Interventional Pulmonology

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| The Lung Center |

HARVARD MEDICAL SCHOOL

Relevant disclosures

- Scientific Advisory Board
  - Ambu A/S (one of the manufacturers of single-use bronchoscopes)

Outline

- Advanced diagnostic bronchoscopy
- Advanced therapeutic bronchoscopy
- Advanced pleural procedures

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Advanced diagnostic bronchoscopy:

1. The mediastinum & EBUS (endobronchial ultrasound)

- EBUS-TBNA = FNA of a lymph node or other structure under *real-time* US guidance
  - Approx. 90% sensitivity for malignancy
    - Comparable to mediastinoscopy
    - Provides enough tissue for molecular testing
  - Approx. 80-85% for sarcoidosis
    - Incremental benefit w/ EBBX/TBBX
  - Approx. 70% for lymphoma
    - Closer to 75% for recurrent, 65% for incident

- Complication rate: <1% (i.e., highly favorable)
  - Bleeding, pneumothorax, pneumomediastinum, infection

Advanced diagnostic bronchoscopy:

1. The mediastinum & EBUS (endobronchial ultrasound)

- **ACCP 2013 guidelines: In NSCLC patients with suspected* mediastinal LN involvement + no distant metastases, a needle technique (e.g., EBUS-TBNA or trans-esophageal FNA) is recommended as the best first test**
  - *Remark:* In cases where the clinical suspicion of mediastinal node involvement remains high after a negative result using a needle technique, surgical staging (e.g., mediastinoscopy, video-assisted thoracic surgery [VATS], etc.) should be performed.

*Grade 1B for high suspicion | Grade 2B for intermediate suspicion

EBUS-TBNA: To ROSE or not to ROSE

- ROSE = Rapid On-Site Evaluation – typically by a cytology tech using “Diff-Quik” staining
  - An optional accompaniment to EBUS-TBNA
    - Provides real-time assessment of specimen adequacy

Which of the following is true about the use of rapid on-site evaluation (ROSE) in EBUS?

A. Increases diagnostic sensitivity for malignant lymph node involvement in NSCLC
B. Decreases procedure time
C. Increases procedure time
D. Decreases number of sites sampled

Which of the following is true about the use of rapid on-site evaluation (ROSE) in EBUS?

A. Increases diagnostic sensitivity for malignant lymph node involvement in NSCLC
B. Decreases procedure time
C. Increases procedure time
D. Decreases number of sites sampled
   - By ensuring diagnosis is attained from a given site

Collins BT, et al. Cancer Cytopathol 2013. PMID: 23825066.

Advanced diagnostic bronchoscopy:

2. The lung parenchyma & peripheral bronchoscopy

1. **Conventional bronchoscopy**
   - Flexible bronchoscopy (with TBBX, TBNA, brushing, and/or BAL)
2. **Guided (e.g., navigational) bronchoscopy (needs pre-op CT)**
   - CT-based rendering for tracking of scope/instrument location
3. **Robotic bronchoscopy (needs pre-op CT)**
   - CT-based tracking + thinner, more maneuverable scope

