

Interventional Pulmonology Update

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Disclosure

- Pulmonx: Consultant
- Olympus: Consultant
- Cook Medical: Consultant

Objectives

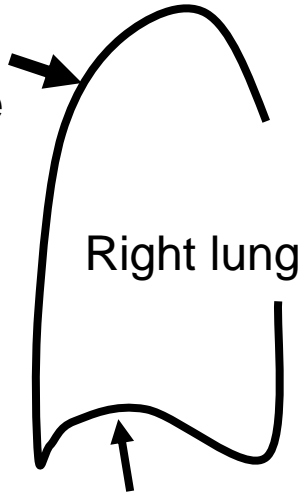
- Upon completion of this learning activity, participants should know the selection criteria for bronchoscopic lung volume reduction
- Upon completion of this learning activity, participants should be able to recognize the complications for bronchoscopic lung volume reduction in severe emphysema
- Upon completion of this learning activity, participants should know the role of robotic bronchoscopy in the diagnosis of the peripheral lung nodule

Agenda

- Bronchoscopic Lung Volume Reduction with Valves
- Robotic Bronchoscopy

Before Emphysema

**Normal
Lung Size
and Shape**

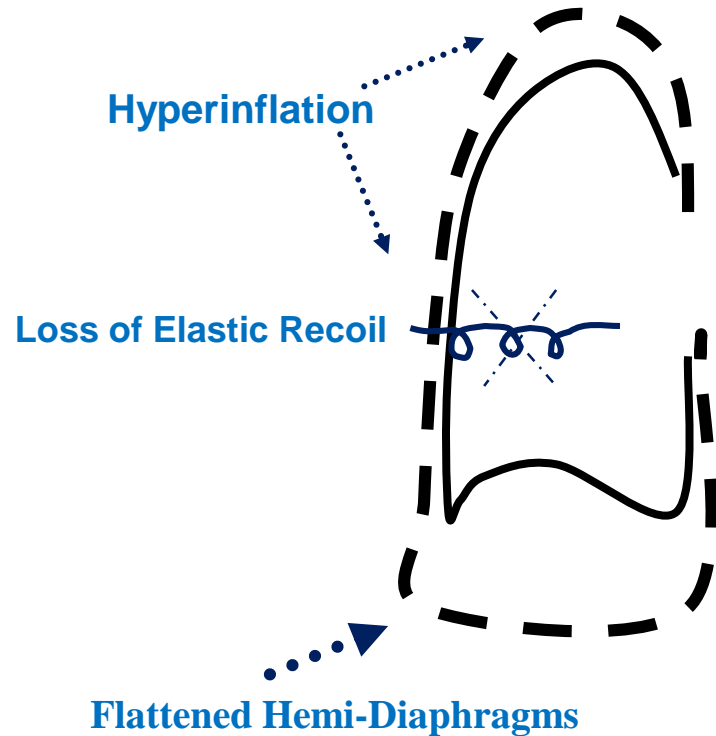


Right lung

Diaphragm with normal curvature



After Emphysema

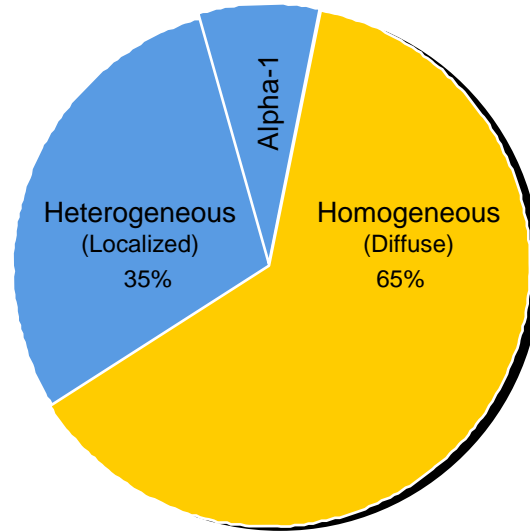
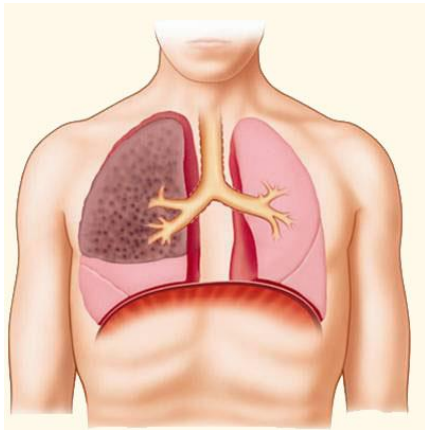


Emphysematous Lungs

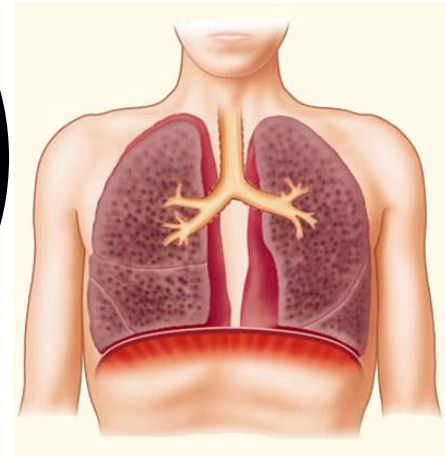


Emphysema Types

Heterogeneous

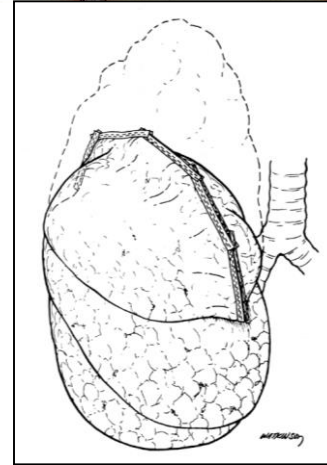
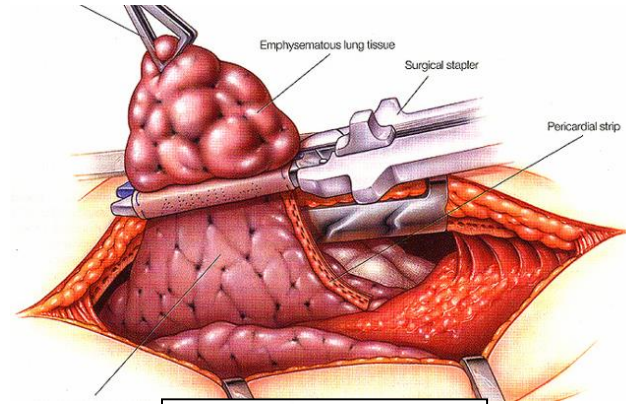


Homogeneous



The Concept of lung Volume Reduction

- Lung volume Reduction
 - Removal of the most destroyed hyperinflated poorly perfused areas of the lung can enhance the function of the remaining “normal” lung and leads to functional and symptomatic improvement
 - Applicable in heterogeneous emphysema (upper lobe predominant)
- Multiple retrospective and prospective studies reported success with surgical lung volume reduction



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A Randomized Trial Comparing Lung-Volume–Reduction Surgery
with Medical Therapy for Severe Emphysema

National Emphysema Treatment Trial Research Group*

- Best evidence provided by the NETT (National Emphysema Treatment Trial) published in 2003
 - Randomized controlled multi-center trial

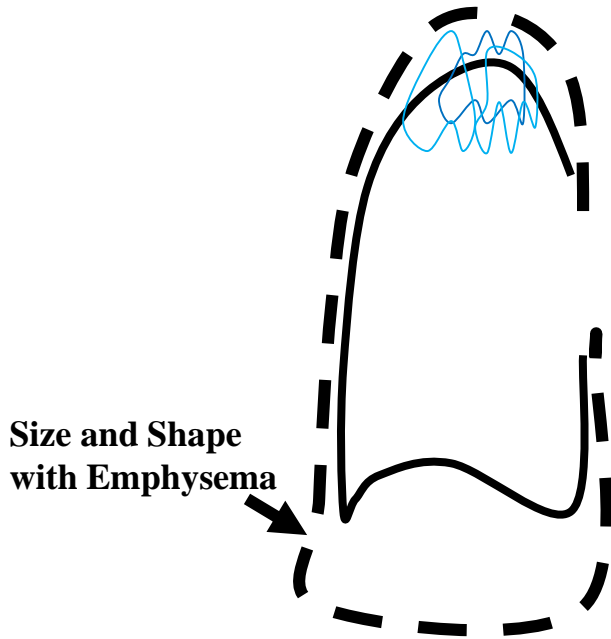
The NETT Results

- 1218 patients with emphysema randomized to either continued medical treatment or lung volume reduction surgery
- At 24 months, exercise capacity improved by >10 W in 15% of patients in the surgery group Vs. 3% in the medical group
- Dyspnea and subjective symptoms improvement in nearly all patients
- Quality of life improvement comparable to heart valve replacement surgery

Surgical Lung Volume Reduction

- Overall, lung volume reduction surgery offered no survival benefit
- There was a survival advantage in patients with upper lobe disease and low exercise capacity
- Mortality rate 5.5%
- Mortality from surgery was found to be higher than the medical group in patients with:
 - Non-upper-lobe-emphysema (homogenous emphysema)
 - High exercise capacity
- An average hospital stay of 10 to 14 days

Emphysema and Lung Volume Reduction

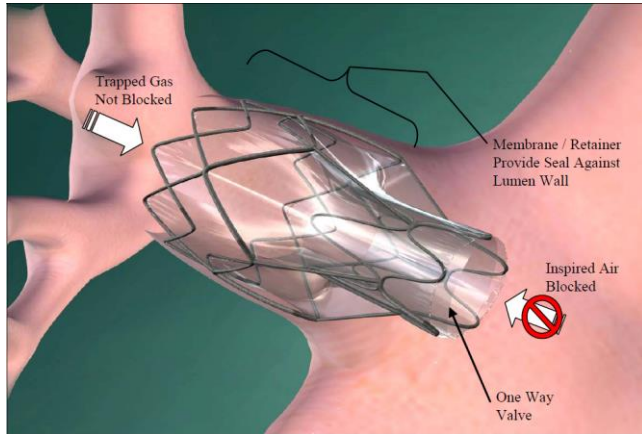


Size and Shape
with Emphysema

Can lung volume reduction
be achieved without
surgery?

