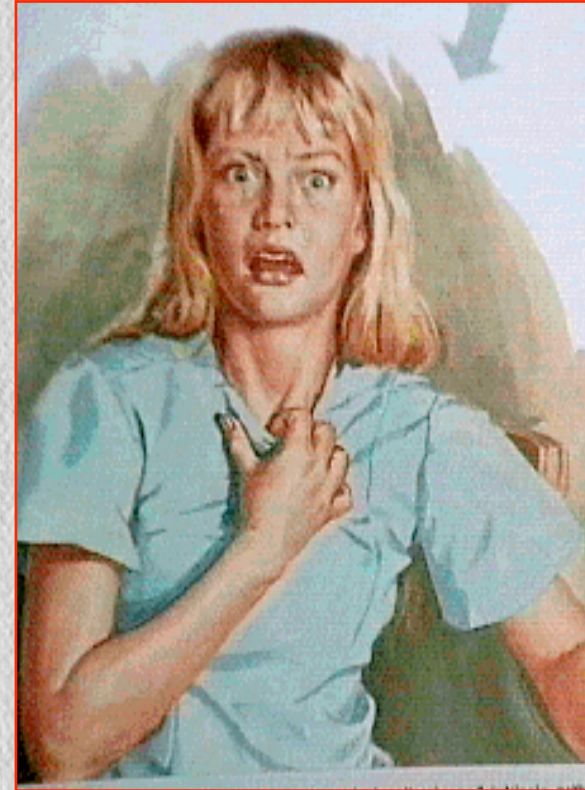


# LA RIDUZIONE ENDOSCOPICA DI VOLUME: TRUCCHI E TRAPPOLE



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Università Politecnica delle Marche  
S.O.D. di Pneumologia  
Azienda Ospedali Riuniti  
Ancona - Italy*



Some years ago...  
**SEVERE COPD AND ASTHMA:**

**CONTRAINDICATION FOR BRONCHOSCOPY !?!?**



# INTERVENTIONAL PULMONOLOGY

## NEW FRONTIERS FOR THERAPY (COPD)



**VALVES**



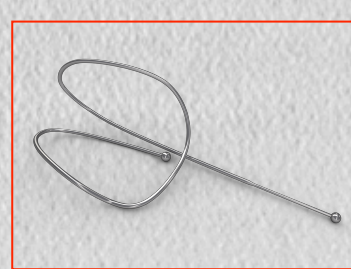
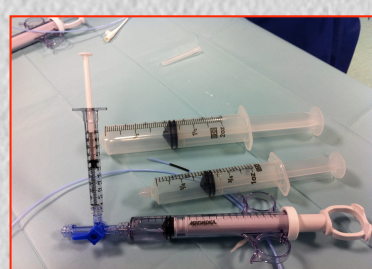
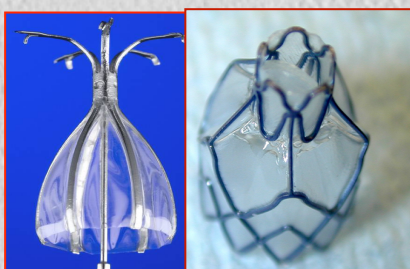
**SEALANT**



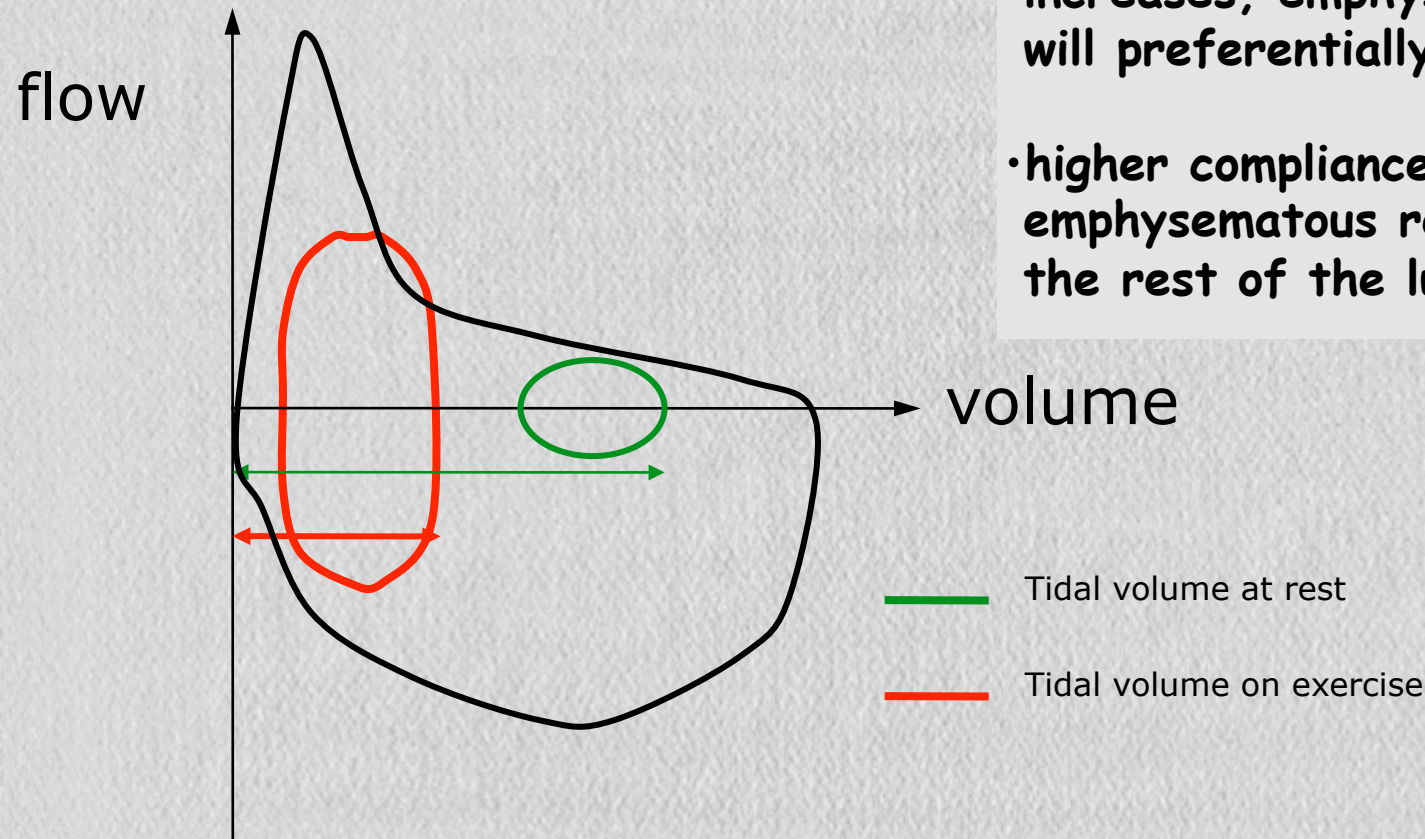
**COILS**



**STEAM**



## Emphysema: Pathophysiological background



- on exercise, as Tidal Volume increases, emphysematous areas will preferentially hyperinflate
- higher compliance of the emphysematous regions relative to the rest of the lung

**Hyperinflation: one the main factors determining dyspnea in emphysema**

**Hyperinflation increases on exercise (dynamic hyperinflation)**

**Inhaled bronchodilators: modest impact on hyperinflation**

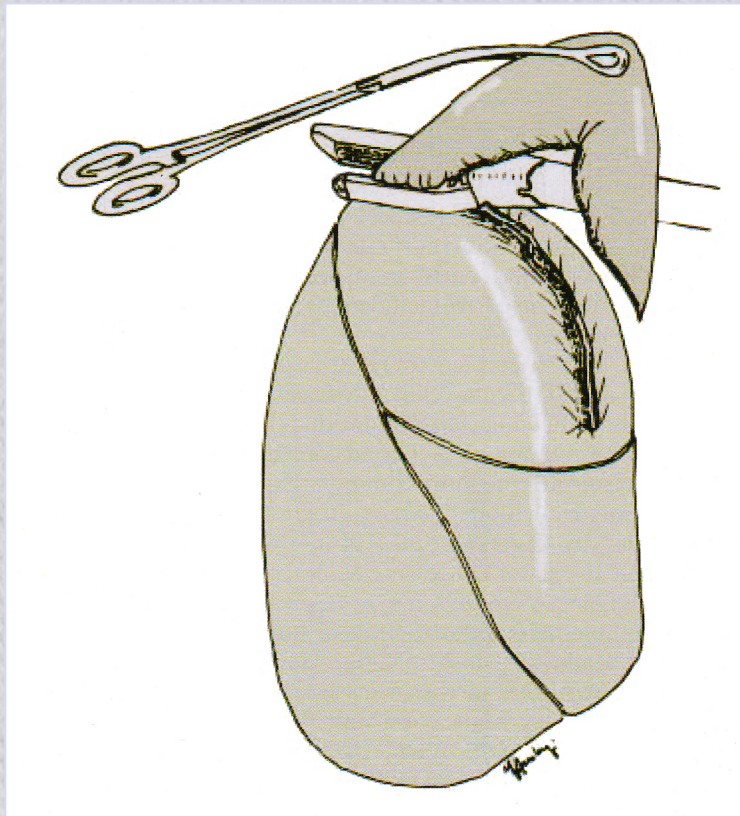


# BILATERAL PNEUMECTOMY (VOLUME REDUCTION) FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASES

Cooper JD et al, J Thorac Cardiovasc Surg 1995; 109: 106-119

## RESULTS OF 150 CONSECUTIVE BILATERAL LUNG VOLUME REDUCTION PROCEDURES IN PATIENTS WITH SEVERE EMPHYSEMA

Cooper JD, Patterson GA et al. J Thorac Cardiovasc Surg 1996; 112: 1319-30



Heterogeneous emphysema,  
Severe hyperinflation,  
 $FEV_1 > 20-25\%$  pred,  
No pulmonary hypertension



Reduction of dyspnea  
Increase of  $FEV_{1.0}$   
Improvement in exercise capacity  
Improvement in quality of life

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 22, 2003

VOL. 348 NO. 21

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

National Emphysema Treatment Trial Research Group\*

- 1218 randomized patients:  
best medical therapy vs. surgical volume reduction.
- LVRS increases exercise capacity in 15% of surgical treated patients vs. 3% of control group
- No differences in terms of overall survival.
- Better survival with LVRS in group of patients with predominant emphysema in upper lobes and low exercise capacity.
- Patients with non-upper-lobe emphysema and high exercise capacity are poor candidate for LVRS for negligible functional gain and increased risk of mortality.



# LUNG VOLUME REDUCTION SURGERY

**Table 2. – Operative results after bilateral stapled lung volume reduction surgery**

First author [Ref.]	Surgical approach	Patients n	Mortality %	Prolonged air leaks %	Hospital stay	FEV <sub>1</sub> increase %
COOPER [25]	Sternotomy	150	4	46	13.5	51
MILLER [26]	Sternotomy	53	5.6	40	10–59	96
BINGISSER [14]	VATS-OS	20	0	35	15	42
BRENNER [27]	VATS-OS	145	4.2		8.8	62
WISSER [28]	VATS-OS	15	13.3		12.3	60
KOTLOFF [15]	Sternotomy	80	4.2		22	40
	VATS-OS	40	2.5		17.3	37
Mc KENNA [22]	VATS-OS	79	2.5	47	10.0	57
DE PERROT [17]	Thoracotomy-OS	18	0	33	21	54
POMPEO [29]	VATS-ST	26	0	52	18.4	39
	VATS-OS	33	3.0	39	11.7	52
CICCONE [12]	Sternotomy	250	4.8	45.2	9 <sup>#</sup>	57

FEV<sub>1</sub>: forced expiratory volume in one second; VATS: video-assisted thoracoscopic surgery; OS: one-stage; ST: staged; Hospital stay data is expressed as mean, or <sup>#</sup>: median range.

# **BRONCHOSCOPIC LUNG VOLUME REDUCTION: WHY?**

- To obtain the same results of surgery (?)
- To reduce risks
- To reduce costs
- To reduce hospital stay
- Effective for patients who do not meet the criteria for LVRS (e.g. lower lobe emphysema)
- Out-patient procedure
- Potentially reversible (?)