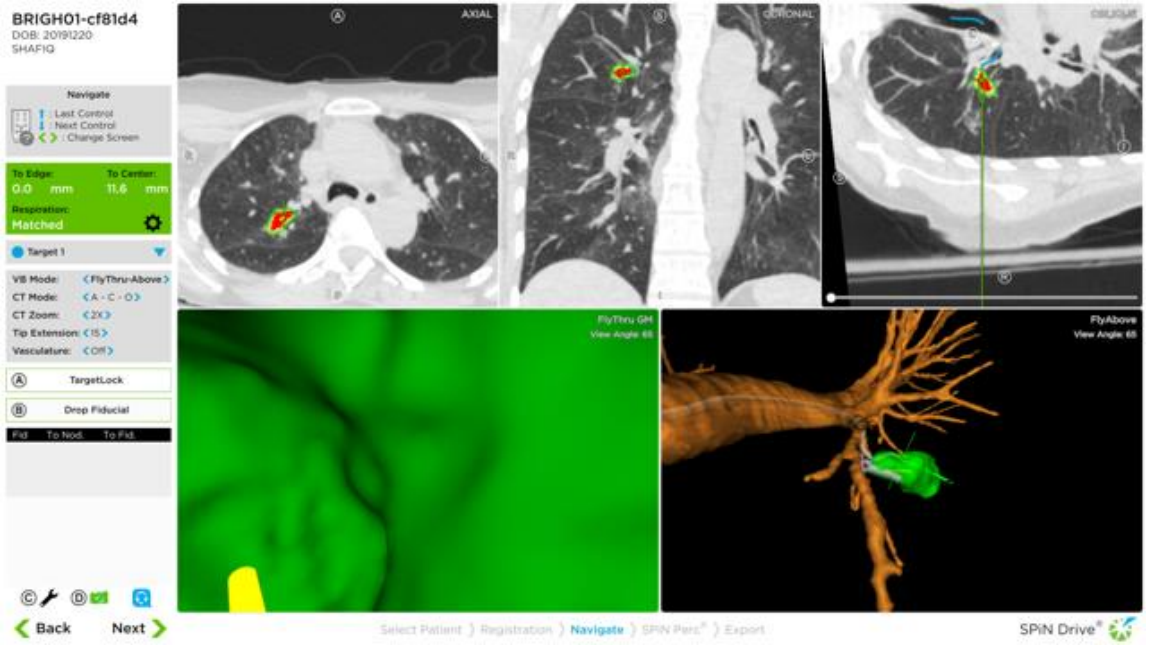
❑**Add-on: Radial EBUS (different from "linear" EBUS)**

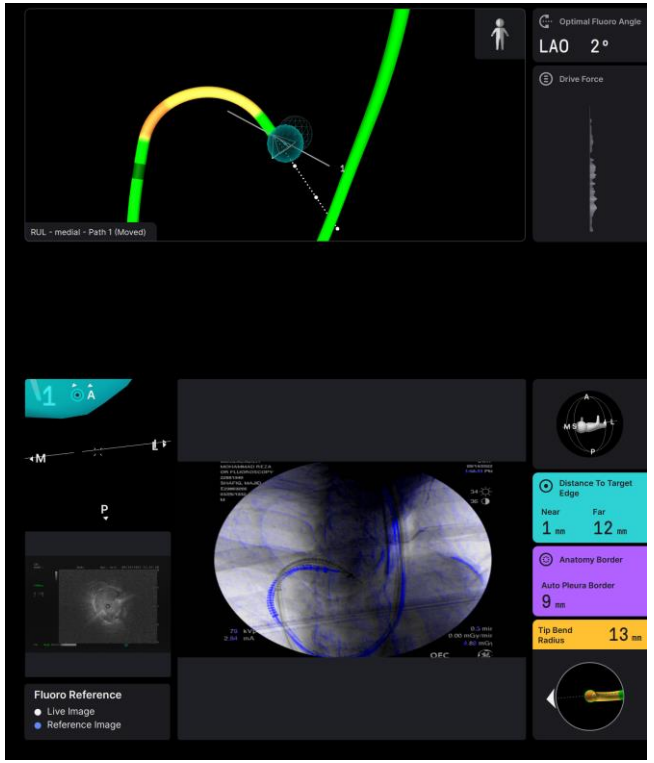
- Real-time visualization of lesion (but not of "tool-in-lesion")

❑**Add-on: Cone-beam CT (and related variants)**

- Real-time visualization of tool-in-lesion (but not of live sampling)

Guided bronchoscopy (using EM navigation) vs. robot





Peripheral bronchoscopy:
Sensitivity for a malignant lung nodule

1. **Conventional bronchoscopy**
   - Around 35% (variable estimates)
2. **Guided bronchoscopy**
   - Around 70%
3. **Robotic bronchoscopy**
   - Early data: Around 80-85%

❑**Add-on: Cone-beam CT**
   - Early data: Up to 90% with either #2 or #3

Peripheral bronchoscopy:
What sampling tool to use?

- Sensitivity for cancer: **TBNA > TBBX > brushing** or **BAL**
  - Pathology may be extraluminal, require traversing airway wall
  - Adding TBBX to TBNA may increase pooled sensitivity

➢Unclear how many specimens to obtain for max. sensitivity

- Retrospective data: 3 TBBX samples enough for lung nodules
- In contrast: ≥5 pieces of alveolated tissue (by TBBX) needed for formal assessment of acute rejection post-lung transplant

➢Envisia genomic classifier (using TBBX specimens)

- Can increase TBBX sensitivity (70%), diagnostic confidence, and rate of appropriate antifibrotic therapy recommendation in IPF patients without typical UIP pattern on HRCT

Lancet Respir Med. 2019 Jun;7(6):487-496. | Ann Am Thorac Soc. 2022 Jun;19(6):916-924.