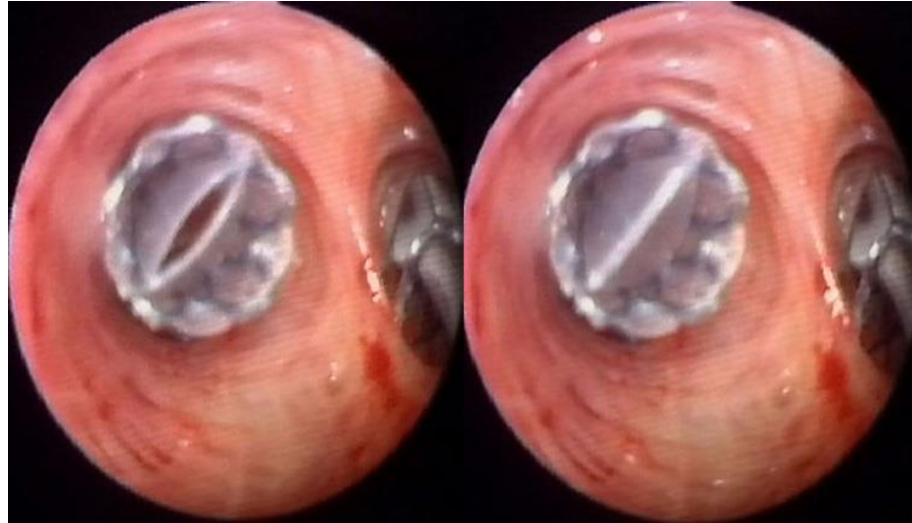
- Many more patients may benefit from a minimally invasive procedure
- Co-morbidities exclude many of the most severely affected patients
- Minimally invasive procedure may allow earlier and staged therapeutic intervention

Endobronchial Valves



First type of valves received FDA approval in June of 2018

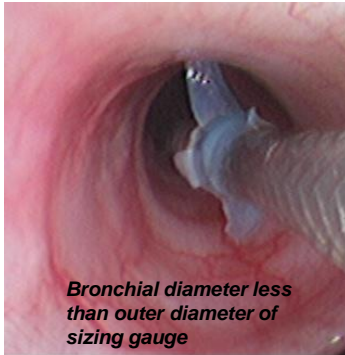
Bronchoscopic View



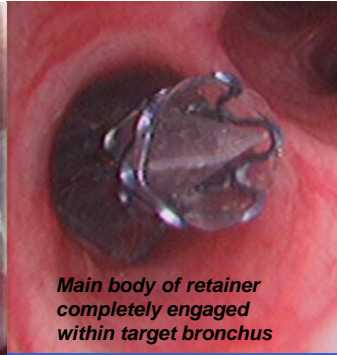
Exhalation

Inspiration

Endobronchial Valve (EBV) Procedure Overview



Advance housing into target segment, confirm sizing using gauges



Confirm EBV positioning and sizing

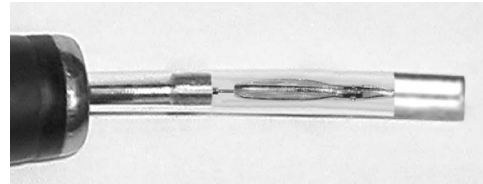
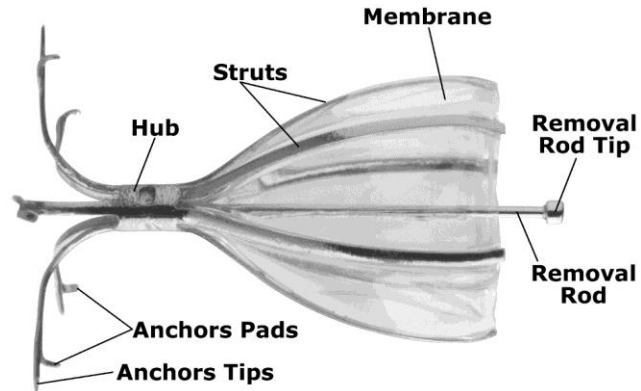
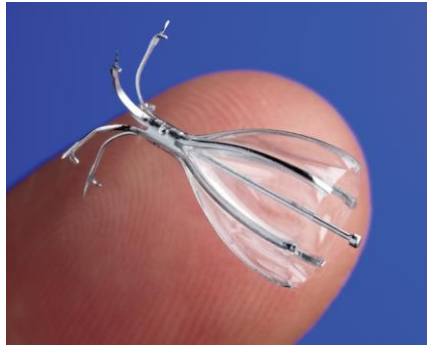
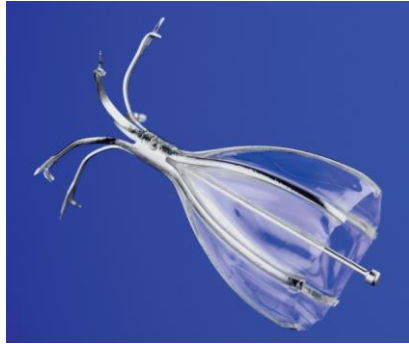


EBV allowing air to exit from during expiration



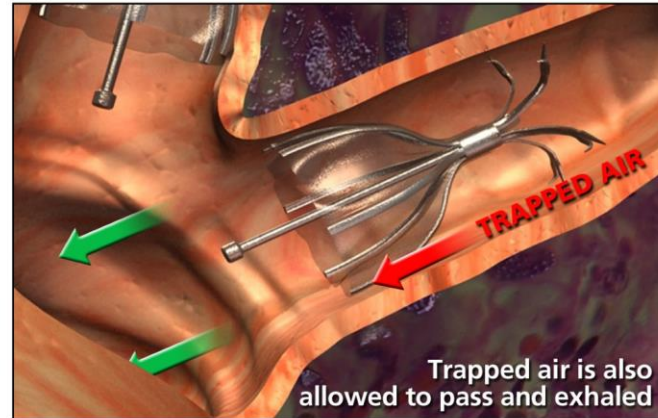
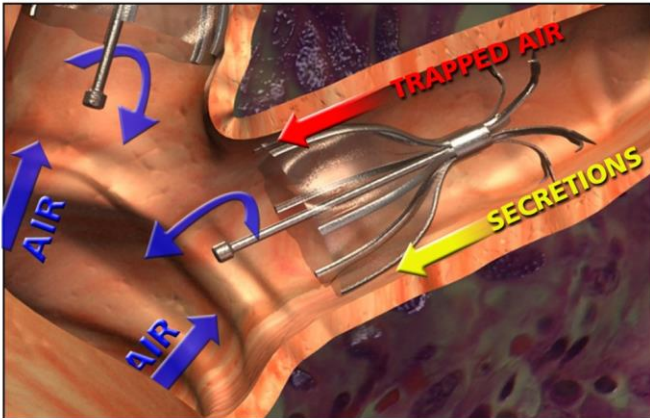
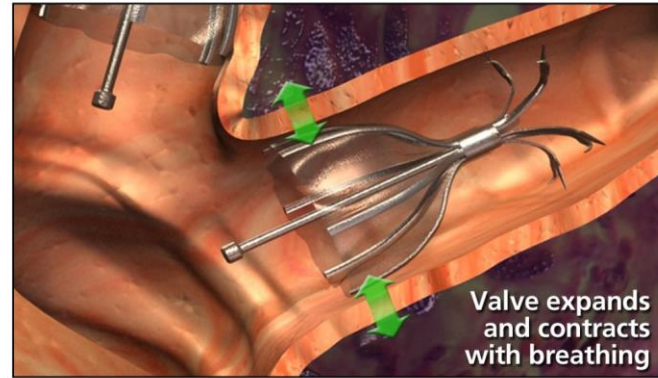
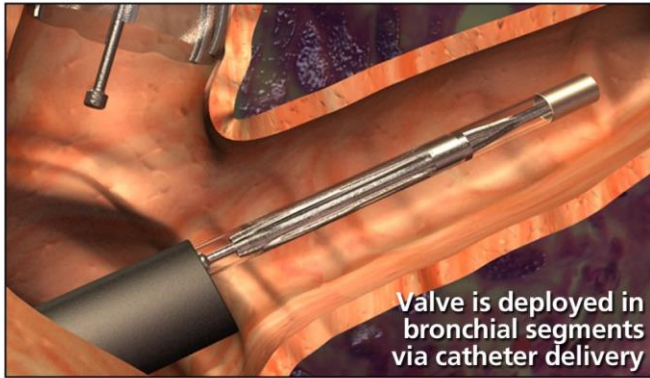
EBV preventing air from entering during inspiration

Another Endobronchial Valve



A second type of valves approved by FDA in 12/2018 for BLVR

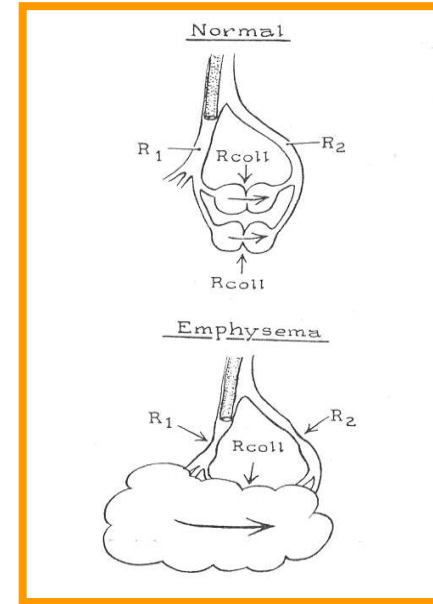
Endobronchial Valve System



Early Experience–Why Are Some of The Valves Failing?

