Befund: schweres Emphysem. Ventile zur Lungenvolumenreduktion – mit oder ohne vorherigem Fissurenverschluss

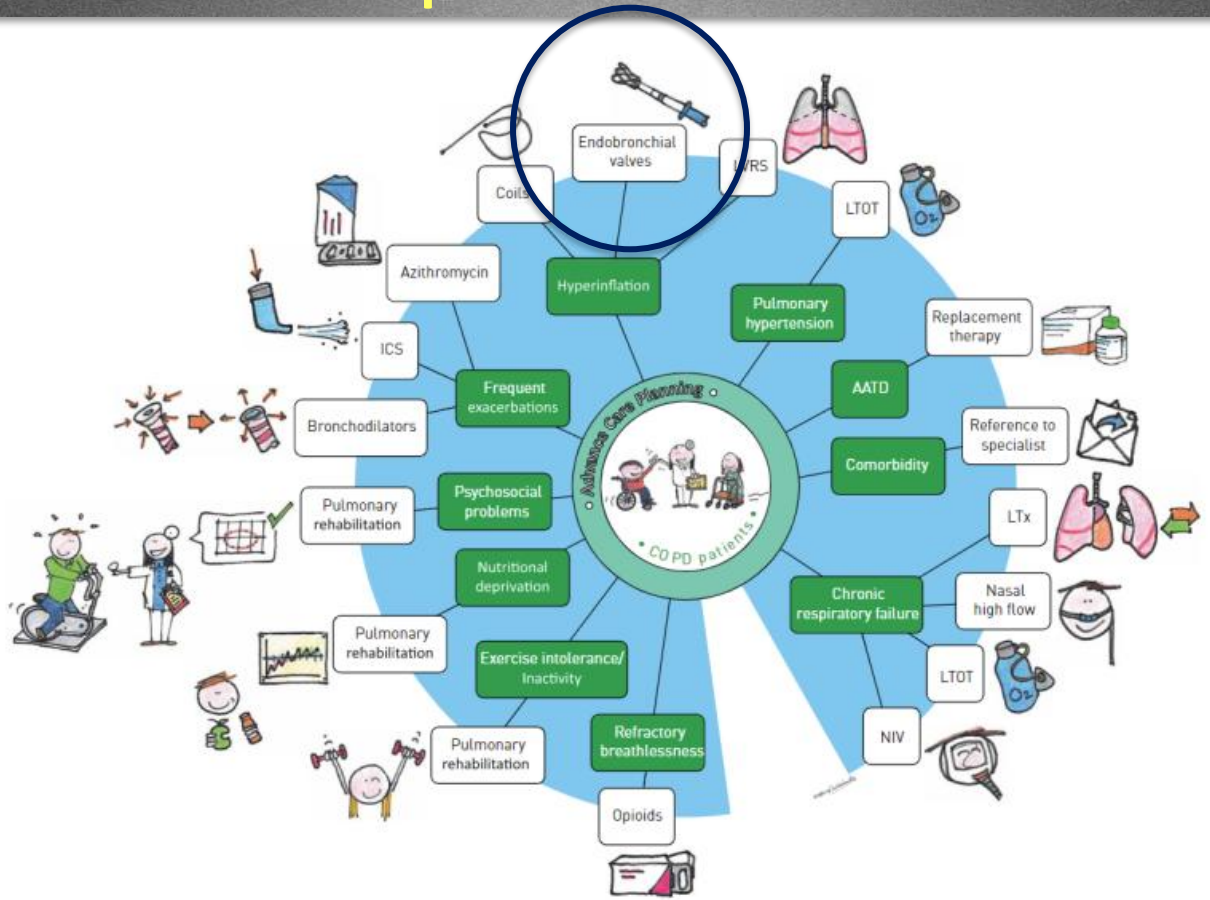
Felix JF Herth
Heidelberg

CoI 2021-2025

Research Support:
Olympus Medical, Pulmonx, Broncus- Uptake Medical, BMBF, DFG, EU, Klaus-Tschirra Stiftung, BMG

Lecturing and Consulting activities:
Pulmonx, Roche Diagnostics, Astra Zeneca, Boehringer Ingelheim, Novartis, Berlin Chemie, Chiesi, Medupdate, Erbe, GSK, streamedup, Merck, Apontis, Olympus Medical, Broncus Medical, Astra Zeneca, J&J, Karger, LÄK, Boston Scientific, Dinova, Nanovation, Sanofi, Erbe, Eolo, Deerfield

Treatable traits in severe copd

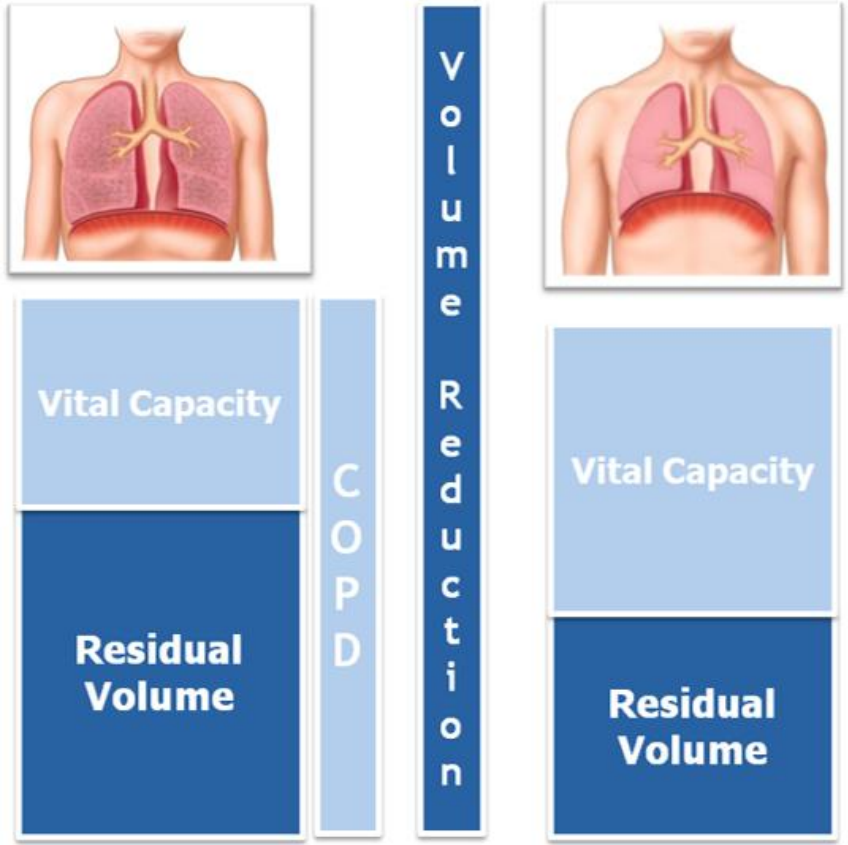


van Dijk M, et al. ERJ Open Res. 2020 Sep 21;6(3):00322-2019.

Bronchoscopic interventions for COPD

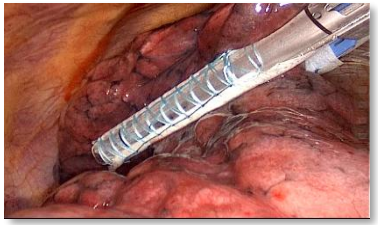
Severe COPD patients, when still symptomatic despite optimal treatment, may benefit from lung volume reduction.

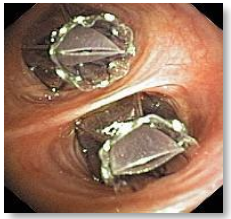
Amount of hyperinflation is key!

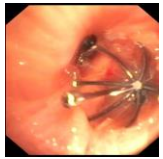


Lung volume reduction - valves

1950 — 1960 — 2002 — 2010 — 2015 — 2018







The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Study of Endobronchial Valves for Advanced Emphysema

Frank C. Sciurba, M.D., Armin Ernst, M.D., Felix J.F. Herth, M.D., Charlie Strange, M.D., Gerard J. Criner, M.D., Charles H. Marquette, M.D., Ph.D., Kevin L. Kovitz, M.D., M.B.A., Richard P. Chiacchierini, Ph.D., Jonathan Goldin, M.D., Ph.D., and Geoffrey McLennan, M.D., Ph.D., for the VENT Study Research Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation

Karin Klooster, Nick H.T. ten Hacken, M.D., Ph.D., Jorine E. Hartman, Ph.D., Huib A.M. Kerstjens, M.D., Ph.D., Eva M. van Rikxoort, Ph.D., and Dirk-Jan Slebos, M.D., Ph.D.

American Journal of Respiratory and Critical Care Medicine

Home > All AJRCCM Issues > Vol. 196, No. 12 | Dec 15, 2017

A Multicenter Randomized Controlled Trial of Zephyr Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM)

Samuel V. Kemp [1,2], Dirk-Jan Slebos [3], Alan Kirk [4], Malgorzata Kornaszewska [5], Kris Carron [6], Lars Ek [7], Gustav Broman [8], Gunnar Hillerdal [9], Herve Mal [3], Christophe Pison [10], Amandine Briault [11], Show All...