•. 2024 Jul;12(7):513-522.

Cryobiopsy for ILD

- TBBX variant using cryoprobe instead of forceps
- Pooled diagnostic yield approx. 73%
- COLDICE (2019): Approx. 70% agreement w/ surgical biopsy for final IPF dx
  - Concern for significant bleeding (15%) & 30d mortality (overall 0.3% but up to 2% if including acutely ill inpatients)
- COLD (2024): Step-up strategy (cryobiopsy first, surgical as needed) with lower unexpected chest tube placement vs straight-to-surgical biopsy (11% vs. 46%)
  - Similar diagnostic yield (89% vs. 88%)
  - Lower LOS (1 day [IQR 1-1] vs. 5 days [IQR 4-6])

➢Value added along with robotic (vs. rigid or flexible) bronchoscopy?

Troy LK, et al. Lancet Respir Med, 2019
Sethi J, et al. J Bronch Intervent Pulmonol, 2019
Kalverda KA, et al. Lancet Respir Med, 2024

Cryobiopsy for ILD: ERS 2022 guidelines

Results In patients with undiagnosed ILD and an indication to obtain histopathological data: 1) TBLC is suggested as replacement test in patients considered eligible to undergo SLB, 2) TBLC is suggested in patients not considered eligible to undergo SLB, 3) SLB is suggested as add-on test in patients with a non-informative TBLC, 4) no recommendation is made for or against second TBLC in patients with a non-informative TBLC, and 5) TBLC-operators should undergo training, but no recommendation is made for the type of training required.

Conclusion TBLC provides important diagnostic information in patients with undiagnosed ILD. Diagnostic yield is lower compared to SLB, at reduced serious adverse events and length of hospitalization. Certainty of the evidence is mostly "very low".

European Respiratory Journal 2022; DOI: 10.1183/13993003.00425-2022

Outline

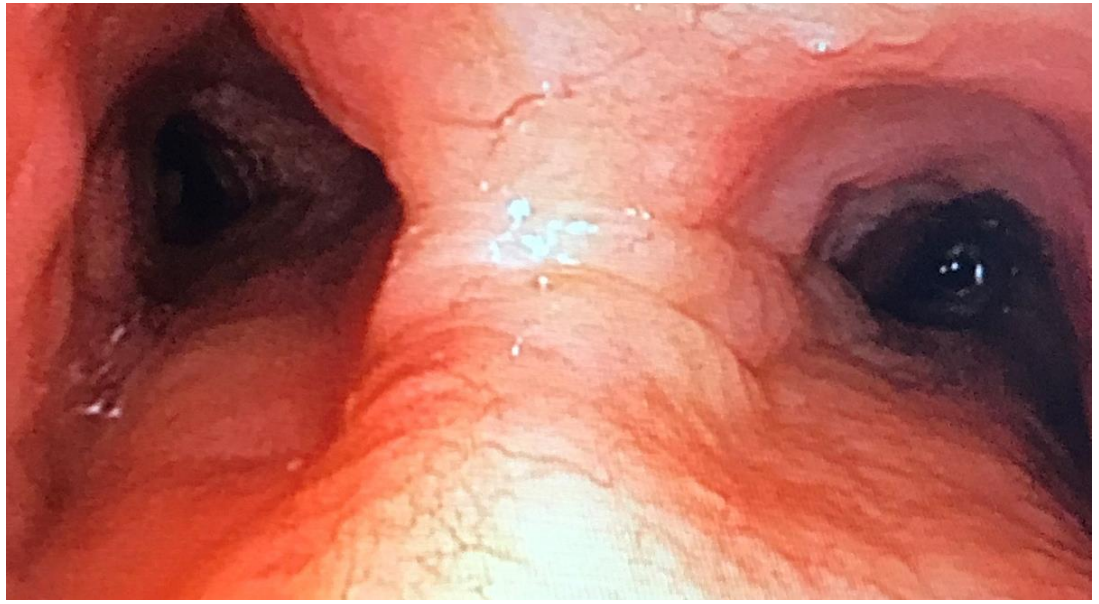
- Advanced diagnostic bronchoscopy
- Advanced therapeutic bronchoscopy
- Advanced pleural procedures