Collateral Ventilation

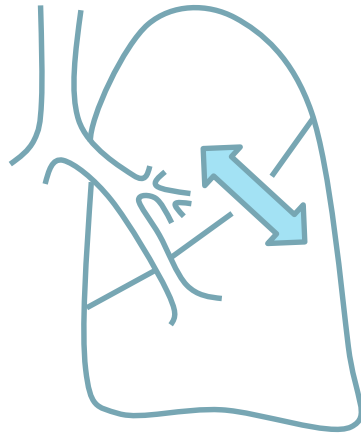
- The ability of gas to move from one part of the lung to another without using the known anatomical airways
- Three levels of collateral ventilation have been described in humans:
 - Intra-alveolar pores
 - Accessory bronchiolar-alveolar connections
 - Interbronchial channels
- Minimal role in normal lungs since the resistance to airflow is higher in collateral channels than in the airways
 - Important role in emphysematous lungs since the resistance to airflow is low in collateral channels
 - Provides important channels for gas distribution in emphysema



What is Collateral Ventilation?

- **Collateral ventilation is airflow between lobes** “through channels that bypass the normal airways”*
- **Only lobes WITHOUT collateral ventilation should be treated with valves**

Collateral Ventilation (CV+)



No Collateral Ventilation (CV-)

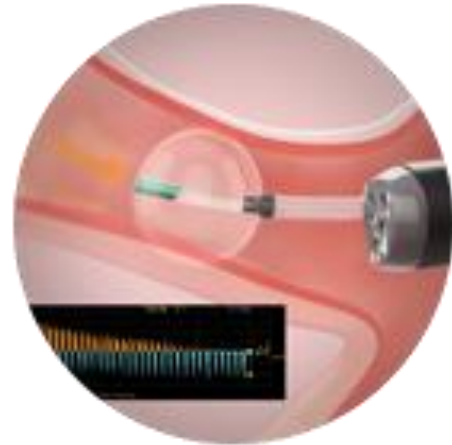


Endobronchial Valve (EBV)

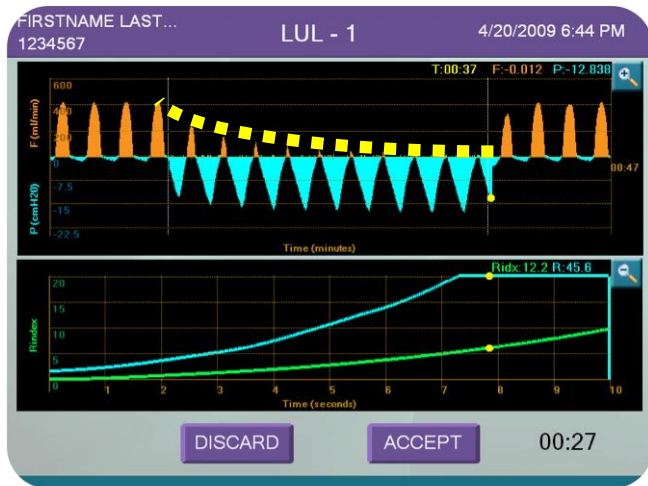
- How to identify a potential subset population that may benefit from the EBV device?
 - HRCT analysis
 - Fissure integrity
 - Heterogeneity
 - Collateral Ventilation (CV) Assessment System

CV Assessment System

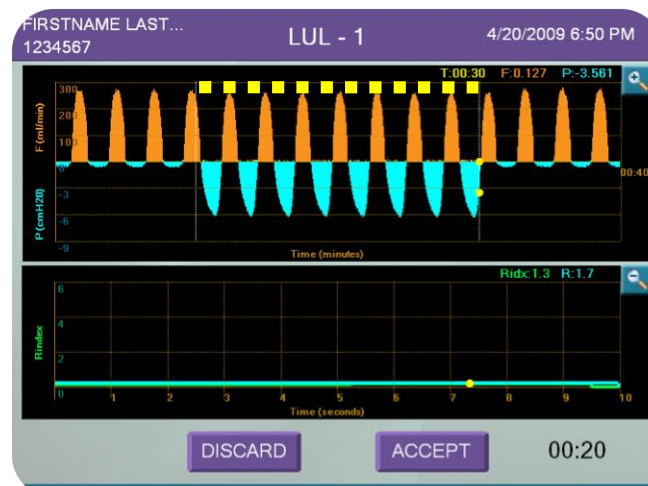
- The balloon catheter is inserted through a bronchoscope to the target airway, and the balloon is inflated to block flow to the target region
- The system calculates airway resistance and measures CV in isolated lobes in the lung. The console displays expiratory air flow (orange), pressure (blue), and resistance measurements



CV Assessment System



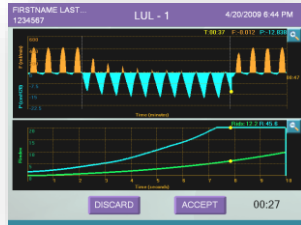
No Collateral Ventilation



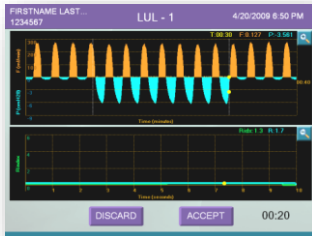
Collateral Ventilation

CV Assessment System: Clinically Validated

Assessment Prediction



Low CV: 9 Patients



High CV: 11 Patients

24 hr Post Procedure Atelectasis Outcome



Atelectasis: 7 Patients



No Atelectasis: 11 Patients

Heidelberg 2008 Study
n=20

Primary Endpoint:
Safety & Feasibility

ENDPOINT MET

Secondary Endpoint:
Correlation of Prediction
to Atelectasis Outcome

90% CORRELATION

A Randomized Study of Endobronchial Valves for Advanced Emphysema (The VENT Study)

- A randomized controlled trial comparing the safety and efficacy of endobronchial valve therapy (EBV) vs. standard medical care (control group) in patients with heterogeneous emphysema
- Unilateral valve placement (one upper lobe only)
- 321 Patients enrolled:
 - 220 in EBV group
 - 101 in control group

A Randomized Study of Endobronchial Valves for Advanced Emphysema

Outcomes at 6 months	EBV Group	Control	Between-Group Difference in Change from Baseline	P Value
FEV1	4.3%	-2.5%	6.8%	0.005
6-min Walk	2.5%	-3.2%	5.8%	0.04
SGRQ Score*	-2.8	0.6	-3.4	0.04

* SGRQ = St. George's Respiratory Questionnaire, scores range from 0-100, higher scores indicate worse quality of life, minimal clinically important difference is 4 points

Safety Profile of Endobronchial Valves

Safety at 90 days	EBV Group	Control	P Value
COPD flares with Hospitalization	7.9%	1.1%	0.03
Hemoptysis	6.1%	0%	0.01
Pneumothorax	1.4%	0%	0.56
Death	0.9%	0%	1.00

Valve-related complications

- Valve expectoration or migration: 4.7%
- Bronchial granulation tissue: 2.3%
- Bronchial trauma: 0.5%
- Pneumonia distal to valve: 0.9%

A Randomized Study of Endobronchial Valves for Advanced Emphysema (The VENT Trial)

- Modest improvement in FEV1 and 6-min walk test
- More improvement was seen in patients with:
 - Higher radiographic heterogeneity of emphysema
 - Radiographic evidence of fissure completeness
 - A surrogate for the lack of interlobar collaterals that negatively affects lobar isolation by the valves
- Improvement comes at a cost of more frequent adverse events (COPD exacerbation, hemoptysis, and pneumonia)
- Didn't received FDA approval

A Multicenter RCT Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE)

- 190 patients with heterogeneous emphysema randomized to standard of care (62) vs. endobronchial valves (128)
 - Collateral ventilation assessment system used in all patients undergoing EBV treatment
- At 12-months, percent of subjects who had an improvement in FEV1 of $\geq 15\%$:
 - 47.7% in the valve group
 - 16.8% in the standard of care group
- Significant improvements were seen in:
 - 6MWT: +39.31 m ($P = 0.002$)
 - St. George's Respiratory Questionnaire, -7.05 points ($P = 0.004$)
 - Hyperinflation (residual volume, -522 ml; $P < 0.001$)

A Multicenter RCT of Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE)

- Pneumothorax was the most common serious adverse event in the Treatment Period (procedure to 45 days), in 26.6% of the valve subjects
- 4 deaths occurred in the valve group during treatment period
 - 1 death in EBV group and 1 death in SOC group between 46 days and 12 months

Adverse Events

		Treatment Period Day of Procedure/Randomization to 45 Days		Longer-Term Period 46 Days from the Study Procedure/Randomization until 12-Month Visit	
	EBV (<i>n</i> = 128)	SoC (<i>n</i> = 62)	EBV (<i>n</i> = 122)		SoC (<i>n</i> = 62)
Death	4 (3.1)*	0 (0.0)	1 (0.8)		1 (1.6)
Pneumothorax	34 (26.6)†	0	8 (6.6)		0
COPD exacerbation	10 (7.8)	3 (4.8)	28 (23.0)		19 (30.6)
Pneumonia	1 (0.8)	0	7 (5.7)		5 (8.1)
Respiratory failure	2 (1.6)	0	1 (0.8)		2 (3.2)
Arrhythmia	0	0	1 (0.8)		2 (3.2)
Diverticulitis	0	0	1 (0.8)		2 (3.2)

How Are We
Doing With
Valves in Real
Life?