+ Author Affiliations

https://doi.org/10.1164/rccm.201707-1327OC PubMed: 28885054

Received: July 01, 2017 Accepted: September 07, 2017

Efficacy predictors of lung volume reduction with Zephyr valves in a European cohort

Felix J.F. Herth, Marc Noppen, Arschang Valipour, Sylvie Leroy, Jean-Michel Vergnon, Joachim H. Ficker, Jim J. Egan, Stefano Gasparini, Carlos Agustí, Debby Holmes-Higgin and Armin Ernst, on behalf of the International VENT Study Group

ORIGINAL ARTICLE

Endobronchial Valve Therapy in Patients with Homogeneous Emphysema

Results from the IMPACT Study

Arschang Valipour[1], Dirk-Jan Slebos[2], Felix Herth[3], Kaid Darwiche[4], Manfred Wagner[5], Joachim H. Ficker[6], Christoph Petermann[6], Ralf-Herto Hubner[7], Franz Stanzel[8], and Ralf Eberhardt[3]; for the IMPACT Study Team*

[1]Ludwig Boltzmann Institute for COPD and Respiratory Epidemiology, Otto Wagner Spital, Vienna, Austria; [2]Department of Pulmonary Diseases, University of Groningen, and University Medical Center Groningen, Groningen, the Netherlands; [3]Department of Pneumology and Critical Care Medicine, Thoraxklinik, University of Heidelberg and Translational Lung Research Center Heidelberg, German Center for Lung Research, Heidelberg, Germany; [4]Department of Interventional Pneumology, Ruhrlandklinik, West German Lung Center, University Clinic Essen, Essen, Germany; [5]Department of Respiratory Medicine, Allergology and Sleep Medicine, General Hospital Nuernberg, and Paracelsus Medical University, Nuremberg, Germany; [6]Lungenabteilung, Thoraxzentrum Hamburg, Asklepios Klinik, Hamburg, Germany; [7]Charité Campus Virchow-Klinikum, Berlin, Germany; and [8]Lungenklinik Hemer, Hemer, Germany

Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial

Claire Davey*, Zaid Zoumot*, Simon Jordan, William H McNulty, Dennis H Carr, Matthew D Hind, David M Hansell, Michael B Rubens, Winston Banya, Michael I Polkey, Pallav L Shah, Nicholas S Hopkinson

LIBERATE Endobronchial Valve Study

Clinical Research Study for Severe Emphysema

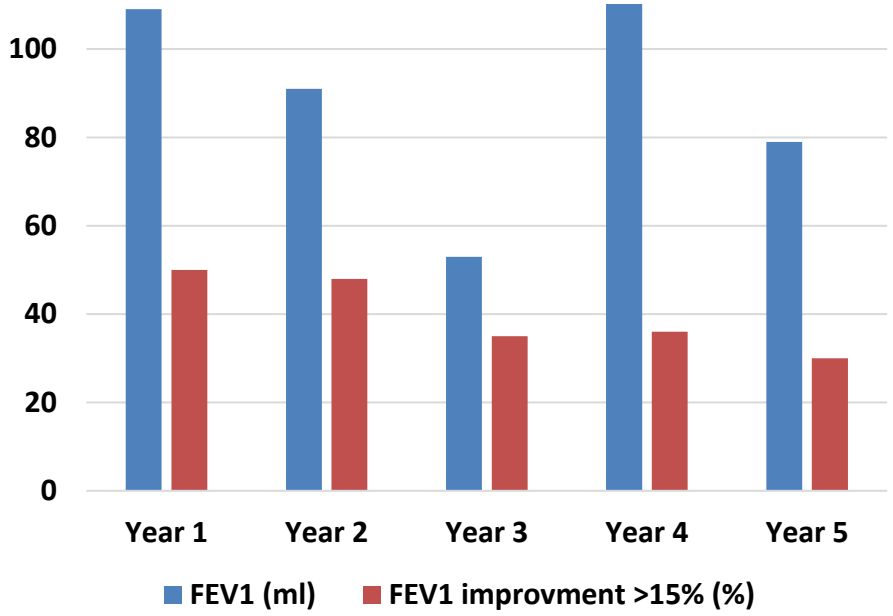
ATS 2018 SAN DIEGO

The LIBERATE Study is evaluating the Zephyr® Endobronchial Valve in patients with severe emphysema. The Zephyr valve is an investigational device designed to reduce the volume of the diseased region of the lung by blocking airflow. As a result, healthy regions may expand and function more efficiently, resulting in improved breathing.

ELVR with valves – Liberate trial 5 years

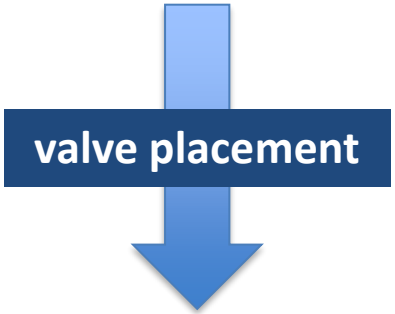
- Most common SAEs beyond Year 1
- COPD exacerbations (range: 13.5 to 23.1%)
- pneumonia (3.8 to 9.6%)
- respiratory failure (1.8 to 11.5%)
- pneumothorax (1.3 to 3.6%)

- 29 deaths after Year 1 to Year 5



ELVR with valves – reducing exacerbationsrate

129 patients with COPD III/IV
valve placement 2016-2019
mean RV 243 %



long-term survival

	n (available data)	Baseline Mean ± SD and median (IQR)	365d FU Mean ± SD and median (IQR)	p-value
FEV_1 (l)	127	0.80 ± 0.25	0.86 ± 0.29	<0.001
FEV_1 (%)	127	30.38 ± 8.55	32.58 ± 11.24	0.002
RV (l)	126	5.31 ± 1.35	4.98 ± 1.29	<0.001
RV (%)	126	243.89 ± 55.11	225.84 ± 59.18	<0.001
VC (l)	127	2.29 ± 0.67	2.36 ± 0.72	0.192
VC (%)	127	69.63 ± 16.88	71.58 ± 19.13	0.197
TLC (l)	127	7.60 ± 1.45	7.40 ± 1.41	0.008
TLC (%)	127	133.69 ± 18.74	130.55 ± 21.31	0.036
DLCO SB (%)	96	34.14 ± 15.15	33.99 ± 11.60	0.905
DLCO/VA (%)	96	50.43 ± 22.24	52.32 ± 36.99	0.905
mMRC	106	2.91 ± 1.04	2.79 ± 1.17	0.285
CAT	38	26.18 ± 6.27	25.18 ± 6.70	0.050
6-MWD (m)	85	283.49 ± 89.07	289.27 ± 92.41	0.477
exacerbations 1 year before and 1 year after ELVR	129	2.5 ± 2.2 2.0 (1.0)	1.8 ± 2.2 1.0 (3)	0.009

