Severe Emphysema and Bronchoscopic Lung Volume Reduction (BLVR)

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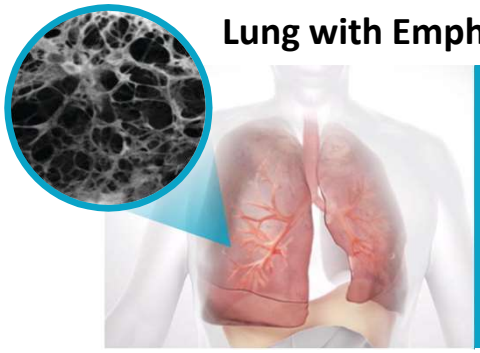
Interventional Pulmonology

Air Trapping and Hyperinflation in Emphysema

Healthy Lung

Tissue is elastic with large surface area

Breathing is easy; lung expands and contracts normally

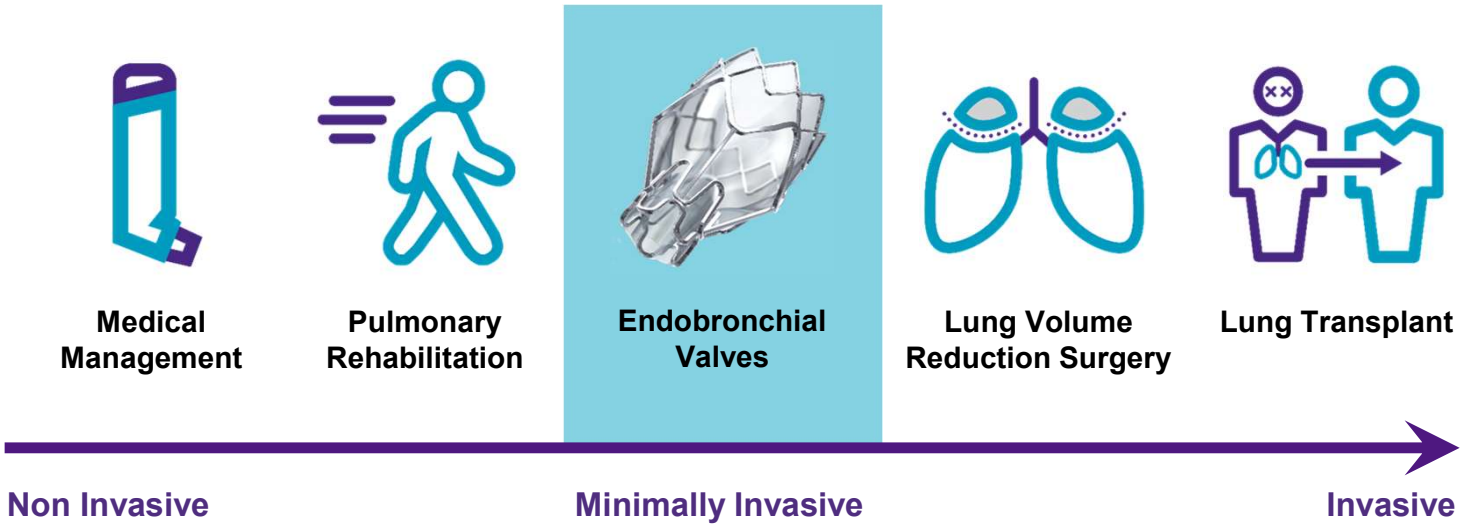


Lung with Emphysema

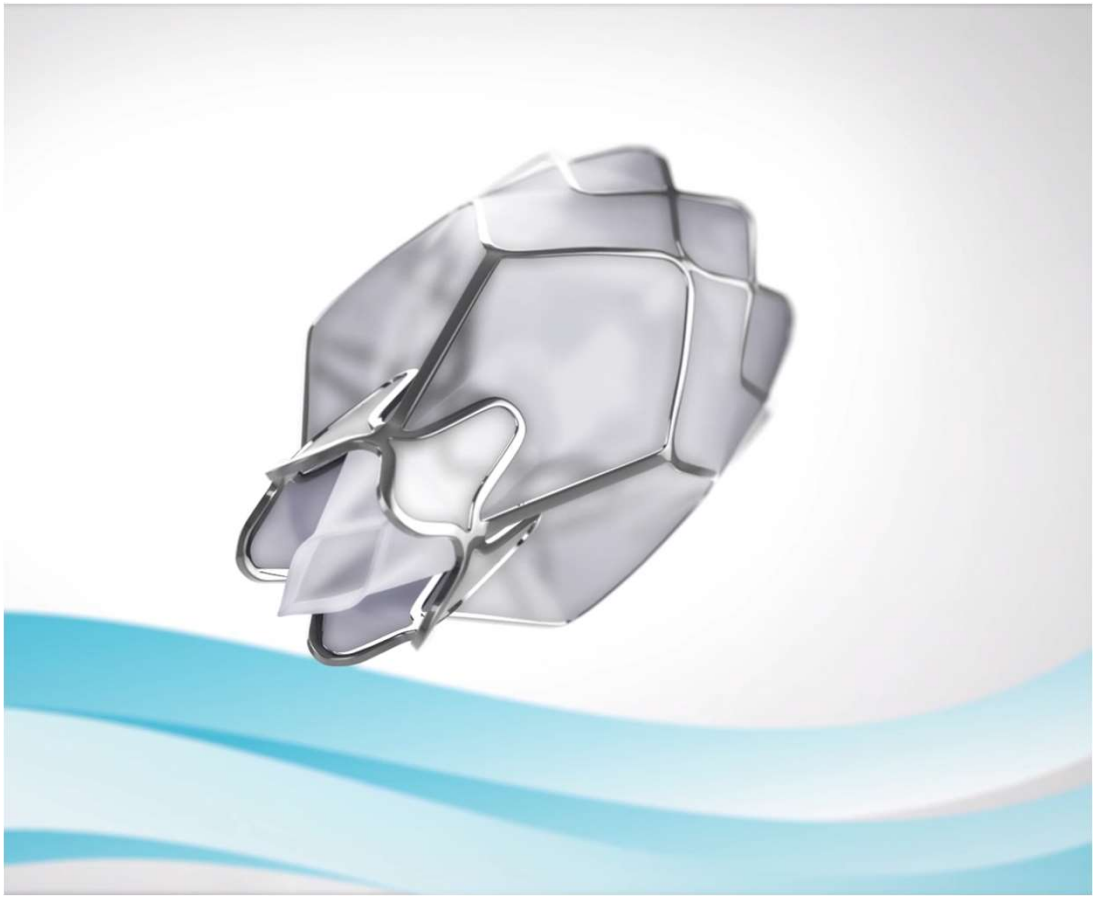
Tissue destruction reduces elasticity and gas exchange