Outpatient Work Up



- First visit:
 - History and physical
 - Chest CT
 - PFTs
- Second visit:
 - Perfusion scan or SPECT scan
 - 6MWT
 - ABG on RA
 - Echo (for most patients)

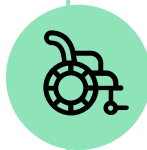
Patients Selection

Stability of Disease



- Less than two hospitalizations for COPD exacerbations over the last year
- Stable with ≤ 20 mg prednisone (or equivalent) daily

Functional Status



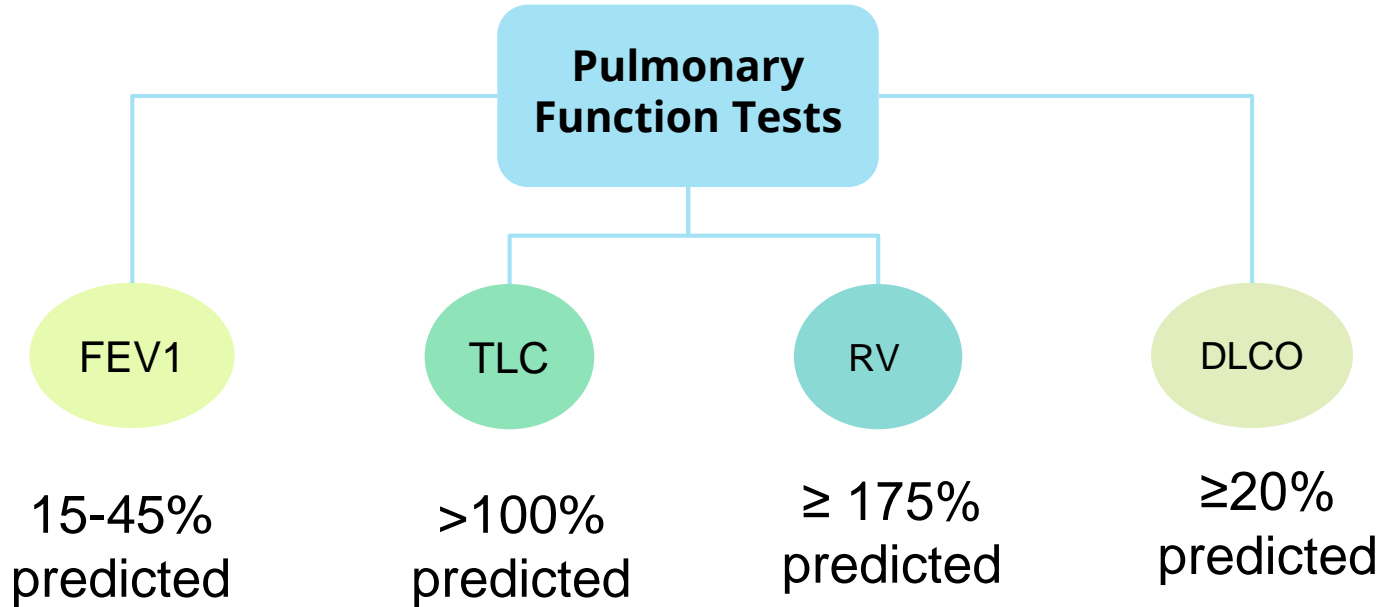
- Has participated in a pulmonary rehabilitation program or in maintenance phase
- mMRC: 2-5 (a scale of breathlessness of 1-5)
- 6MWD 100-500m

Co-Morbidities



- No active smoking for at least 4 months
- BMI < 35 kg/m²
- No active CAD or severe pulmonary HTN (sPAP >45mm Hg)

Physiological Impairment - PFT First Clinic Visit



Chest CT-First Clinic Visit

- Confirms the diagnosis of emphysema
- Characterizes the emphysema as homogenous or heterogeneous
- Detects additional findings on chest CT



Unfavorable Chest CT Findings-Lung Nodules

- Most common finding
- Solitary lung nodule or multiple lung nodules
- Suspicious lung nodules should be addressed immediately
- Small sub-centimeter lung nodules need to be followed
 - Either delay BLVR until nodules are declared stable based on Fleischner Guidelines
 - Or ensure that these nodules are not present in your target lobe

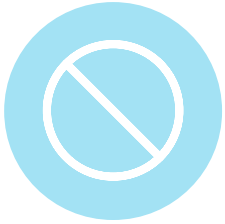


Unfavorable Chest CT Findings

- Large bullae encompassing greater than 30% of either lung
- Moderate to severe ILD
- Significant bronchiectasis



Exclusions and Warnings



- Exclusions

- Patients with evidence of active pulmonary infection
- Patients with known allergies to Nitinol, Nickel, Titanium, or Silicone
- Patient who have not quit smoking
- Severe hypercapnia ($\text{PaCO}_2 \geq 50$ mm Hg on room air) and/or severe hypoxemia ($\text{PaO}_2 \leq 45$ mm Hg on room air)

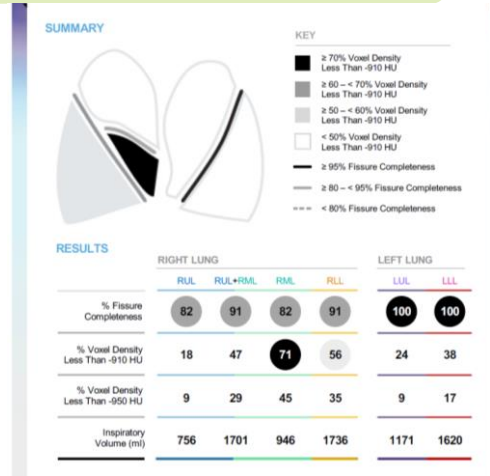


- Warnings (only after careful consideration):

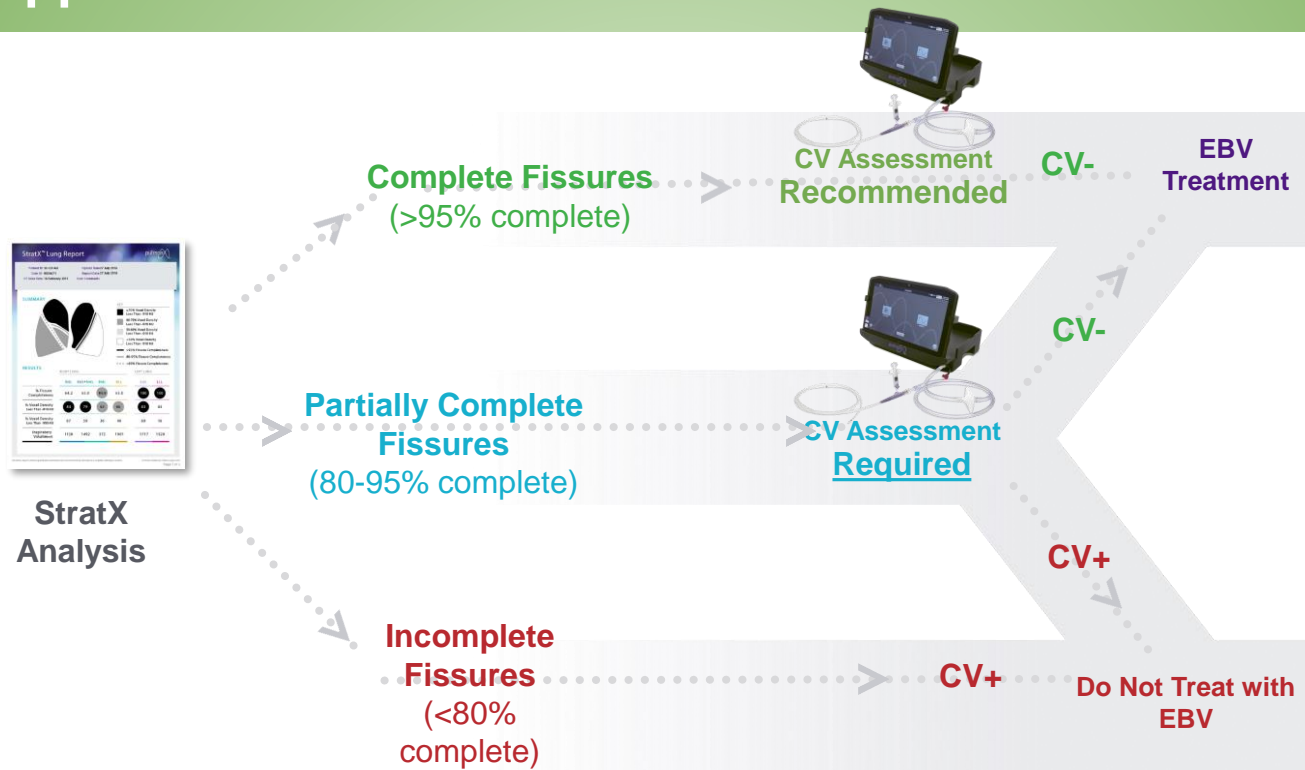
- Prior lung transplant, LVRS, median sternotomy or lobectomy

Analysis of Target Lobe

- If all criteria are met, upload the chest CT into the analysis software (StratX or SeleCT)
- Carefully study the report alongside the perfusion report