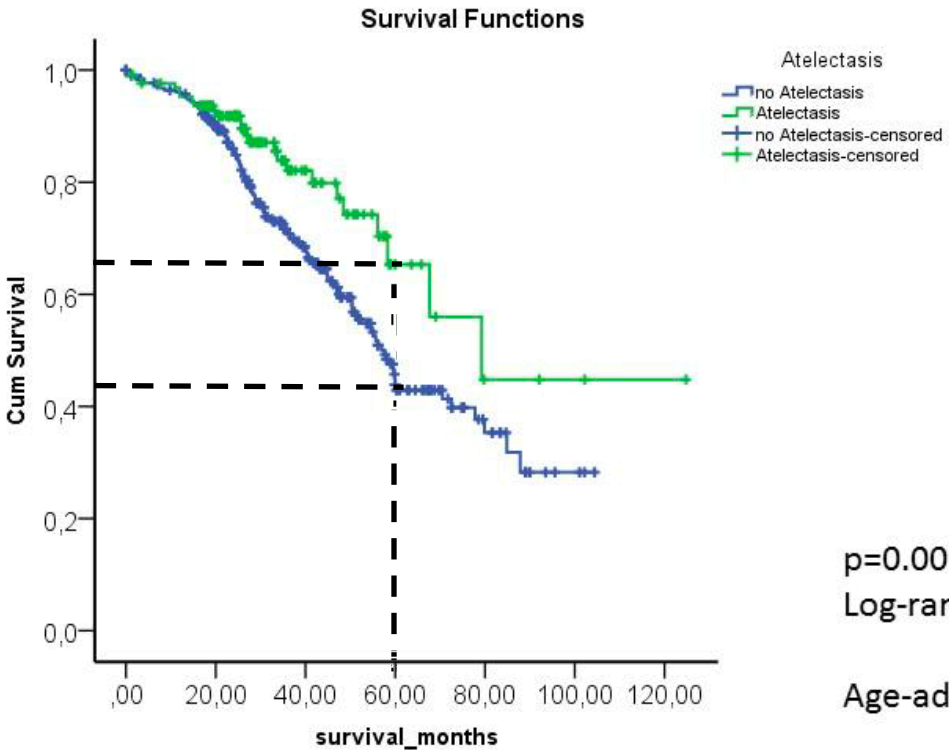
Brock et al., Res Med 2023

ELVR with valves – longterm results

449 patients with COPD III/IV
valve placement 2005-2013
mean RV 259 %

valve placement

long-term survival

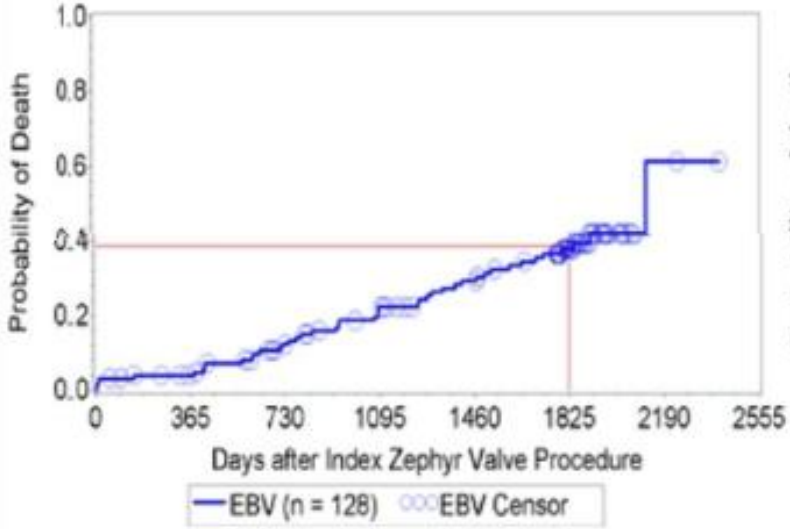


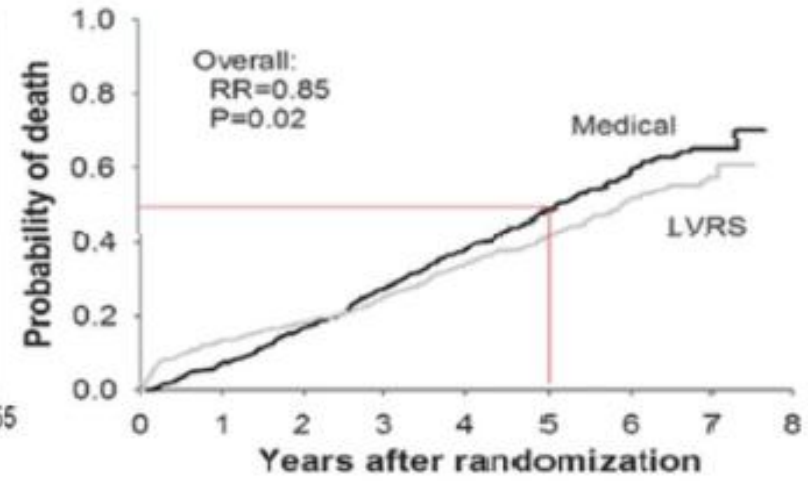
p=0.009
Log-rank test

Age-adjusted p=0.019

ELVR with valves – Liberate trial 5 years

Figure 2: Mortality Comparison: BLVR vs Control Arm in NETT

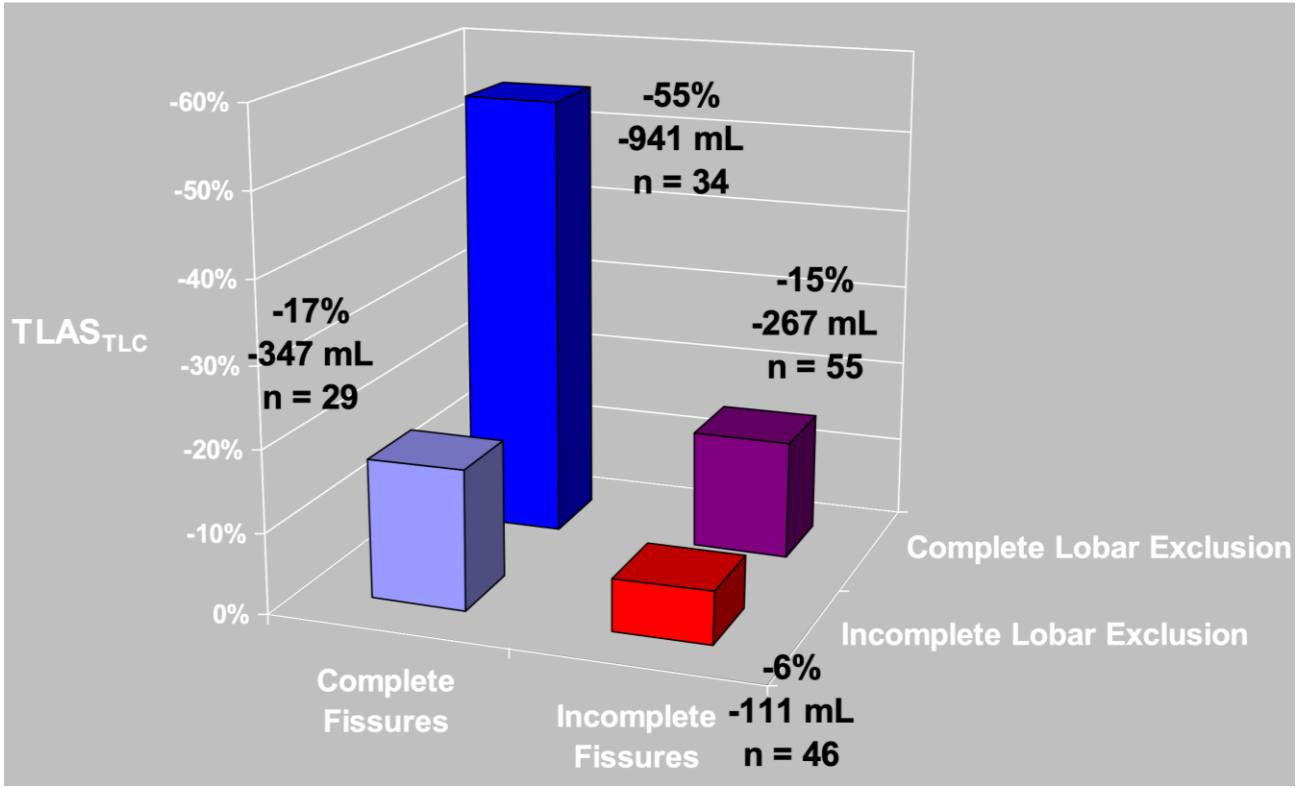




Factors that influence the response to valve therapy

- Collateral ventilation
- Technical success → Lobar exclusion
- Emphysema heterogeneity

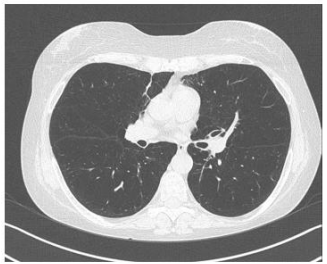
Target Lobe Volume Reduction by Lobar Exclusion and Fissure Integrity