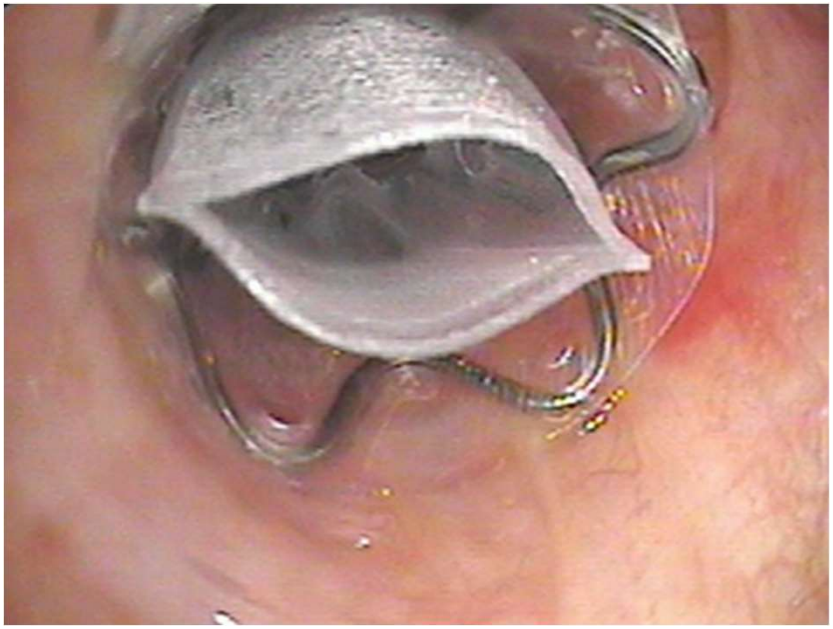
Air is trapped in the diseased portion of the lungs, increasing lung volume and putting pressure on the diaphragm, making patient persistently breathless

Spectrum of Treatment Options



How it Works



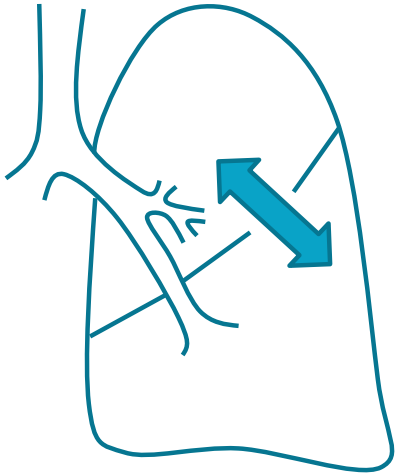


Criner G et al, AJRCC 2018, Published on 22-May-2018 as 10.1164/rccm.201803-0590OC

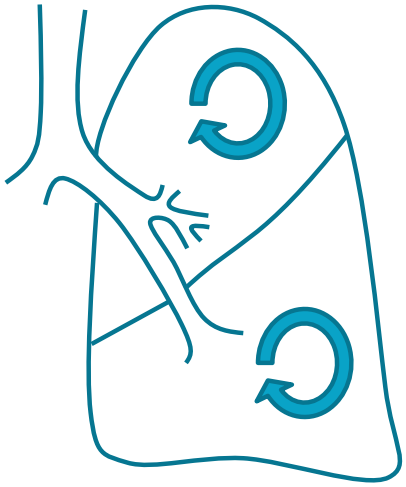
What is Collateral Ventilation?

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

Collateral Ventilation (CV+)



No Collateral Ventilation (CV-)



*E J Cetti, A J Moore, and D M Geddes. *Collateral Ventilation.* Thorax. 2006 May; 61(5): 371–373.