Advanced therapeutic bronchoscopy:
1. Symptomatic tracheobronchomalacia (TBM)

➢ **Controversies aplenty:**

1. Should we distinguish types of expiratory airway collapse?
   - "True" TBM (cartilage) vs. EDAC (posterior membrane)
2. How to diagnose and characterize severity etc.?
   - Dynamic CT, flex bronch, both? How best to protocolize them?
   - What cut-off to use for expiratory collapse?
3. Rx (wt. loss, CPAP, ambulatory PEP device, pursed lips, flutter valve, expectorant):
   - Does surgery (membranous tracheoplasty) have a role?
   - Should an airway stent trial precede selection for surgery? [SOB phenotype]

A tale of 2 CTs reporting “tracheomalacia”



Menon AA, Shafiq M. Am J Respir Crit Care Med. 2022.

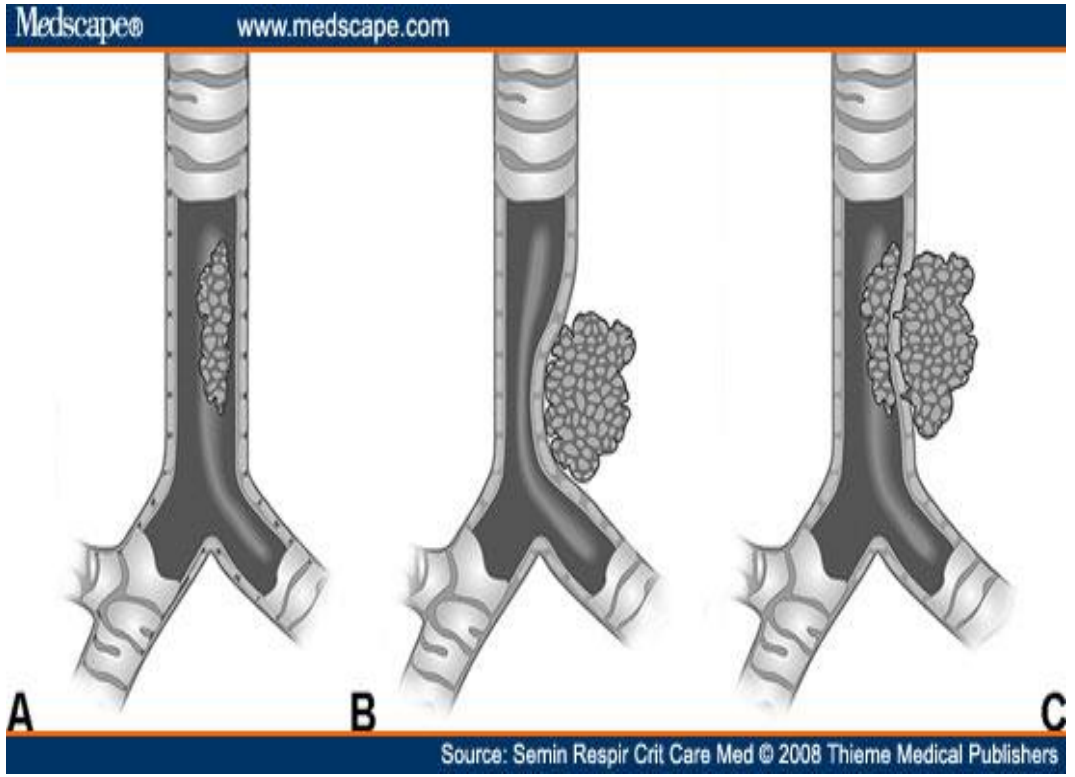
Advanced therapeutic bronchoscopy:

2. Central airway obstruction (i.e., proximal to lobar bronchi)

A. Intraluminal
   - Tumor debulking

B. Extrinsic (compression)
   - Airway stenting

C. Mixed
   - Possibly both

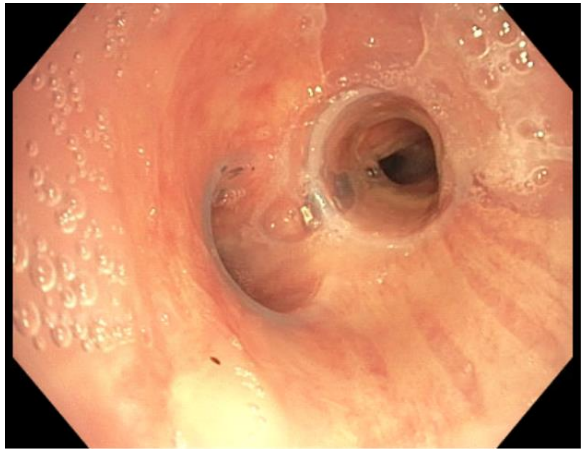


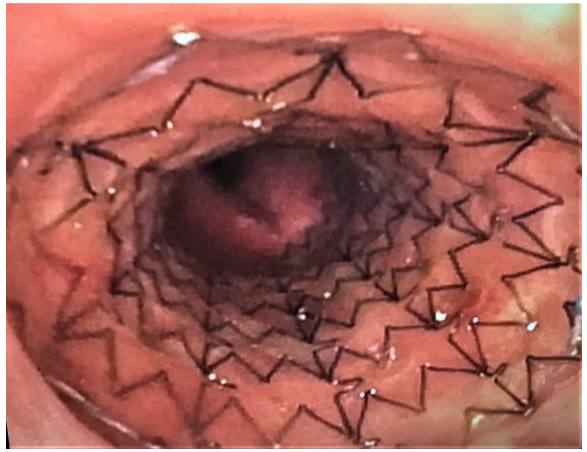
Options in hand:
Tumor debulking

	Mechanical (rigid barrel or forceps)	Electro-cautery	Argon plasma coagulation (APC)	Laser (Nd: YAG, KTP, etc.)	Cryo-therapy (spray vs. contact)	Brachy-therapy (high-dose local XRT)	Photo-dynamic therapy (PDT)
Requires contact	Y	Y	N	N	**Spray**: N **Contact**: Y	N	N
Immediate effect?	Y	Y	Y	Y	**Spray**: Y **Contact**: Y & N	N	N
Depth of effect (mm)	Varies	3-15	3	Varies	10	10-20	5-10
Fire risk (need FiO2 <40%)	N	Y	Y	Y	N	N	Y (during activation)

Options in hand:
Airway stenting

- 2 broad types: Silicone vs. metallic
  - Metallic stents are self-expanding (SEMS) and collapsible; hence can be deployed through a flexible bronchoscope too
  - Most SEMS: Metal frame “covered” w/ silicone/polyurethane





Management considerations post-stenting

- All stents represent a new disease. Complications include:
  - Mucostasis & infection 2/2 compromised airway wall clearance
  - Granulation tissue esp. around edges of stent
  - Migration, fracture, bleeding, epithelialization, perforation, etc.
  - **FDA Black Box (2005):** SEMS in non-malignant tracheal disease
    - Longer lifespan -> more complications, esp. with 1st gen, uncovered SEMS

➢Consider the following post-stenting:

- Expectorant (guaifenesin) and/or saline nebs
- Surveillance bronchoscopy (weak data favors q6weeks) to pro-actively deal with issues

Chaddha U, et al. Respirology. 2024

JANUARY 8, 2020 / NEWS RELEASES

FDA Approves 3D-printed Airway Stents

- Stent material: Silicone
- Allowing customization to patient airway
  - Potentially longer stent life without requiring replacement for stent fracture, migration, or other stent-related issues

vs.

Which of the following is a contraindication to bronchoscopic lung volume reduction using one-way endobronchial valves?

A. Homogeneous emphysema

B. Lower-lobe predominant heterogeneous emphysema

C. Presence of severe chronic bronchitis

D. Presence of an implantable cardioverter-defibrillator (ICD) device

Which of the following is a contraindication to bronchoscopic lung volume reduction using one-way endobronchial valves?