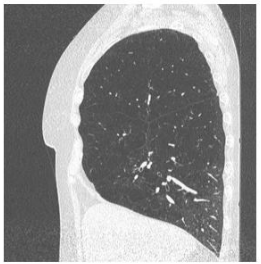
Scriuba F et al., NEJM, 2010

Selecting the Target Lobe

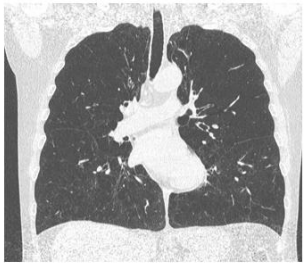
axial



sagittal

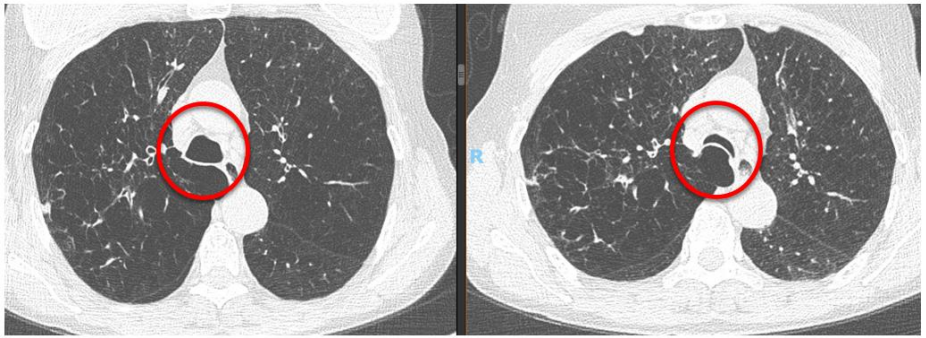


coronal

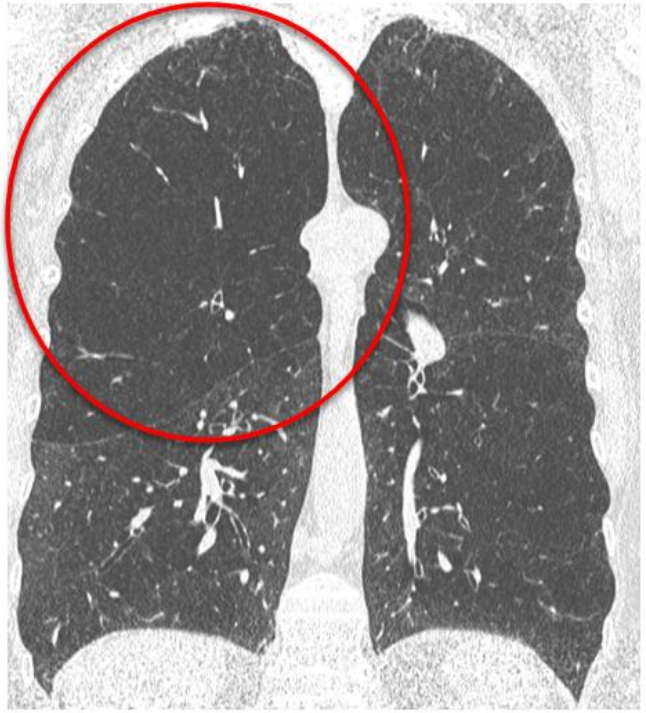


inspiration

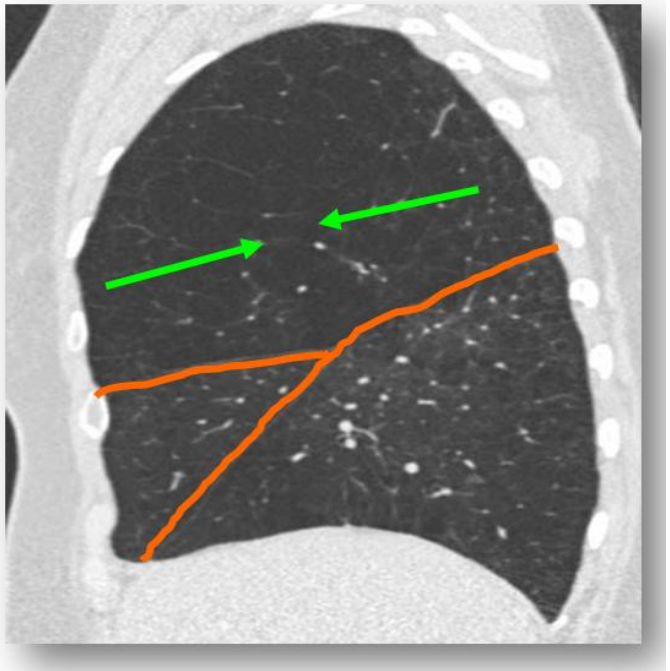
expiration



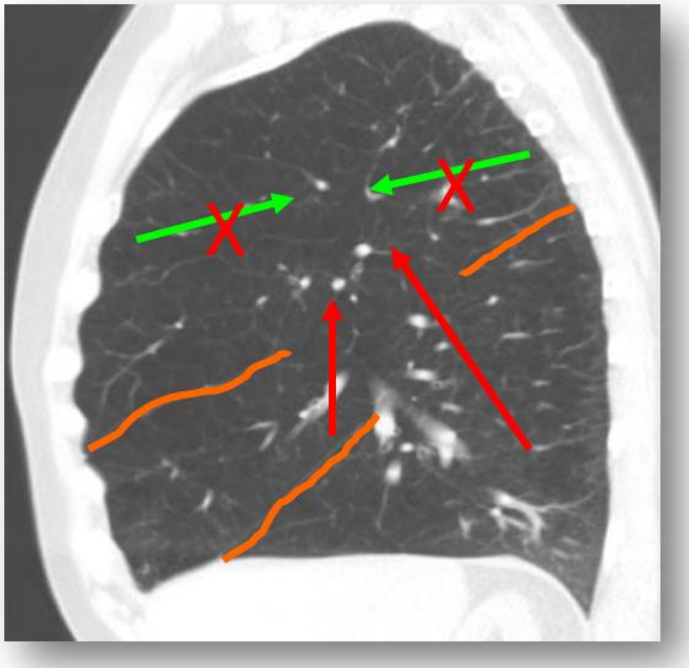
Identify at least one target by ‘eye bolling’



Fissure Integrity: crucial for valves

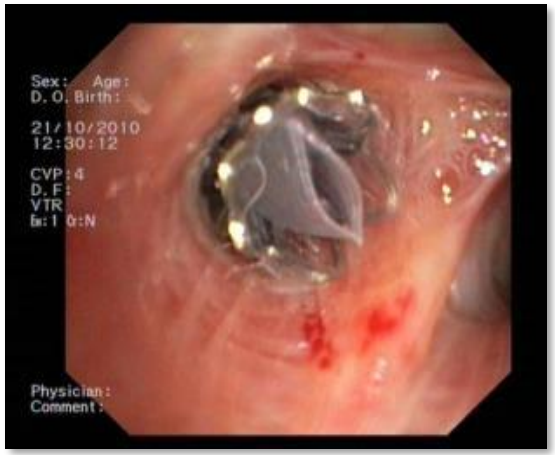


Fissures complete

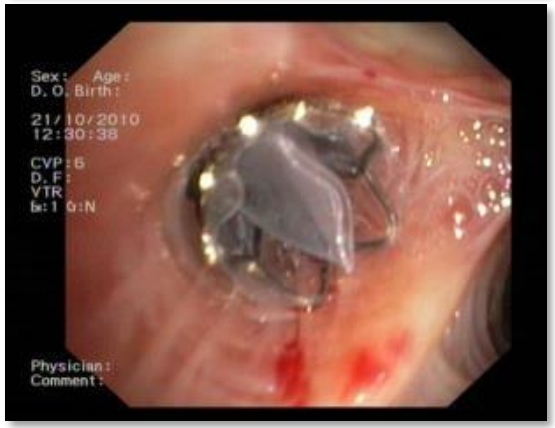


Fissures incomplete

Endobronchial valve treatment



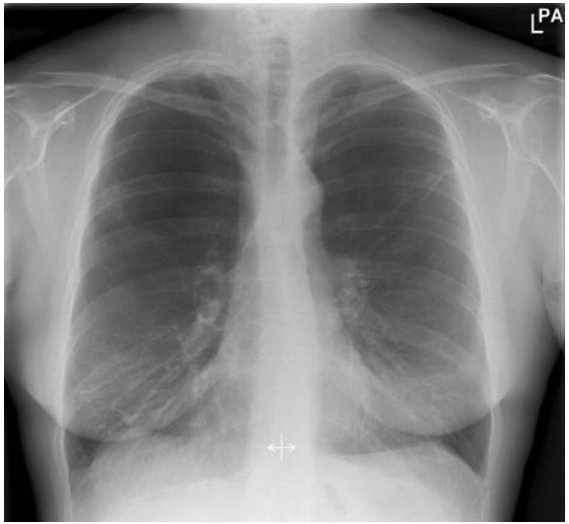
EXPIRATION



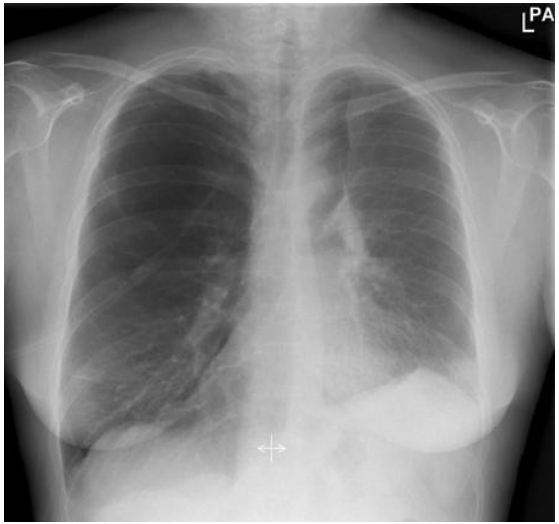
INSPIRATION

Klooster K, Slebos DJ. Chest. 2021 May;159(5):1833-1842.

