BRIGHAM AND WOMEN'S HOSPITAL

The Lung Center

Asthma mimics: Consider tracheobronchomalacia

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Conflicts of interest

- Dr. El Boueiz: None
- Dr. Shafiq: Ambu A/S (Advisory Board)

Case example

- 38F presented with asthma symptoms shortly after the birth of her 3rd child.
- She had smoked cigarettes for 10 years, quitting 10 years ago.
- She does not work outside of the house; she has two Golden Retrievers.
- Exam was significant for diffuse expiratory wheezes and a non-productive cough. BMI 45.
- She was treated with inhaled steroids and LABA.
- Allergy testing was positive for dust mites.
- She had frequent hospital admissions with episodes of SOB and wheezing, usually triggered by respiratory tract infections, complicated on one occasion by respiratory failure necessitating a brief period of intubation and mechanical ventilation.

Case example – Continued

- Despite treatment with anti-IgE monoclonal antibody and low-dose daily steroids, she continued with loud, persistent cough, difficulty clearing chest secretions, wheezing on a nearly daily basis, and marked exertional dyspnea.
- Normal vital signs (SpO_2 96% at rest)
- Intermittent diffuse expiratory wheezes audible without a stethoscope. Loud cough.
- Variable PFTs, sometimes with mild restriction, other times with mild airflow obstruction.
- Normal indirect laryngoscopy

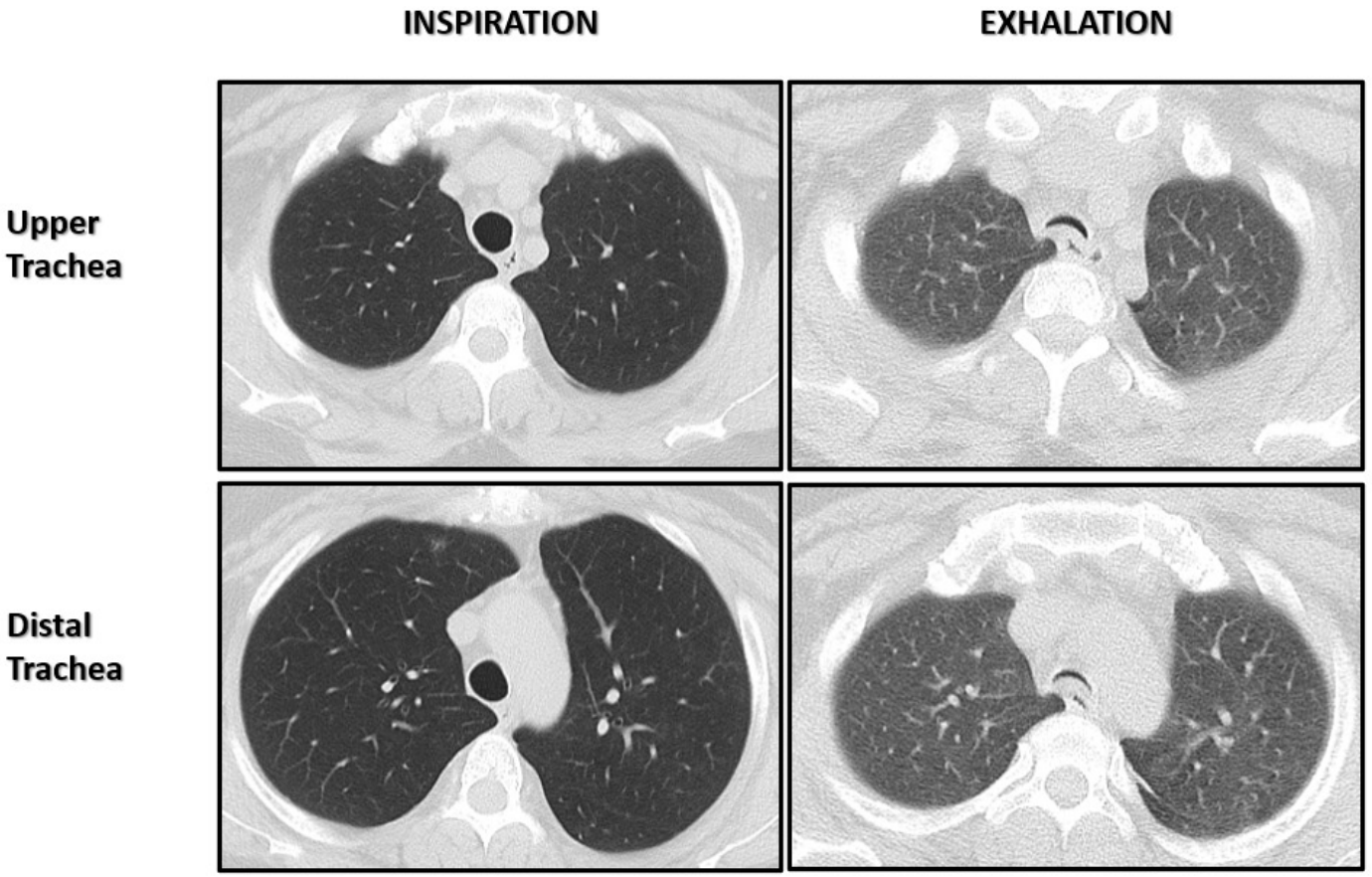
Asthma mimics

- Upper airway:
  - Vocal cord dysfunction
  - Tracheal tumor / stricture
  - Foreign body aspiration
  - Vascular sling
- Lower airway:
  - COPD
  - Bronchiectasis
  - Constrictive bronchiolitis

- Other:
  - Heart failure
  - Sarcoidosis
  - Eosinophilic bronchitis
  - Pulmonary embolism
  - LAM
  - Disseminated strongyloidiasis

… and consider TBM

Case example – Continued - Dynamic CT chest



Outline –
Asthma mimics: Consider tracheobronchomalacia

- Definition
- Etiology / Risk factors
- Clinical manifestations
- Evaluation
- Treatment options

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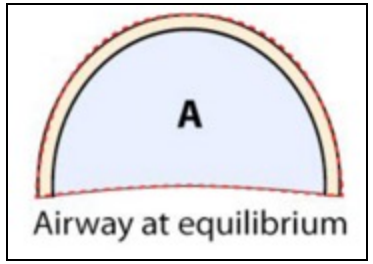
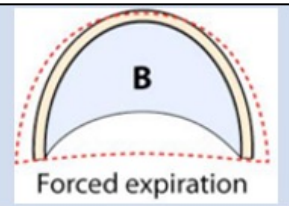
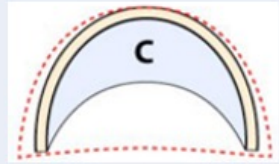
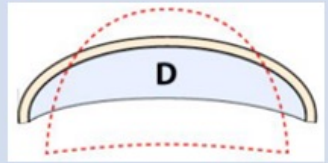
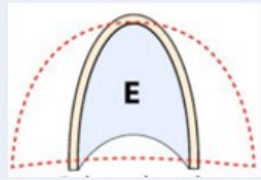
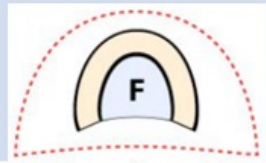
Tracheal collapse

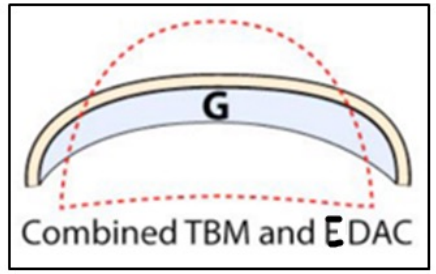
- Dynamic Central Airway Obstruction:
  - Luminal narrowing < 50% during expiration
- Tracheomalacia (TM) or Tracheobronchomalacia (TBM):
  - In Greek, the word "malakia" means softness → TM / TBM: Cartilage weakness / softening of the trachea and/or mainstem or lobar bronchi
  - Cartilaginous injury → airways excessively susceptible to the influence of pleural pressure and transairway pressures → airway collapse during active exhalation and airway expansion on inhalation
- Excessive Dynamic Airway Collapse (EDAC):
  - Excessive laxity of the posterior membranous wall with an intact integrity of the cartilaginous support
  - Bulging of the posterior membrane into the airway lumen during exhalation
- Excessive central airway collapse (ECAC):
  - If is often difficult radiologically or bronchoscopically to assign the degree to which airway narrowing is being caused by TBM, EDAC, or both.

Chest 2005;127(3):984-1005 // Treat Respir Med 2006;5(2):103-115

Classification of collapse



DAC	Physiologic CSA narrowing	
EDAC	Pathologic bulging of posterior membrane	
Crescent-type TBM	Anterior cartilage softening	
Saber-sheath TBM	Lateral cartilage wall softening	
Circumferential TBM	Both anterior and lateral wall collapse	



Respirology 2006;11(4):388-406

Optimal diagnostic threshold for luminal narrowing?

