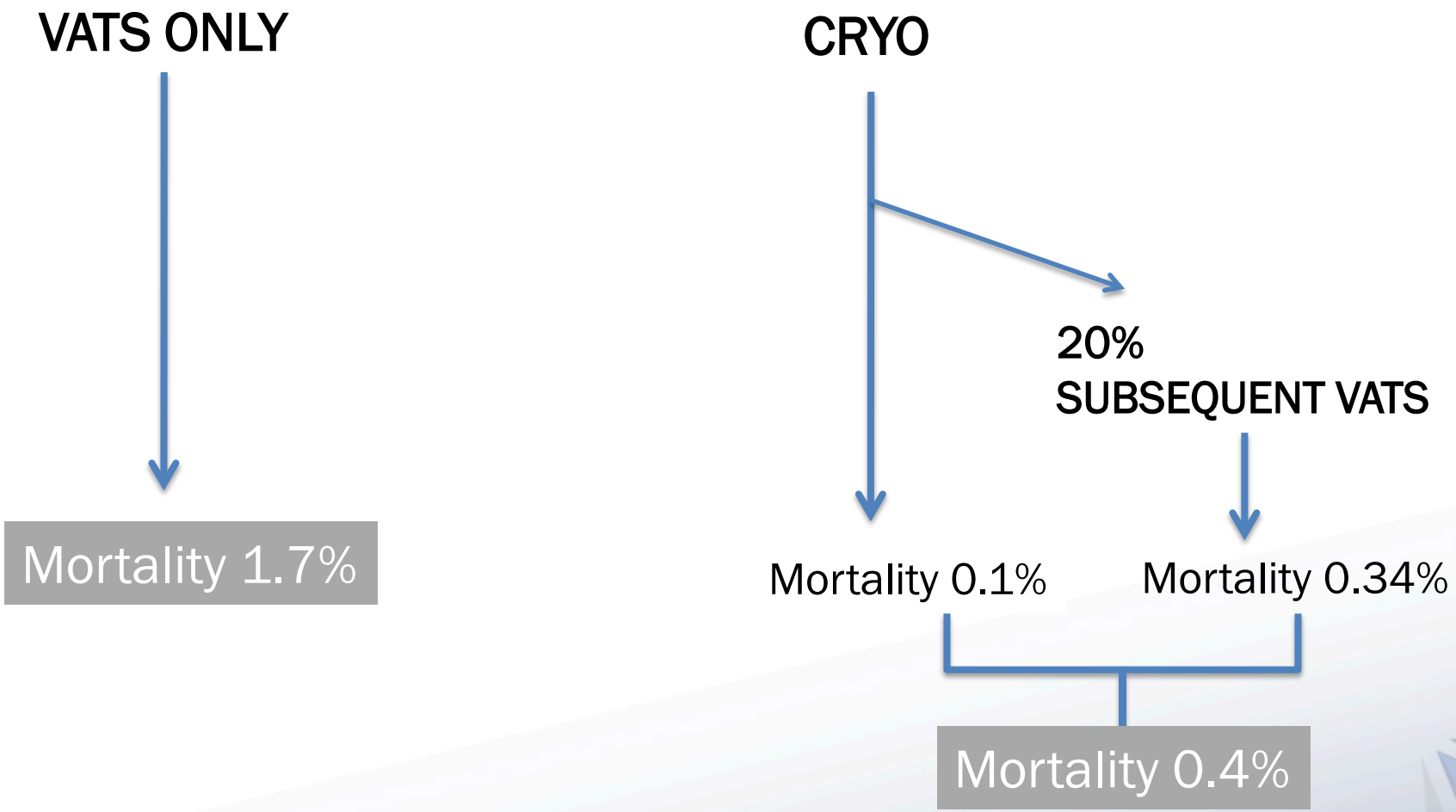
# A systematic review

1 death related to Cryo among 994 pts, 11 studies: **0.1%**



Ravaglia C et al, Respiration 2016

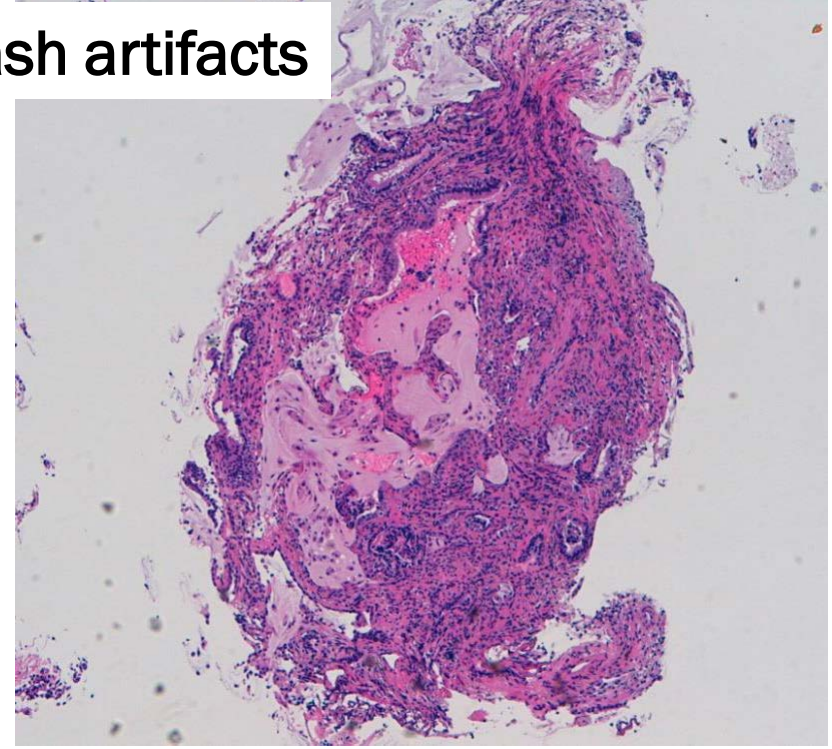
# CRYOBIOPSY HAS A LOWER DIAGNOSTIC YIELD COMPARED TO SLB (80% vs 98%), BUT IS SIGNIFICANTLY SAFER