Key Entry Criteria

Inclusion

- Age 40 to 75 years
- BMI < 35 kg/m2
- Stable with < 20mg prednisone daily
- Nonsmoking for 4 months
- Post-bronchodilator FEV_1 ≥15% or ≤ 45% of predicted
- RV ≥ 175% predicted (body pleth)
- TLC ≥ 100% predicted
- DLCO ≥ 20% predicted
- PaCO2 ≤ 50mm Hg room air

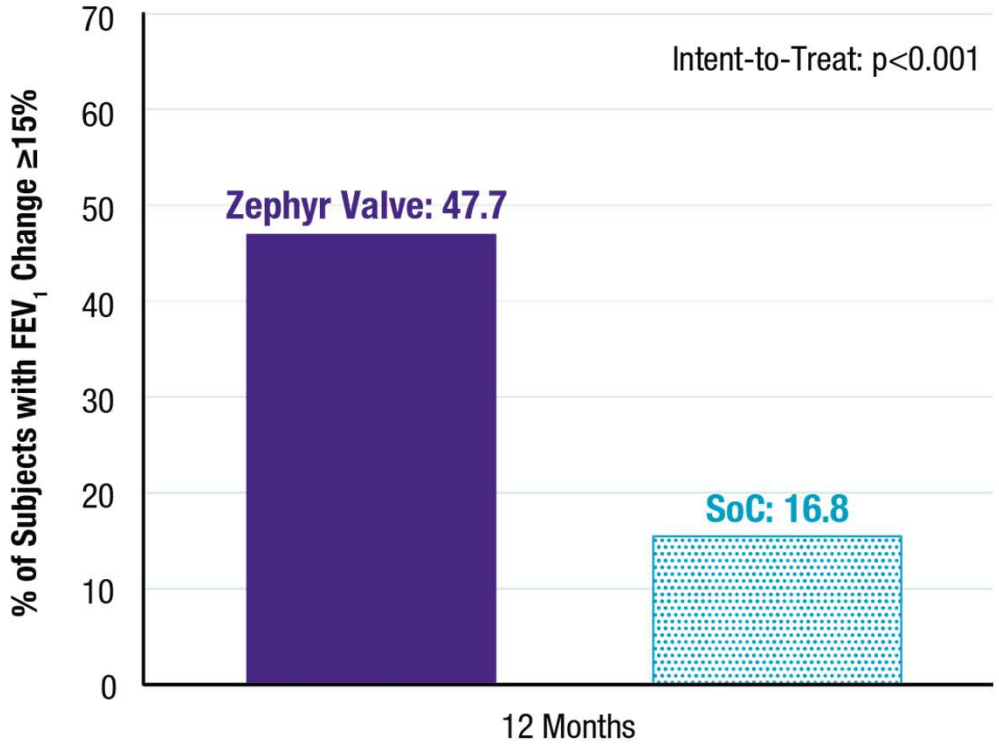
Exclusion

- >2 pneumonia episodes in last year
- MI or CHF < 6 months
- Unable to discontinue anti-coagulants or platelet activity inhibitors for 7 days
- Pulmonary hypertension (SPAP >45 mm Hg)
- Pulmonary nodule requiring surveillance
- WBC >10,000 cells/μL
- 6 MWD < 100 or > 500 meters after PR
- Presence of A1ATD
- Plasma cotinine level >13.7 ng/ml or carboxyhgb >2.5% if using nicotine products

Criner G et al, AJRCCM, 2018

LIBERATE: Primary Outcome

Percent of Subjects with FEV_1 Change from Baseline to 12-months of ≥15%



Criner G et al, AJRCCM, 2018

Serious Adverse Events

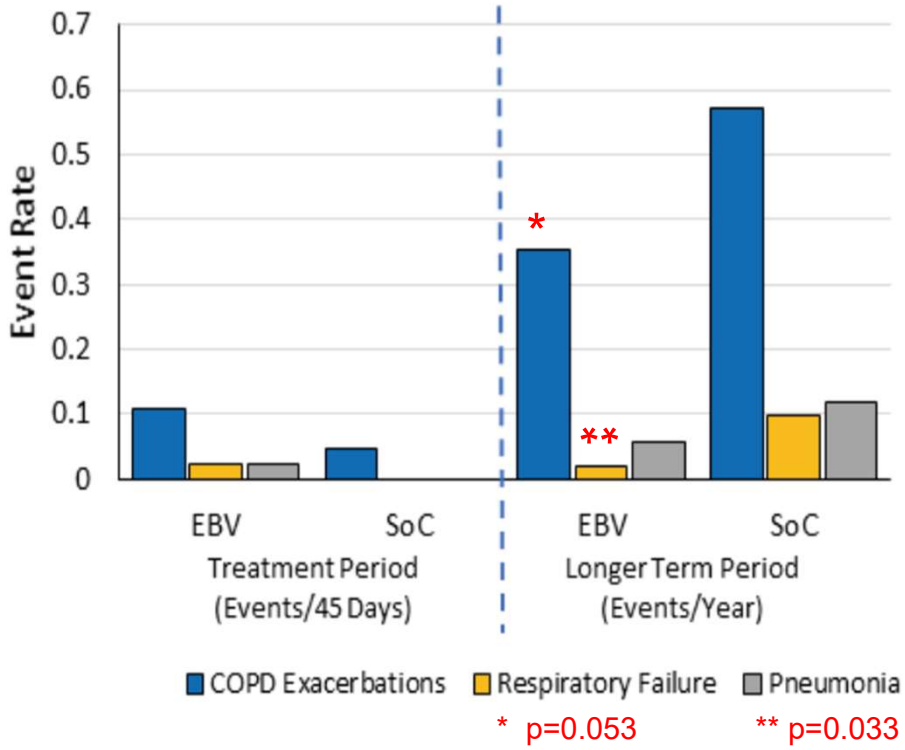
Serious Adverse Events Occurring in at Least 3.0% of Subjects in Either Group