- No universally accepted cut-off value to define normal and abnormal airway narrowing.
- Defined by at least 50% decrease in the area from inspiration to expiration.
  - If forced expiration, cutoff is 70%
  - No clear cutoff for bronchial collapse
  - Accepted by convention, but may not be true, and ~80% of normal individuals exceeded the current diagnostic criterion
- When do we measure it ???!!!
  - During tidal breathing
  - During forced expiration
  - During coughing
  - During suspended exhalation

Radiology 2009;252(1);255-262
Clin Chest Med 2013;34:527-555

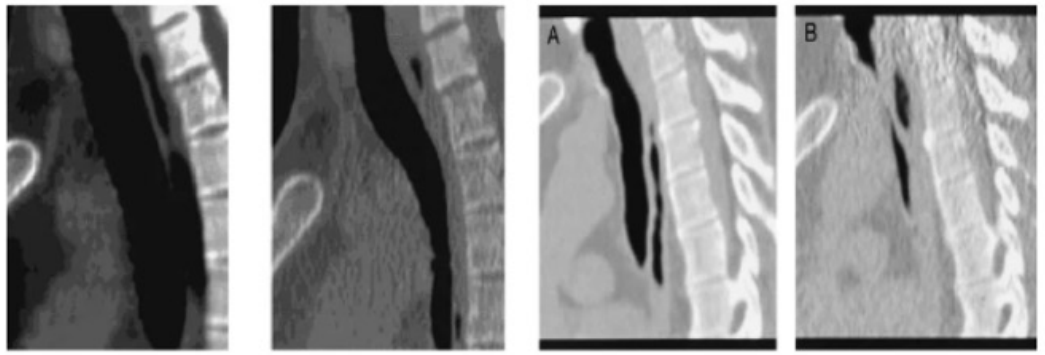
Classification by severity and distribution

Severity

Severity

- <50% (normal)
- 50-75% (mild)
- 76-90% (moderate)
- 91-100% (severe)

Distribution



Diffuse TM

Excessive collapse of a long segment of the intrathoracic trachea during expiration

Segmental TM

Segmental tracheal collapse during exhalation

Chest 2005;127:984-1005 // Chest 2007;131:1118-1124 // Chest 2007;132:609-616 // Radiology 2009;252:255-262 // Radiology 2010;257(2):560 // Chest 2012;142(1):168-174

FEMOS classification

- FEMOS:
  - **F**unctional class:
    - NYHA I-IV
  - **E**tiology:
    - Primary, secondary
  - **M**orphology:
    - Saber sheath, crescentic, circumferential …
  - **O**rigin:
    - TM, BM, TBM (focal/multifocal/diffuse)
  - **S**everity:
    - Mild, moderate, severe

Respirology 2006;11(4):388-406

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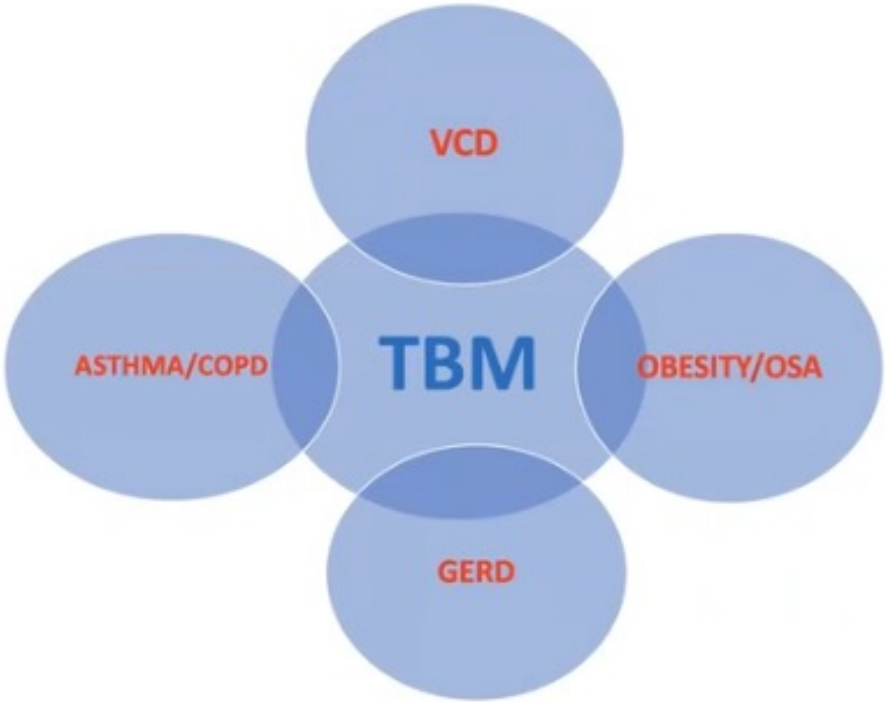

VCD
ASTHMA/COPD
TBM
OBESITY/OSA
GERD

Etiology

Primary or Congenital
Genetic, such as polychondritis (See also Pediatric table)
Idiopathic "Giant Trachea" or Mounier-Kuhn
Secondary or Acquired
Post-traumatic
Post intubation
Post tracheostomy
External chest trauma
Post lung transplantation
Emphysema
Chronic Infection/Bronchitis
Chronic Inflammation
Relapsing Polychondritis
Chronic External Compression of the Trachea
Malignancy
Benign Tumors
Cysts
Abscesses
Aortic aneurysm
Vascular Rings, previously undiagnosed in childhood

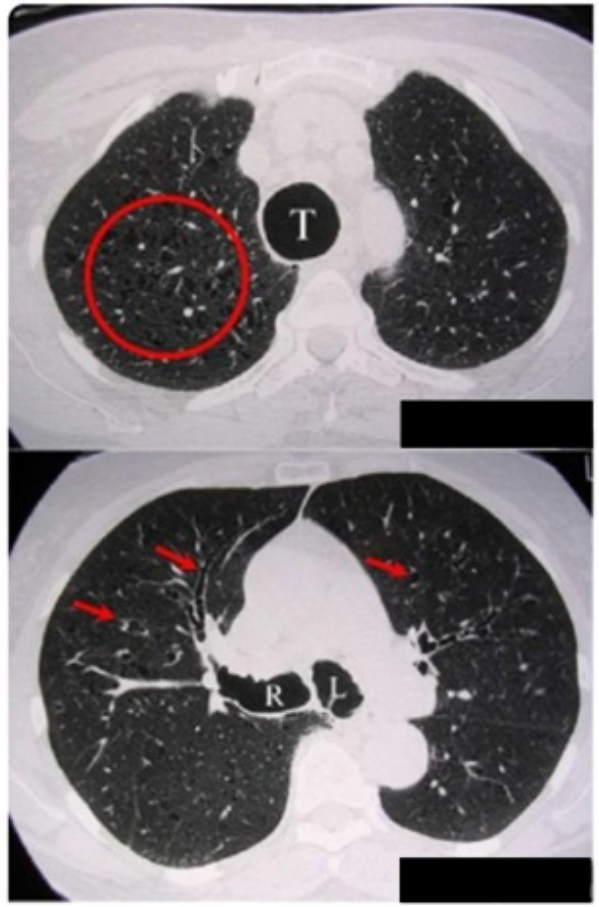
Respirology 2006;11(4):388-406

Etiology

- Localized:
  - Prolonged intubation / tracheostomy
  - Vascular sling
  - Resection of anterior mediastinal mass
- Diffuse:
  - COPD (saber-sheath trachea)
  - Tracheomegaly
  - Ehlers-Danlos syndrome
  - EDAC:
    - ? Inhaled steroids
    - ? Obesity
    - ? Smoking
- Diffuse tracheal wall thickening, sparing the posterior membrane:
  - Relapsing polychondritis
  - Tracheobronchopathia osteochondroplastica
- Diffuse circumferential tracheal wall thickening:
  - Sarcoidosis
  - Granulomatosis with polyangiitis (GPA)
  - Amyloidosis
  - Inflammatory bowel disease

Tracheobronchomegaly - Mounier-Kuhn syndrome

- 3rd or 4th decade of life
- Atrophy of longitudinal elastic fibers and thinning of the muscularis mucosa
- Diagnostic criteria:
  - Right mainstem > 2.4 cm
  - Left mainstem > 2.3 cm
  - Trachea exceed > 3 cm
- Secretions are poorly mobilized, leading to the chronic accumulation of secretions
  - Recurrent infections
  - Bronchiectasis
  - Rarely pulmonary fibrosis