Optimal Approach for CV Assessment

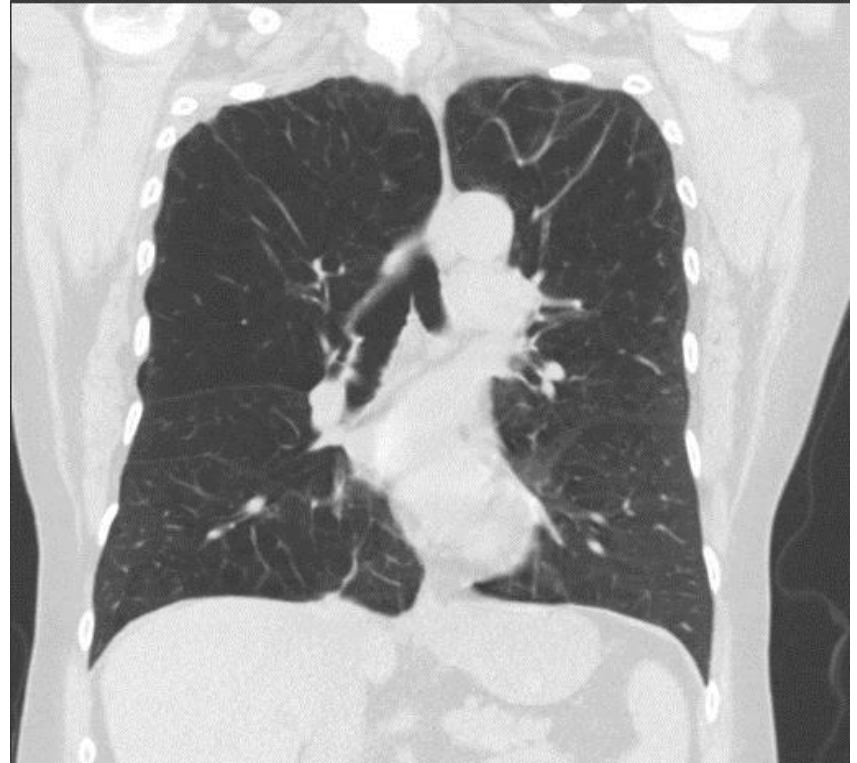


Case Discussion

- 73 Y.O. woman with emphysema diagnosed 3 years ago
- Significant DOE, mMRC =3
- Only hospitalization for COPD was in 2019
- No COPD exacerbation over the last year
- Participated in pulmonary Rehab in 2019, maintaining exercise at home (walking on treadmill three times a week)
- On Albuterol, Formoterol/Budesonide and tiotropium
- Quit smoking 13 years ago
- BMI: 26
- No known cardiac co-morbidities

Case Discussion

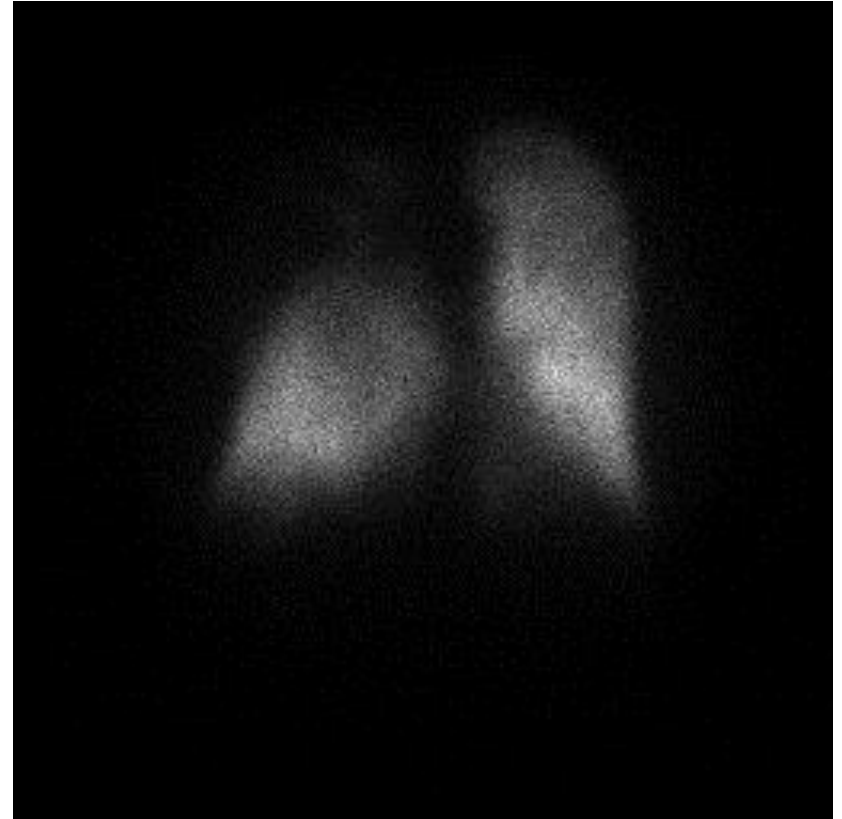
- PFTs: FEV1 42%, TLC 128%, RV 186%, DLCO 56%
- 6MWT: 265 M
- ABG: 7.41/PCO2 41/PO2 68
- Echo: normal
- Chest CT: Severe heterogeneous emphysema and hyperinflation, stable 6 mm nodule in the lingula (compared to one year ago)



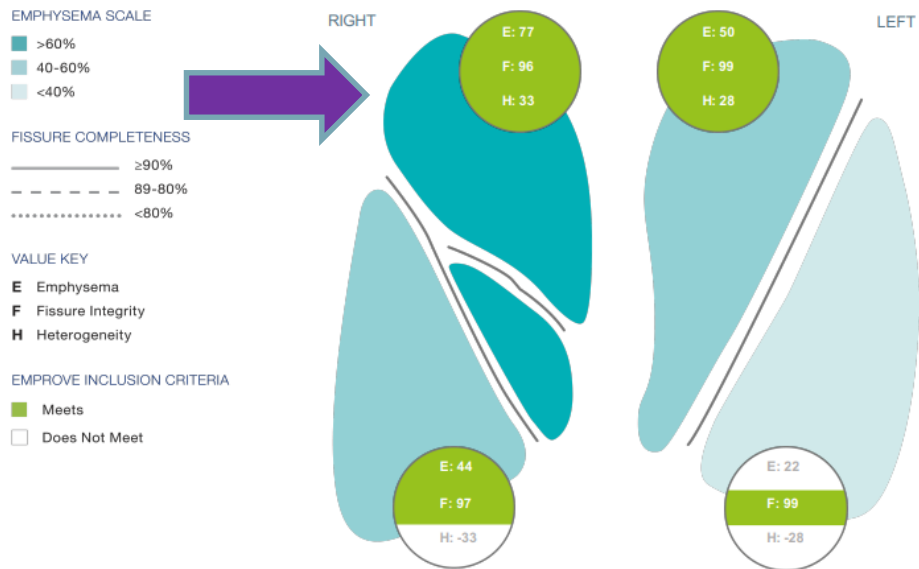
Case Discussion

Perfusion scan

- Left upper zone: 9% Right upper zone: 2.5%
- Left mid zone: 30.3% Right mid zone: 20.2%
- Left lower zone: 18.6% Right lower zone: 19.5%
- Total left lung: 57.9% Total right lung: 42.1%



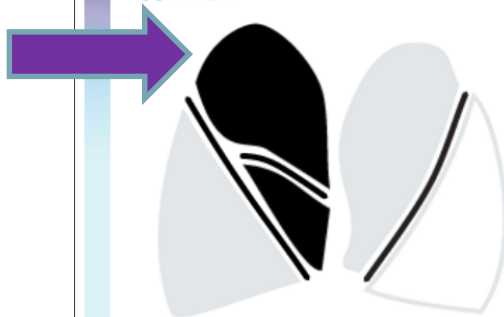
SeleCT Report-Endobronchial Valves



	EMPROVE THRESHOLDS	RUL	RML	RLL	LUL	LLL
EMPHYSEMA (%)	≥ 40%	77	66	44	50	22
FISSURE SCORE (%)	≥ 90%	96	N/A	97	99	99
HETEROGENEITY (%)	≥ 10%	33	N/A	-33	28	-28
VOLUME (cc)	-	1414	393	1237	1229	1128