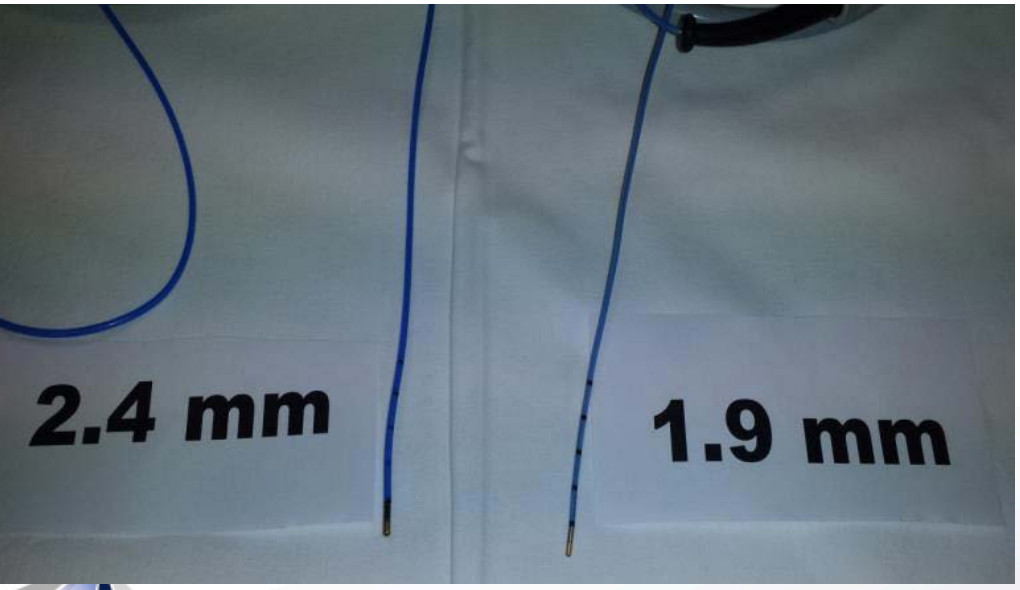


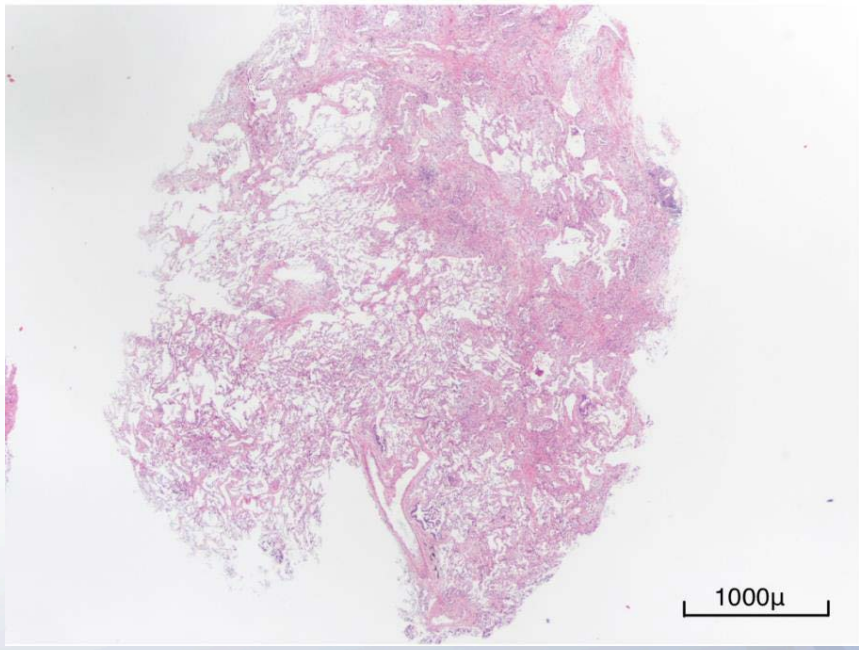


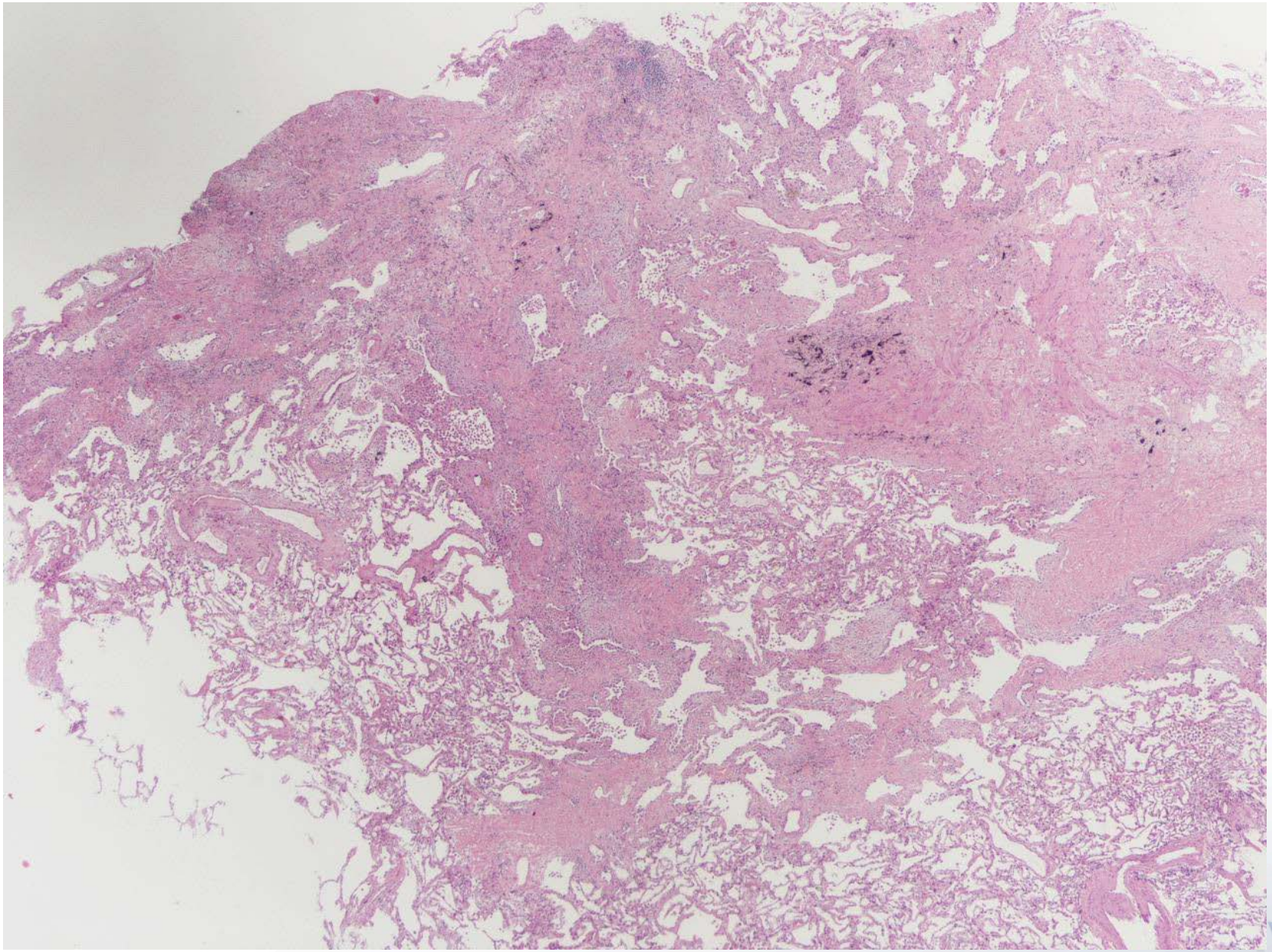

Ravaglia C et al, Respiration 2016

# Crash artifacts





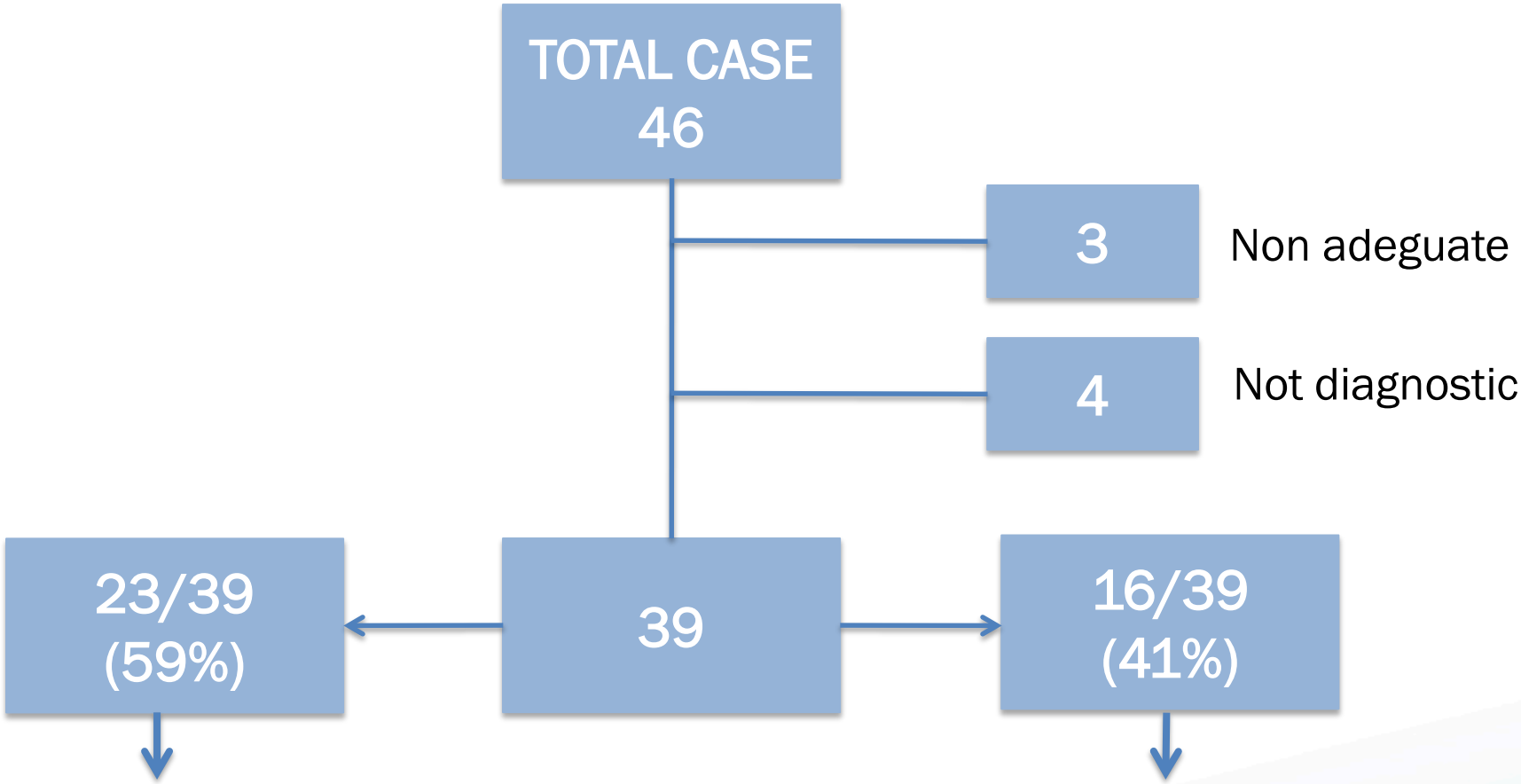