Br J Radiol. 1984;57(679):640-4

Relapsing polychondritis

- Inflammatory condition affecting cartilage across the body
- Cellular and humoral response against collagen type II, IX, and XI (30-70% of pts)
- Involves tracheal rings in 56% of cases, but respiratory symptoms on presentation in only 14% of cases:
  - Sparing of the posterior wall
  - Smooth, long-segment involvement
  - May calcify (typically thick)
  - Worse prognosis and poorer response to steroids (5-year survival rate: 45-74%)
- Delay in diagnosis ~ 3 years; Asthma imitator. When suspected, look for:
  - Auricular cartilage inflammation
  - Nasal chondritis
  - Seronegative polyarthritis
  - Ocular inflammation
  - Audio-vestibular damage

Chest 2009;134(4):1024-1030

COPD and TBM/EDAC

- 214 patients with chronic bronchitis:
  - 50/214 with TBM
- 2,150 patients with TBM:
  - 53% concurrent chronic bronchitis
- 8,820 subjects from 21 clinical centers involved in the COPDGene study
  - Paired inspiratory / expiratory dynamic CT
  - Measurements at the aortic arch, carina, and BI
  - EDAC in 443/8,820 subjects (5%)
  - SGRQ worse in EDAC; No difference in 6MWD
  - Patients with EDAC had increased frequency and severity of respiratory exacerbations

J Otorhinolaryngol Relat Spec. 1976;38(3):178-186 // Ann Clin Res. 1977;9(2):52-57 // JAMA 2016;315(5):498-505

Dynamic expiratory tracheal collapse in morbidly obese COPD patients

- N = 100 (48 F) patients with obesity and COPD
- N = 53 normal volunteers
- Expiratory collapse:
  - Significantly associated with BMI:
    - 69 ± 12% tracheal collapse among 20 morbidly obese patients with BMI ≥ 35

    vs.
    - 57 ± 19% in others *(P-value = 0.002)*
  - No significant difference in collapse between healthy volunteers with BMI ≥ 35 and < 35

COPD 2013;10(5):604-610

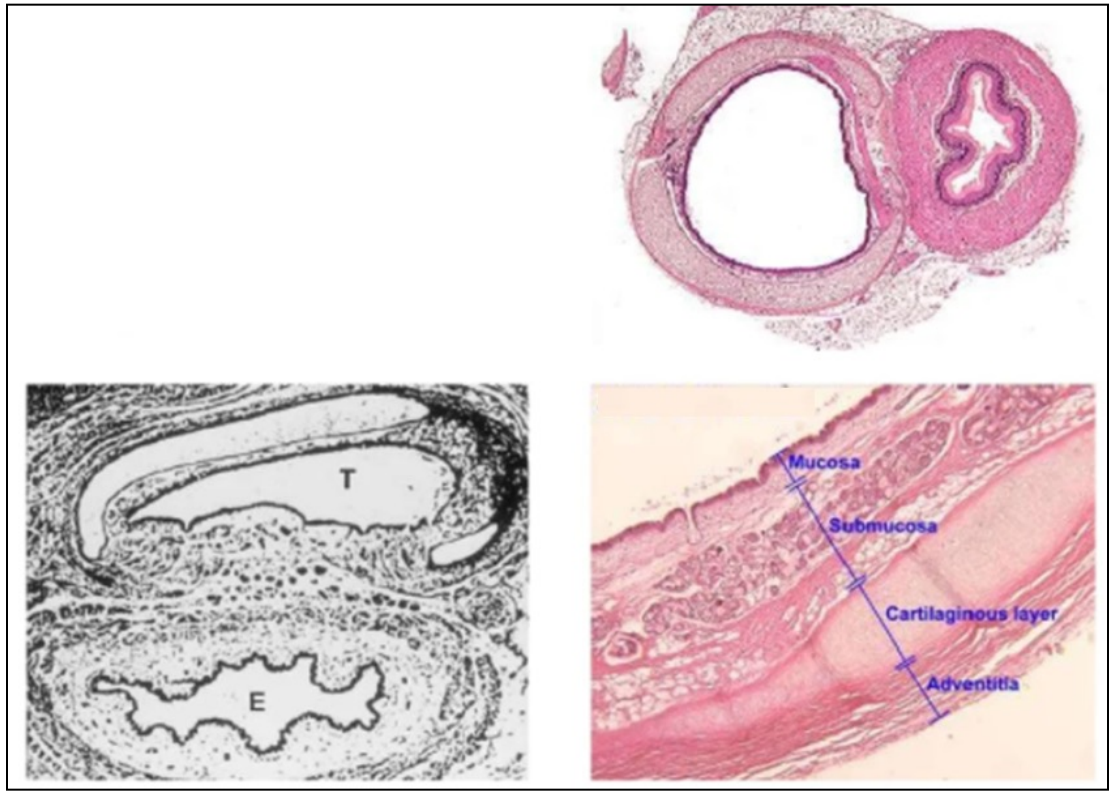
GERD and TBM/EDAC

- 45.3% prevalence of GERD (with abnormal esophageal pH test result) in patients with TBM/EDAC
- There was no reflux symptom correlation in > 50% of patients
- All patients with unsuccessful surgical treatment of TBM had severe GERD
- 46% with GERD reported improvement in respiratory symptoms following maximal medical therapy or anti-reflux surgery without requiring further treatment for TBM/EDAC.
  - ✓ Aggressive reflux treatment should be considered in TBM/EDAC patients prior to considering invasive airway procedures or surgery

Chest 2019; 155(3): 540–545.

Histopathology

- Atrophy of the longitudinal elastic fibers
- Fragmentation of the tracheal cartilage
- Tracheal cartilage-to-soft tissue ratio:
  - Normal: ~ 4.5:1
  - In TBM: Often as low as 2:1
- TBM may result from a fibrotic process as evidenced by the increases in Collagens I and III but not IV, as noted in pulmonary fibrosis.
  - Mechanism is unclear but may involve epithelial mesenchymal transition



Courtesy: University of Illinois Medical Center

J Thorac Imaging 201126(4):278-89

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Clinical manifestations

- Non-specific
- Asymptomatic
- Dyspnea → Respiratory failure
- Cough *(barking seal cough)*  → Syncope
- Wheezing / Stridor
- Mucostasis → Recurrent infections
- Unexplained extubation failure

Ann Clin Res 1977;9:359-364
Chest 2005;127:984-1005
Chest 2007;132:609-616
Chest 2008;134(4):801-807

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Evaluation

- Functional assessment
- Pulmonary function testing
- Airway oscillometry
- Chest CT (dynamic inspiratory / expiratory imaging)
- Bronchoscopy