	TREATMENT PERIOD Day of Procedure/Randomization to 45 Days		LONGER-TERM PERIOD 45 Days from the Study Procedure/Randomization until 12-month Visit Date	
	EBV (N=128)	SoC (N=62)	EBV (N=122)	SoC (N=62)
Death	4 (3.1%)[a]	0 (0.0%)	1 (0.8%)	1 (1.6%)
Pneumothorax	34 (26.6%)*	0	8 (6.6%) Includes 5 pneumo-thoraces from revision procedures	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%)

Criner G et al, AJRCCM, 2018

* P<0.05

Adjudicated Events



* p=0.053 ** p=0.033

US-EN-574 v1

Diagnostic Work Up

Pulmonary function testing

- Spirometry (Post-BD FEV_1 >15 and ≤ 45%)
- Body Plethysmography (RV ≥ 175% , TLC ≥ 100%)
- DLCO

Arterial Blood Gas level

- Collected on room air, D/C supplemental O_2 for 10 minutes prior to sampling
- $PaCO_2$ < 50 mm HG, PaO_2 > 45 mm HG

- **6-Minute Walk Test (100-500m)**
- **HRCT**
  - Thin slice (≤ 1.0 mm preferred)
  - Complete lungs with no artifacts
  - Supine only
- **Perfusion Scan (if available)**
- **Echocardiography**
  - No congestive heart failure, LVEF <45%
  - No uncontrolled pulmonary hypertension, sPAP >45mm Hg

Patient Selection Process

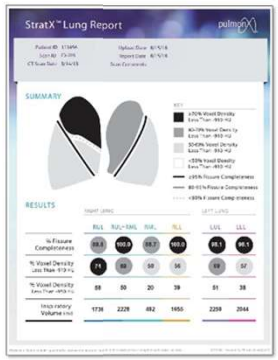
Clinical Screening

15-45% FEV1
≥175% RV
≥ 100% TLC
(Spirometry, PFTs)

Diagnosis of Emphysema
(CT Scan)

Medically Stable, No Disqualifying Comorbidities

Lobe Evaluation



Noninvasive:
StratX® Analysis Platform

Lobes with 80+% Fissure Completeness

Procedure:
Chartis® Pulmonary Assessment System

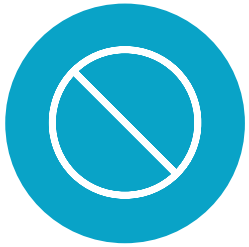
Treatment

Patient Selection Criteria For Zephyr Valve Based on Multiple RCTs

- Diagnosis of emphysema confirmed by CT
- BMI < 35 kg/m2
- Stable with ≤ 20mg prednisone (or equivalent) daily
- Residual volume ≥ 175% predicted (≥ 200% if homogeneous)
- FEV1 15-45% predicted
- TLC ≥ 100% predicted
- 6MWD 100-500m (150-500m if homogeneous)
- Not actively smoking (for at least 4 months)
- Target lobe with little or no collateral ventilation (as measured by Stratx and/or Chartis Assessment)

Criner et al. Am J Resp Crit Care Med 2018 in press, Kemp et al. Am J Resp Crt Care Med 2017: (196)12 1535-1543, Valipour et al. Am J Respir Crit Care Med 2016; Vol 194, Iss. 9 pp 1073-1082 and data on file at Pulmonx, Klooster et al. N Engl J Med. 2015; 373: 2325-2336 + Supplementary Appendix,

Indications for Use



- Contraindications

The Zephyr Valve is contraindicated for:

  - Patients for whom bronchoscopic procedures are contraindicated
  - Patients with evidence of active pulmonary infection
  - Patients with known allergies to Nitinol, Nickel, Titanium, or Silicone
  - Patient who have not quit smoking
  - Patients with large bullae encompassing greater than 30% of either lung

Warnings

The Zephyr Valve should be used with caution and only after careful consideration in patients with:

- Prior lung transplant, LVRS, median sternotomy or lobectomy
- Congestive heart failure (Left Ventricular Ejection Fraction <45%); myocardial infarction
- FEV_1< 15% of predicted value