# BRONCHOSCOPIC TREATMENT OF EMPHYSEMA

## 1. Bronchial blockers devices

### Valves

- IBV
- Zephyr



## 2. Devices that works on lung parenchima

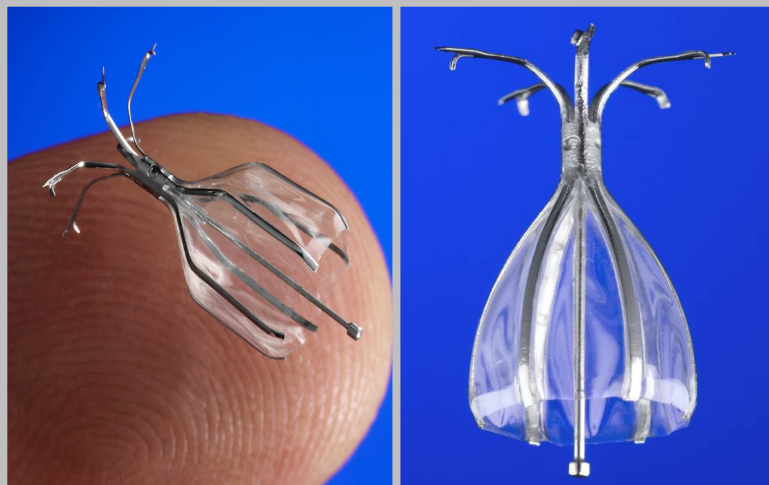
Sealants

Coils

Steam



# One-way endobronchial valves



**IBV valve**



**ZEPHYR valve**



# VENT: Bronchial Valve for Emphysema Palliation Trial

ORIGINAL ARTICLE

N Engl J Med 2010; 363: 1233-1244

## 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\*

- Multi-center
- Prospective/Randomized
  - 2:1 treatment to control / non-blinded
- All subjects received optimal medical management prior to baseline
- Key Entry Criteria
  - Severe heterogeneous disease determined by HRCT, Pulmonary Function testing
  - Clinically Stable (i.e. no severe concurrent acute events)



# VENT:

## Effectiveness Results (6 months)

	Treatment n = 220 Mean $\pm$ SD	Control n = 101 Mean $\pm$ SD	Between- group difference from baseline	p value <sup>1</sup>
<u>Co-Primary Endpoints</u>				
% Change in FEV <sub>1</sub>	4.3% (1.4 to 7.2)	-2.5% (-5.4 to 0.4)	6.8	0.005
% Change in 6MWT	2.5% (0.2 to 1.8)	3.2% (-8.9 to 2.4)	5.8	0.002
<u>Secondary Endpoints</u>				
SGRQ	-2.8 (-4.7 to -1.0)	0.6 (-1.8 to 3.0)	-3.4	0.04
mMRC	-0.1 (-0.21 to 0.09)	0.2 (0.01 to 0.37)	-0.3	0.04

Sciurba et al. N Engl J Med 2010; 363: 1233-1244



# VENT:

## Effectiveness Results (6 months)

SUBGROUPE	Difference between EBV group and Control group	
<u>High-heterogeneity</u>		
FEV1.0	10.7% (1.4 to 7.2)	<0.001
6MWT	12.4% (4.8 to 20.1)	0.08
<u>Low-heterogeneity</u>		
FEV1.0	2.5% (3.1 to 8.2)	0.64
6MWT	-1.0 (-6.4 to 8.4)	0.84
<u>Complete fissure</u>		
FEV1.0	16.2 (8.8 to 23.8)	<0.001
6MWT	7.7 (-1.8 to 17.2)	0.31
<u>Incomplete fissure</u>		
FEV1.0	2.0 (-3.9 to 7.9)	0.41
6MWT	5.3 (-1.5 to 12.2)	0.20

# 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 Agusti, Debby Holmes-Higgin and Armin Ernst, on behalf of the International VENT Study Group

Eur Respir J 2012; 39: 1334-1342

European cohort of VENT Study: 161 pts  
111 valves  
60 control group

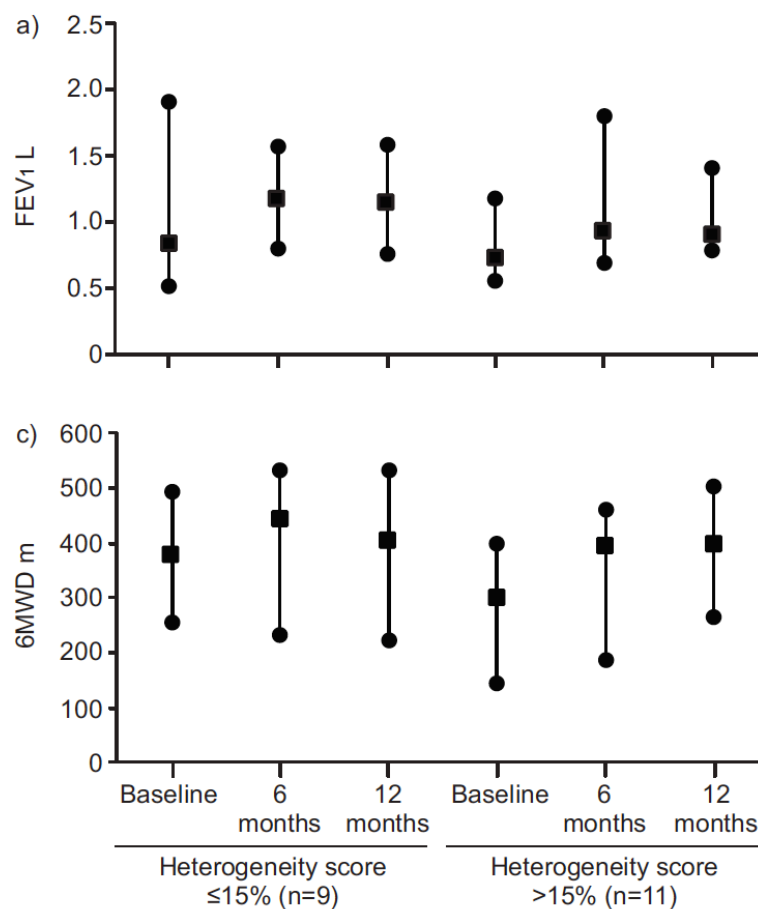
	Treatment n = 111	Control n = 60	p value
% Change in FEV <sub>1</sub>	+7.0%	+0.5%	0.067
% Change in cycle erg	+2±14 W	-3±10 W	0.04
<u>Fissure integrity</u>			
FEV <sub>1</sub>			
<u>Lobar occlusion and Fissure integrity</u>			
FEV <sub>1</sub>			

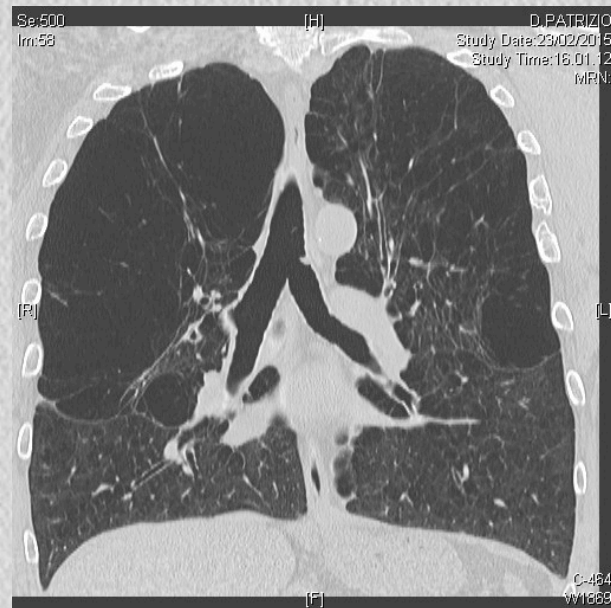
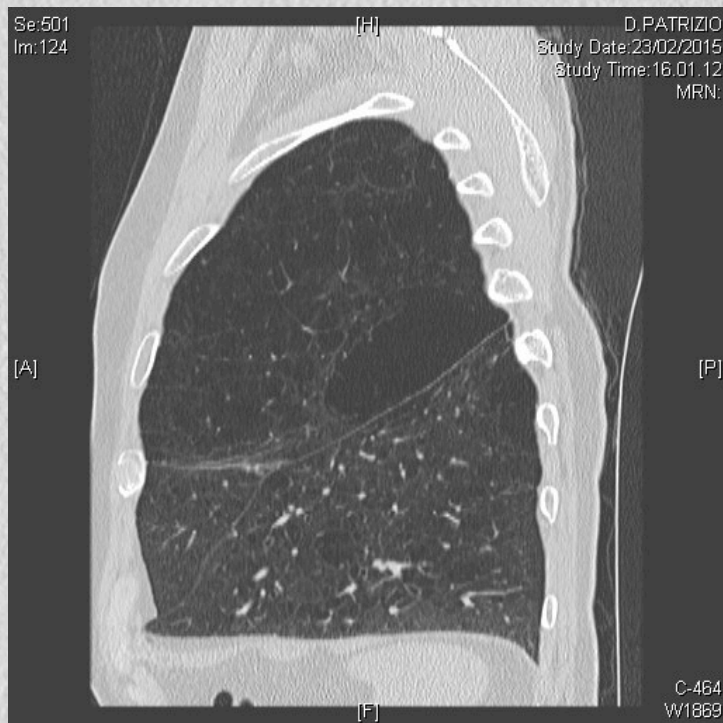


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Eur Respir J 2012; 39: 1334-1342





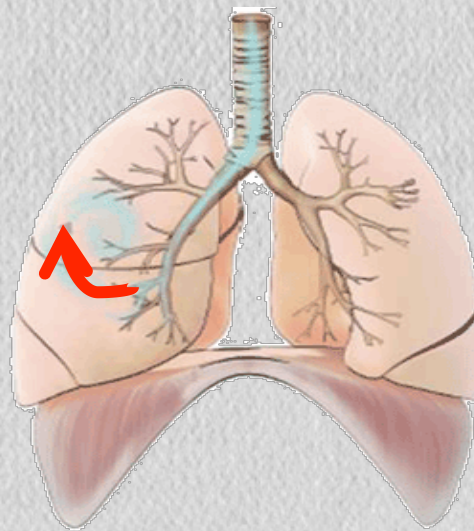


# COLLATERAL VENTILATION

All the studies with endobronchial valves emphasized the role of collateral ventilation as main factor affecting outcome

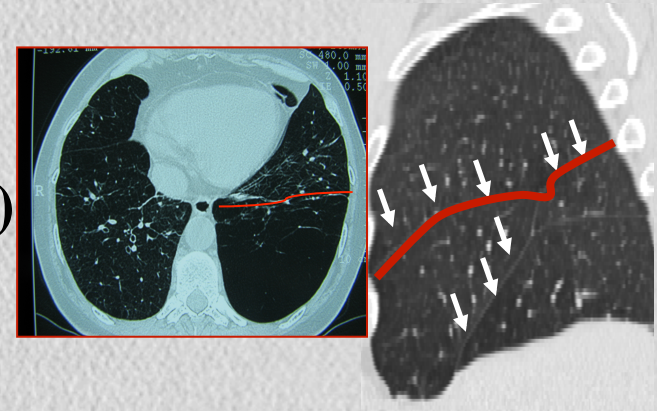
The post hoc analysis of two earlier trials with valves (Vent EU / Vent USA) showed better response rates in pts who had intact fissure

The later trials (BeLieVeR Hifi 2015, IMPACT 2016, STELVIO 2015) altered their inclusion criteria to only select pts without collateral ventilation

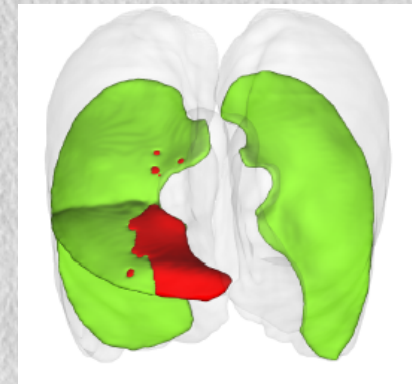


# TRICK: HOW TO ASSESS COLLATERAL VENTILATION

- 1) Visual assessment of interlobar scissures by HRCT (sagittal, axial and coronal view)

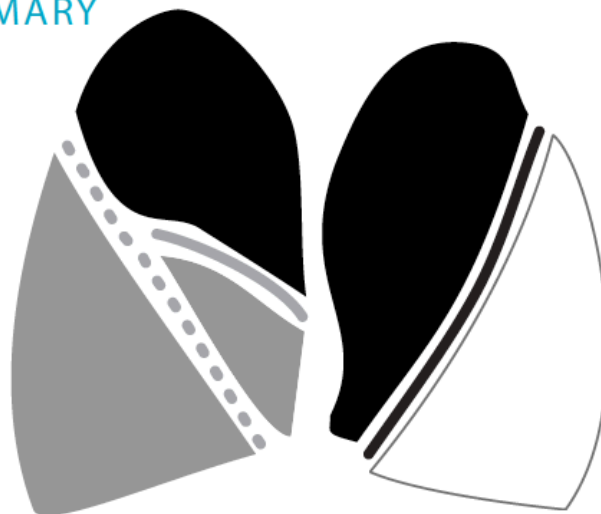


- 2) Quantitative CT and automatic lobar segmentation (software is available)





## SUMMARY



### KEY

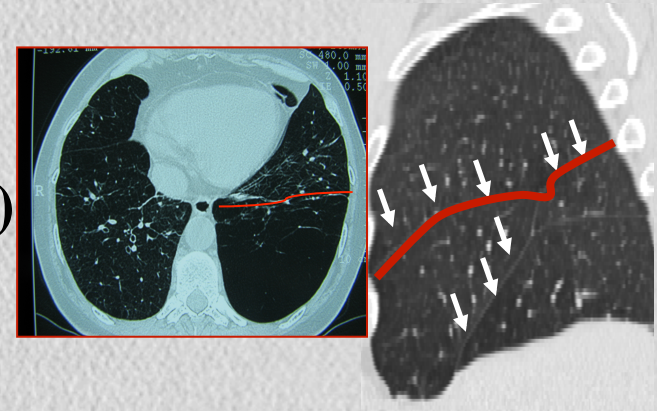
- $\geq 70\%$  Voxel Density  
Less Than -910 HU
- 60-70% Voxel Density  
Less Than -910 HU
- 50-60% Voxel Density  
Less Than -910 HU
- $< 50\%$  Voxel Density  
Less Than -910 HU
- $> 95\%$  Fissure Completeness
- 80-95% Fissure Completeness
- $< 80\%$  Fissure Completeness

## RESULTS

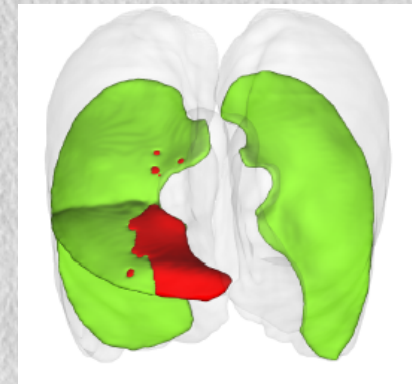
	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	64.2	65.0	84.9	65.0	100	100
% Voxel Density Less Than -910 HU	84	79	63	66	83	43
% Voxel Density Less Than -950 HU	67	59	36	40	69	16
Inspiratory Volume(ml)	1120	1492	372	1901	1717	1520