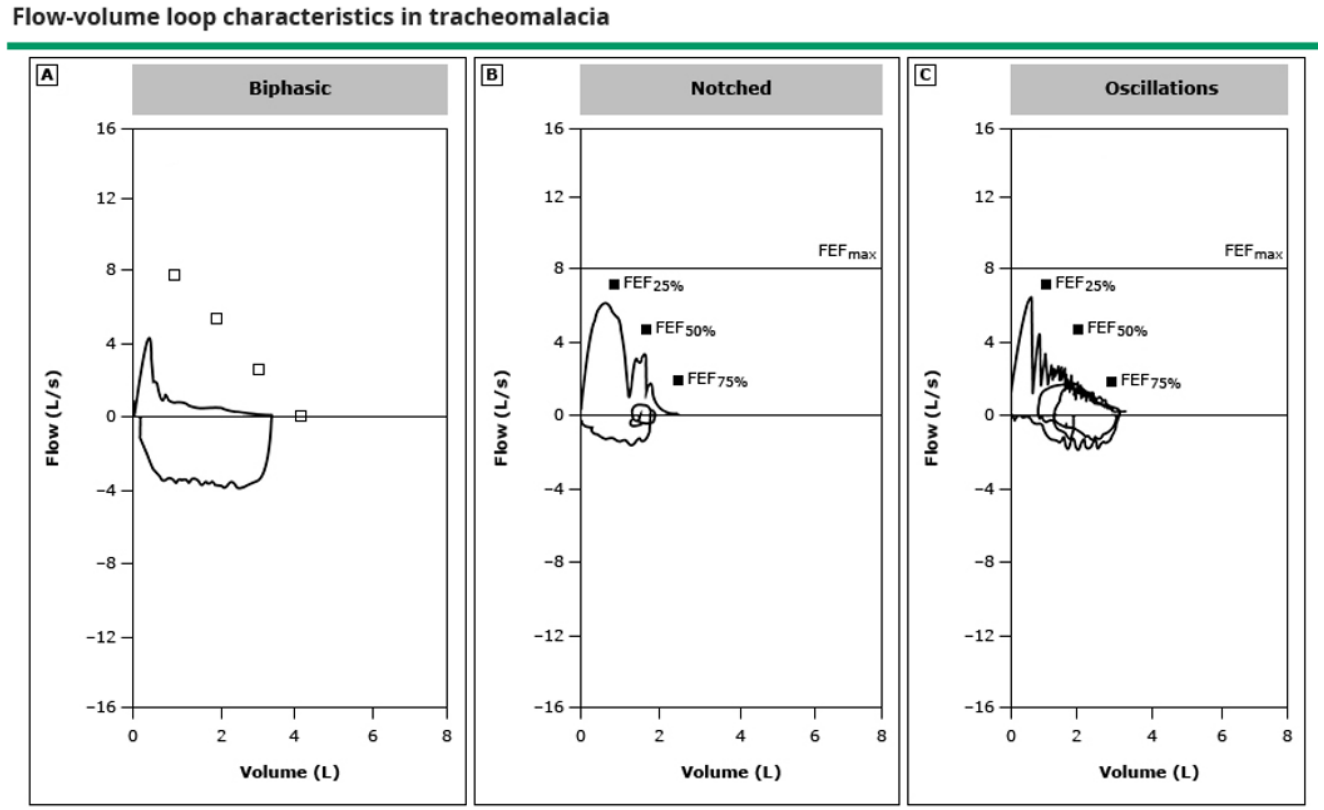
Assessment of symptoms

- Saint George Respiratory Questionnaire (SGRQ)
- Dyspnea index (DI)
- Cough Quality of Life Questionnaire (CQLQ)
- Karnofsky performance status
- …

MINIMALLY CLINICALLY IMPORTANT DIFFERENCE (MCID)

PFT

- Supportive but not diagnostic:
  - 44% obstructive ventilatory defect
  - 18% restrictive defect
  - 17% mixed
  - 21% normal
- Diminished expiratory flow
- Notching / Biphasic / or flow oscillations
- Flow oscillations ("saw-tooth" pattern):
  - TBM
  - OSA
  - Structural or functional disorders of the larynx
  - Neuromuscular diseases

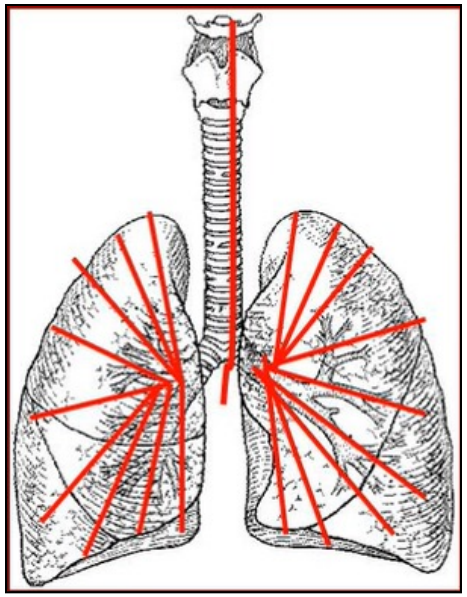


Respiratory Care 2013 VOL 58 NO 9

Airway oscillometry

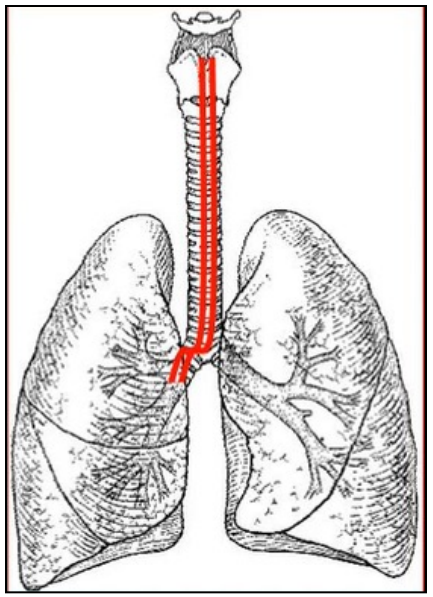
Slow impulses

5 Hz



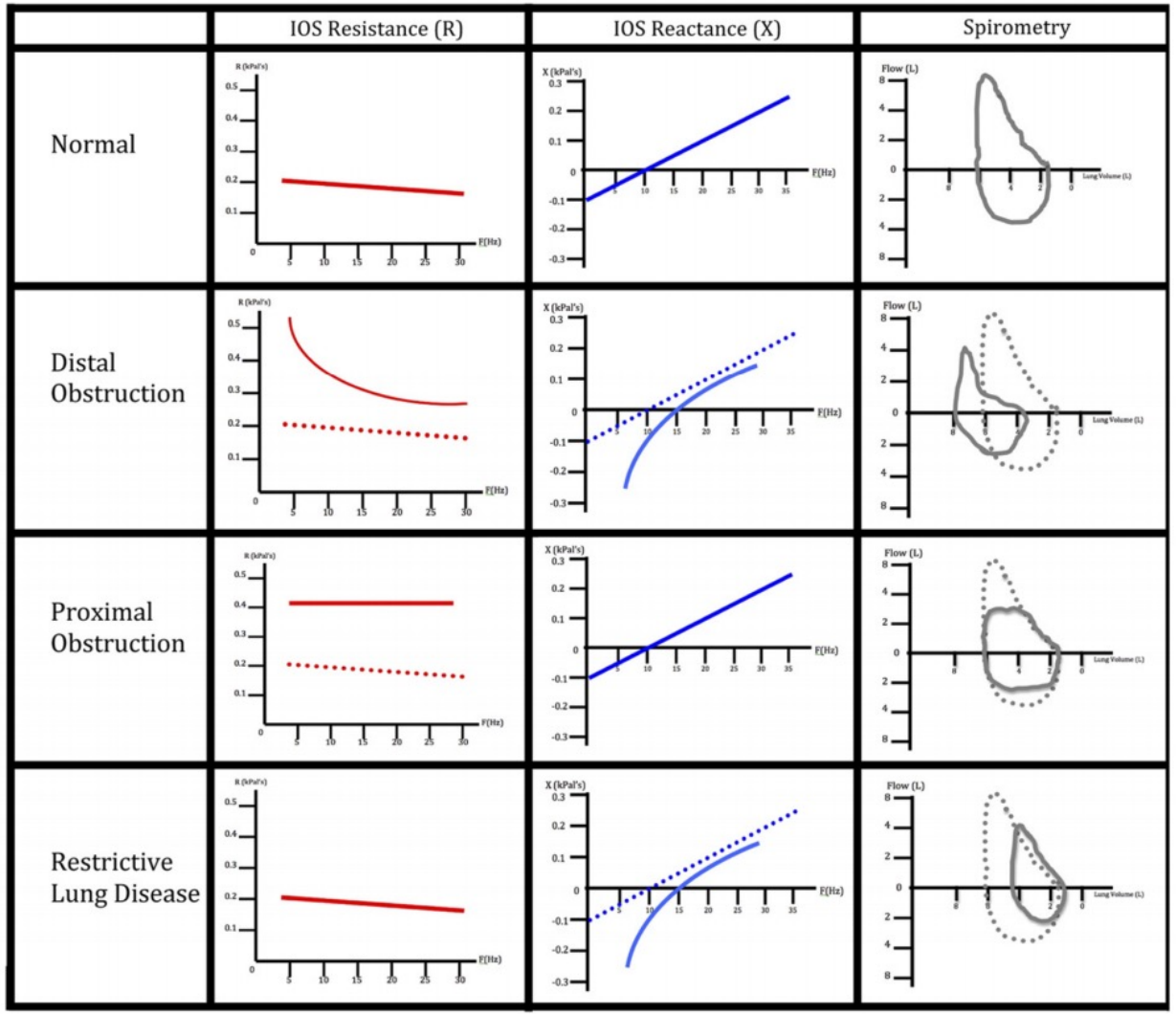
Fast impulses

20 Hz



- High frequencies:
  - low penetration
  - upper (central) airway
- Low frequencies:
  - deep penetration
  - total airways (central and peripheral)

Higher oscillation frequencies are reflected from the larger airways.
Lower frequencies travel more peripherally before returning to the mouth.



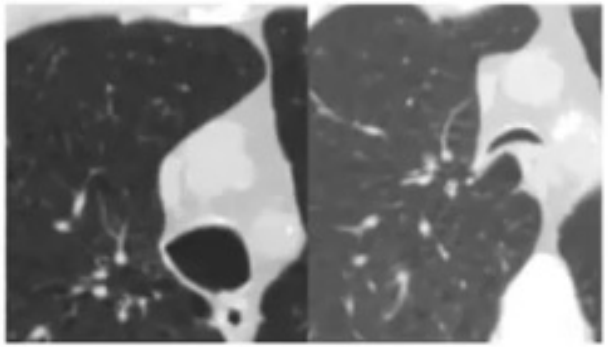
- Obstruction of the small airways in the peripheral lung causes an increase in resistance (R) with a downward shift in reactance (X). In the presence of heterogeneity, R becomes curved.