**Cryo has a meaningful impact on MDT diagnosis of ILDs, comparable to that of SLB.**



Tomassetti S, et al. Am J Respir Crit Care Med 2016

# San Giuseppe experience (july 2015 – 2017)

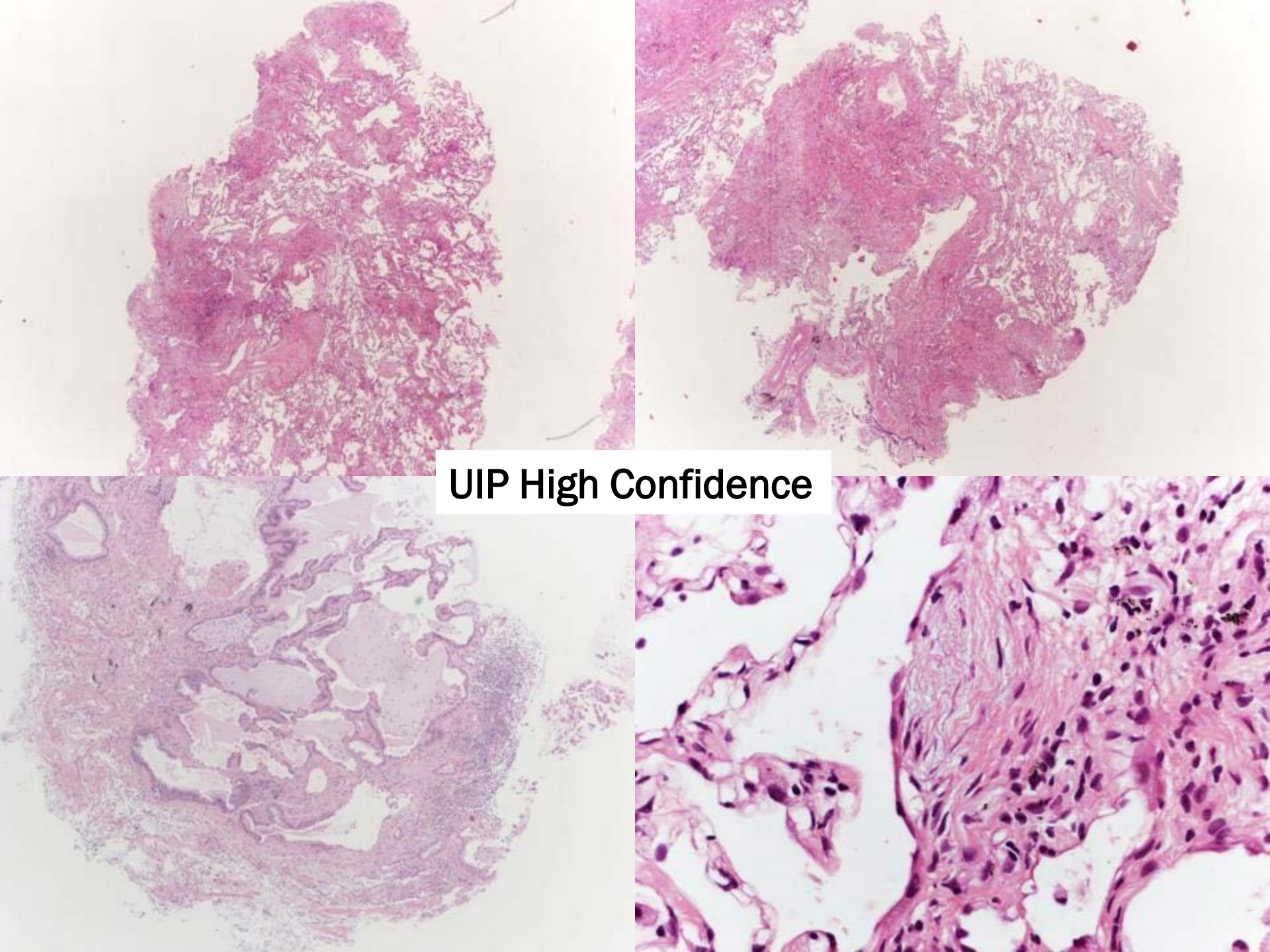


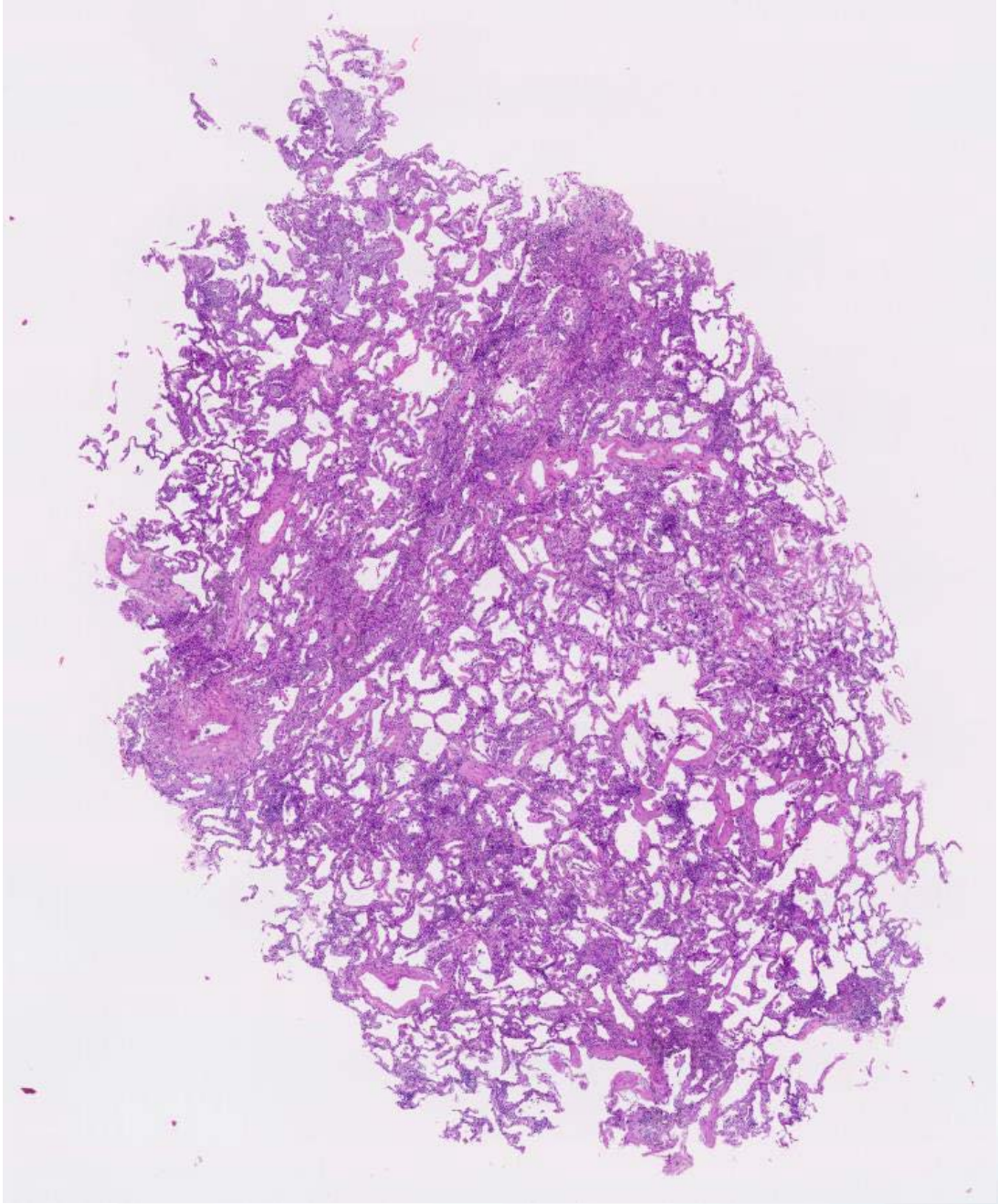

**UIP**

19/23 UIP High confidence
4/23 UIP low confidence

**NOT UIP**

7/16 NSIP
3/16 DIP/RB-ILD/PLCH
2/16 HP
2/16 SARCOIDOSIS
2/16 OTHERS


UIP High Confidence



# NSIP

# San Giuseppe experience: Complicances

Bleeding: minor 8/46 (17.4%)
major 1/46 (2.2%)

Pnx: 4/46 (8.7%), 2 (4.3%) with need of drenage tube

# Conclusions

**Cryo is ready for clinical use, but only in an adequate setting**

Cryobiopsy in ILDs is feasible (diagnostic yield, approx 80%), safe (mortality, approx 0.1%) and less complications compared to SLB.

However the technique needs standardization and should be performed by IPs trained in expert centres and in the appropriate settings (that should include biopsy technique and the ability to manage emergencies, i.e. bleeding and pneumothorax)