# HOW TO ASSESS COLLATERAL VENTILATION

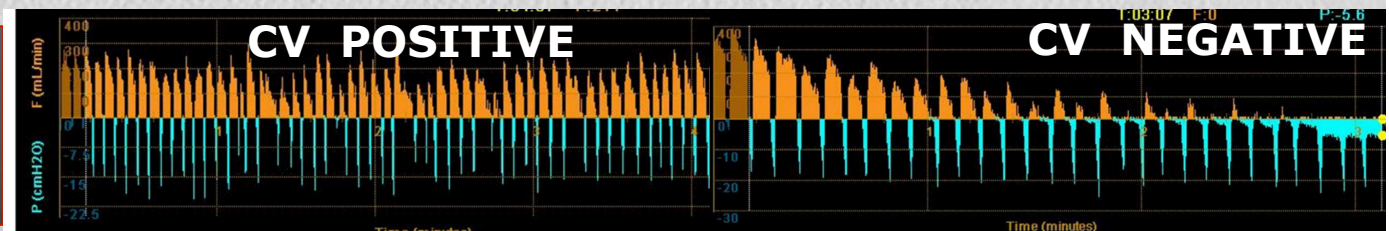
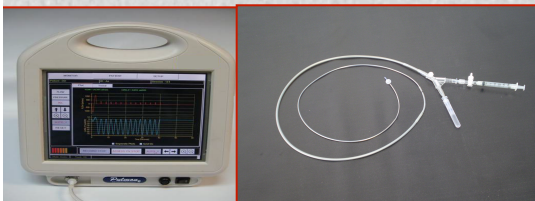
1) Visual assessment of interlobar scissures by HRCT (sagittal, axial and coronal view)



2) Quantitative CT and automatic lobar segmentation (software is available)



3) Chartis System





# HOW TO ASSESS COLLATERAL VENTILATION

## HRCT vs Chartis

Respiration. 2016;91(6):471-9. doi: 10.1159/000446288. Epub 2016 Jun 1.

### **Fissure Integrity and Volume Reduction in Emphysema: A Retrospective Study.**

de Oliveira HG<sup>1</sup>, de Oliveira SM, Rambo RR, de Macedo Neto AV.

Retrospective analysis of 38 patients:

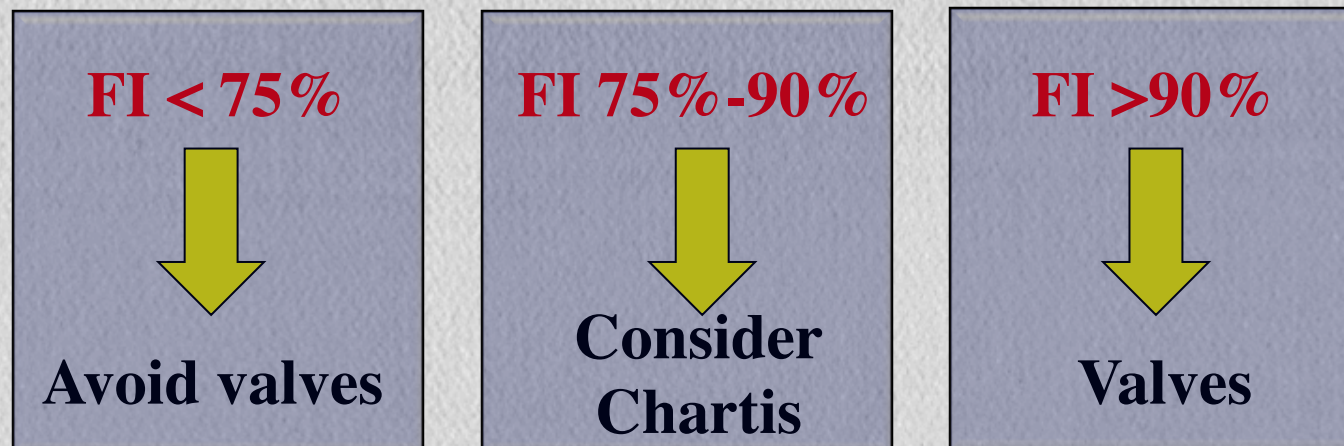
Accuracy of fissure integrity (FI) in predicting volume reduction:

FI 75%-90%: accuracy = 70%

FI >90%: accuracy = 90.5%

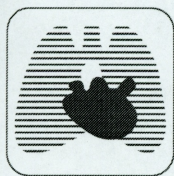
None of the pts with FI < 75% achieved a volume reduction  $\geq$  350 ml

### **Suggested algorithm for assessing CV**



*By Herth F*

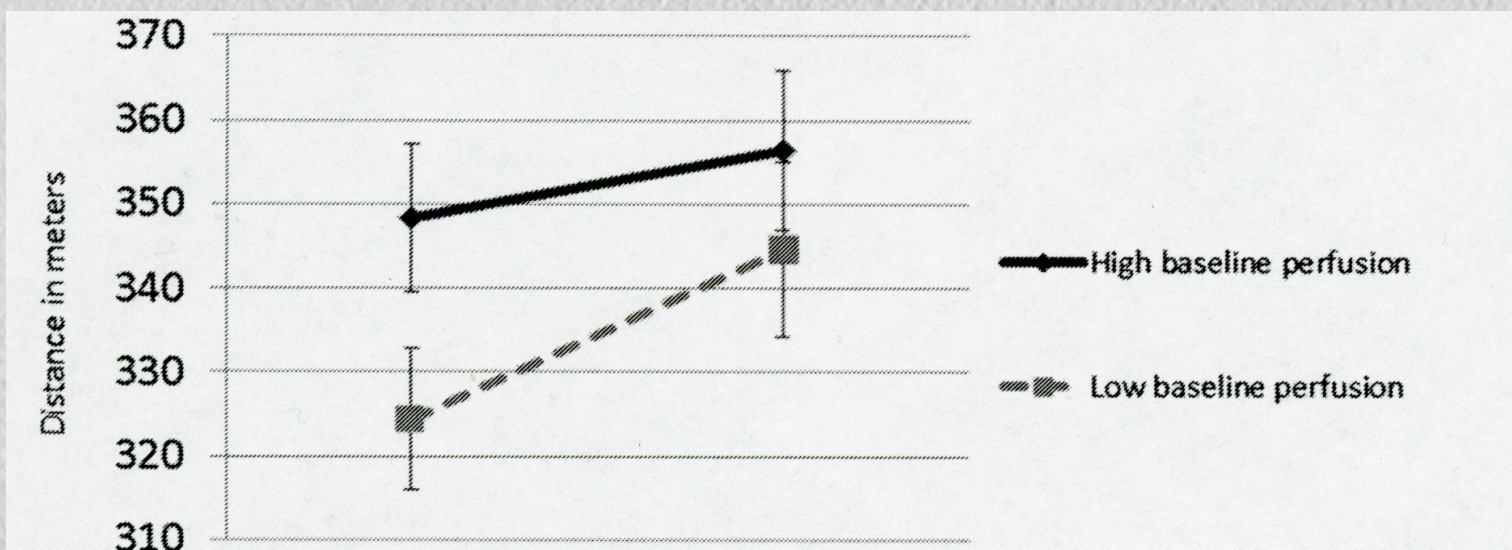




## Baseline Regional Perfusion Impacts Exercise Response to Endobronchial Valve Therapy in Advanced Pulmonary Emphysema

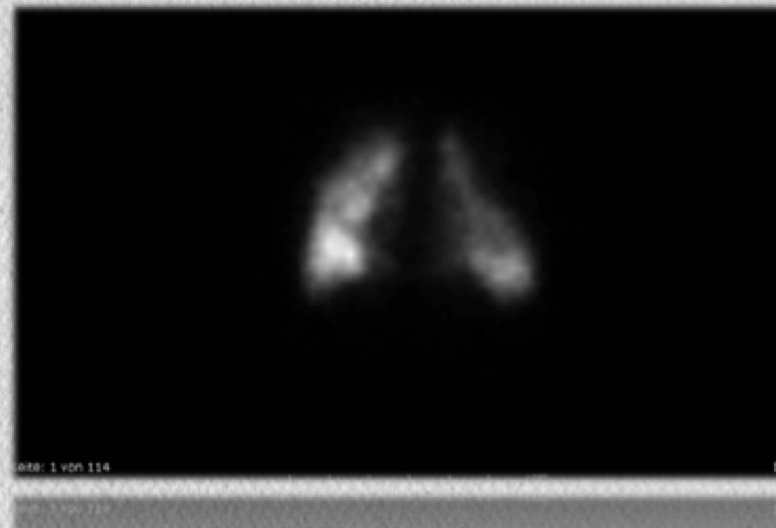
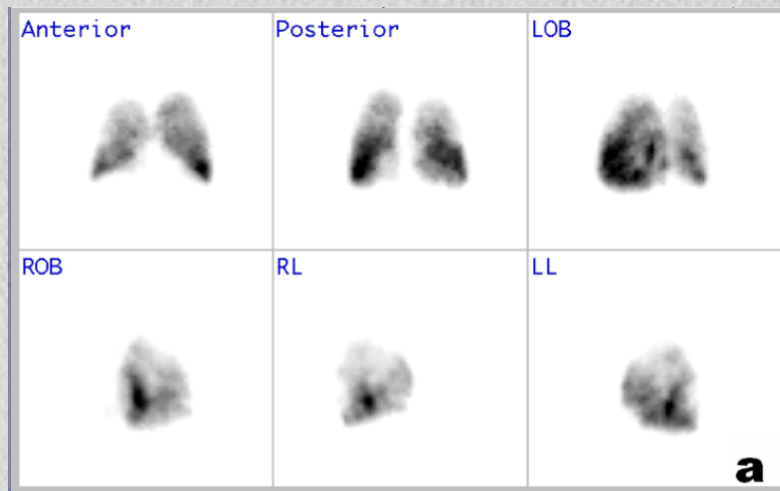
*Rahul G. Argula, MBBS, MPH; Charlie Strange, MD, FCCP;  
Viswanathan Ramakrishnan, PhD; and Jonathan Goldin, MD, PhD*

- Retrospective analysis of 169 pts (VENT study) treated with valves
- Pts with a low target lobe regional perfusion: significant improvement in 6mWTD in comparison with pts with high target lobe perfusion (30.24 m vs. 3.72 m)

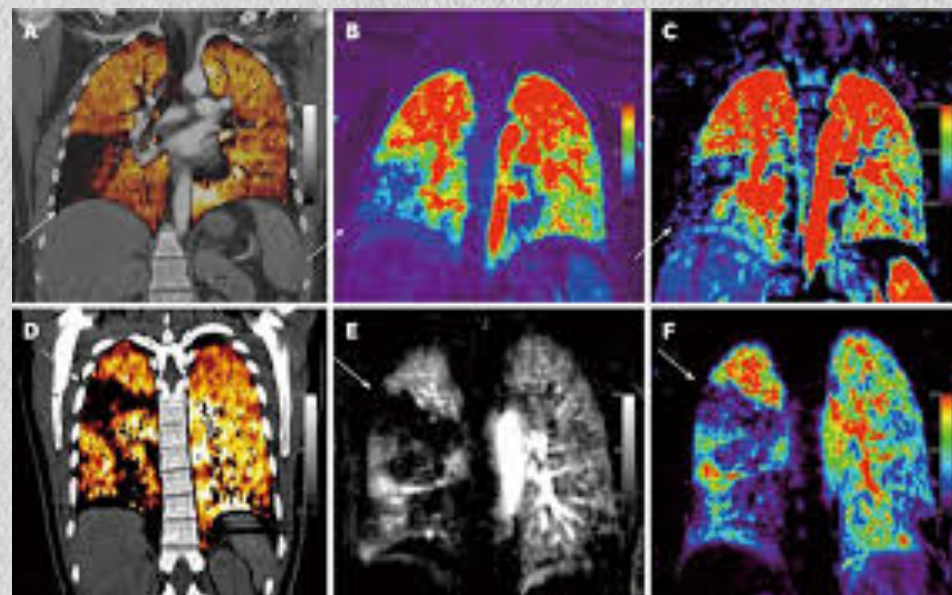




# HOW TO ASSESS PERFUSION DISTRIBUTION?



## PERFUSION SCINTIGRAPHY



## CT DUAL ENERGY

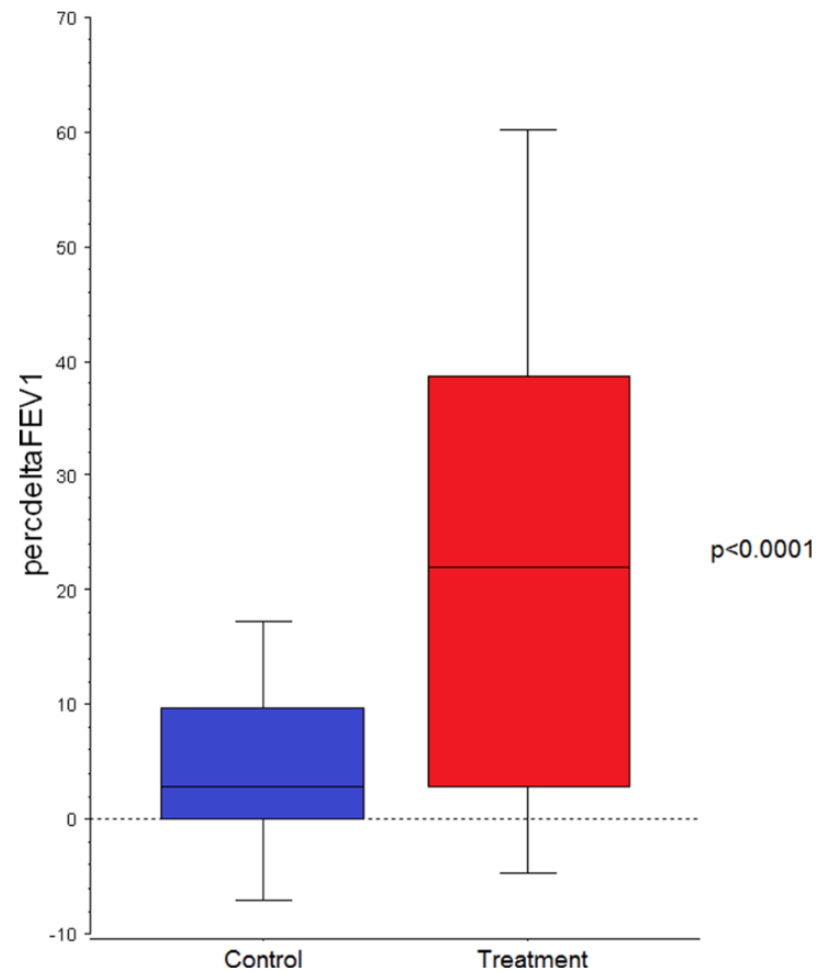
# **Endobronchial valves for emphysema: an individual patient-level reanalysis of randomised controlled trials**