SeleCT Report - Endobronchial Valves

SUMMARY



KEY

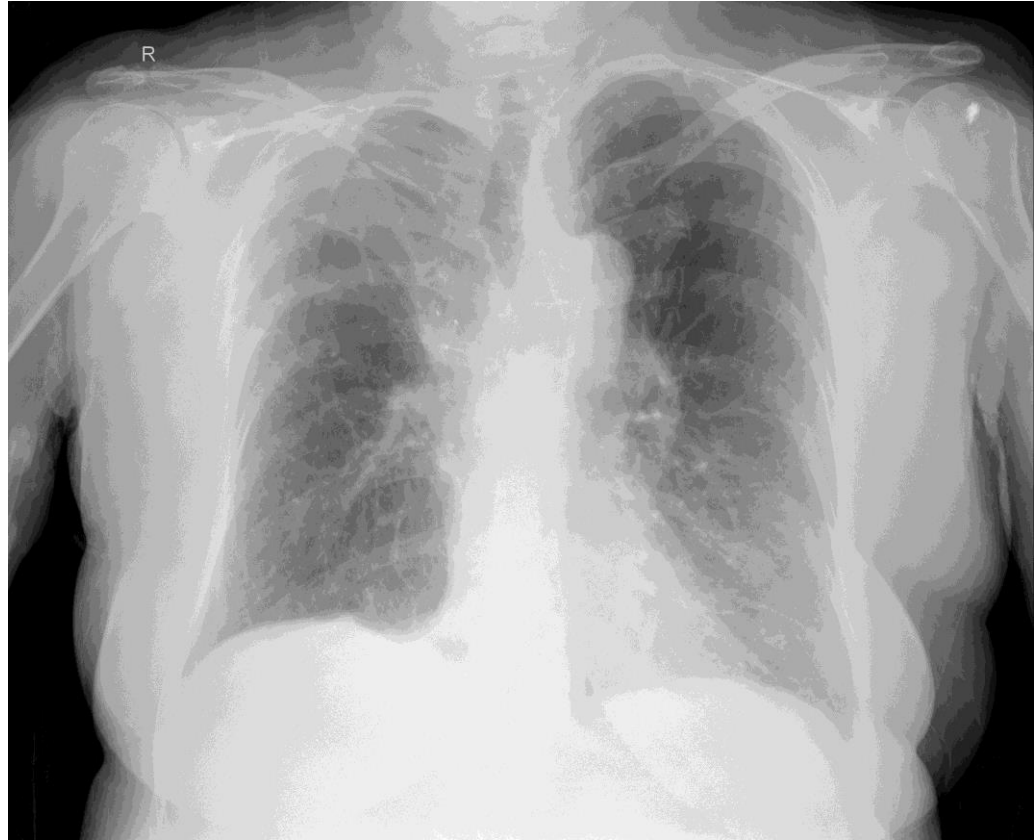
- ≥ 70% Voxel Density
Less Than -910 HU
- ≥ 60 - < 70% Voxel Density
Less Than -910 HU
- ≥ 50 - < 60% Voxel Density
Less Than -910 HU
- < 50% Voxel Density
Less Than -910 HU
- ≥ 95% Fissure Completeness
- ≥ 80 - < 95% Fissure Completeness
- < 80% Fissure Completeness

RESULTS

	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	96	97	99	97	99	99
% Voxel Density Less Than -910 HU	80	78	72	51	56	27
% Voxel Density Less Than -950 HU	62	58	44	23	31	11
Inspiratory Volume (ml)	1414	1807	393	1237	1229	1128

Case Discussion

- Patient underwent bronchoscopy with placement of valves in the RUL
- Developed complete atelectasis of the RUL within 1 day
- No pneumothorax

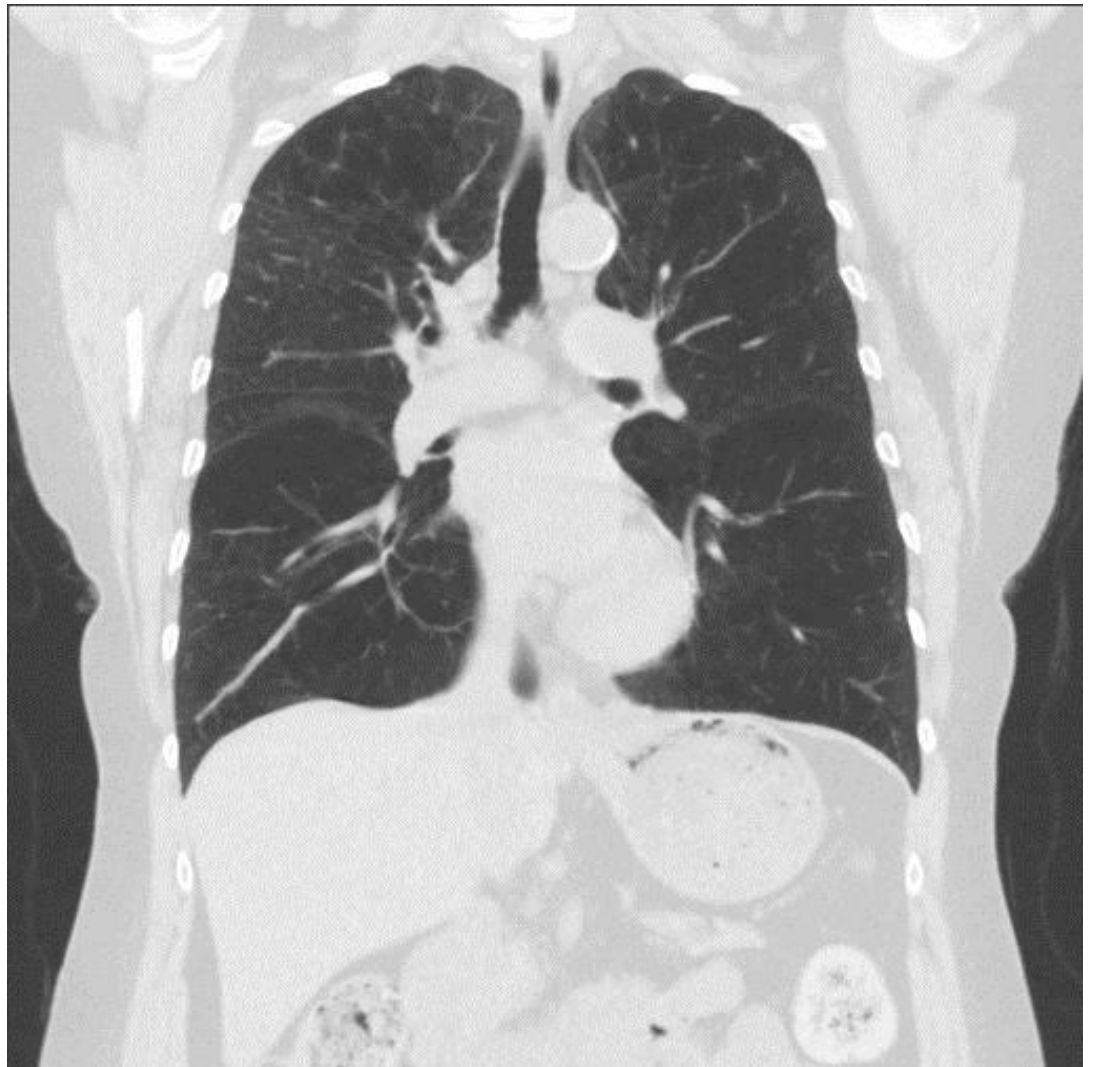


Case 2

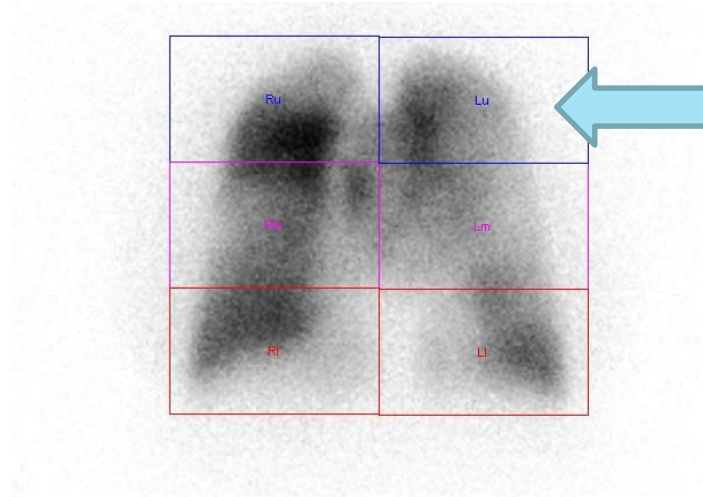
- 62 Y.O. Woman with severe centrilobular emphysema
- 30 Pack-year smoking history, quit in 2013
- She has chronic daily cough and severe dyspnea on exertion; on O2 supplementation (2-3 LMP)
- No hospitalizations for COPD
- Develops COPD exacerbation 2-3 times a year
- Participates in a maintenance pulmonary rehab program

Patient Profile

- PFTs:
 - FEV1 23%
 - FVC 71%
 - TLC 110%
 - RV 176%
 - DLCO 35%
- ABG on RA:
 - PO₂: 72



Perfusion Scan



Right Lung		Anterior Kct			
%	Kct	Right	Left	%	Kct
17.2	125.68	18.3	135.16	13.9	102.61
24.5	178.43	24.1	178.24	15.7	116.21
19.0	138.86	16.3	120.65	11.6	85.50
60.7	442.98	58.8	434.04	41.2	304.32

Stratx Report

SUMMARY



KEY

- $\geq 70\%$ Voxel Density
Less Than -910 HU
- $\geq 60 - < 70\%$ Voxel Density
Less Than -910 HU
- $\geq 50 - < 60\%$ Voxel Density
Less Than -910 HU
- $< 50\%$ Voxel Density
Less Than -910 HU
- $\geq 95\%$ Fissure Completeness
- $\geq 80 - < 95\%$ Fissure Completeness
- - - $< 80\%$ Fissure Completeness

RESULTS

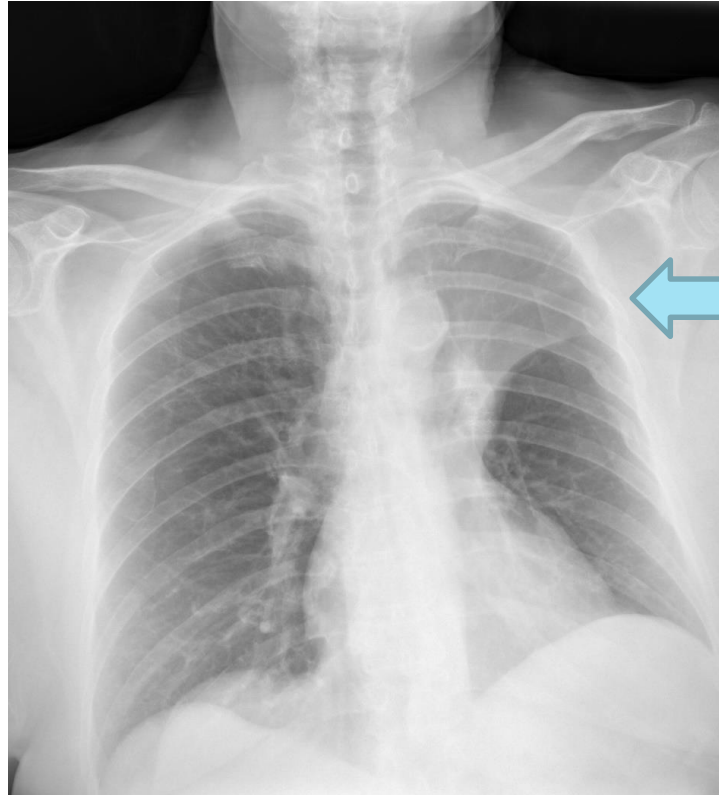
	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	57	91	59	91	100	100
% Voxel Density Less Than -910 HU	46	50	59	52	65	58

Bronchoscopy

- Patient underwent bronchoscopy:
 - CV assessment: Complete cessation of flow from LUL was documented at 3 minutes confirming lack of collateral ventilation
 - Three valves were placed in the LUL bronchus:
 - The left upper lobe apico-posterior and anterior segments were occluded using two 4.0-LP endobronchial valves.
 - The lingula was occluded using one 4.0 endobronchial valve.