- Obstruction of the large, central airways causes a parallel upward shift in resistance (R) while reactance (X) remains largely unchanged.

Ann Allergy Asthma Immunol 2011;106(3):191-199

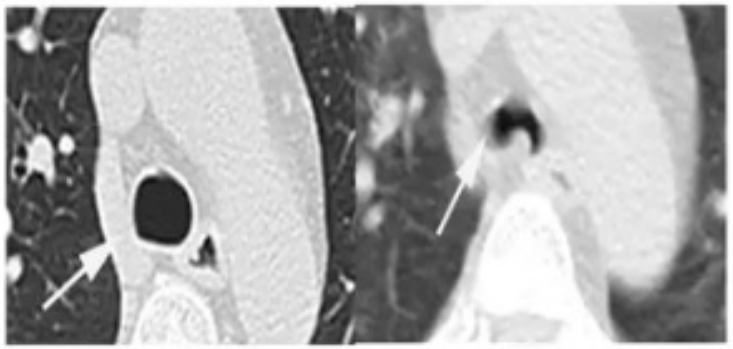
Dynamic CT chest

Tracheobronchomalacia (TBM)



Collapse of anterior cartilage

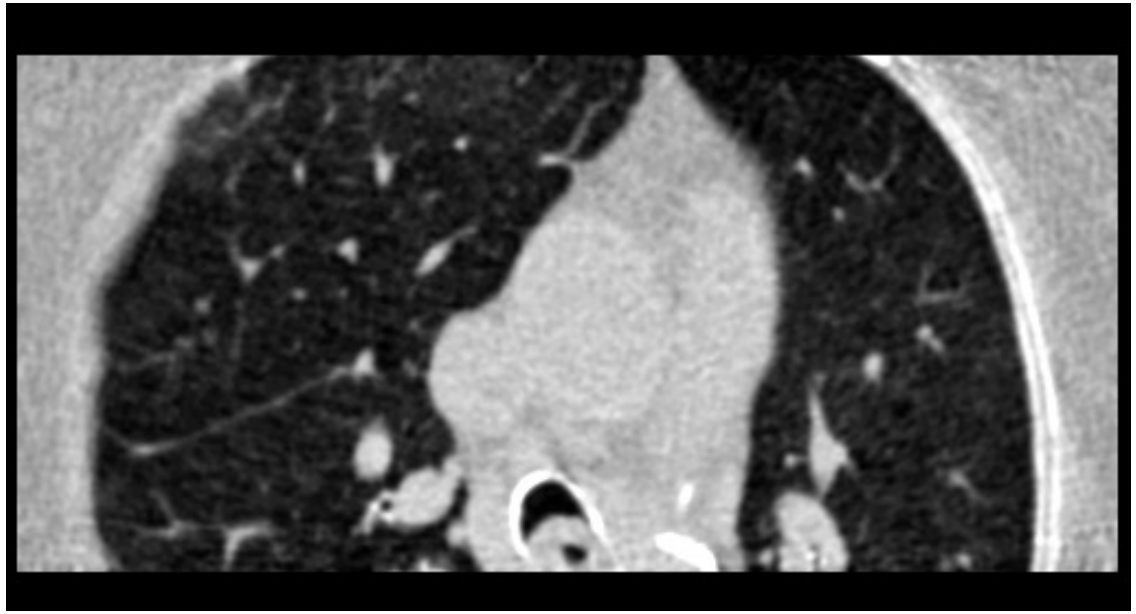
Excessive Dynamic Airway Collapse (EDAC)