Karin Klooster,<sup>1</sup> Dirk-Jan Slebos,<sup>1</sup> Zaid Zoumot,<sup>2</sup> Claire Davey,<sup>3</sup> Pallav L Shah,<sup>3</sup>  
Nicholas S Hopkinson<sup>3</sup>

- **Analysis of two randomized trials in pts with heterogeneous emphysema and absence of collateral ventilation**
- **Data from Stelvio trial and BelieVeR-HiFi study**
- **114 pts evaluated**



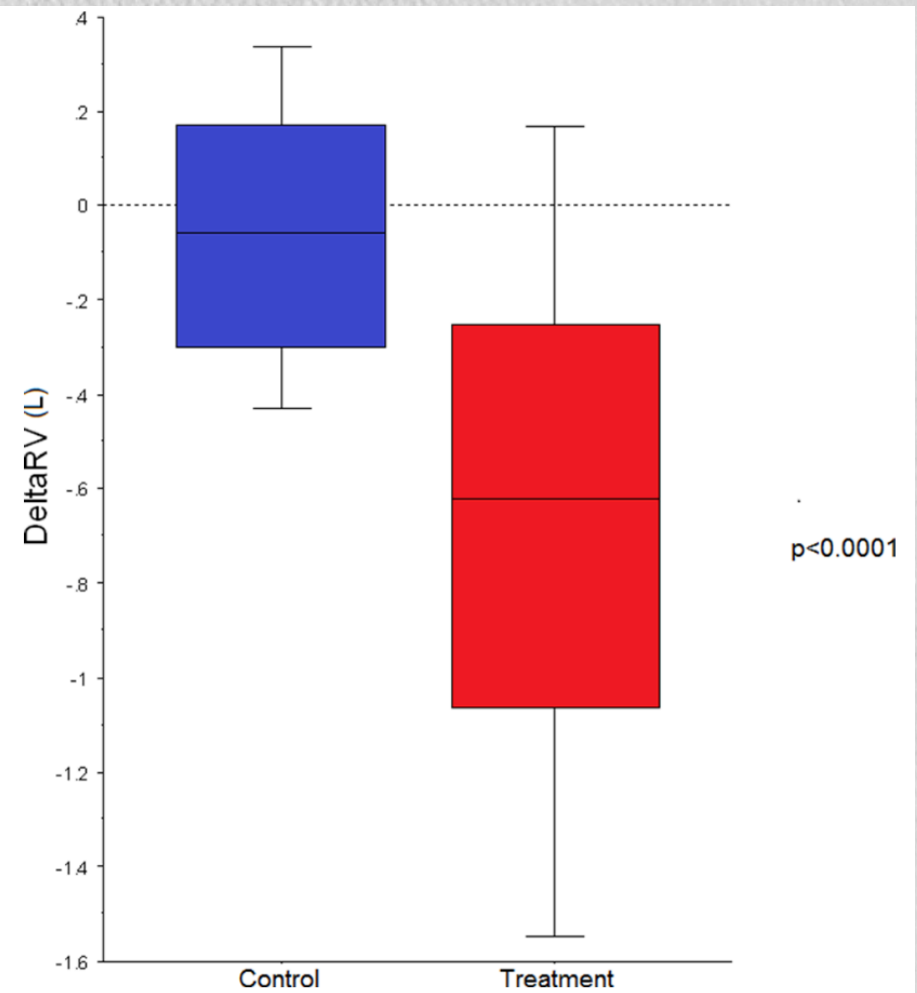
**$\Delta FEV_{1.0}$**



**+ 5.3%    + 23.1%**

***P<0.0001***

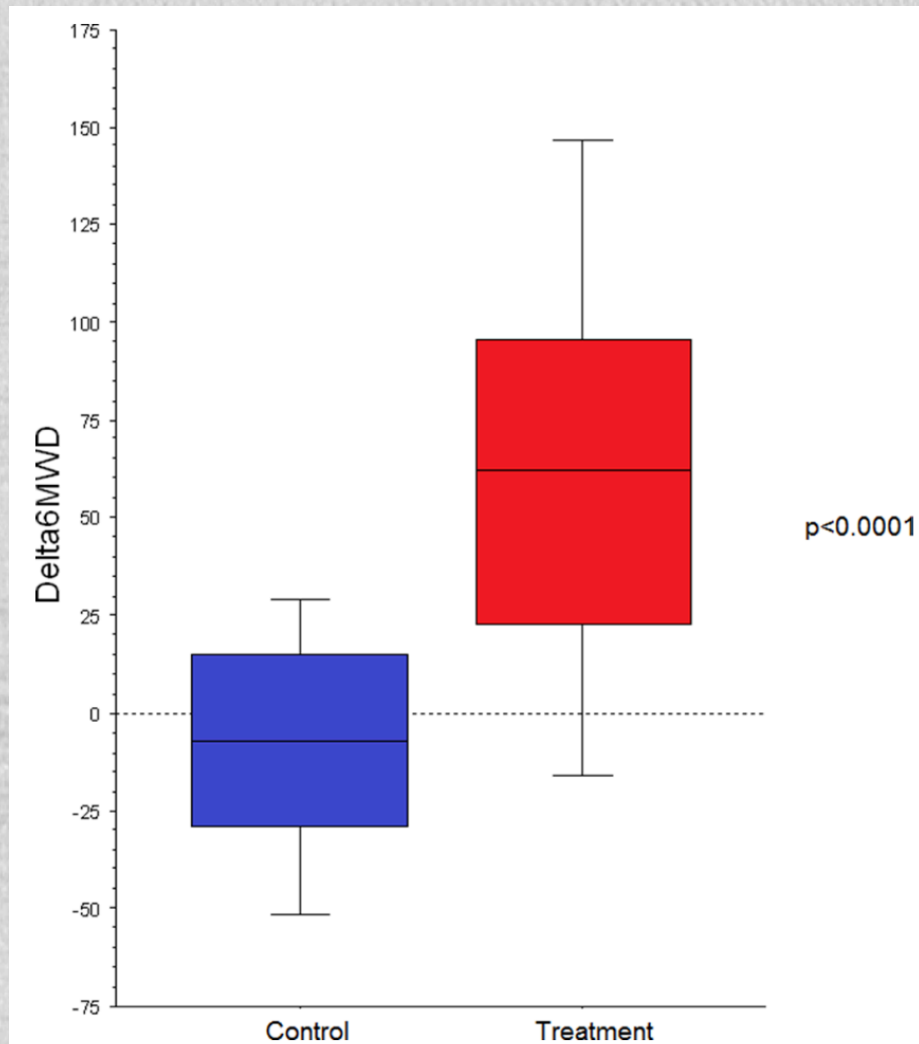
**$\Delta RV$**



**-0.06%    -0.7%**

***P<0.0001***

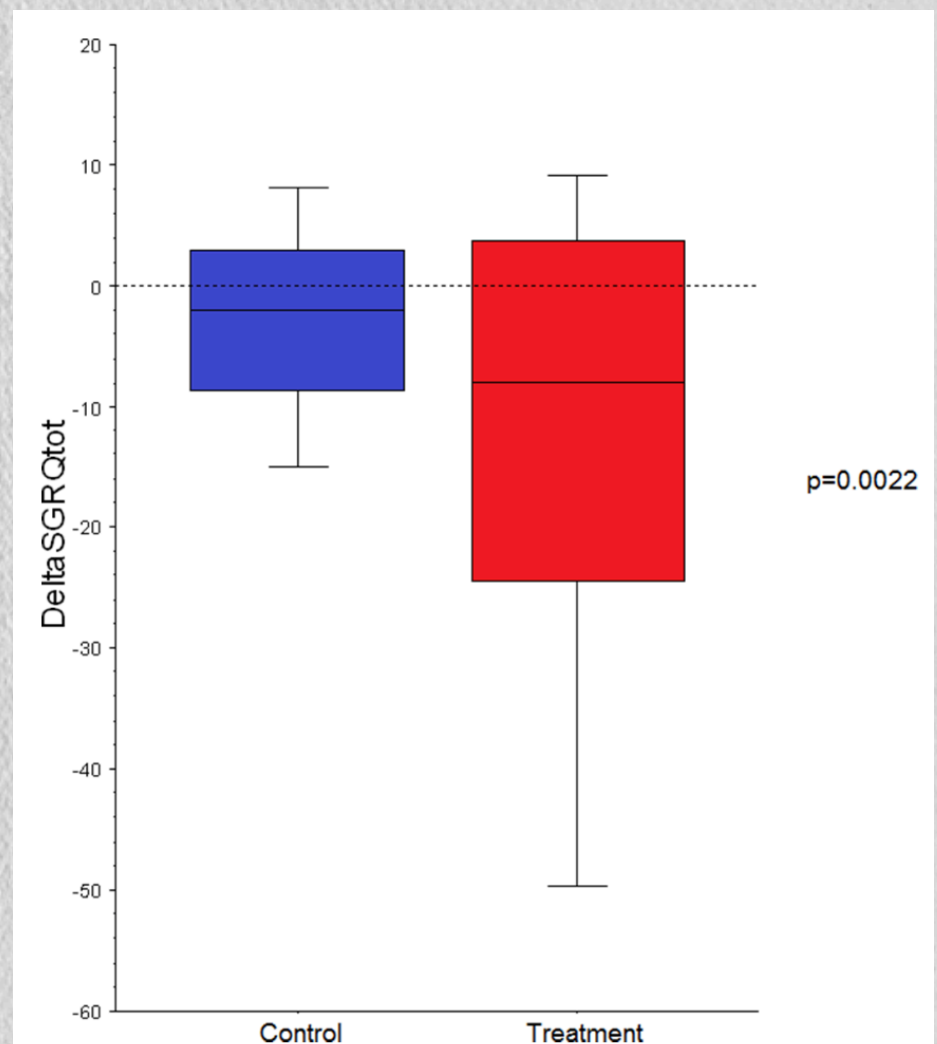
## $\Delta$ 6minWD



- 5.6 m    + 58.6 m

$P < 0.0001$

## $\Delta$ SGRQ



-3.2    -12.7

$P = 0.0022$

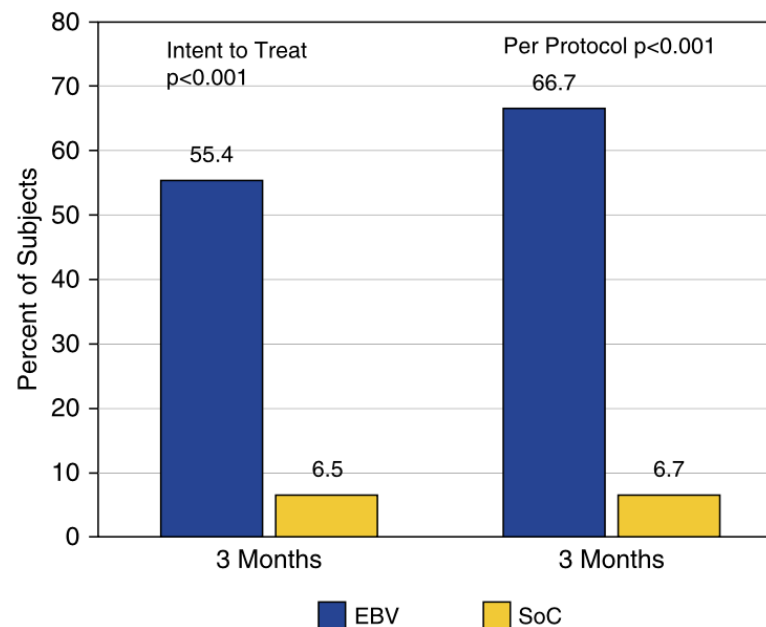


# A Multicenter Randomized Controlled Trial of Zephyr Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM)

*Kemp SV et al.*

*Am J Respir Crit Care Med 2017; 196: 1535-1543*

- Prospective, multicenter 2:1 randomized controlled trial
- EBV plus standard of care vs. standard of care alone
- 97 patients (65 EBV; 32 SoC) with heterogeneous emphysema
- Primary outcome at 3 months: percentage of subjects with FEV<sub>1.0</sub> improvement from baseline of 12% or greater