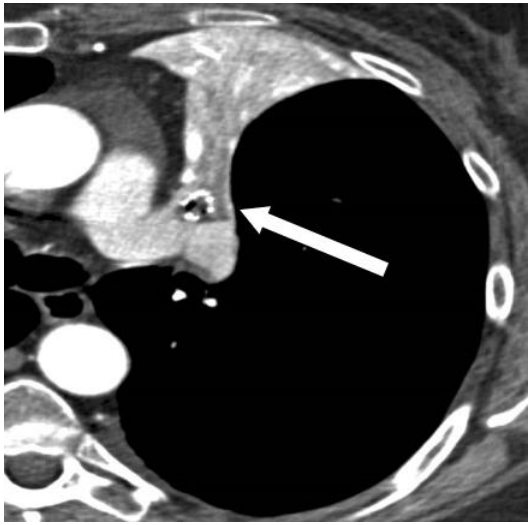
Achieve an atelectasis



before

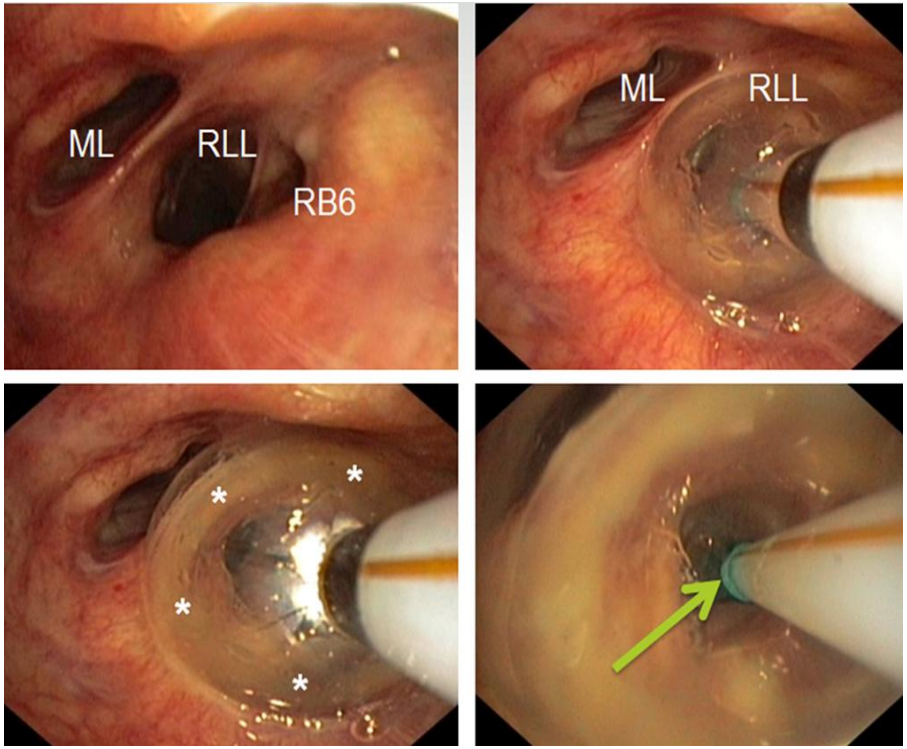


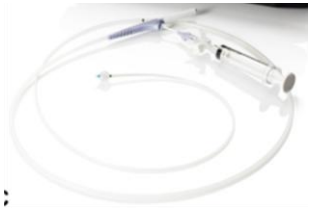
after valve treatment

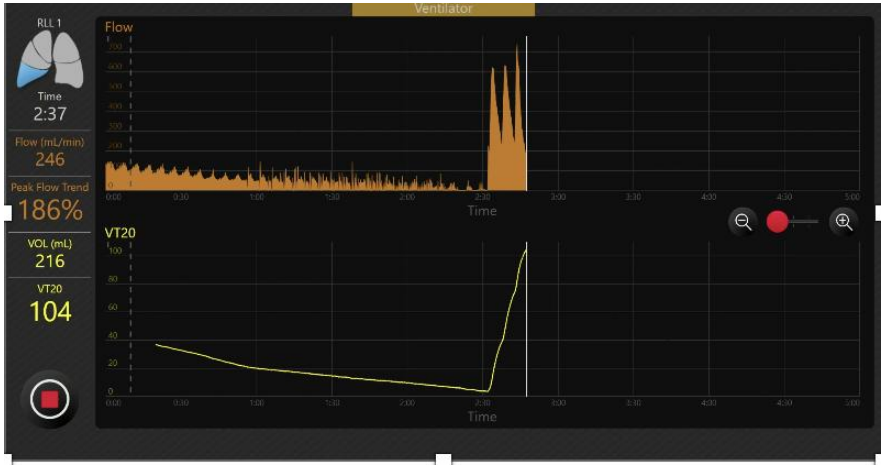


Measurement of collateral ventilation

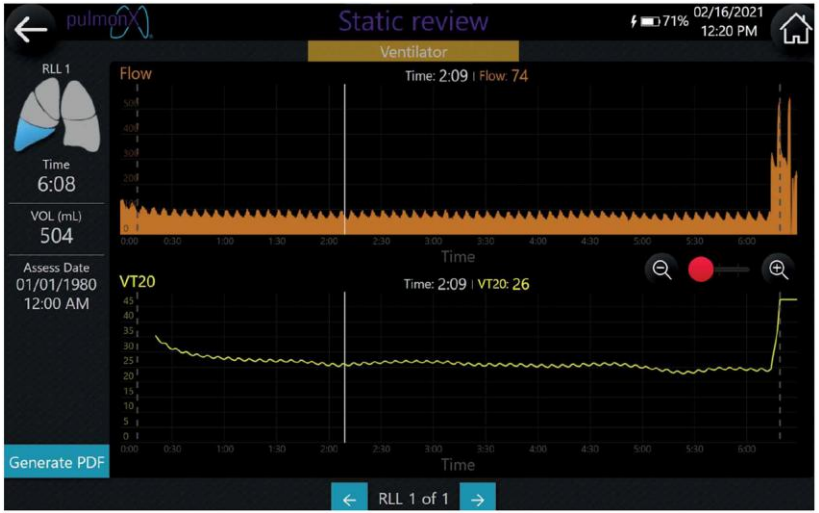
Chartis System measurement

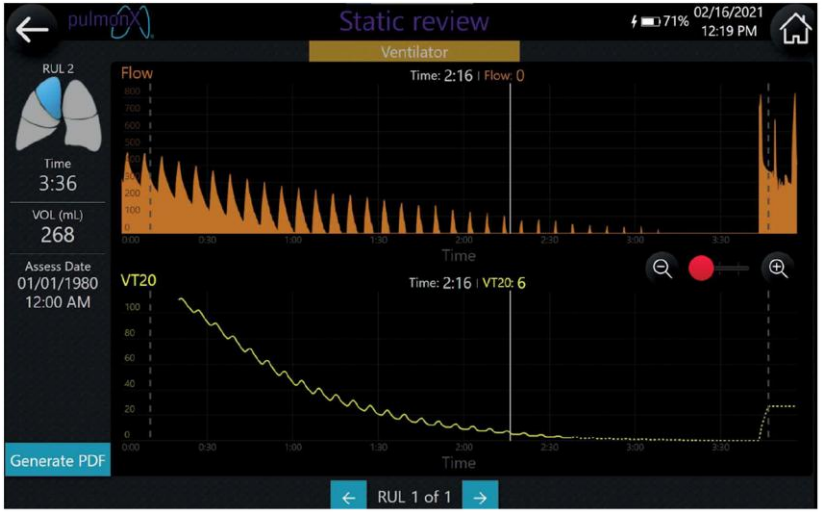






Outcome chartis system assessment



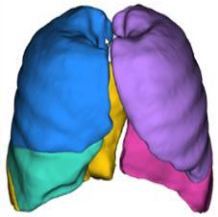


NOT eligible

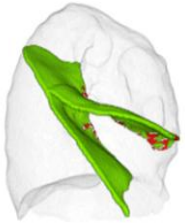
eligible

Ct scan | Quantitative analyses report

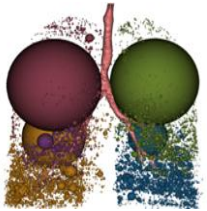
Lobar volumes

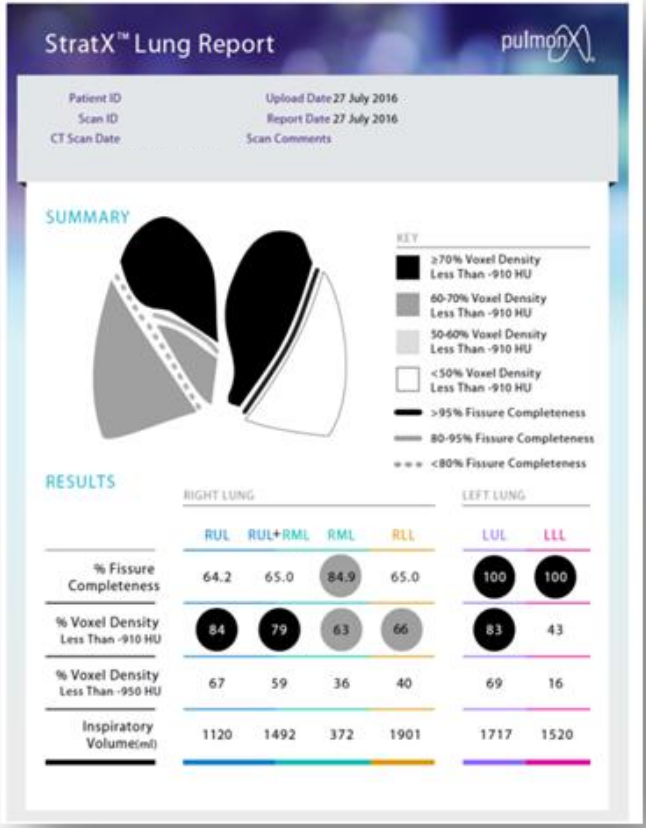


Fissures

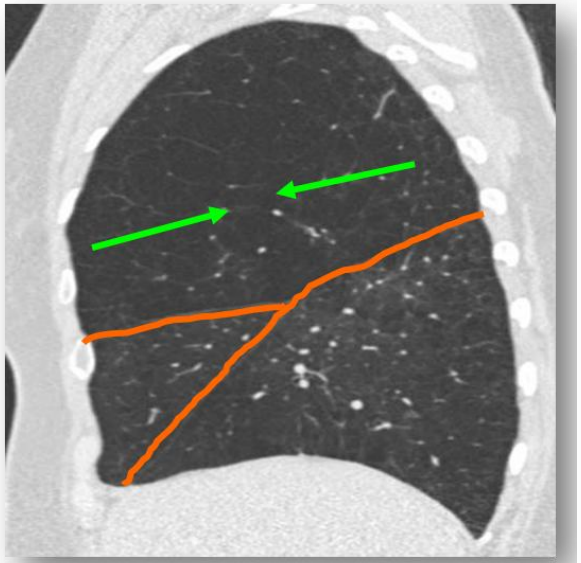


Emphysema

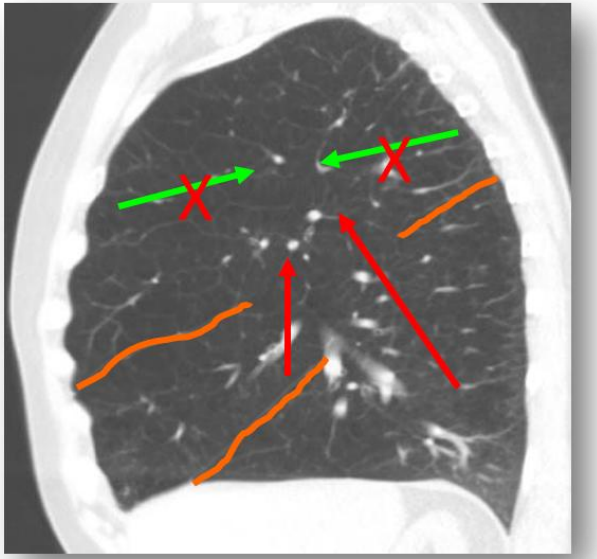




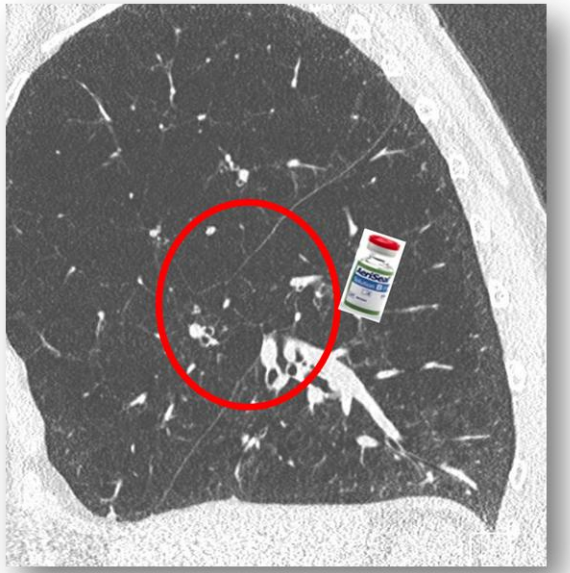
Fissure Integrity: crucial for valves



Fissures complete



Fissures incomplete



Closing the fissure

Reversal of collateral ventilation

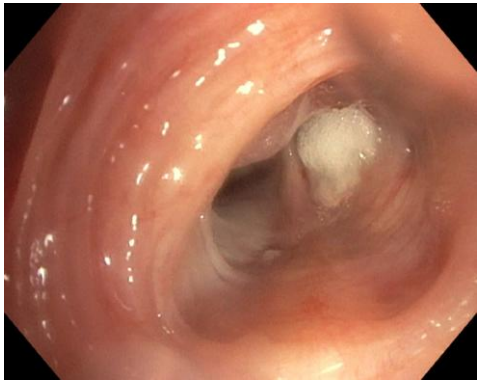
- **Single center, parallel group study: CVpos patients treated with AeriSeal (30mL; LUL only) followed 4 weeks later with Zephyr valves, and CVneg patients treated with Zephyr valves.**