A. Homogeneous emphysema

- FDA-approved for both heterogeneous and homogeneous emphysema

B. Lower-lobe predominant heterogeneous emphysema

- RCTs show benefit in non-upper lobe disease too (unlike LVRS, i.e., LVR Surgery)

C. Presence of severe chronic bronchitis

- Endobronchial valves can impede mucus clearance, increasing short-term risk of pneumonia

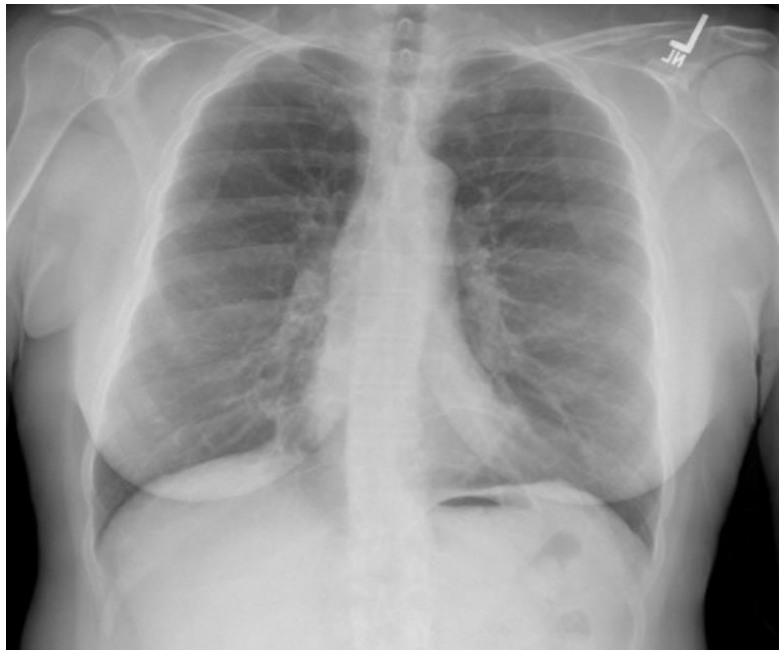
D. Presence of an implantable cardioverter-defibrillator (ICD) device

- Nitinol is a non-ferromagnetic alloy and not expected to interfere with ICD functioning

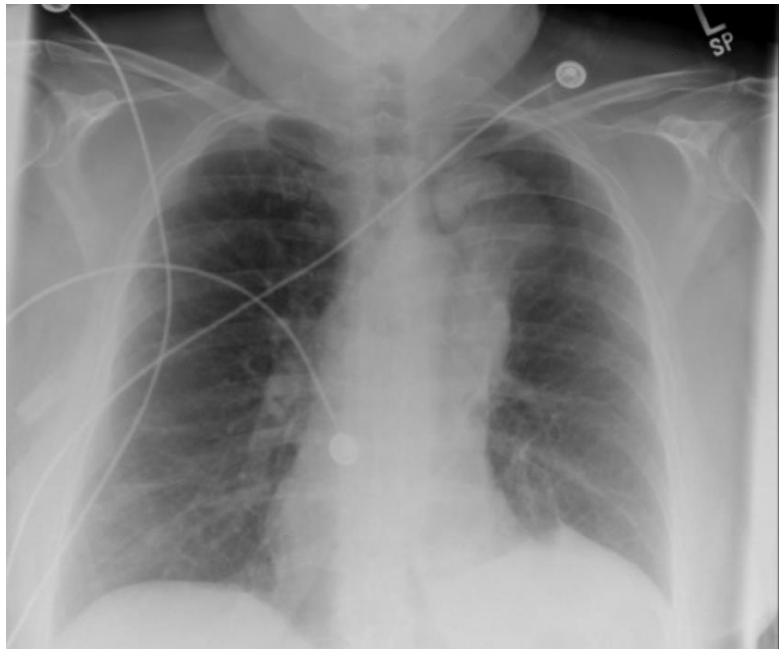
Advanced therapeutic bronchoscopy:
3. Emphysema with hyper-inflation

- Bronchoscopic lung volume reduction (BLVR) via one-way valves improves FEV1 (in 50%), 6MWD, symptom scores
  - To date, not shown to reduce mortality (unlike surgical LVR)
  - But more favorable peri-op M&M compared to surgery
- **Major challenge**: Not valve placement, but patient selection!
  - Need complete lobar fissure to avoid back-door air entry into the treated lobe through collateral ventilation
- **Major complication**: PTX in 1/3rd (on top of poor baseline)
  - Keep patient hospitalized for 3 days post-op; consider sending out with MedicAlert bracelet; ensure close follow up