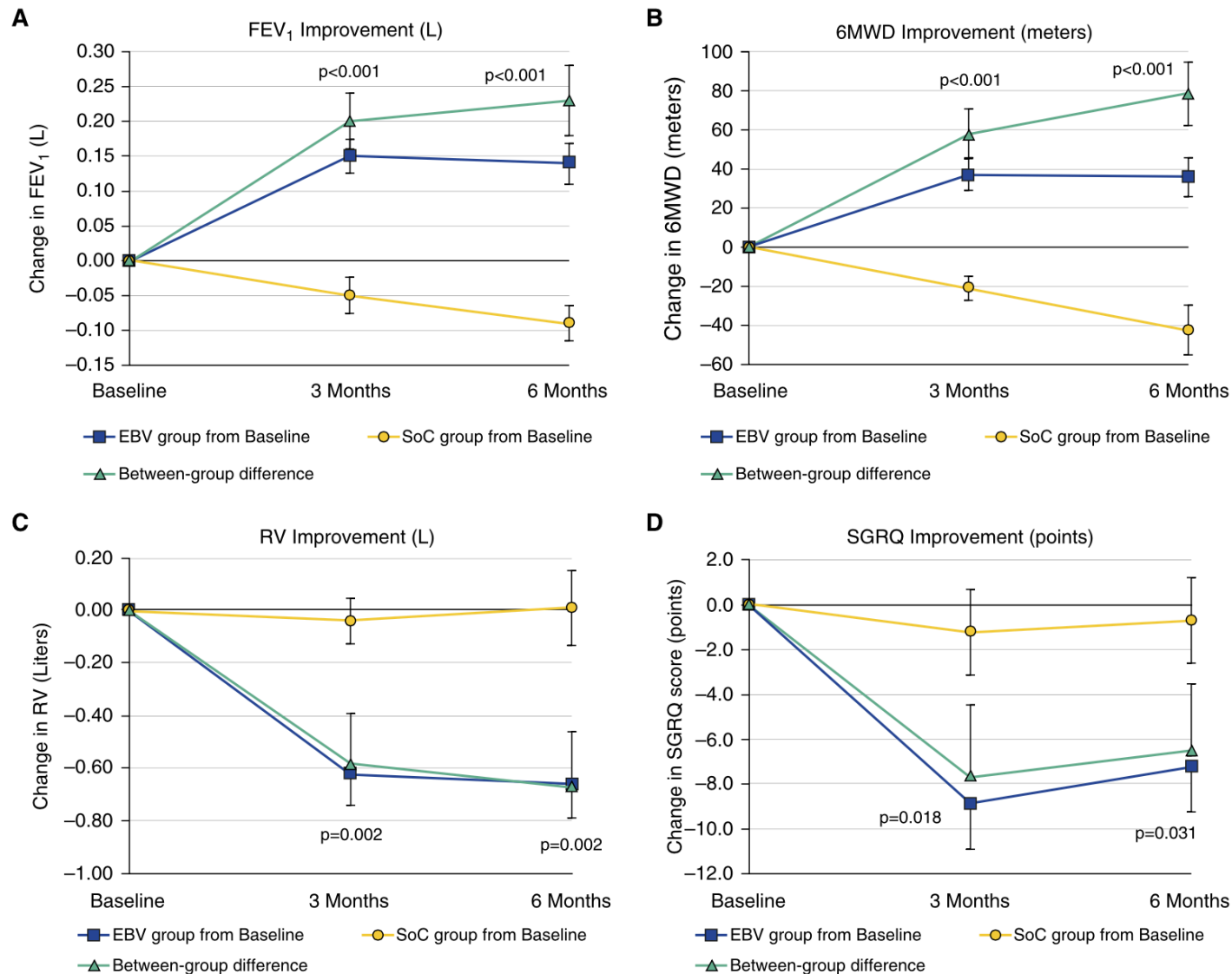


**Figure 1.** Primary endpoint: percentage of subjects achieving a 12% or greater improvement in FEV<sub>1</sub> (liters) at 3 months. EBV = Zephyr endobronchial valve; SoC = standard of care only.

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

Kemp SV et al.

*Am J Respir Crit Care Med* 2017; 196: 1535-1543





# **Endobronchial Valve Therapy in Patients with Homogeneous Emphysema**

**Results from the IMPACT Study**

**AJRCCM 2016; 194;1073-1082**

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

- **To evaluate the efficacy of EBV in pts with homogeneous emphysema with absence of collateral ventilation**
- **Prospective multicenter randomized trial (EBV vs standard care)**
- **93 pts: 43 EBV vs 50 standard care**

- **$\Delta$  FEV<sub>1.0</sub> = + 17%**
- **$\Delta$  6mWD = + 40 m**
- **$\Delta$  SGRQ = - 9.6**

## **CONCLUSIONS:**

**EBV in patients with homogeneous emphysema without collateral ventilation results in clinically meaningful benefits of improved lung function, exercise tolerance and quality of life**

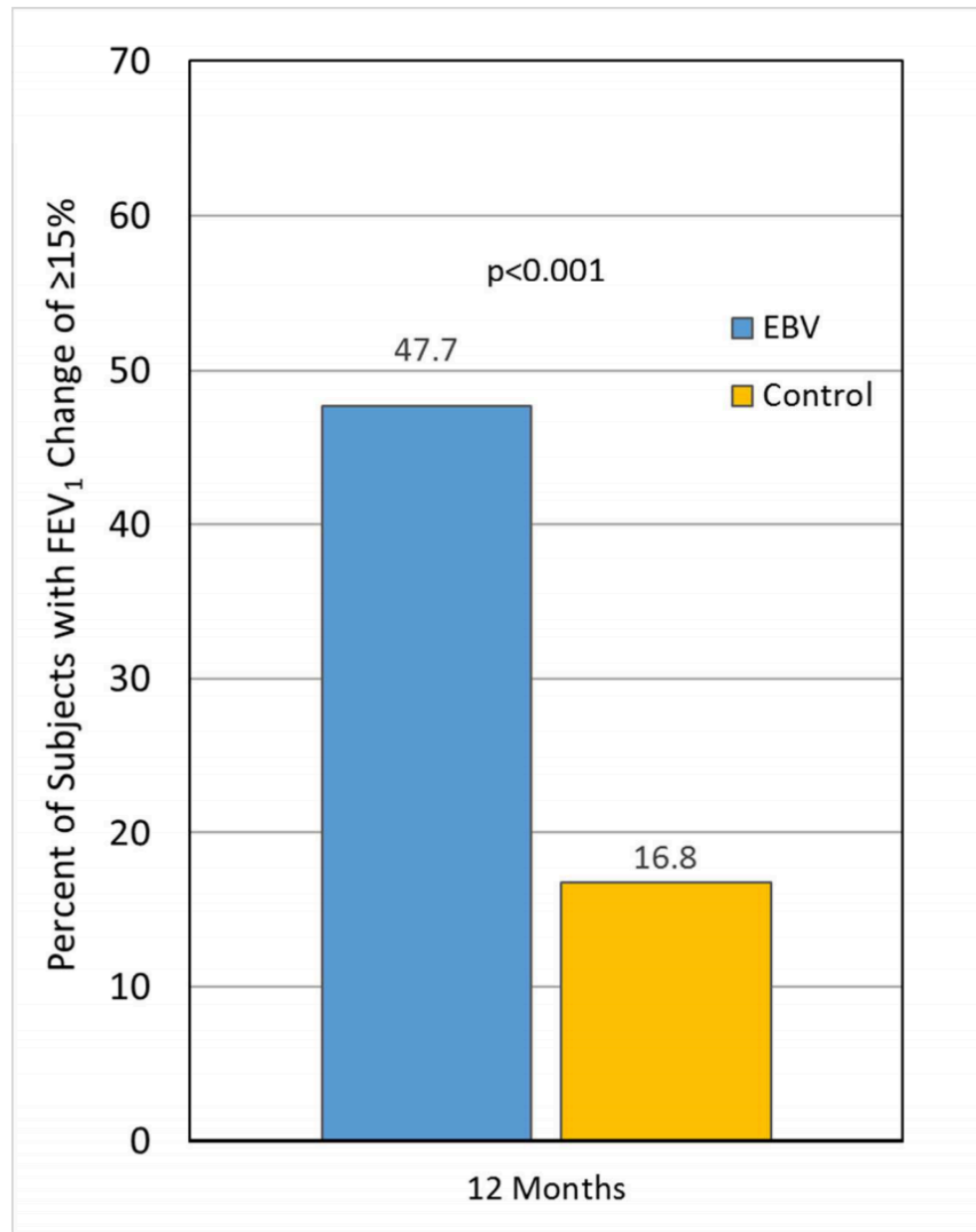
# A Multicenter RCT of Zephyr® Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE)

*Criner GJ et al. Am J Respir Crit Care Med 2018; 198:1151-1164*



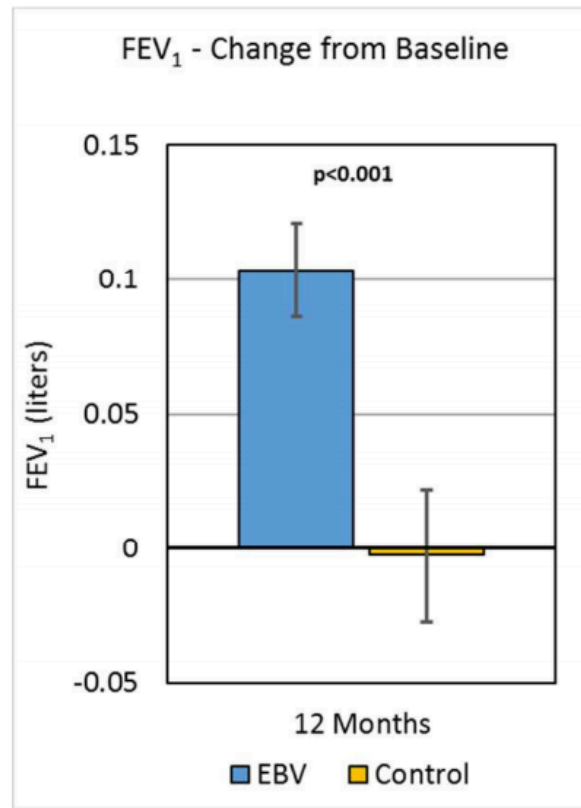
- **Randomized study: valves vs best standard of care**
- **Heterogeneous emphysema with little to no collateral ventilation**
- **Primary endpoint at 12 months:**  
    **number of subjects with FEV1.0 improvement > 15%**
- **Secondary endpoints:**  
    **change in FEV1.0, 6 min WD, SGRQ score**
- **190 pts:      128 valves**  
                  **62 control**



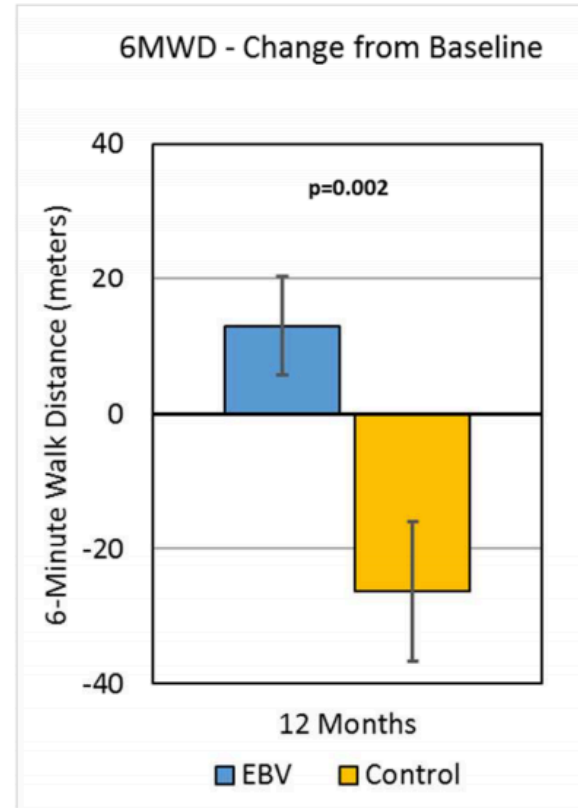


**Percent of Subjects with FEV<sub>1</sub> Change from Baseline to 12-months of ≥15%.**

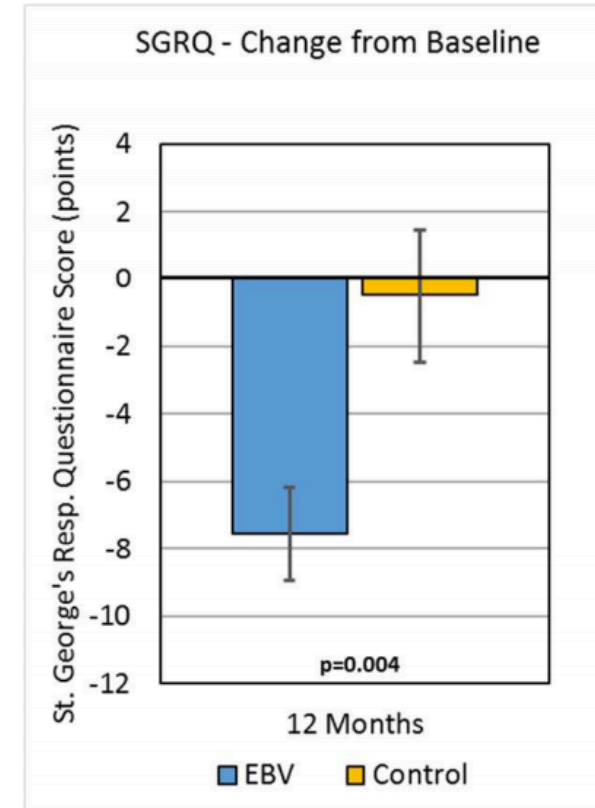
3a



3b



3c



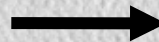
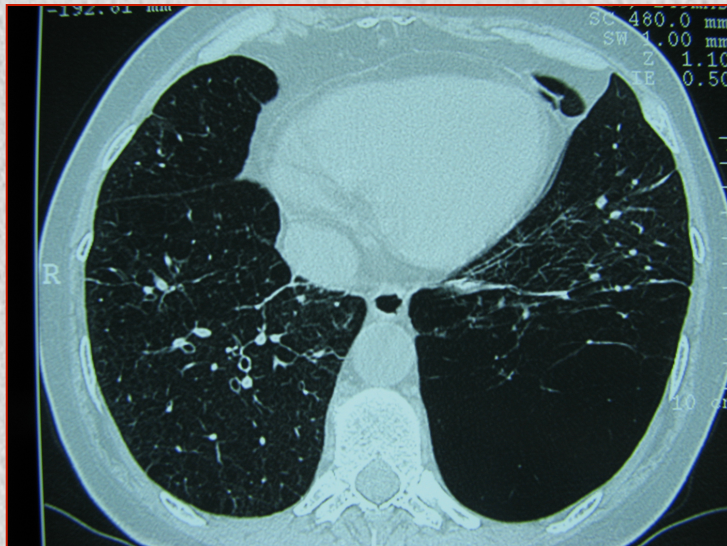
## CONCLUSIONS