Source: Zephyr Valve IFU

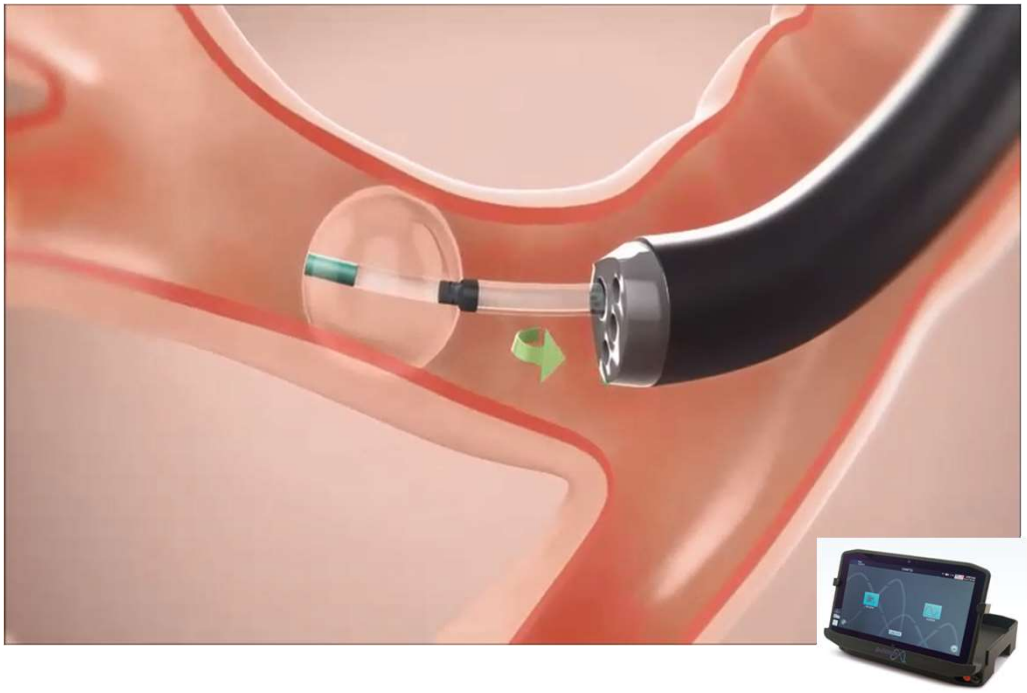
Patient Exclusion Criteria Zephyr Valve Based on Multiple RCTs

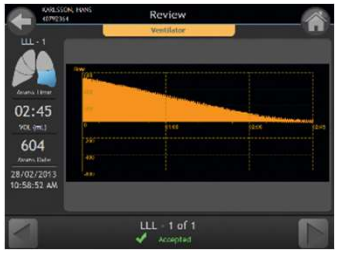
Patients should be excluded from the treatment with the Zephyr Valve based on the following criteria:

- Medical conditions or other circumstances make it likely that the patient will be unable to complete the preoperative and postoperative pulmonary diagnostic and therapeutic program required for the procedure
- Severe hypercapnia (PaC02 ≥50 mm Hg on room air) and/or severe hypoxemia (PaO2 ≤45 mm Hg on room air)
- Unstable cardiac arrhythmia or stoke
- Unstable pulmonary hypertension (sPAP>45mg Hg)

Criner et al. Am J Resp Crit Care Med 2018 in press, Kemp et al. Am J Resp Crt Care Med 2017: (196)12 1535-1543, Valipour et al. Am J Respir Crit Care Med 2016; Vol 194, Iss. 9 pp 1073-1082 and data on file at Pulmonx, Klooster et al. N Engl J Med. 2015; 373: 2325-2336 + Supplementary Appendix,

Assessing Collateral Ventilation – Chartis System





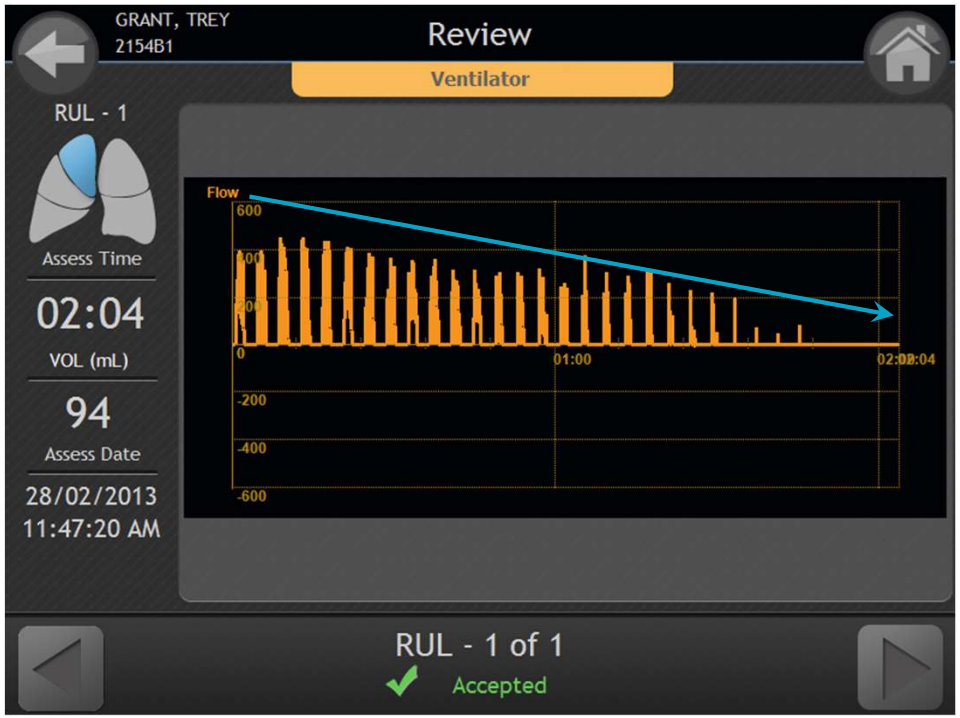
No collateral airflow, high likelihood of good treatment response