Immediate Post-Operative CXR



24 Hours Later...



- Next day, she developed acute left sided chest pain and worsening SOB

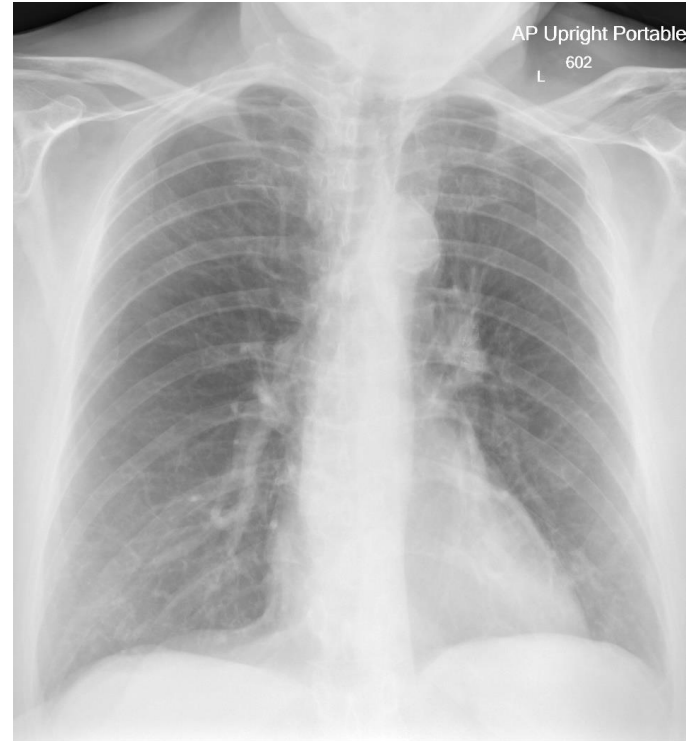


Hospital Course

- An air leak persisted for 7 days post-procedure
- Leak was continuous on inspiration and expiration
- What will you do next?
 1. Place a second chest tube
 2. Consult thoracic surgery for VATS pleurodesis
 3. Perform talc pleurodesis via chest tube
 4. Remove One valve

Hospital Course

- Bronchoscopy was performed with removal of lingular valve
- Air leak stopped within three days
- Patient discharged home with clinic follow up appointments arranged



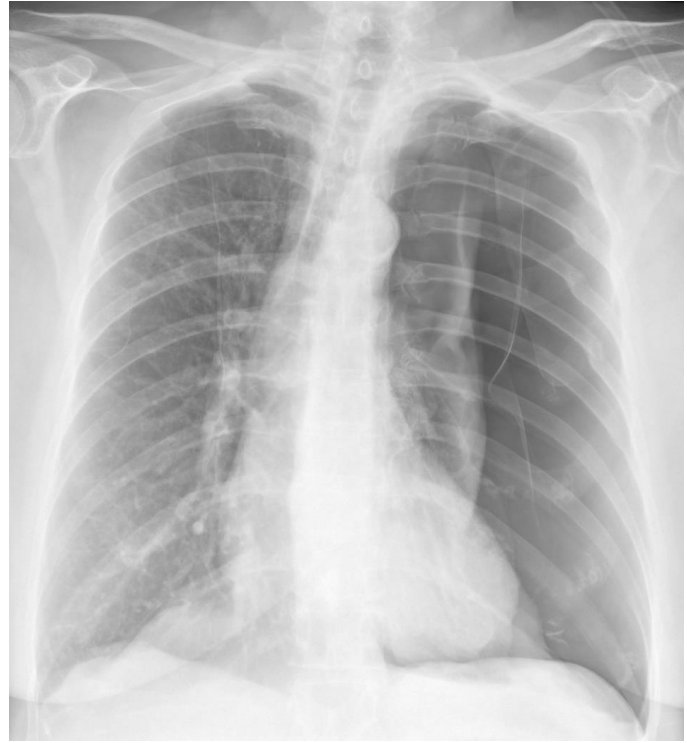
Post-Hospital Course

- She returned to clinic 3 weeks later
- She reported that she felt “amazing” with incredible breathing in those 24 hours prior to the occurrence of pneumothorax
- She asked for the lingular valve to be replaced



Second Bronchoscopy

- Bronchoscopy was performed with replacement of lingular valve
- Left pneumothorax developed at almost exactly the same time as last time (24 hours later)



Second Hospitalization Course

- Air leak persisted for 7 days post-procedure
- Air leak was intermittent and only with expiration



Resolution

- Patient was sent home with chest tube and Heimlich valve
- Air leak stopped and chest tube was removed at day 10
- Patient doing very well

Improvement after BLVR

Before

- FEV1: 0.54 L
- RV: 176%
- 6MWT: 350 M

After

- FEV1: 0.64 L
- RV: 150%
- 6MWT: 390 M

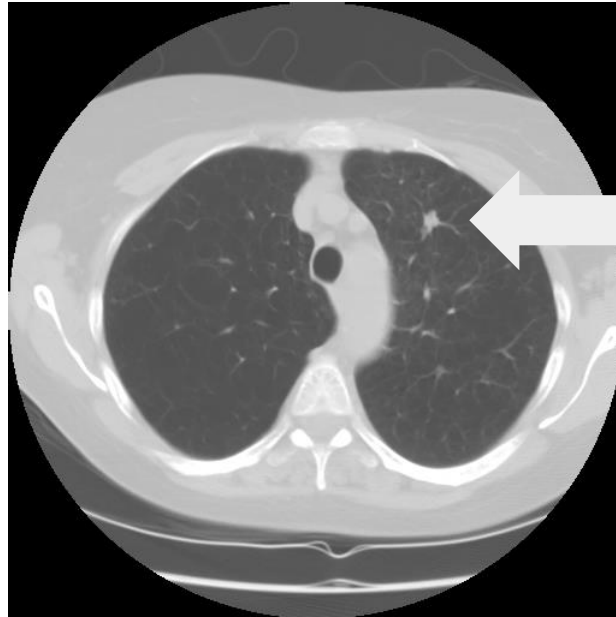
Summary

- Bronchoscopic lung Volume Reduction with valves is now a viable option for patients with advanced emphysema and air trapping
- Patient selection is critical to ensure best outcome and to minimize complications
- The technical work of placing the valves is easily learned
- Much more energy should be spent on learning patient selection, target lobe selection and post-operative care and complications

Robotic Bronchoscopy

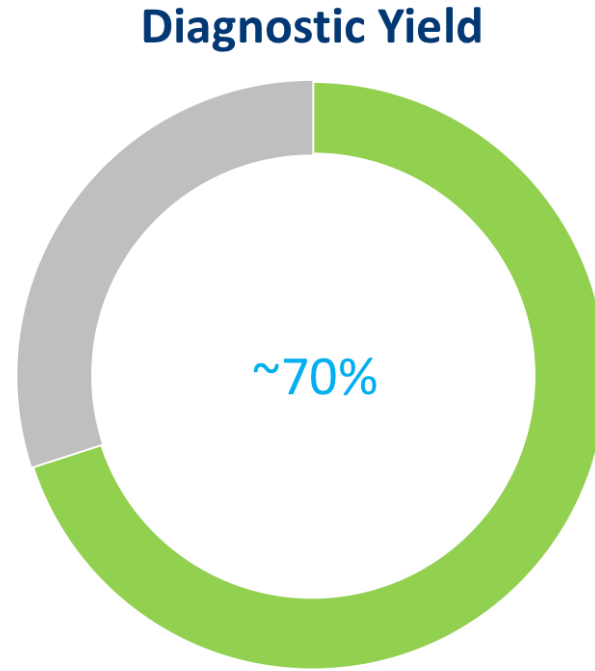
The Clinical Problem We Are Trying to Solve...

Access to The Peripheral Lung Nodule



Why Do You Care about New Tools?

- Guided Bronchoscopy:
 - SuperDimension Navigation System
 - Veran SPiN Thoracic Navigation System
 - Broncus LungPoint System
 - Radial EBUS



Comparison of Yield of Guided Bronchoscopic Sampling for the SPN

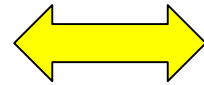
- Meta analysis of the diagnostic yield of guided Bronchoscopic techniques
- 39 studies with 3052 patients included
- Pooled diagnostic yield: 70% (CI: 67.1%-86.2%)
 - ENB: 67%
 - Radial EBUS: 71.1%
- Yield increases as the lesion size increases:
 - For lesion \leq 20 mm: 61.3%
 - For lesions $>$ 20 mm: 82.2%

Reasons for Modest Performance

- Reliance on chest CT
 - Not real time
- Respiratory Variation
- Location of nodules
 - Bronchus sign is associated with higher yield
- Ability to maneuver tools in the periphery

What Can the Robots Solve?