**Zephyr EBV provides clinically meaningful benefits in lung function, exercise tolerance, dyspnea and quality of life out to at least 12-months, with an acceptable safety profile in patients with little or no collateral ventilation in the target lobe.**

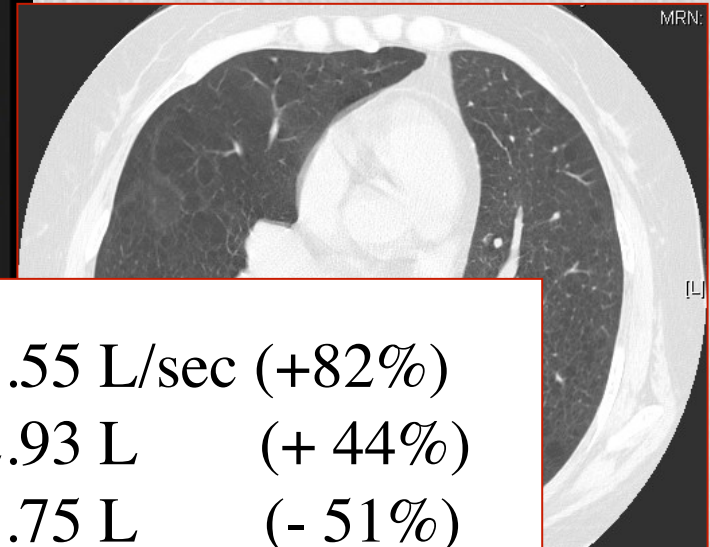
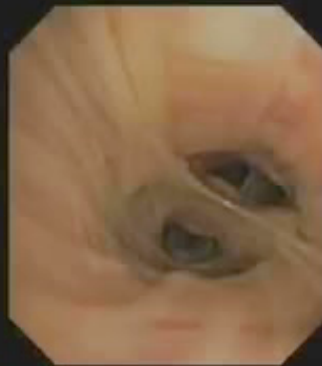
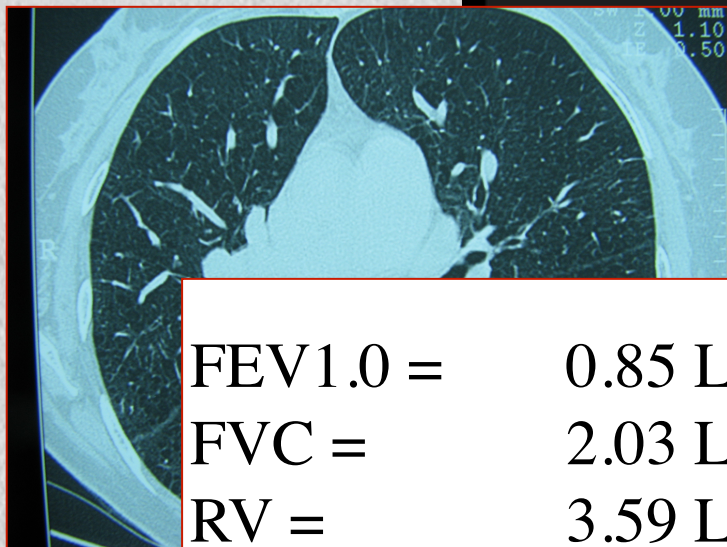
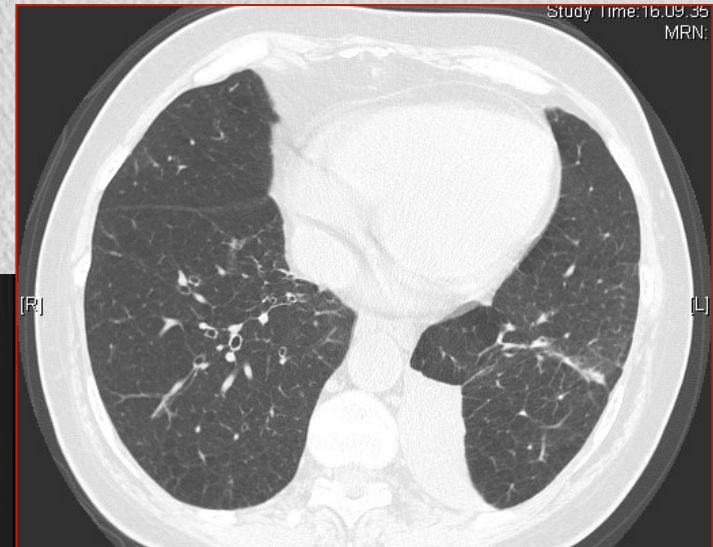


Woman, 62 yrs

PRE BLVR



POST BLVR (30 days)



FEV1.0 =	0.85 L/sec	→	1.55 L/sec (+82%)
FVC =	2.03 L		2.93 L (+ 44%)
RV =	3.59 L		1.75 L (- 51%)
6 minWT =	250 m		490 m (+ 96%)

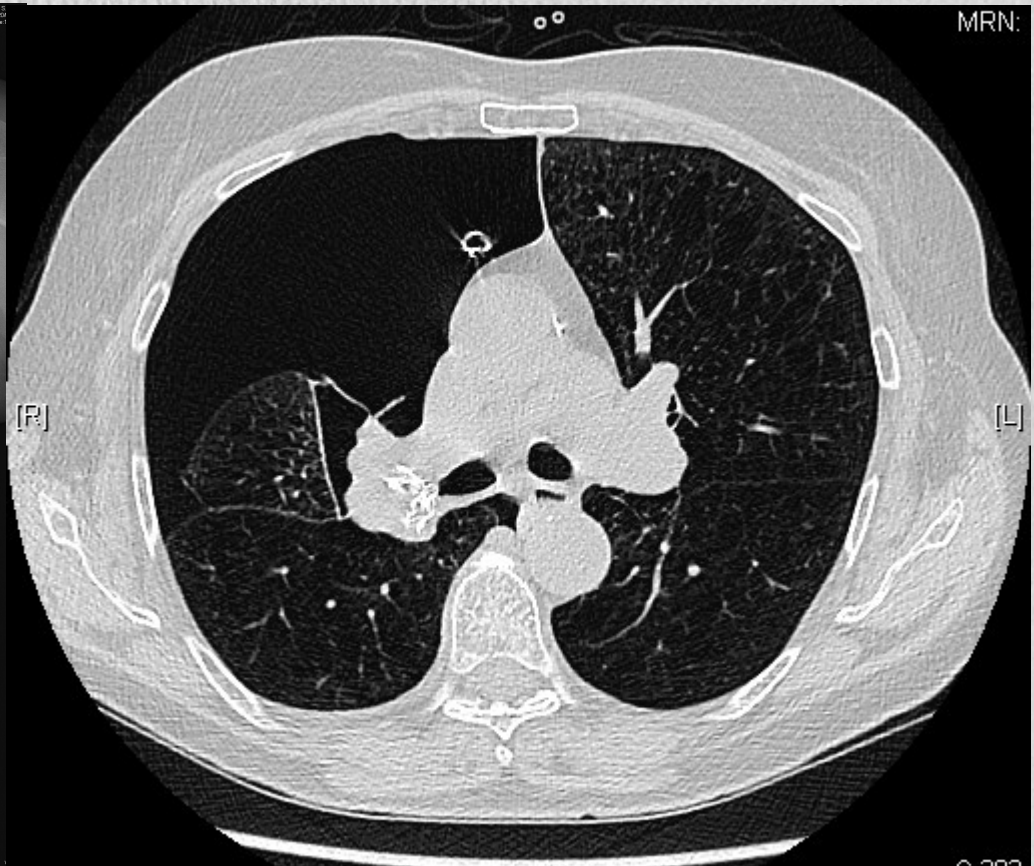


# COMPLICATIONS

**Pneumothorax: 29%**

**COPD Exacerbation: 19%**

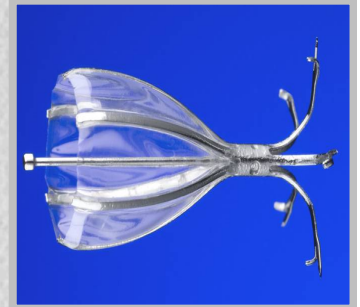
**Pneumonia: 4.7%**







# VALVES: EVIDENCE



- **Widely evaluated devices**
- **No comparative studies on models of valve (but majority of studies with Zephyr valves)**
- **Easily removable**
- **Can be used also for lower lobe predominant emphysema**
- **Best results are correlated with:**
  - **no collateral ventilation (fissure integrity/Chartis)**
  - **low target lobe regional perfusion**
  - **development of anatomic atelectasis (true volume reduction)**
- **Pts with homog. emphysema may have benefit? Some evidence**
- **Collateral ventilation is a major problem that limits the use of this device**

# BRONCHOSCOPIC TREATMENT OF EMPHYSEMA

## 1. Bronchial blockers devices

### Valves

- IBV
- Zephyr

## 2. Devices that works on lung parenchima

### Sealants

Coils

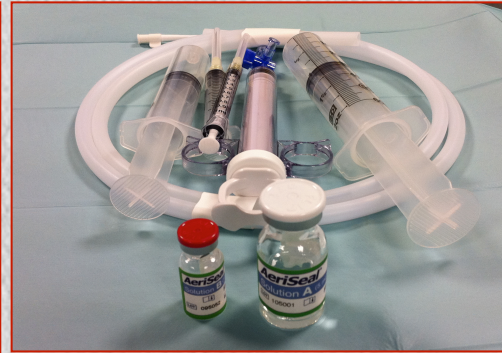
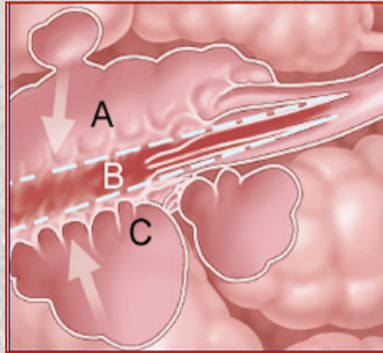
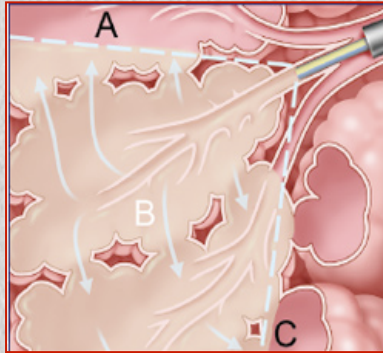
Steam





# Polymeric Lung Volume Reduction

## AERISEAL SYSTEM

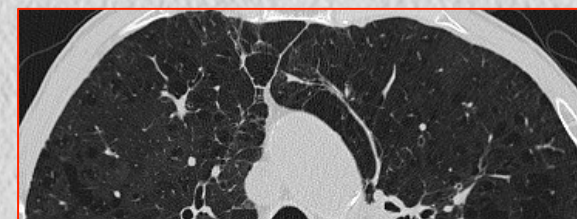
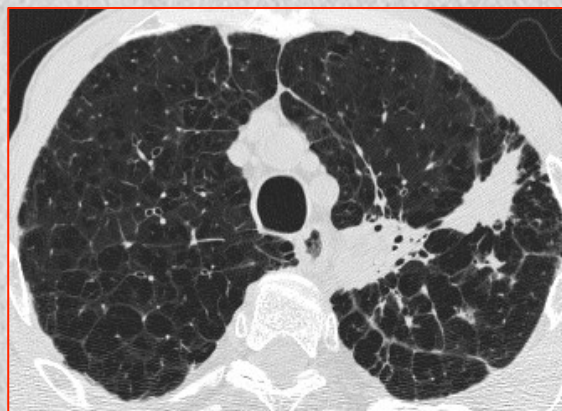




Basal

1 month

12 months



<b>FEV1.0:</b>	<b>0,74</b>	<b>→ 0,79 (+6%)</b>	<b>→ 0,75 (+1%)</b>
<b>VC:</b>	<b>1,91</b>	<b>→ 2,47 (+29%)</b>	<b>→ 2.00 (+4%)</b>
<b>RV:</b>	<b>6,18</b>	<b>→ 5,37 (-13%)</b>	<b>→ 6.00 (-3%)</b>