Collateral airflow, low likelihood of good treatment response

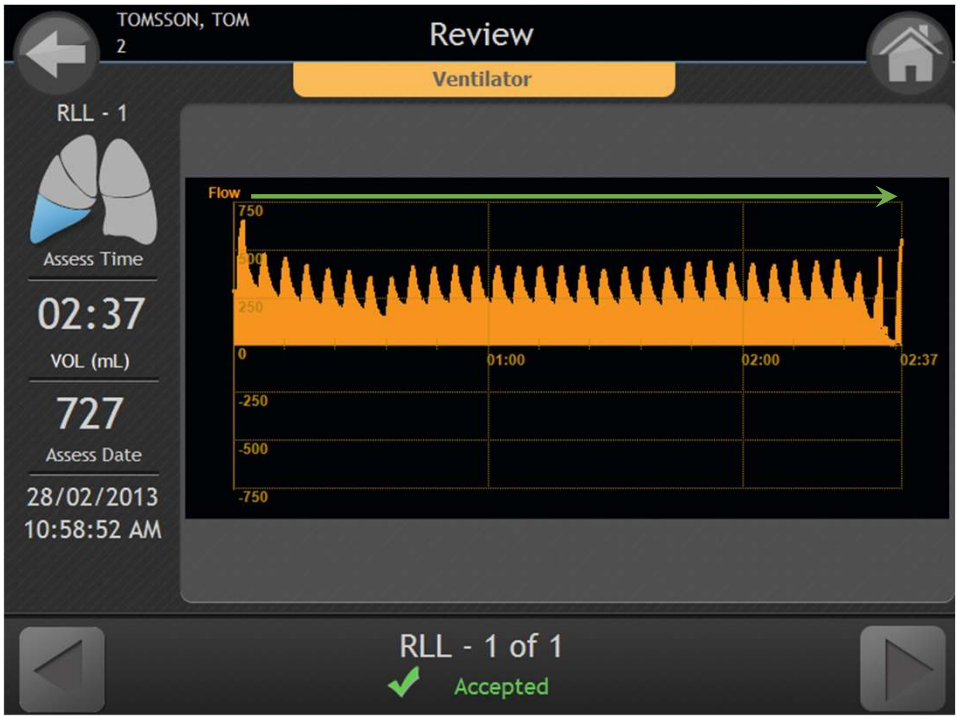
Availability of Chartis console models may vary by country

Chartis Assessment — Volume Ventilation

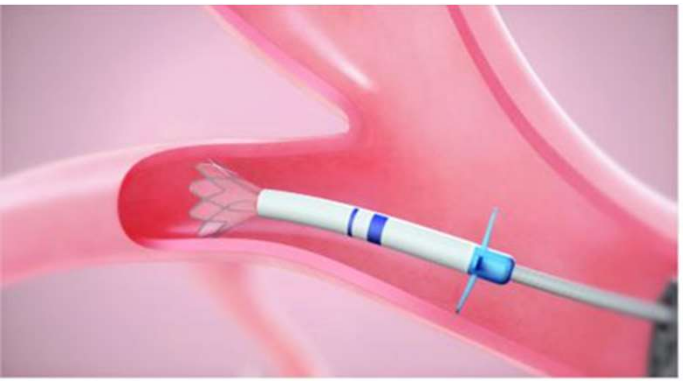
Even downward trend of airflow
CV-

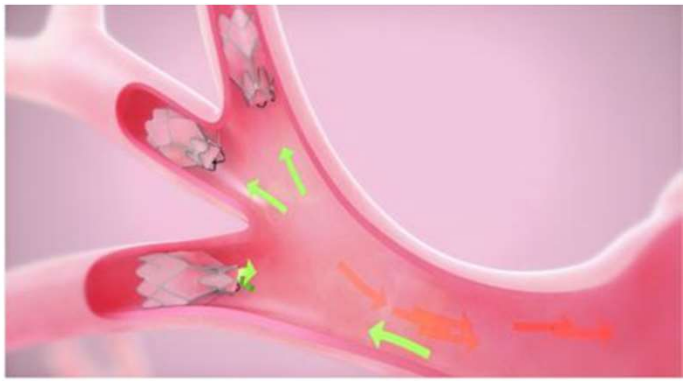


No downward trend
CV+



Zephyr Valve Procedure





Post-Valve Placement Recommendations

- Inpatient Care
- Length of stay
  - Minimum of 3 hospital nights post-procedure for observation
  - Possibly longer stay based on physician's discretion and if there is persistent chest discomfort or pain on the treated side
- Chest tube
  - Chest tube kit should be kept by bedside
  - Chest tube should be able to be placed 24/7 within 15-30 minutes
- Continuous monitoring of vitals signs and pulse oximetry
- Obtain chest x-ray immediately post extubation
- Give Nebulized treatment of ipratropium & albuterol immediately post extubation & q4h
- Give corticosteroid/antibiotic at the discretion of the attending physician if needed
- Have pulmonary physician perform physical exam and check x-ray for pneumothorax before transferring to medical floor/ICU