- Reliance on chest CT
 - Not real time
- Respiratory Variation
- Location of nodules
 - Bronchus sign is associated with higher yield
 - Very peripheral lesions are hard to access
- Ability to maneuver tools in the periphery



The Search for New Tools

- Robotic Bronchoscopy:
 - The Monarch Platform Auris Health: FDA-Approved in March 2018
 - Ion Endoluminal System Intuitive Surgical: FDA-Approved in February 2019

Robotic Bronchoscopy

- **Potential advantages**
 - More precision
 - Higher degree of movement of peripheral guide sheath
 - The ability to hold the endoscope/catheter in a locked curved position allowing biopsy tools to stay on target without the straightening that currently affects other systems



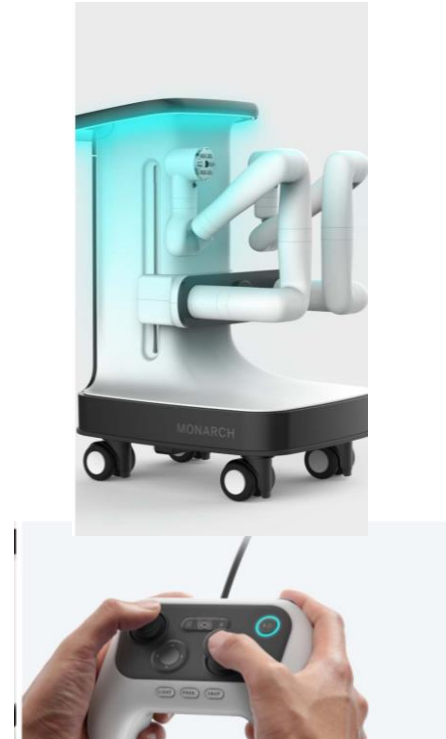
Robotic Bronchoscopy

- Potential disadvantages
 - Has not solved the issue of “finding The best path” to the lesion”
 - Lack of tactile feedback
 - Steep learning curve
 - Cost



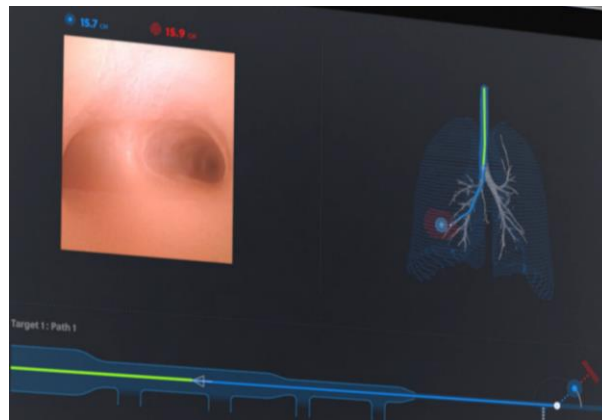
Currently Available System – Auris Monarch

- A robotically propelled outer sheath (5.7-mm) with an inner telescoping endoscope (4.4 mm)
- It uses electromagnetic navigation for guidance with an external EM field generator
- The physician uses a small hand-held controller to guide the robotic scope
- The scope has continuous optical capabilities and a separate suction channel (working channel 2.1 mm)



Currently Available Systems – Intuitive

- An articulating, robotic-assisted catheter allows navigation along a planned path through the airways to a predetermined location
- This system uses a navigation system based on shape sensing technology, rather than the traditional electromagnetic
- The working channel of this biopsy channel is 2.0 mm



Where Are We with the Evidence?



The Need for Data

Feasibility study

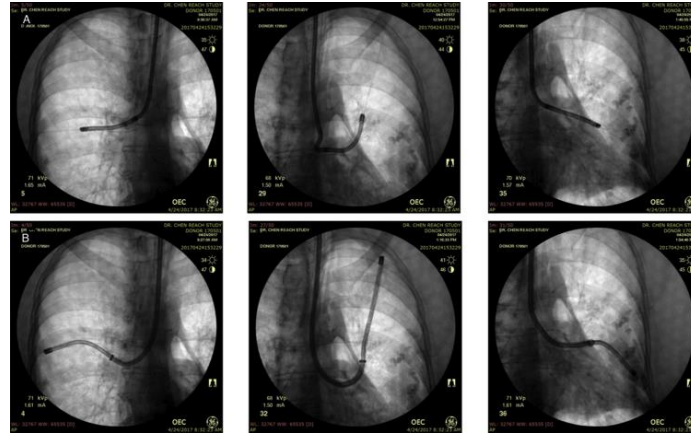


- Large multi-center registry studies
- Comparative studies-Robotic vs. current available technology
- Patient/lesion factors associated with success

REACH - Cadaver Study

- Assessed the reach of Auris robotic system within 2 human cadaveric lungs compared with conventional thin bronchoscopes
- The robotic endoscope was advanced beyond the conventional thin bronchoscope in all segments, particularly in bronchi with increased angulation such as RB1
- Mean generation count:
 - Robot: 8
 - Thin Bronchoscope: 3.5

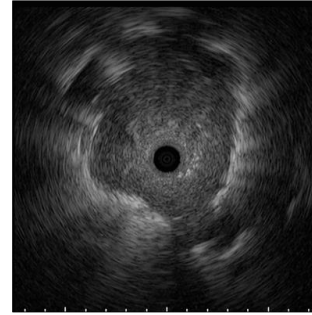
Thin
Bronchoscopy



Robotic
Bronchoscopy

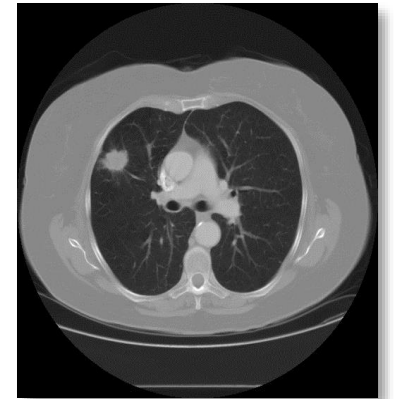
Precision-1 - Cadaver Study

- A Prospective Single-Blinded Randomized Comparative study of Three Guided Bronchoscopy Approaches for Investigating Pulmonary Nodules in a human cadaver model
- Ultrathin bronchoscope and R-EBUS (UTB-EBUS)
VS
Electromagnetic navigation
VS
Robotic bronchoscopy-Ion System



Precision-1 - Cadaver Study

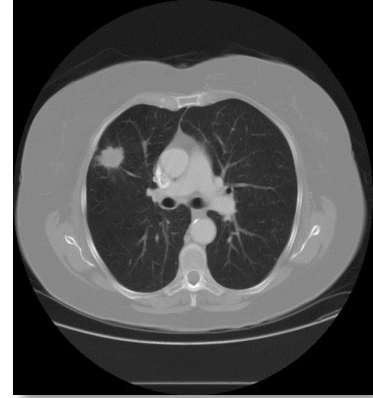
- 60 procedures were performed to target 20 pulmonary nodules
 - Cone beam CT was used to confirm nodule localization and puncture
 - Nodules were distributed across all lobes with a mean nodule size of 16.5mm
- Localization of the nodule:
 - Defined as successful if the proceduralist had sufficient confidence to attempt a needle puncture pass
- Nodule localization rate:
 - Robotic bronchoscopy: 100%
 - EMN: 85%
 - UTB-EBUS: 65%



Precision-1-Cadaver Study

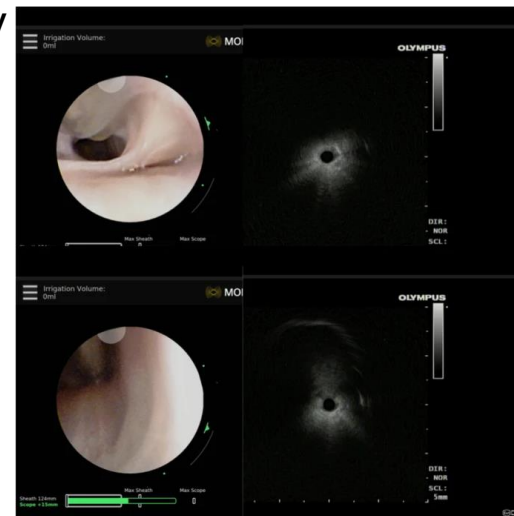
- Nodule puncture rate:
 - Robotic bronchoscopy: 80%
 - EMN: 45% (p-value 0.022)
 - UTB-EBUS: 20% (p-value<0.001)

- Need validation in human studies



Retrospective Clinical Study

- Retrospective review of robot-assisted bronchoscopy (Auris) to sample peripheral lung lesions in 4 centers
- 167 lesions in 165 patients
- Average size of nodule 25 mm
- Navigation was successful in 88.6% of the cases
- Diagnostic yield: 69.1% to 77%
- Pneumothorax occurred in 3.6%



Prospective Clinical Study

- Prospective multicenter pilot study
- Peripheral pulmonary lesions
Median lesion size was 23 mm
(interquartile range, 15 to 29 mm)
- Robotic bronchoscopy was able to locate lesions in 96.2% of the lesions as confirmed by radial EBUS
- Pneumothorax occurred in 3.7%
- Data on diagnostic yield will be reported after appropriate follow up period



Robotic Bronchoscopy

- Feasible
- Safe
- Unequivocal data about diagnostic yield or value over current technology



Alternative Technology