## Sealant: Polymeric Lung Volume Reduction Evidence

- Published data: only 47 pts (!!)
- Better results in less severe patients (GOLD III)
- Not influence by collateral ventilation
- Easy to perform - Irreversible
- Not indicated if large bullae (>5cm)
- No indication for lower lobe emphysema
- Homogeneous emphysema? (data just on 10 pts)
- Long term efficacy?
- Safety (COPDE: 15-40%; pneumonia:10-12%)
- High scattering of results (high SD, greater than mean)

**All the studies on Sealant have been terminated  
on November 13, 2013!!!!**

# BRONCHOSCOPIC TREATMENT OF EMPHYSEMA

## 1. Bronchial blockers devices

### Valves

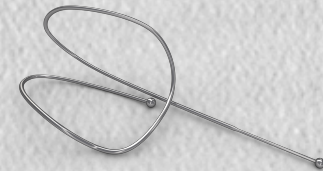
- IBV
- Zephyr

## 2. Devices that works on lung parenchima

### Sealants

### Coils

### Steam

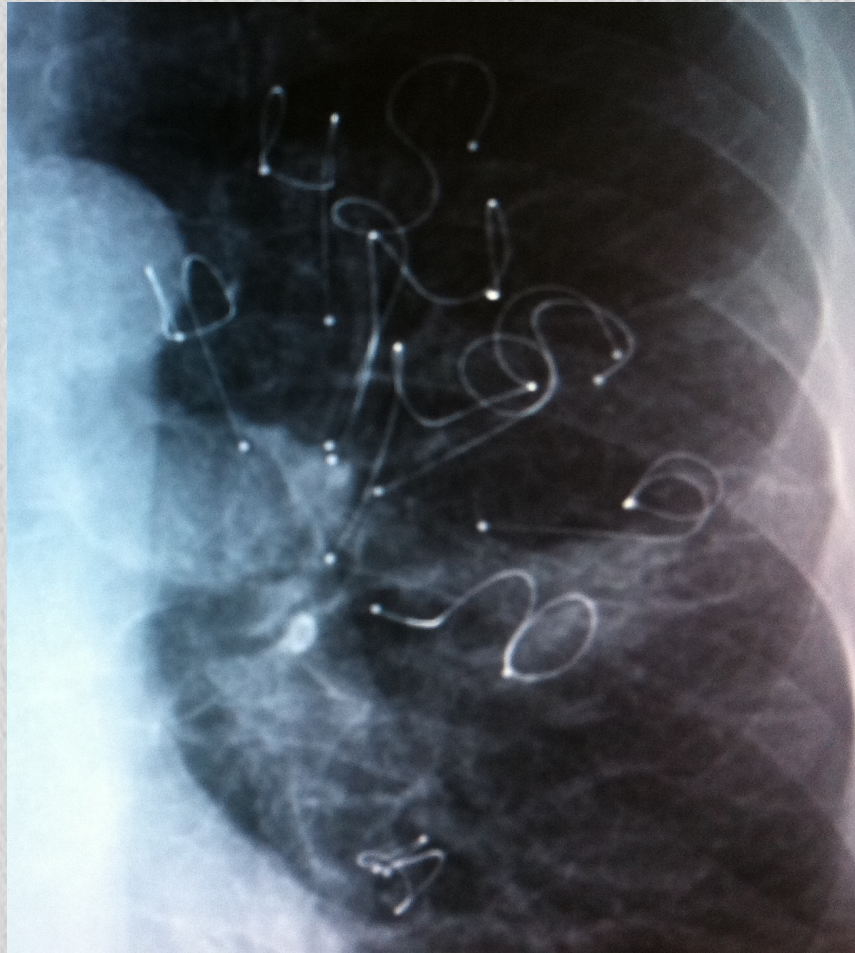




# COILS




## MAN, 67 yrs



FEV1.0 (L/sec):	0.46	→	0.79	(+41%)
RV (L):	7,620	→	5,340	(-29 %)
6mWT (m):	90	→	120	(+25%)



# Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial

Dr [Pallav L Shah](#) MD [a](#) [b](#) , [Zaid Zoumot](#) MBBS [a](#) [b](#), [Suveer Singh](#) PhD [b](#), [Stephen R Bicknell](#) MD [c](#), [Ewen T Ross](#) MD [c](#), [John Quiring](#) PhD [d](#), [Nicholas S Hopkinson](#) PhD [a](#), [Samuel V Kemp](#) MBBS [a](#) [b](#), for the RESET trial Study Group

The Lancet Respiratory Medicine, 2013; 3: 233-240

## Randomised study

**47 patients (heterogeneous and homogeneous) (RV>220%) :**

- BLVR with coils (23 pts; 21 bilateral)
- Best medical treatment (24 pts)

## Between-group difference in change from baseline:

**SGRQ: = -8.36**

**6 minWT: = 63 m (p<0.001)**

**FEV1.0 = 10.6%**

**RV(L) = -0.31**

## No between-group difference in serious adverse events

**Exacerbation 2 (5%)**

**Lower respiratory tract infections: 2 (5%)**

**Pneumothorax: 2 (5%)**

ORIGINAL ARTICLE

# Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial

Gaëtan Deslee,<sup>1</sup> Karin Klooster,<sup>2</sup> Martin Hetzel,<sup>3</sup> Franz Stanzel,<sup>4</sup> Romain Kessler,<sup>5</sup> Charles-Hugo Marquette,<sup>6</sup> Christian Witt,<sup>7</sup> Stefan Blaas,<sup>8</sup> Wolfgang Gesierich,<sup>9</sup> Felix J F Herth,<sup>10</sup> Juergen Hetzel,<sup>11</sup> Eva M van Rikxoort,<sup>12</sup> Dirk-Jan Slebos<sup>2</sup>



*Thorax* 2014; 69: 980

- **Prospective multicenter trial (11 Centers)**
- **60 patients (55 treated bilaterally; 5 treated unilaterally)**  
(upper or lower lobe predominant heterogeneous emphysema)  
(RV>175% of predicted) (10 coils per lobe; range: 5-15)

Variable	6 months	12 months
FEV1.0 (% change)	+15.36	+16.04
RV (% change)	-11.31	-13.75
6minWD (m)	+29.7	+51.4
SGRQ	-12.1	-11.1



# **Lung Volume Reduction Coil Treatment vs Usual Care in Patients With Severe Emphysema**

## **The REVOLENS Randomized Clinical Trial**

Gaëtan Deslée et al. JAMA 2016; 315: 175-184

**Multicenter 1:1 randomized superiority trial comparing coils with usual care at 10 university hospitals in France**

**10 coils per lobe were placed in 2 bilateral lobes in 2 procedures**

**100 patients, (mean age, 62 years) were included**

**Results (mean between group differences):**

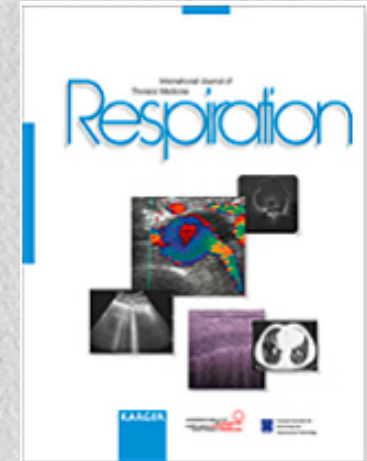
<b>6 months -</b>	<b>6mWD:</b>	<b>+ 21 m</b>
	<b>FEV1.0:</b>	<b>+ 90 ml</b>
	<b>sGRQ:</b>	<b>- 13.4</b>
<b>12 months -</b>	<b>6mWD:</b>	<b>+ 21 m</b>
	<b>FEV1.0:</b>	<b>+ 80 ml</b>
	<b>sGRQ:</b>	<b>- 10.6</b>

# Lung Volume Reduction Coil Treatment in Chronic Obstructive Pulmonary Disease Patients with Homogeneous Emphysema: A Prospective Feasibility Trial

Klooster K. · ten Hacken N.H.T. · Franz I. · Kerstjens H.A.M. · van Rikxoort E.M. · Slebos D.-J.

Respiration (DOI:10.1159/000362522)

*Respiration* 2014; 88: 116



## Prospective feasibility study

**10 patients (homogeneous emphysema)**

**Bilateral treatment (median: 11 coils in each lung)**

## Results at 6 months:

**SGRQ:** 63 → 48 (p=0.028)

**6 minWD (m):** 289 → 350 (p=0.005)

**FVC (L):** 2.17 → 2.55 (p=0.047)

**RV(L):** 5.04 → 4.44 (p=0.007)

## Serious adverse events:

**COPD exacerbation:** 2

**Small pneumothorax:** 1



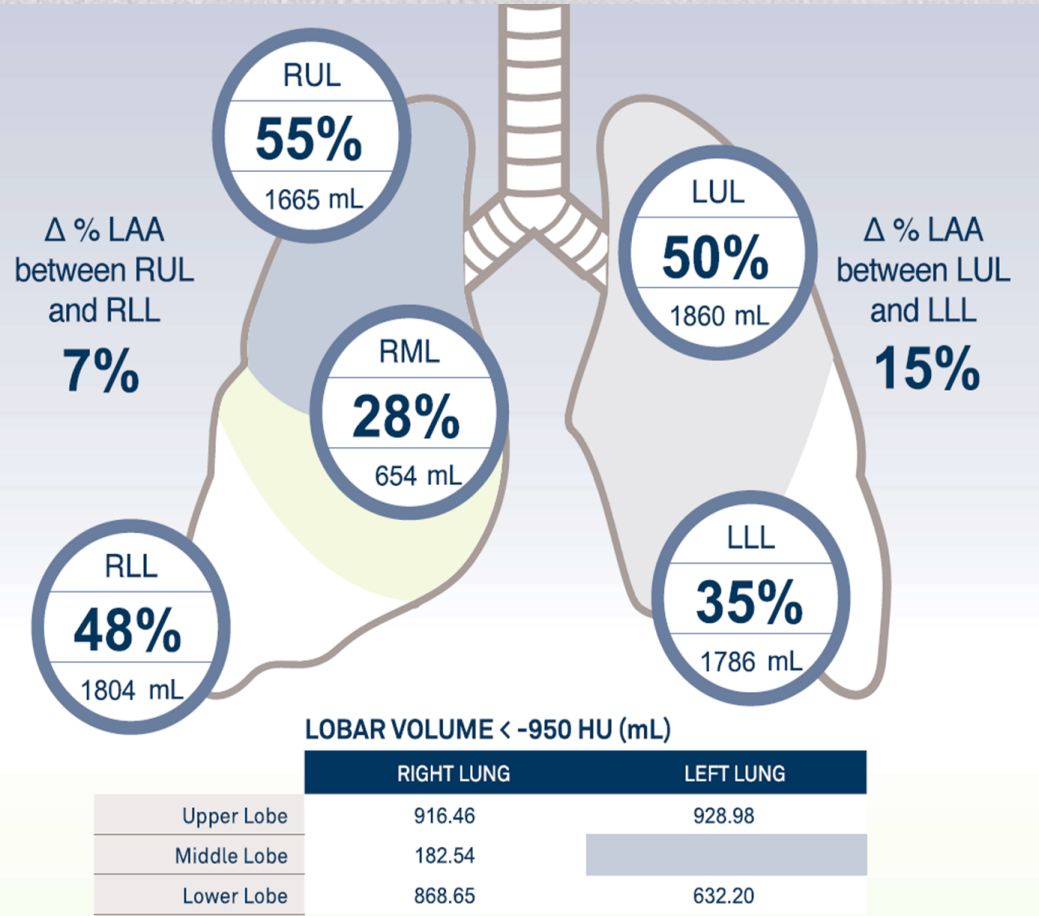
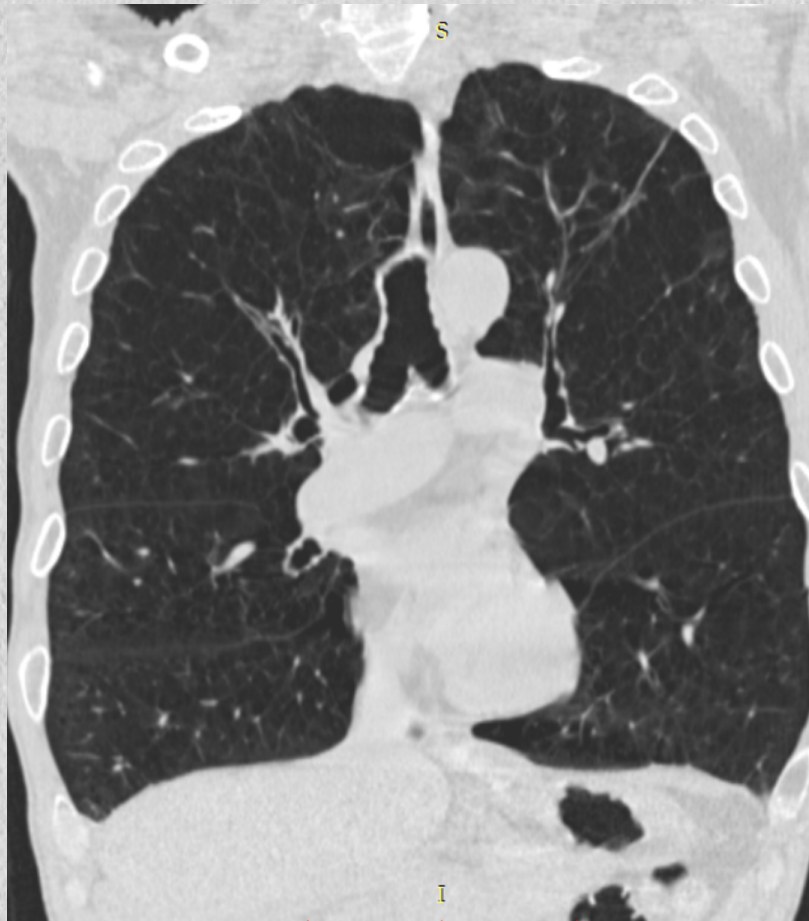
## Coils: Evidence