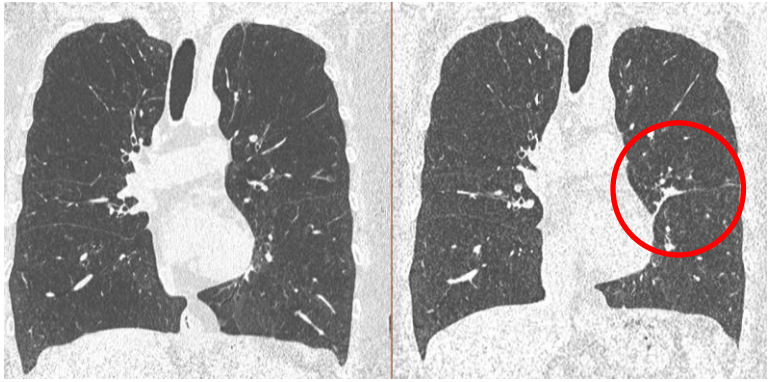
- **Baseline characteristics:**
  - **Age: 71.8 yrs**
  - **FEV_1: 28.2%**
  - **RV: 217.2%**
  - **SGRQ: 62.2 pts.**
  - **6MWD: 299 m**
  - **Fissure integrity (LUL): 88.6%**

KEY FINDINGS Conversion Rate: 9/14 (64%)		
	Change from Baseline to 6-Months	
	CVneg + Valves n=14	CVpos + Aeriseal + Valves n-=14
FEV_1	+27.7%	+19.7%
RV	- 20.1%	-16.2%
SGRQ (pts)	-16.6	-15.1
6MWD (m)	82.3	77.2
TLVR (LUL)	-46.1%	-43.4%

Reversal of collateral ventilation

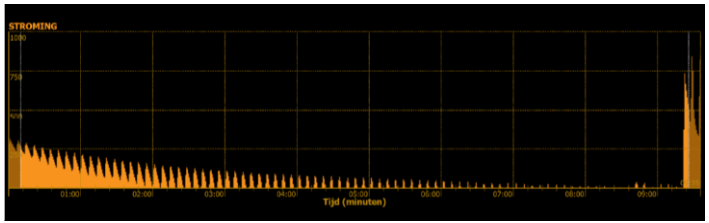
AeriSeal in segment LB5





pre-AeriSeal **4 weeks post-AeriSeal**

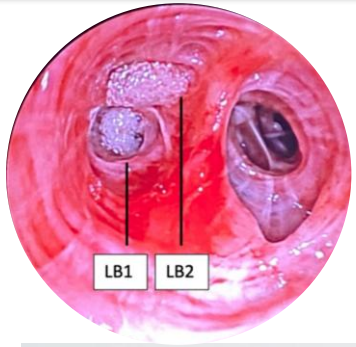
Chartis measurement → CV-



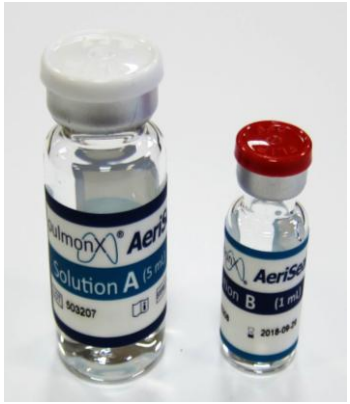
UNDER INVESTIGATION

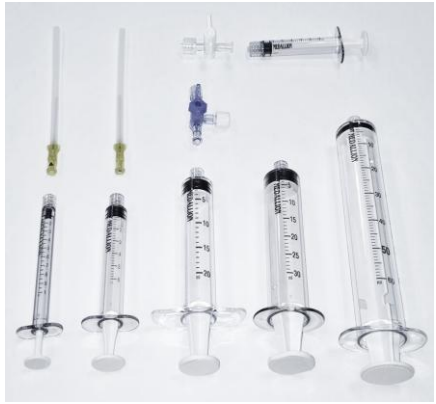
AeriSeal® System

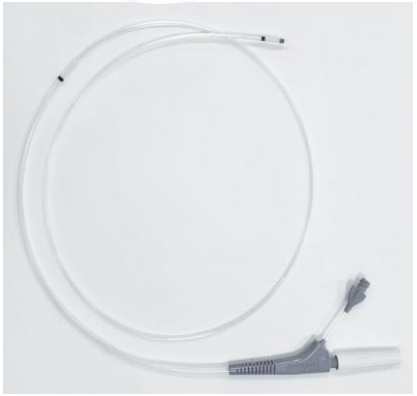
The AeriSeal® Foam is a polymerizing sealant (composed of aminated polyvinyl alcohol and glutaraldehyde) that functions by blocking both small airways and collateral channels which limits the collateral ventilation of a target lobe.