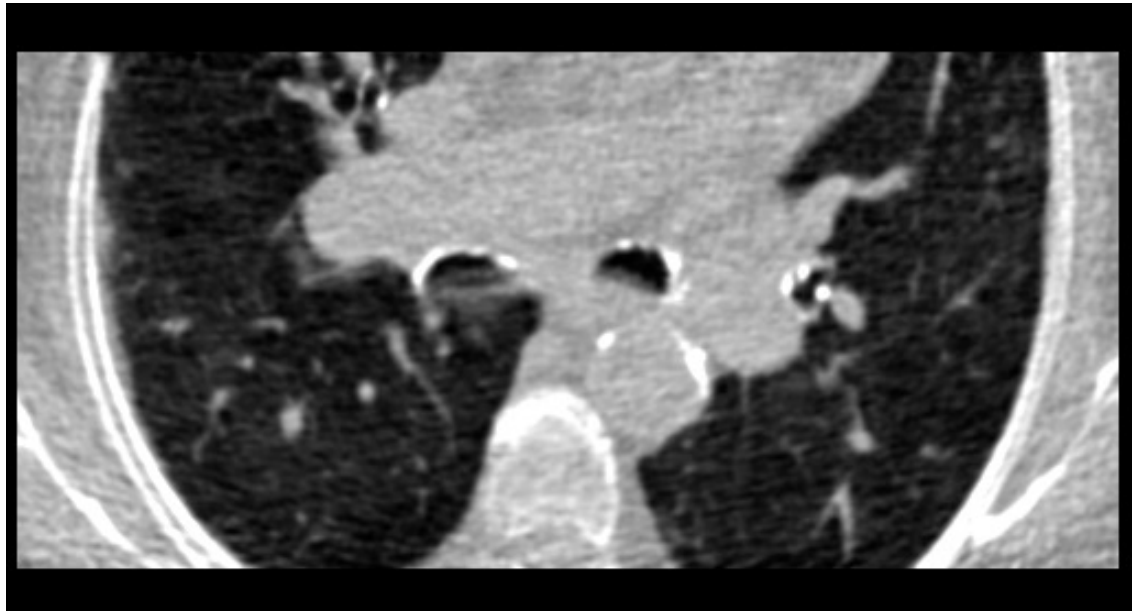


Excessive invagination of posterior membrane

Dynamic CT chest

Volume acquisition during tidal breathing

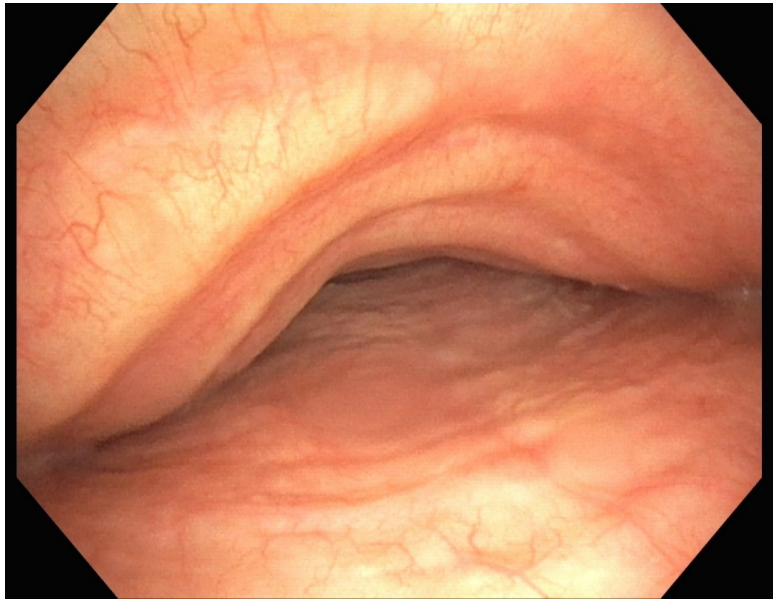


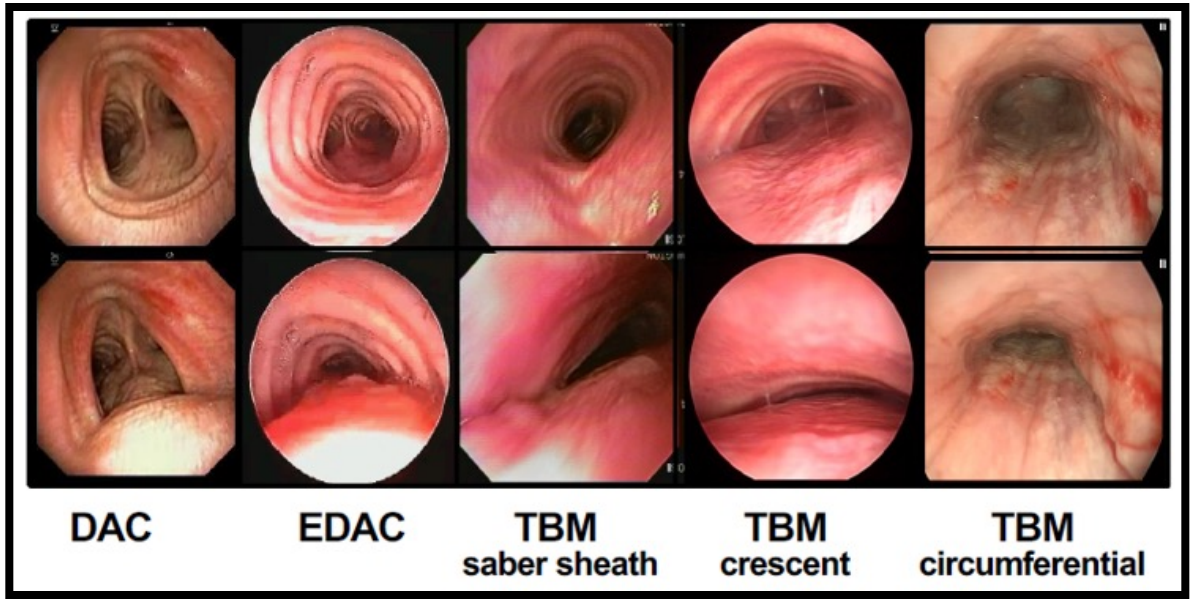


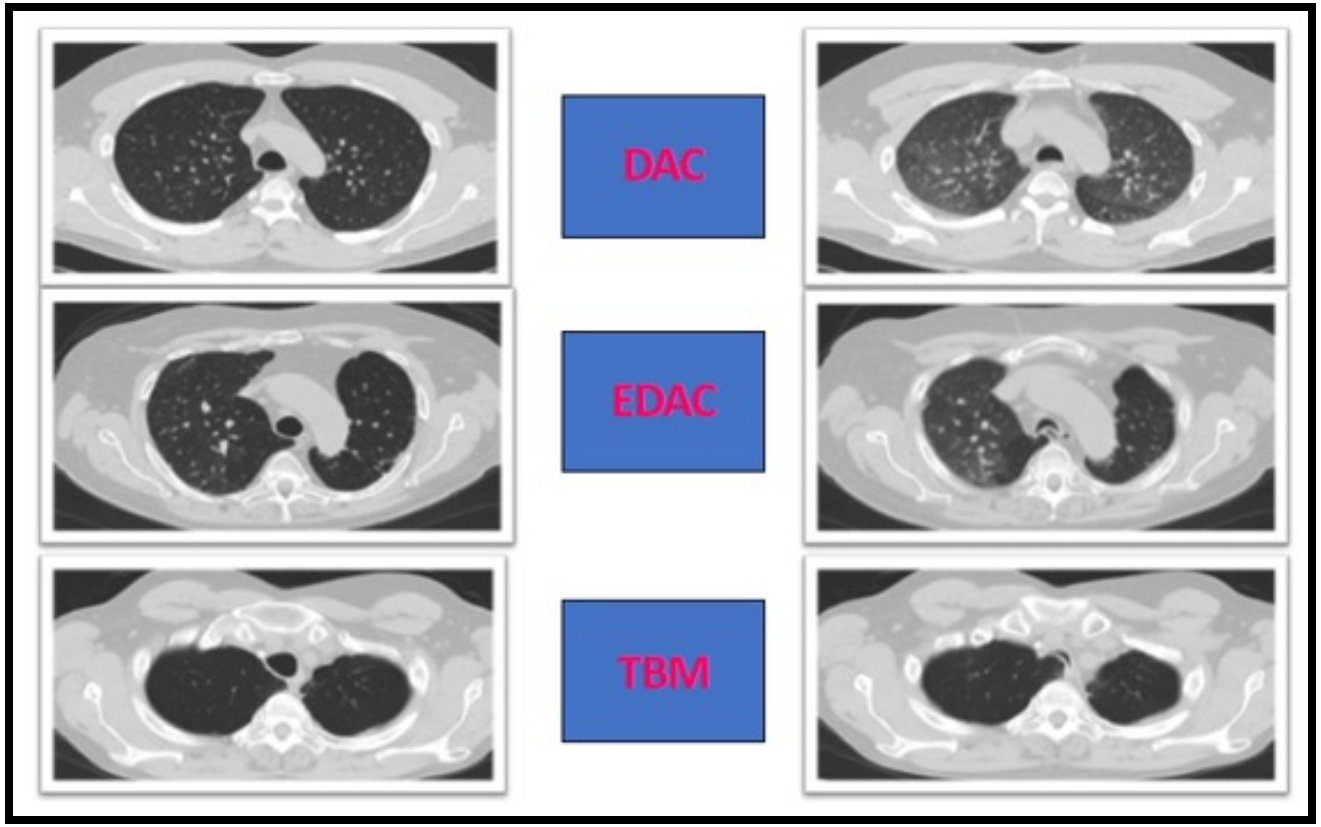
Images courtesy of Dr. Mark Hammer, Thoracic Radiology, BWH

Bronchoscopy as a diagnostic tool

1. “Gold standard” for assessment of airway collapse:
    - Approaches to sedation: “awake” (± specific maneuvers) vs. GA (e.g., TIVA)
    - What to look for:
        - Degree of collapse (50% reduction? By diameter or CSA?)
        - Extent of airway involvement (central airways only vs. involvement of lobar airways and beyond)



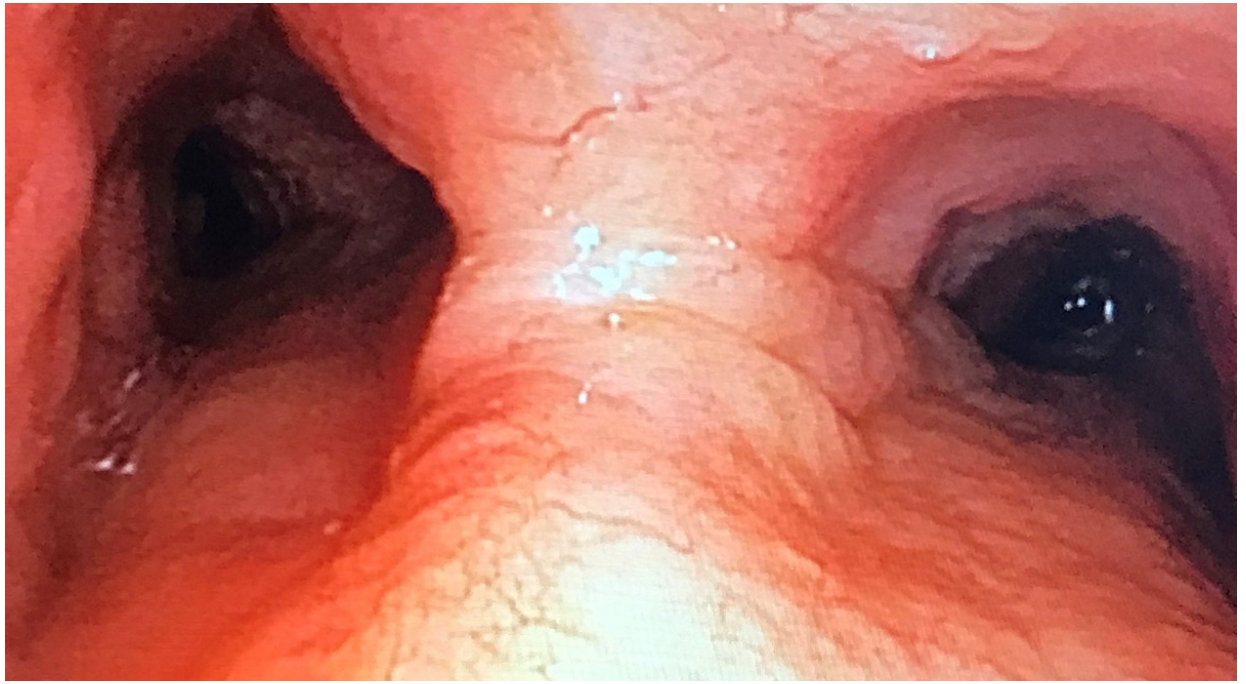




Bronchoscopy	Computed Tomography
1. **Direct visualization of the airway mucosa**	1. No details about the mucosa
2. Can be performed in critically ill patients at the bedside	2. **Reveals adjacent parenchyma and vascular structures**
3. Lack of ionizing radiation	3. Paired dynamic CT requires patient cooperation
4. **Allows assessment of CPAP response**	4. Exposure to ionizing radiation