Day of Discharge

- Obtain CXR and have physician check for pneumothorax before discharge
- Go over the discharge medications
- Give patient ID card with emergency info (stating # of valves inserted & in which treated lobe with phone # of physician)
- Schedule patient to return for follow-up visit with treating pulmonary physician in a week
- Inform patient to call if he/she has any increased symptoms of shortness of breath, cough, purulent sputum, fever, chills or hemoptysis
- Inform patient to go to the nearest ER if symptoms are severe or persist

Long Term Follow-Up

- It is critical for primary pulmonologist and treating center to communicate regarding the procedure, outcomes, and potential complications
- Treating physician and referring physician should decided together on optimal approach for follow-up
- Assess if patient is stable, restart maintenance pulmonary rehabilitation at outpatient center and maintenance at home with app (if available)
- Treating physician should see patient at 1 week, 30-45 days, schedule 3, 6 and 12 month visit (and annual visits)

Case

- 68 yo woman with emphysema referred for Zephyr evaluation
- Met all inclusion criteria with no contraindications
- Valves were inserted 4/19/22

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JUST IN Empty folders marked classified among items found in FBI search of Trump home

Lung valves allow some emphysema patients in Nebraska to do more

Julie Anderson Aug 28, 2022 0

Over the last few years, Susan Steffel had noticed that she got winded more easily.

"Just a flight of stairs, I'd have to catch my breath after," said Steffel, 68, who lives in a two-story house in Beaver Lake.

In April, Steffel, who has emphysema, had three tiny, one-way valves placed in the airways of the left lower lobe of her lung. The use of the procedure is part of a relatively new program at Creighton University Medical Center-Bergan Mercy.

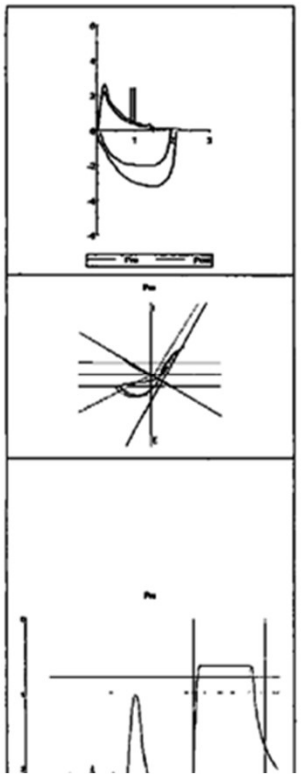
A duckbill valve like those in a whoopie cushion, a Zephyr valve is designed to let air out of — but not back in — less functional parts of the lungs, which become hyperinflated over time in people with emphysema. The hyperinflated areas take up more than their share of space in the chest, crowding the functional parts of the lung and hampering their ability to expand and contract normally with breathing.

Steffel

JULIE ANDERSON, THE WORLD-HERALD

Pre-procedure testing

	Pre-Bronch				Post-Bronch		
	Pred	Actual	LLN	%Pred	Actual	Pred%Chng	
---- SPIROMETRY ----							
FVC (L)	3.13	1.98	2.44	63	2.24	71	+12
FEV1 (L)	2.39	0.93	1.80	38	1.02	42	+10
FEV1/FVC (%)	77	47	67	60	46	59	-2
FEF 25-75% (L/sec)	2.08	0.30	0.84	14	0.43	20	+42
FEF Max (L/sec)	5.93	2.40	4.21	40	2.62	44	+9
FEF50%/FIF50% (%)	90-100	19			15		-20
Expiratory Time (sec)		9.65			10.73		+11
— LUNG VOLUMES –							
TLC (Pleth) (L)	4.85	6.43	3.93	132			
SVC (L)	3.13	2.03	2.44	64			
IC (L)	2.07	1.91		92			
TGV (L)	2.32	4.53	1.16	195			
ERV (L)	1.06	0.12		11			
RV (Pleth) (L)	1.90	4.40	0.94	232			
RV/TLC (Pleth) (%)	39	68	25	174			
Raw (cmH2O/L/s)	1.86	3.22	1.15	173			
sGaw (1/cmH2O*s)	0.20	0.07	0.14	34			
— DIFFUSION —							
DLCOunc (ml/min/mmH	23.16	12.35	13.08	53			
DLCOcor (ml/min/mmH	23.16	12.24	13.08	52			
DL/VA (ml/min/mmHg/	4.52	3.60		79			
VA (L)	4.82	3.40		70			
Hgb (gm/dL)	12-18	13.7					



☐ Male ☒ Female	Age: 67	Height: 64 inches 162.6 cm	Weight: 200 lbs 90.9 kg
Diagnosis: COPD	Forehead Probes Used: Yes ☒ No ☐		Room: Clinic PFT Lab

Laps: X X X X + 5 6 7 8 9 10 11 12 13 14 15

Predicted six-minute walk test (6MWT) distance: Pred: 415 Meters Actual: 270 Meters %Pred: 65 %

Baseline Resting (pre-walk):

BP 128/80 SpO2 99% HR 82 Borg Fatigue 2 Borg Dyspnea 2

O2 flow rate and delivery device Ø Assist device used to ambulate Ø

Medications taken before the test (dose & time) Ø

Immediately Post Test:

BP 136/84 SpO2 89% HR 110 Borg Fatigue 2 Borg Dyspnea 4-5

Recovery:

BP 110/80 SpO2 99% HR 84 Borg Fatigue 2 Borg Dyspnea 2-3

Summary Data:

SpO2 on room air at rest 99% Lowest SpO2 on room air with activity 89%

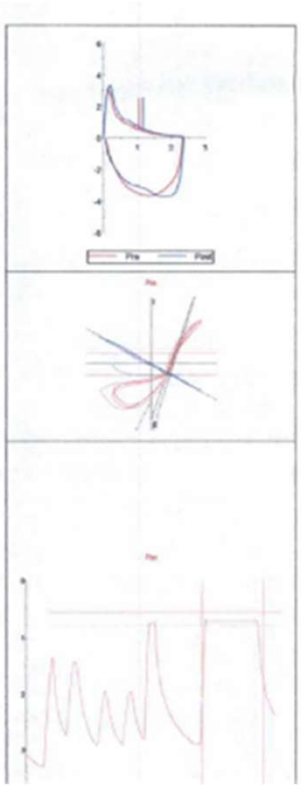
SpO2 on supplemental O2 at rest N/A SpO2 on supplemental O2 with activity N/A

Lowest SpO2 on O2 with activity, if applicable N/A SpO2 on4 lpm, if applicable N/A

Minute	SpO2	HR	O2/Device	Symptoms/ Comments/ Stopped or Paused
1	97%	89	Room Air	
2	92%	101	Room Air	Paused briefly due to SOB.
3	90%	99	Room Air	
4	90%	105	Room Air	Paused briefly due to SOB.
5	90%	107	Room Air	
6	89%	110	Room Air	
BODE SCORE FOR EXERCISE CAPACITY				BORG SCALE

Post-procedure testing

	Pre-Bronch				Post-Bronch		
	Pred	Actual	LLN	%Pred	Actual	Pred%Chng	
---- SPIROMETRY ----							
FVC (L)	3.06	2.34	2.37	76	2.39	77	+2
FEV1 (L)	2.33	1.08	1.74	46	1.19	51	+10
FEV1/FVC (%)	76	46	67	60	50	65	+8
FEF 25-75% (L/sec)	1.99	0.37	0.75	18	0.47	23	+27
FEF Max (L/sec)	5.79	3.16	4.08	54	3.56	61	+12
FEF50%/FIF50% (%)	90-100	13			18		+38
Expiratory Time (sec)		9.80			9.74		+0
---- LUNG VOLUMES --							
TLC (Pleth) (L)	4.83	5.64	3.91	116			
SVC (L)	3.06	2.25	2.37	73			
IC (L)	2.02	1.24		61			
TGV (L)	2.34	4.39	1.19	187			
ERV (L)	1.04	1.01		96			
RV (Pleth) (L)	1.92	3.39	0.96	176			
RV/TLC (Pleth) (%)	40	60	25	151			
Raw (cmH2O/L/s)	1.86	1.81	1.15	97			
sGaw (1/cmH2O*s)	0.20	0.11	0.14	55			
---- DIFFUSION ----							
DLCOunc (ml/min/mmH	22.77	11.55	12.69	50			
DLCOcor (ml/min/mmH	22.77	11.38	12.69	49			
DL/VA (ml/min/mmHg/	4.46	3.49		78			
VA (L)	4.81	3.26		67			
Hgb (gm/dL)	12-18	13.9					



Male ☒ Female | Age: 68 | Height: 64 inches cm | Weight: 199 lbs kg

Diagnosis: COPD, Asthma; Zephyr | Forehead Probes Used Yes ☒ No ☐ | Room: Clinic PFT

Laps: / / / / / 6 7 8 9 10 11 12 13 14 15 + 15 m

Predicted six-minute walk test (6MWT) distance: Pred: 410 Meters Actual: 340 Meters %Pred: 83 %

Baseline Resting (pre-walk):

BP 120/78 SpO2 98 HR 68 Borg Fatigue 3 Borg Dyspnea 0

O2 flow rate and delivery device none Assist device used to ambulate none

Medications taken before the test (dose & time) Albuterol neb @ 1143

Immediately Post Test:

BP 144/74 SpO2 91 HR 106 Borg Fatigue 4 Borg Dyspnea 2

Recovery:

BP 122/76 SpO2 100 HR 71 Borg Fatigue 2 Borg Dyspnea 2

Summary Data:

SpO2 on room air at rest 98 Lowest SpO2 on room air with activity 90

SpO2 on supplemental O2 at rest — SpO2 on supplemental O2 with activity —

Lowest SpO2 on O2 with activity, if applicable — SpO2 on4 lpm, if applicable —

Minute	SpO2	HR	O2/Device	Symptoms/ Comments/ Stopped or Paused
1	94	89	Room Air	
2	93	94		
3	92	99		
4	91	100		↓ 90
5	92	103		
6	91	106		
BODE SCORE FOR EXERCISE CAPACITY				BORG SCALE

Case Summary

- Pre-testing
  - FEV1 1.02 L (42%)
  - FVC 2.24 L (71%)
  - TLC 6.43 L (132%)
  - RV 4.40 L (232%)
  - 6 MWT 270 m (65%)
- Post-testing
  - FEV1 1.19 L (51%)
  - FVC 2.39 L (77%)
  - TLC 5.64 L (116%)
  - RV 3.39 L (176%)
  - 6 MWT 340 m (83%)