AeriSeal® Foam in airways



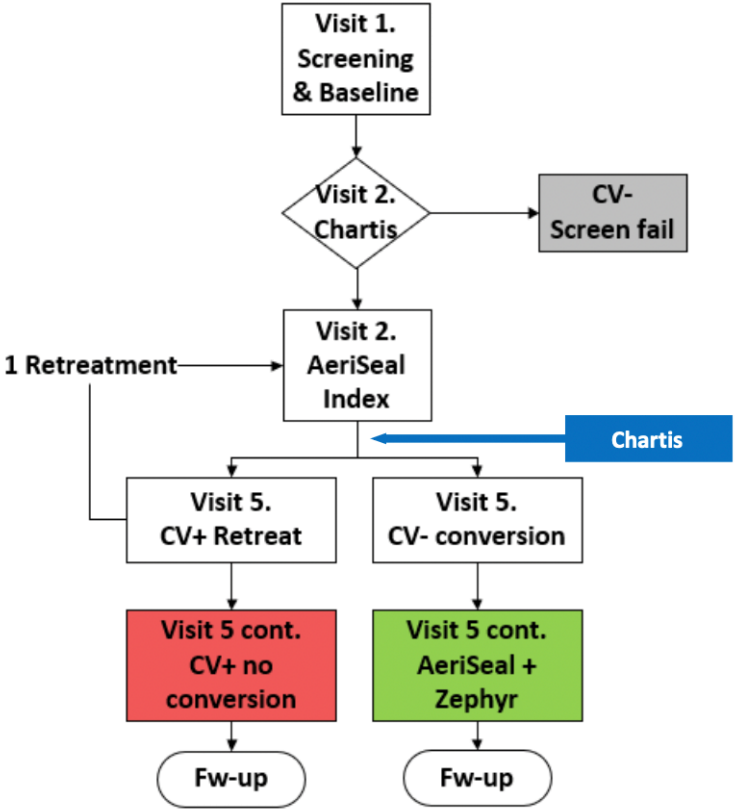




AeriSeal is delivered as a foam that polymerizes at time of delivery via a balloon catheter through a therapeutic bronchoscope (2.8mm working channel) to segmental or subsegmental bronchi.

CONVERT I trial

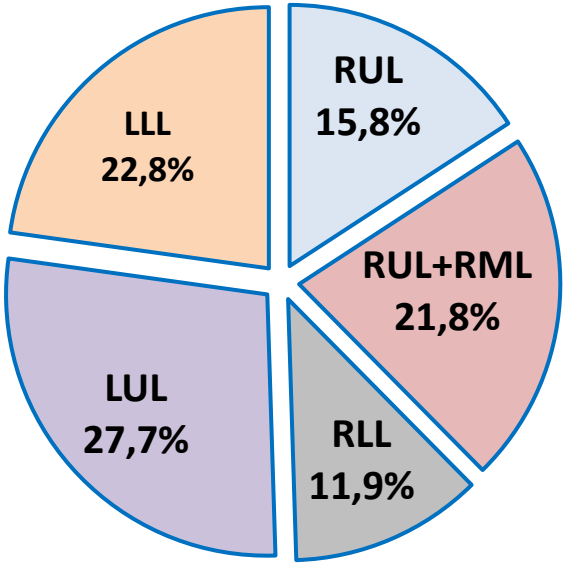
Baseline Demographics - Intent-to-treat Population (n=101)	
Variable	N[%] or mean ± SD
Age (years)	65.1 ± 6.86
Gender (M / F)	57 [56.4%] / 44 [43.6%]
BMI (kg/m^2)	23.5 ± 3.86
Smoking History (pack years)	45.1 ± 24.3
Post-BD FEV_1 (%pred.)	30.7 ± 9.2
TLC (% pred.)	136.9 ± 17.48
RV (% pred.)	235.7 ± 46.48
6MWD (meters)	347 ± 74.5
SGRQ (points)	58.9 ± 15.27
Emphysema Subtype (Heterogeneous / Homogeneous)	43 [42.6%] / 58 [57.4%]



CONVERT I trial

Lobe Status				
	Fissure Completeness (%)*	Emphysema Destruction at -910 HU*	AeriSeal Treated (n=101)	Zephyr Valve Treated (n=76)
RUL	68.2 ± 16.26	66.6 ± 12.40	16 (15.8%)	12 (15.8%)
RML	75.3 ± 15.76	59.2 ± 15.70	0	0
RUL + RML	87.0 ± 7.91	65.7 ± 11.12	22 (21.8%)	15 (19.7%)
RLL	87.0 ± 7.91	57.7 ± 13.97	12 (11.9%)	8 (10.5%)
LUL	87.6 ± 11.25	63.6 ± 11.28	28 (27.7%)	22 (27.6%)
LLL	87.6 ± 11.25	56.9 ± 14.25	23 (22.8%)	20 (26.3%)
Treated Lobe	**88.3 ± 5.94**	**70.6 ± 8.12**		

*: mean ± SD



CONVERT I trial

Table 2: Serious Adverse Events			
Event	AeriSeal Only	AeriSeal + Zephyr Valves	
	Stage 1† Post-AeriSeal only	Short-term (45-days post-Zephyr Valve)	Long-term (≥46-days post-Zephyr Valve)
	N=102	N=77	N=65
PAIR*	16 (15.7%)	0	0
Pneumonia	7 (6.9%)	1 (1.3%)	7 (10.8%)
Pneumonitis	6 (5.9%)	0	1 (1.5%)
COPD Exacerbation	6 (5.9%)	0	9 (13.8%)
Hemoptysis	1 (1.0%)	0	2 (3.1%)
Lung consolidation	1 (1.0%)	0	0
Pneumothorax	0	15 (19.5%)	4 (6.2%)
Respiratory failure	1 (1.0%)	0	1 (1.5%)

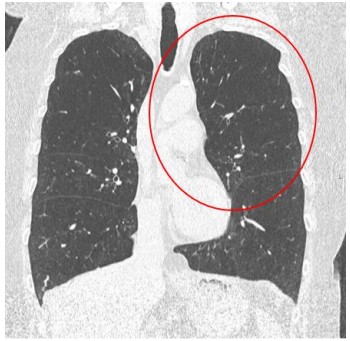
† Stage 1: Period from first AeriSeal treatment to final CV determination at 45 days (single AeriSeal treatment) or 90 days (repeat AeriSeal treatment) post-procedure.
* PAIR (Post-Treatment Acute Inflammatory Response)

CONVERT I trial

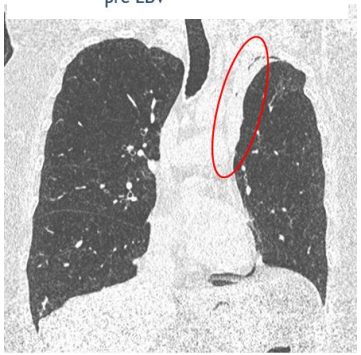
- 77.6% successfully converted and were treated with ZV
- 89% of CV- converted patients achieved a TLVR equal to or greater than 350mL, the minimal clinical important difference, at 6-months following valve implantation

- Improved lung function of 80mL or 10.2% over the baseline as measured by FEV1
- Improvement of 6.3 points in QoL (SGRQ)
- Mean treated lobe volume reduction (TLVR) of 1062 ±649 ml at 6 months