- Acts at alveolar rather than the airway level
- Not influenced by collateral ventilation
- Effective also in lower lobe emphysema
- Homogeneous emphysema (?)
- Irreversible?
- **Not indicated if lung is too destroyed**  
(Coils need tissue)



# Quantitative analysis

## Low Attenuation Area%



**Limit for treatment: Low Attenuation Area > 70 %**



# BRONCHOSCOPIC TREATMENT OF EMPHYSEMA

## 1. Bronchial blockers devices

### Valves

- IBV
- Zephyr

## 2. Devices that works on lung parenchima

### Sealants

### Coils

### Steam



# Steam

Regional collapse with steam





# Segmental volume reduction using thermal vapour ablation in patients with severe emphysema: 6-month results of the multicentre, parallel-group, open-label, randomised controlled STEP-UP trial

**Lancet Respir Med 2016**

*Felix J F Herth, Arschang Valipour, Pallav L Shah, Ralf Eberhardt, Christian Grah, Jim Egan, Joachim H Ficker, Manfred Wagner, Christian Witt, Uta Liebers, Peter Hopkins, Wolfgang Gesierich, Martin Phillips, Franz Stanzel, William H McNulty, Christoph Petermann, Greg Snell, Daniela Gompelmann*

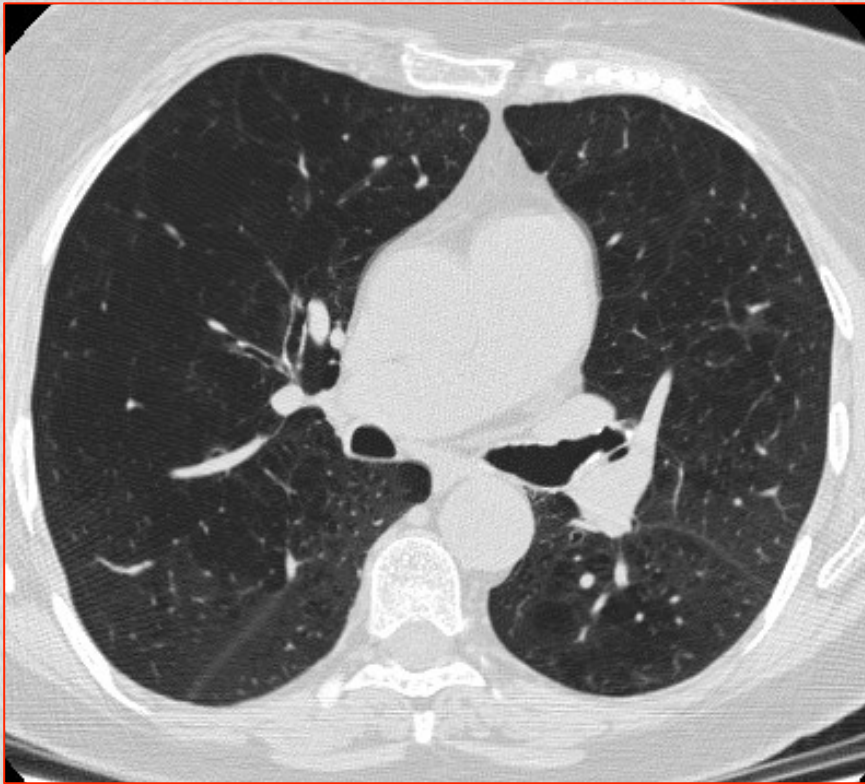
	Bronchoscopic vapour ablation group		Control group		Difference between groups (95% CI)	p value
	Patients, n	Mean (SD)	Patients, n	Mean (SD)		
FEV <sub>1</sub> , %						
3 months*	43	8.2% (17.5%)	22	-1.8% (10.1%)	10.1% (3.2 to 16.9)	0.0047
6 months	41	11.0% (16.2%)	23	-3.7% (11.1%)	14.7% (7.8 to 21.5)	<0.0001
SGRQ-C, points						
3 months*	44	-7.2 (12.2%)	22	-0.6 (11.0)	-6.6 (-12.4 to -0.9)	0.0243
6 months	42	-9.7 (14.4)	23	-0.0 (9.8)	-9.7 (-15.7 to -3.7)	0.0021

FEV<sub>1</sub>=forced expiratory volume in 1 s. SGRQ=St George's Respiratory Questionnaire.\*3-month data were collected before the second treatment session was administered.

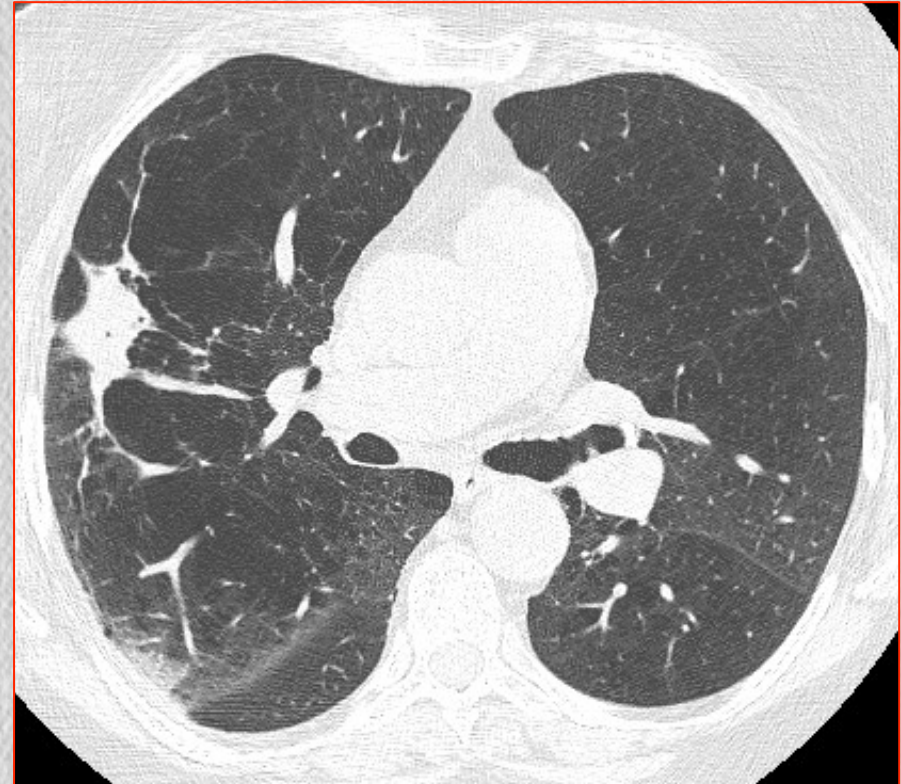
**Table 3: Results for primary efficacy endpoints**



**Basal**



**One month after treatment**



**FEV1.0 = 0.87 L/sec**

**6 minWT = 240 m**

**1.02 L/sec (+17%)**

**280 m (+16.6%)**



# HOW TO PERSONALIZE APPROACH FOR ELVR

Emphysema optimal medical RX  
FEV1<50% and RV>175% , RV/TLC>0.58, 6MWT 150-400m

CT Features

## GRADE OF HYPERINFLATION (RV%pred)

Study	VENT USA	VENT EUR	IMPACT valves	STELVIO valves	BeLieVeR valves	REVOLENS coils	RENEW coils	RESET coils	TRANSF ORM valves
<b>Inclusion criteria</b>	>150	>150	>200	>150	>150	>220	>225	NA	≥180
<b>Study pop. mean RV</b>	216	240	277	216	219	271	246	236	249

# HOW TO PERSONALIZE APPROACH FOR ELVR

Emphysema optimal medical RX  
FEV1<50% and RV>175% , RV/TLC>0.58, 6MWT 150-400m

CT Features

Heterogenous

Homogeneous

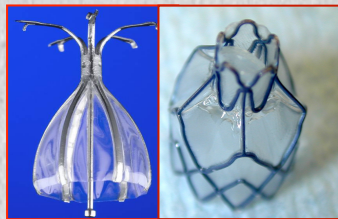
No Collateral Ventilation

Collateral Ventilation

No Collateral Ventilation

Collateral Ventilation

VALVES

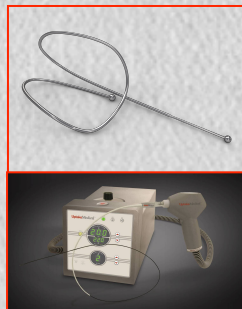


No results

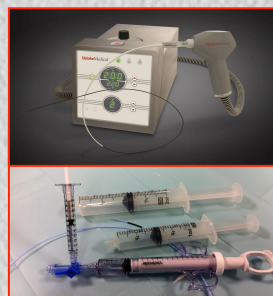
Tissue represented

No tissue

COILS  
STEAM



STEAM  
Glue?



=?

But in clinical trials  
or registers

*Herth FJF et al. Respiration, 2016 (modified)*



**And for non-hyperinflated patients?**

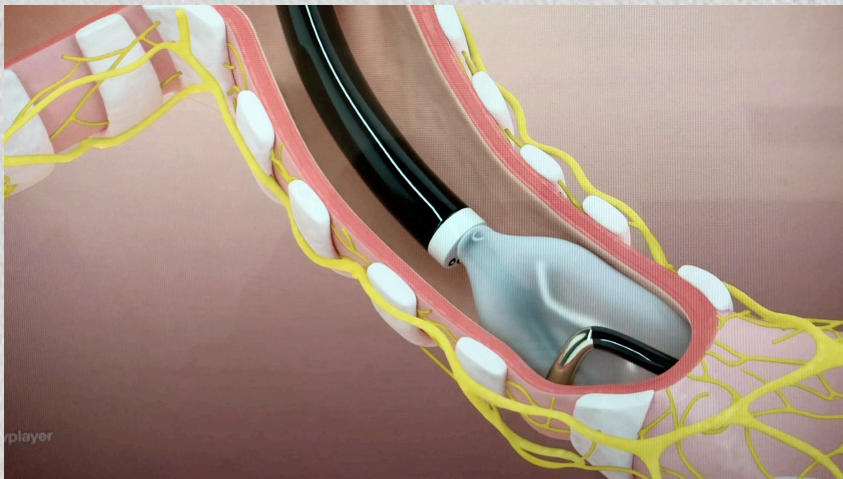




# TARGETED LUNG DENERVATION

**A radio-frequency-energy releasing system designed to disrupt parasympathetic pulmonary nerves surrounding the main bronchi.**

**Purposes: decreasing the release of acetylcholine in the airways, resulting in a permanent anti-cholinergic effect**



- **Relaxation of airways**
- **Decrease in mucus production**
- **Decrease in airway wall inflammation**



# Targeted lung denervation for moderate to severe COPD: a pilot study

*Slebos DJ et al. Thorax 2015; 70: 411*

**22 patients (FEV1.0: 30%-60% pred)**

**Improvement in FEV1.0 > 15% after ipratropium**

**Results at 1 year**

**15 W energy:**

**FEV1.0 = + 0.02%**

**Cycle endurance: + 2.6 min**

**SGRQ: - 0.9 points**

**20 W energy:**

**FEV1.0 = + 11.6%**

**Cycle endurance: + 6.8 min**

**SGRQ: - 11.1 points**

**The first randomized sham controlled trial assessing this technology is currently underway (ClinicalTrials.gov identifier: NCT02058459)**

## **Liquid nitrogen metered cryospray**

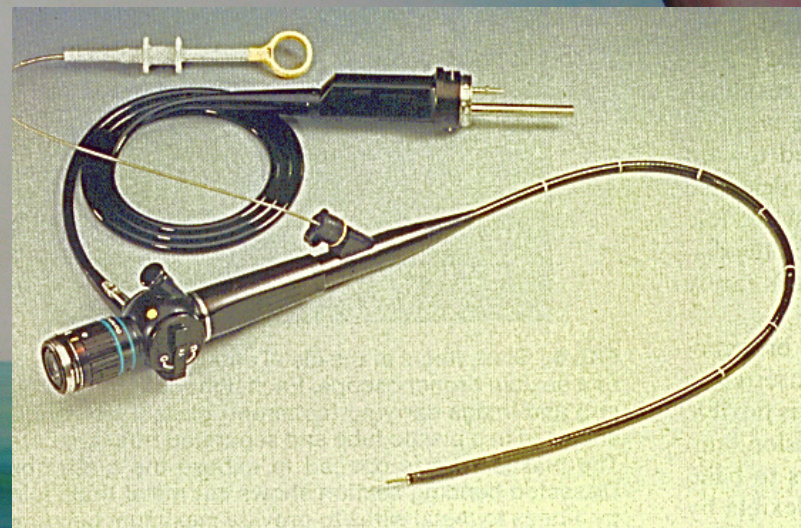
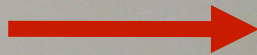
**Liquid Nitrogen Metered Cryospray( Rejuvenair System) is a method designed to bronchoscopically deliver liquid nitrogen to the central airways in such a way that is leads to a cryoablation depth of 0.1 to 0.5 mm for the treatment of chronic bronchitis.**

**This treatment is intended to induce a regenerative airway tissue healing effect, by initially destroying the hyperplastic goblet cells and excess submucous glands by cryo necrosis. After treatment rapid rejuvenation of normal epithelium occurs.**

**The first in human trials testing this system and its hypothesis are currently underway (NCT02106143, NCT02483052, and NCT02483637)**



## THE DREAMS OF BRONCHOSCOPIST





**GRAZIE !**