Bronchoscopy as a diagnostic tool

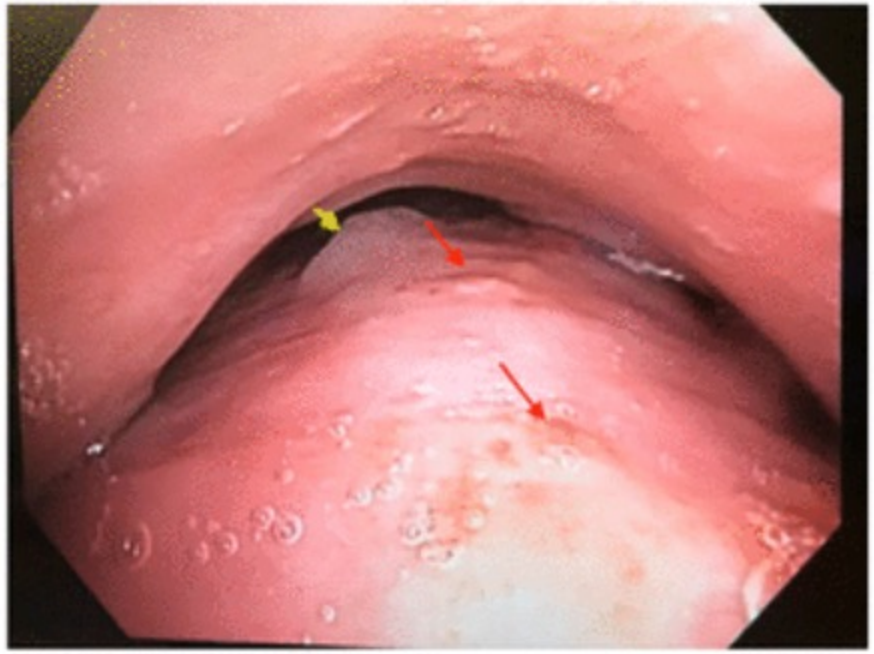
2. Better identification of underlying etiology
    - Visualization ± sampling of airway abnormalities



Tracheobronchial amyloidosis (AL type)

Bronchoscopy as a diagnostic tool

3. Assessment of TBM's (EDAC's) functional impact
   - Retained secretions
   - "Kissing ulcers"



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

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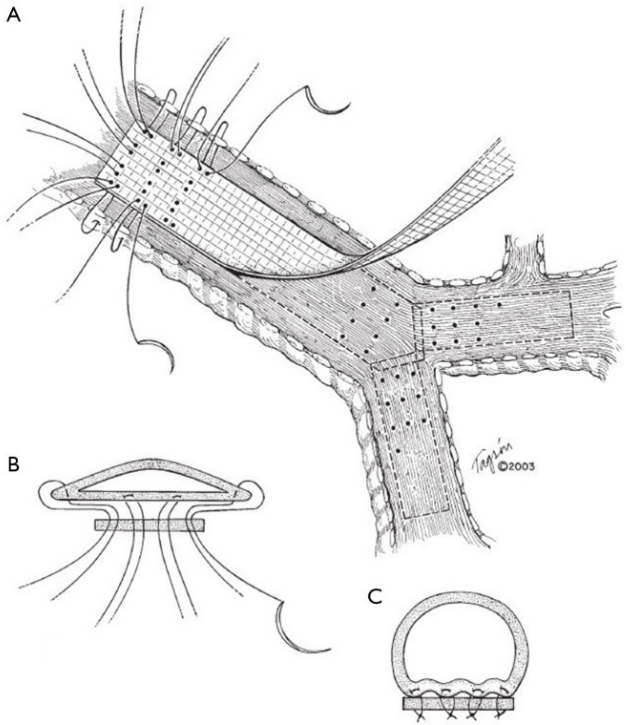
Treatment options

- Surgical
- Medical

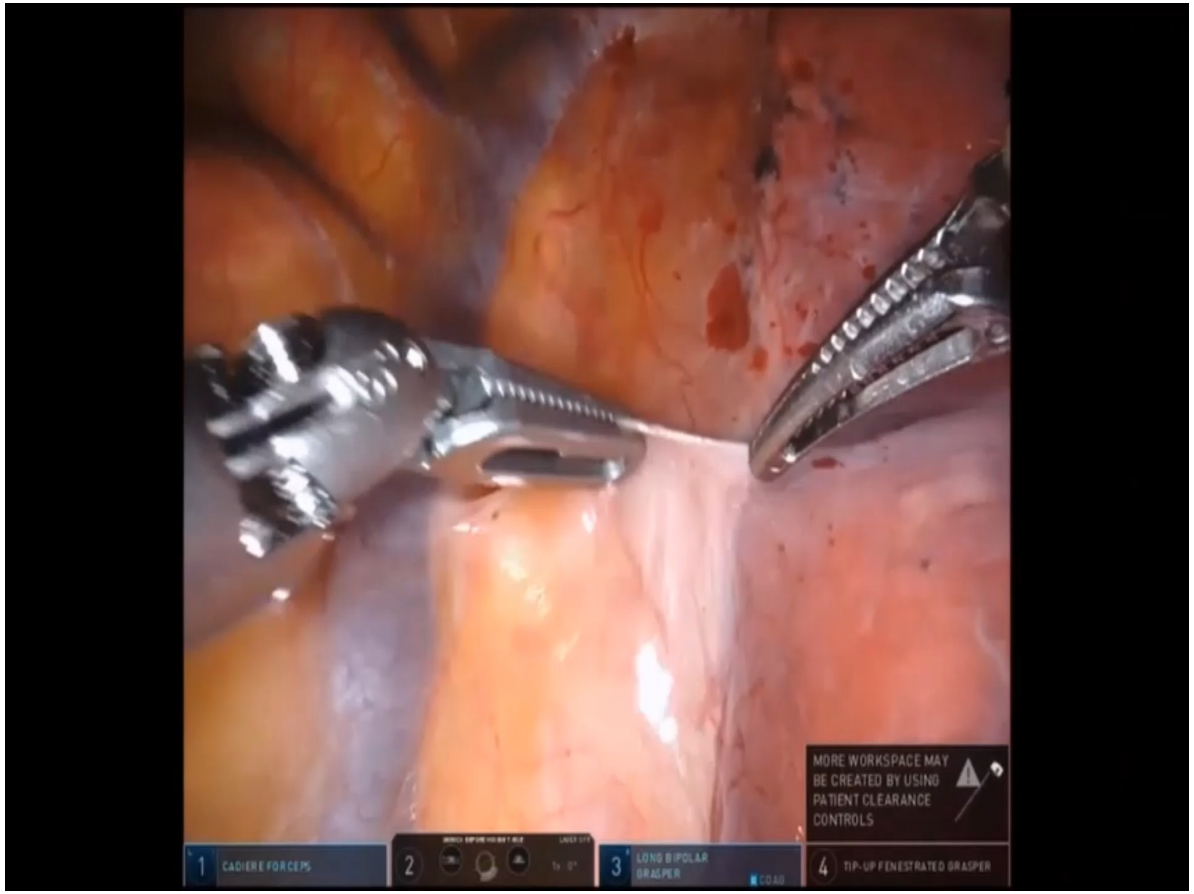
Gold standard: Surgical tracheobronchoplasty

- What?
  - Prolene mesh connecting one end of each cartilaginous ring to the other (to restore horseshoe shape)
  - Plication of posterior membrane to this mesh (to prevent expiratory collapse)
- How?
  - Open (thoracotomy) – *traditional approach*
  - Minimally invasive:
    - ~~VATS~~
    - Robotic – *newer, less invasive approach*



Minimally invasive thoracic surgery

- VATS vs. Robotics
- Surgery is in 3-D space-pitch, roll and yaw
  - VATS instruments do not bend
  - Robotic instruments are “wristed”
- Imaging
  - VATS-2-D view (cannot tell depth)
  - Robotic-3-D view (binocular)



Video courtesy of Dr. M. Blair Marshall, Thoracic Surgery, BWH (now at Sarasota Memorial Health Care System)

Robotic tracheobronchoplasty: Initial data

- Retrospective study out of New York
- 435 underwent dynamic CT for suspected TBM
- 42 (10%) eventually underwent robotic TBP
  - All had severe collapse (>90%) on awake bronchoscopy

Robotic tracheobronchoplasty: Benefits

- At 4 months: Significant improvement in PFTs (longer f/u unpublished)
- At 13 months: 82% satisfied | 72% improved cough | 57% improved SOB