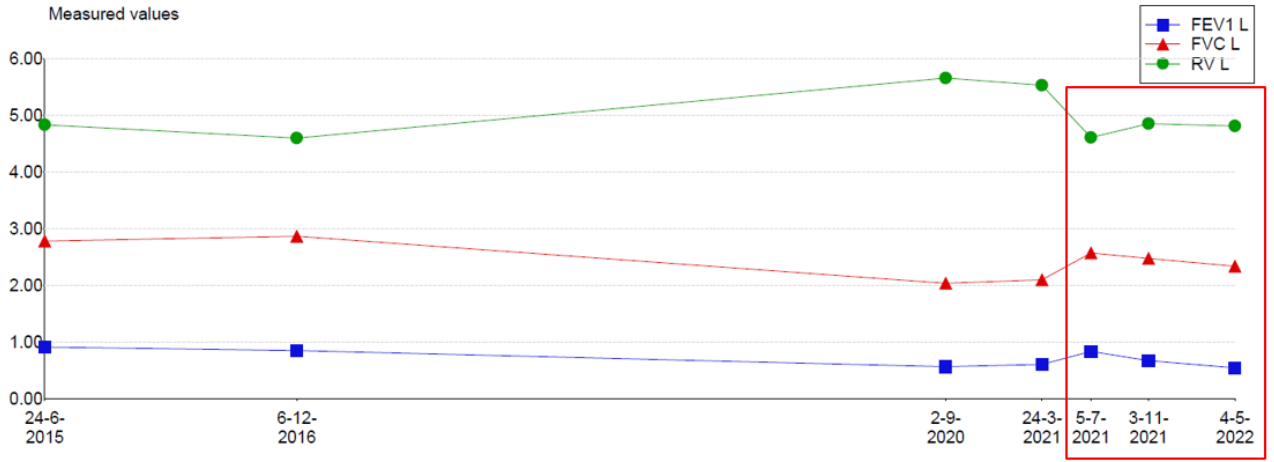
Reversal of collateral ventilation

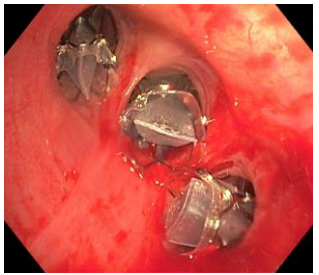


pre-EBV

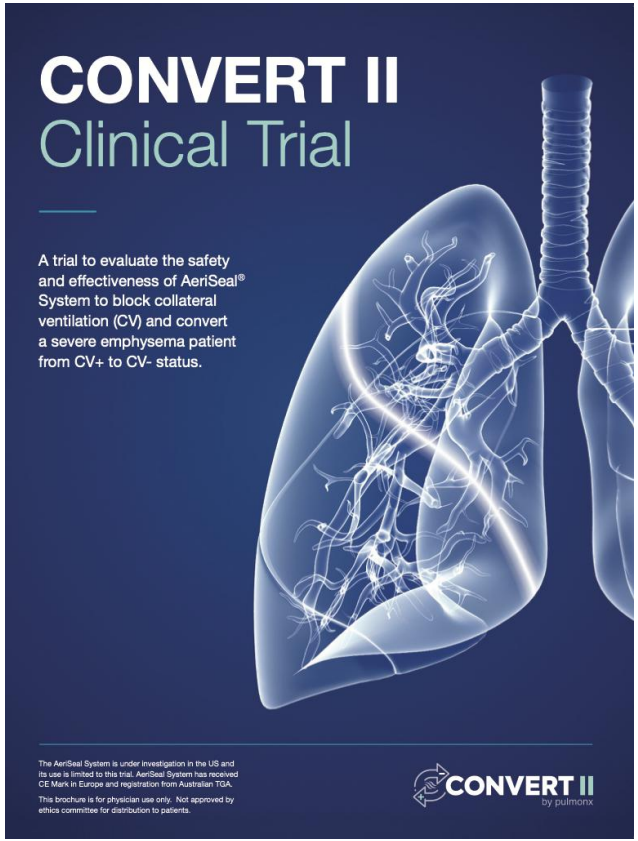


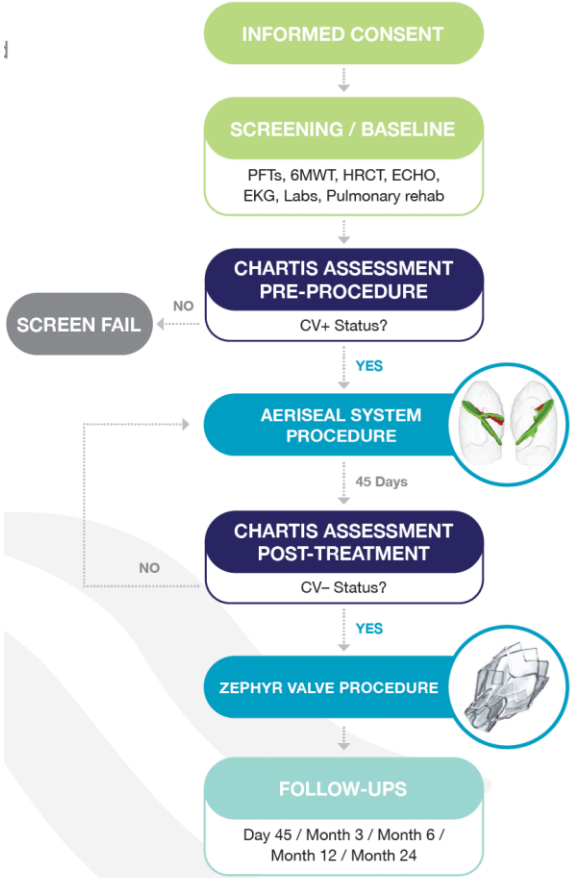
post-EBV + AeriSeal





Convert II


CONVERT II
Clinical Trial
A trial to evaluate the safety and effectiveness of AeriSeal® System to block collateral ventilation (CV) and convert a severe emphysema patient from CV+ to CV- status.
The AeriSeal System is under investigation in the US and its use is limited to this trial. AeriSeal System has received CE Mark in Europe and registration from Australian TGA.
This brochure is for physician use only. Not approved by ethics committee for distribution to patients.
CONVERT II
by pulmonx


INFORMED CONSENT
SCREENING / BASELINE
PFTs, 6MWT, HRCT, ECHO, EKG, Labs, Pulmonary rehab
CHARTIS ASSESSMENT PRE-PROCEDURE
CV+ Status?
NO
SCREEN FAIL
YES
AERISEAL SYSTEM PROCEDURE
45 Days
CHARTIS ASSESSMENT POST-TREATMENT
CV– Status?
NO
YES
ZEPHYR VALVE PROCEDURE
FOLLOW-UPS
Day 45 / Month 3 / Month 6 / Month 12 / Month 24

Conclusion

- ELVR with valves work in CV negative patients

- Reduced Hyperinfaltion, Reduced Exacerbation rate
- Improved QoL, prolonged survival

- AeriSeal®Foam can safely and effectively occlude collateral channels and convert a CV+ lobe

- Emphysema patients with a defined fissure gap in the target lobe may have an option for BLVR with Zephyr Valves after closure of the fissure gap with AeriSeal Foam

Komplikationen bei der Behandlung mit dem Zephyr Endobronchialventil können u. a. sein: Pneumothorax, Verschlechterung der COPD-Symptome, Hämoptyse, Pneumonie, Dyspnoe und in seltenen Fällen Tod.

Wichtige Sicherheitsinformationen:
Das **Zephyr Endobronchialventil (EBV)** ist ein implantierbares Bronchialventil, das den Luftstrom kontrollieren soll, um die Lungenfunktion bei Patienten mit Überblähung im Zusammenhang mit einem schweren Emphysem mit geringer oder keiner Kollateralventilation zu verbessern und/oder Fisteln zu reduzieren. Das Zephyr-Ventil ist kontraindiziert bei: Patienten, bei denen bronchoskopische Verfahren kontraindiziert sind; Patienten mit Hinweis auf eine aktive pulmonale Infektion; Patienten mit bekannten Allergien gegen Nitinol (Nickel-Titan) oder dessen Metallbestandteile (Nickel oder Titan); Patienten mit bekannten Allergien gegen Silikon; aktiven Rauchern. Der Gebrauch ist geschulten Ärzten vorbehalten. Vor dem Gebrauch sind alle weiteren Angaben zu Anwendungsbereichen, Gegenanzeigen, Warnhinweisen, Vorsichtsmaßnahmen und Nebenwirkungen in der Gebrauchsanleitung für das Zephyr® Endobronchialventilsystem zu beachten.

Das **Chartis-System** ist indiziert für den Gebrauch von dem durchführenden Arzt bei einer diagnostischen Bronchoskopie bei erwachsenen Patienten mit chronisch obstruktiver Lungenerkrankung (COPD) und Emphysem in einer Bronchoskopie-Einheit. Das System besteht aus dem Chartis-Katheter und der Chartis-Konsole und ist für Druck- und Strömungsmessungen ausgelegt, um den Luftstromwiderstand zu berechnen und die Kollateralventilation in isolierten Lungenkompartimenten zu quantifizieren. Der Chartis-Katheter wird durch den Arbeitskanal eines Bronchoskops eingebracht und ist mit der Chartis-Konsole verbunden. Die Chartis-Konsole ist ein wiederverwendbares Gerät für die Anzeige der Patientendaten. Das Chartis-System ist bei aktiver Infektion oder gravierender hämorrhagischer Diathese kontraindiziert. Es sind keine Störsubstanzen bekannt. Der Gebrauch ist geschulten Ärzten vorbehalten. Vor dem Gebrauch sind alle weiteren Angaben zu
Anwendungsbereichen, Gegenanzeigen, Warnhinweisen, Vorsichtsmaßnahmen und Nebenwirkungen in der Gebrauchsanleitung/dem Benutzerhandbuch für das Chartis-System zu beachten.

Das **AeriSeal-System** ist zur Reduzierung des Lungenvolumens bestimmt, um die Lungenfunktion und die Lebensqualität von Patienten mit fortgeschrittenem Emphysem zu verbessern. Seine Funktion beruht auf einer physischen Okklusion sowohl von kleinen Atemwegen als auch von kollateralen Luftkanälen, was bewirkt, dass der behandelte Bereich aufgrund einer Resorptionsatelektase kollabiert. Es handelt sich dabei um ein System für den Einmalgebrauch, das für die Verwendung durch Lungenspezialisten und Thoraxchirurgen in einer Bronchoskopie-Sitzung oder im OP bestimmt ist. Das AeriSeal-System ist kontraindiziert bei Patienten mit heterogenem Emphysem, das sich nicht überwiegend im Oberlappen befindet; bei Nachweis einer aktiven Atemwegsinfektion oder starken Blutungsneigung; bei vorliegender COPD-Exazerbation oder Bronchospasmen; bei Patienten, die bronchoskopische Verfahren oder die notwendige Anästhesie nicht vertragen, die eine bekannte Allergie gegen die Bestandteile des Gerätes haben oder die aktive Raucher sind. Die Anwendung ist geschulten Ärzten vorbehalten. Vor der Anwendung sind alle weiteren Angaben zu Anwendungsgebieten, Gegenanzeigen, Warnhinweisen, Vorsichtsmaßnahmen und Nebenwirkungen in der Gebrauchsanweisung für das AeriSeal System zu beachten.

Prof. Herth ist ein bezahlter Berater für Pulmonx.

zephyr®
by pulmonx