Successful LUL volume reduction via endobronchial valve placement



BEFORE



AFTER

Advanced therapeutic bronchoscopy:
4. Severe asthma

- AIR-2 RCT (sham-controlled): Bronchial thermoplasty improves AQLQ symptom scores + decreases exacerbations, ED visits, hospitalizations, and days missed from work/school
  - Excluded patients with >10mg/d OCS, >3 hospitalizations/year
  - Newer data post-FDA approval: Sustained effects at 5 years
  - **BT10+ study (2021): Sustained effects (10+ yrs), excellent safety profile**
  - Unclear what asthma subtype(s) benefits most

- Major short-term complication: Asthma exacerbation
  - Pre-op spiro (consider postponing if post-BD FEV1 <85% of recent)
  - 5 days of steroid burst starting 3 days pre-treatment

Chaudhuri R, et al. Lancet Respir Med 2021. PMID: 33524320.

Advanced therapeutic bronchoscopy:

5. Miscellaneous modalities in various stages of investigation

- Bronchoscopic application of Aeriseal (sealant)
  - Convert lobar fissures from incomplete to complete to permit valve placement
- Bronchoscopic coil placement for BLVR
  - Coils unfurl post-deployment -> not reversible (unlike valves)
- Bronchial rheoplasty for chronic bronchitis
  - Pulsed Electric Fields -> ablation of mucus-producing airway cells
- Ablation of lung nodules (e.g., via microwave, PEF, or RFA)
  - Needs confirmation of tool-in-lesion
- Targeted lung denervation for COPD (GOLD stage B or D)
  - Peri-bronchial parasympathetic n. ablation (RFA) -> bronchodilation
  - AIRFLOW-3 (international sham-controlled RCT) underway

Outline

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Advanced pleural procedures

1. Indwelling pleural catheter (IPC)

- Symptomatic management for recurrent effusion
  - Role established in both malignant or non-malignant effusions
- IPC compared with chemical (e.g., talc) pleurodesis:
  - Done as outpatient; fewer hospital days overall
  - More cost-effective if shorter life expectancy (around <3mo)
  - IPC can lead to “auto-pleurodesis” in up to half of all cases
  - IPC-Plus = Talc via IPC: Auto-pleurodesis faster, more likely
- IPC-related pleural infection rate approx. 5%
  - Usually treated pharmacologically without catheter removal

Advanced pleural procedures

2. Pleuroscopy for malignant pleural effusion

✓ Diagnostic role:

- High sensitivity for malignant effusion (around 95%)
  - Pleural fluid cytology (approx. 50%), closed pleural biopsy: much lower sensitivity (esp. for mesothelioma)

x Therapeutic role:

- TAPPS RCT (JAMA 2019): No difference between talc slurry (chest tube) vs. talc poudrage (pleuroscopy) in terms of pleurodesis success for malignant effusion

Medical pleuroscopy	Video-assisted thoracoscopic surgery (VATS)
• Typically single entry port	• Typically 2-3 entry ports
• Patient typically awake, spontaneously breathing	• Patient under GA and single-lung ventilation
• Typically limited to parietal pleura (biopsy) and pleural space (talc, indwelling catheter)	• Encompasses lung biopsy or resection, diaphragm repair, sympathectomy, etc.

Why choose medical pleuroscopy* over VATS for pleural biopsy (e.g., for undiagnosed effusion)?

- Similar diagnostic performance
- Similar safety profile
- Shorter hospital LOS & fewer overall costs
  - *With “awake” pleuroscopy i.e., not involving GA

McDonald CM, et al. Ann Thorac Surg. 2018. PMID: 29577922.

Take-home points

- EBUS-TBNA is preferable to surgery as 1st line for mediastinal staging, sarcoidosis eval
- Guided bronchoscopy has lower sensitivity for malignant nodules than TTNA (but lower PTX rate)
  - Will newer modalities (robotic bronch, CBCT) change that?
- Cryobiopsy has better sensitivity, higher risk vs. TBBX for ILD and the opposite vs. surgical biopsy
- Airway stents require meticulous care and follow up
- A complete lobar fissure is essential for endobronchial valve-based BLVR
- Bronchial thermoplasty is a highly safe long-acting (life-long?) therapeutic option for patients with uncontrolled asthma despite optimal medical management
- Pleural biopsy is the only way to reliably exclude malignancy as a cause of an exudative pleural effusion