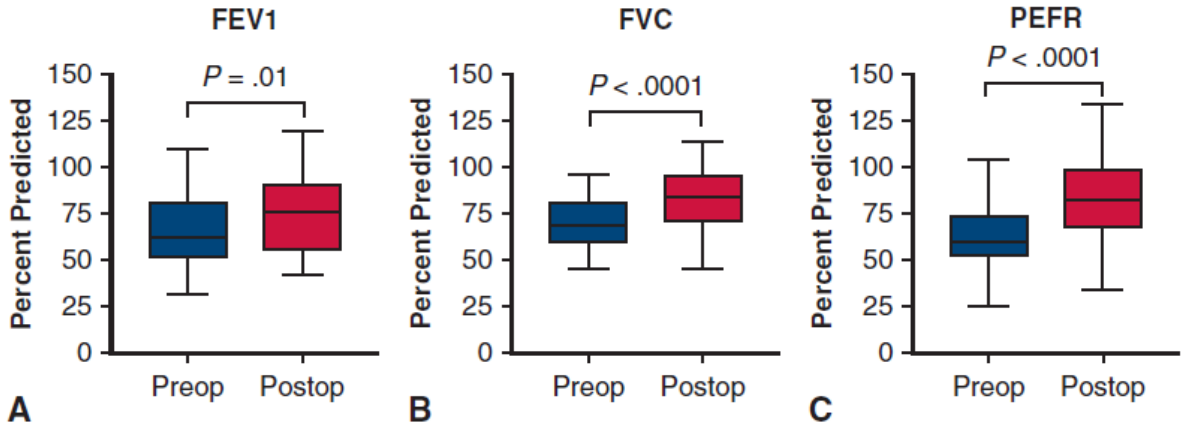


FIGURE 3. Median percent predicted lung function before and after robot-assisted tracheobronchoplasty. A, Forced expiratory volume in 1 second (*FEV1*). B, Forced vital capacity (*FVC*). C, Peak expiratory flow rate (*PEFR*). The median preoperative percent predicted FEV1 was 62.50% (interquartile range [IQR], 51.25%-82.00%) and was 76.00% (IQR, 55.25%-91.75%) after surgery ($P = .01$). The median preoperative percent predicted FVC was 69.50% (IQR, 59.25%-82.25%) and improved to 84.00% (IQR, 70.50%-96.25%) following operation ($P < .0001$). The median preoperative percent predicted PEFR was 60.00% (IQR, 52.00%-73.25%) and rose to 81.00% (IQR, 67.25%-101.75%) after surgery ($P < .0001$). The boxes indicate the IQR, with the upper boarder and lower boarder of the box indicating the upper and lower quartiles, respectively. Whiskers represent the minimum and maximum values. The central line demonstrates the median (n = 40 patients per group).

Robotic tracheobronchoplasty: Costs and risks

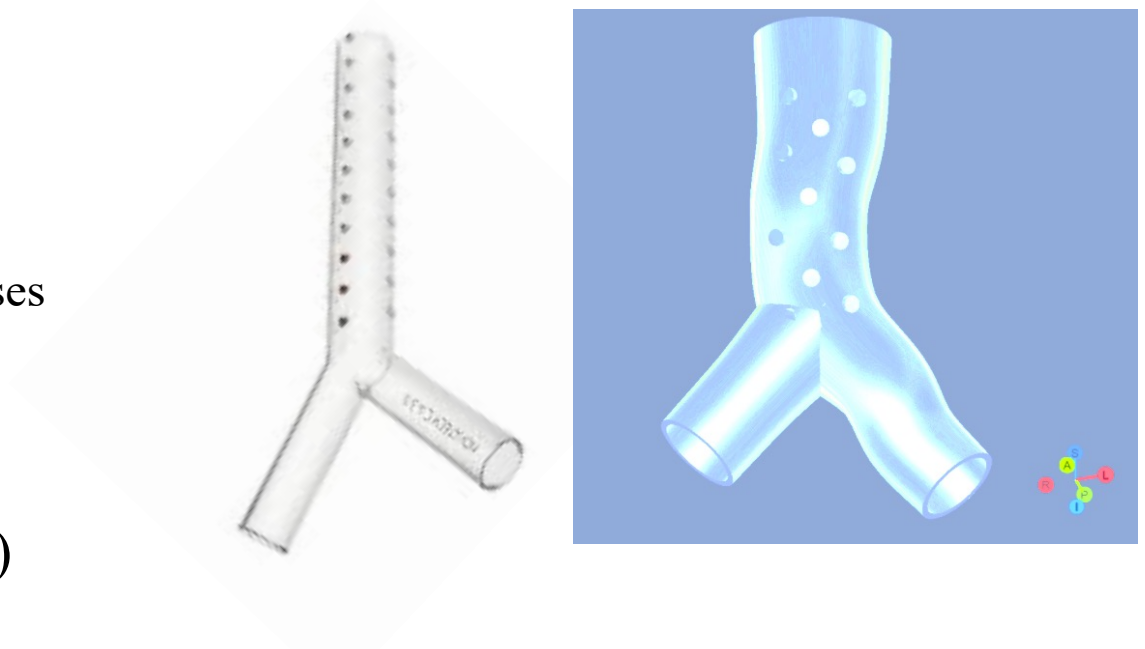
- Median hospital LOS: 3 days
- Complications: 19 (45%)
  - Minor: 11 (26%)
  - Major: 8 (19%)
    - 2 pneumothorax episodes needing chest tube
    - 2 SC emphysema episodes needing infraclavicular blowholes
    - VATS evacuation for hemothorax post-chest tube on POD2
    - Revision surgery for persistent symptoms (POD 125)
    - 1 return to ICU (needing bronchoscopy)
    - 1 return to ICU for arrhythmia (tachy-brady syndrome)
    - 0 deaths
    - 0 reintubations or tracheostomies

Role of airway stenting

1. Stent trial as decision aid for surgery
2. Stenting as destination therapy (?)

Stent trial as decision aid for surgery

- Stent trial protocol
  - 1-2 weeks, then scheduled removal
  - Objective + (mostly) subjective assessment
    - Some centers reserve stent trials for equivocal cases
- Stent options:
  - Silicone Y-stent
    - Off the shelf vs. 3D printed (customized)
  - SEMS (self-expanding metallic stents)
    - Covered vs. uncovered
    - Note: FDA Black Box warning for use in non-malignant airway disease



Standard vs. customized (3D-printed) silicone Y-stent

Stent as destination therapy (?)

- Mucostasis / Respiratory infection
  - Airway clearance can potentially be worse than with TBM itself
  - Mucus plugging can be an airway emergency
- Granulation tissue
  - Hemoptysis
  - Obstruction
- Cough and/or chest pain
- Migration
- Stent fracture
- Epithelialization (uncovered metallic stents only)

Silicone (Y) as destination therapy (?)

- Mucostasis / Respiratory infection
  - Airway clearance can potentially be worse than with TBM itself
  - Mucus plugging can be an airway emergency
- Granulation tissue
  - Hemoptysis
  - Obstruction
- Cough and/or chest pain
- ~~Migration~~
- Stent fracture
- ~~Epithelialization (uncovered metallic stents only)~~

~~Stent~~ Tracheostomy as destination therapy (?)

- Mucostasis / Respiratory infection
  - ~~Airway clearance can potentially be worse than with TBM itself~~
  - Mucus plugging can be an airway emergency
- Granulation tissue
  - Hemoptysis
  - Obstruction
- ~~Cough and/or chest pain~~
- ~~Migration~~
- ~~Stent fracture~~
- ~~Epithelialization (uncovered metallic stents only)~~

Conservative management for non-surgical candidates

- Avoid ICS if possible?
  - Some evidence that long-term ICS may contribute to TBM and/or EDAC (smooth muscle atrophy)
- Weight loss (where applicable)
- Airway clearance regimen:
  - Guaifenesin
  - Hydration ± nebs (e.g., saline)
  - Oscillatory PEP devices (Acapella, Aerobika)
- Positive airway pressure:
  - Pursed lip breathing
  - CPAP (for night/naps/"EDAC attacks")
  - Ambulatory CPAP (Life2000; uses nasal pillows)
  - Ambulatory PEP device (PEP Buddy)

Positive airway pressure, to go

Multi-disciplinary approach to TBM/EDAC
Our BWH TBM/EDAC program

- Collaboration of pulmonary medicine, thoracic surgery, interventional pulmonology, radiology, ENT, and anesthesiology focused on assessment and treatment of TBM/EDAC.
- Provides monthly interdisciplinary review of complex cases.
- Offers novel assessment tools (cine CT of trachea, airway oscillometry) and treatment options (robotic-assisted thoracoscopic tracheoplasty).
- Provides opportunities for advancing the science of TBM/EDAC as well as development of novel interventions.

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- Victoria Forth
- George Washko
- Gary Visner
- Chris Fanta

Interventional Pulmonary:

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- M. Blair Marshall
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- Mark Hammer
- Raul San Jose Estepar

Anesthesiology:

- Philip Hartigan

Conclusions

- TBM / EDAC:
  - Underdiagnosed or misdiagnosed disease.
    - No standardized definition or classification
      - ✓ Distinguish TBM from EDAC on bronchoscopy and CT scan
    - Heterogeneous disease with diverse symptom profile. Under-recognized cause of dyspnea and cough.
    - The combination of recent advancements in CT, bronchoscopy, and a multi-disciplinary approach has facilitated the diagnosis and management.
  - If untreated, has significant morbidity and healthcare utilization
- Tracheobronchoplasty appears to result in symptomatic improvement in patients with TBM
  - The procedure can be performed both open and robotically
    - ✓ Advancements in surgical techniques appear to be making it a lower risk undertaking than in the past
- Continued research efforts will add new knowledge

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THANK
YOU