

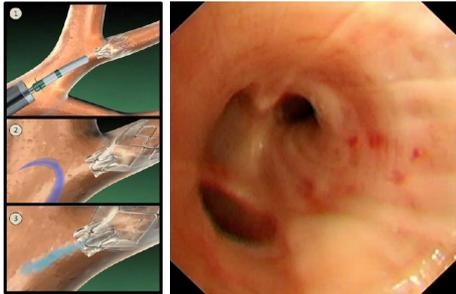
Bronchoscopic Lung Volume Reduction

Techniques Available

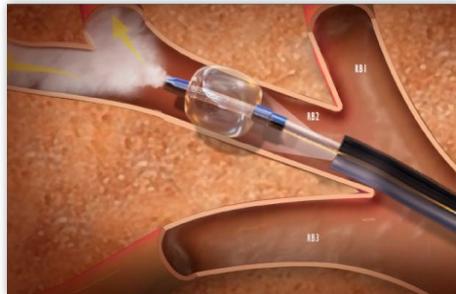
1. Surgery



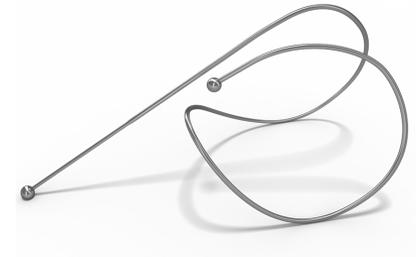
2. Valves



3. BTVA



4. Coils

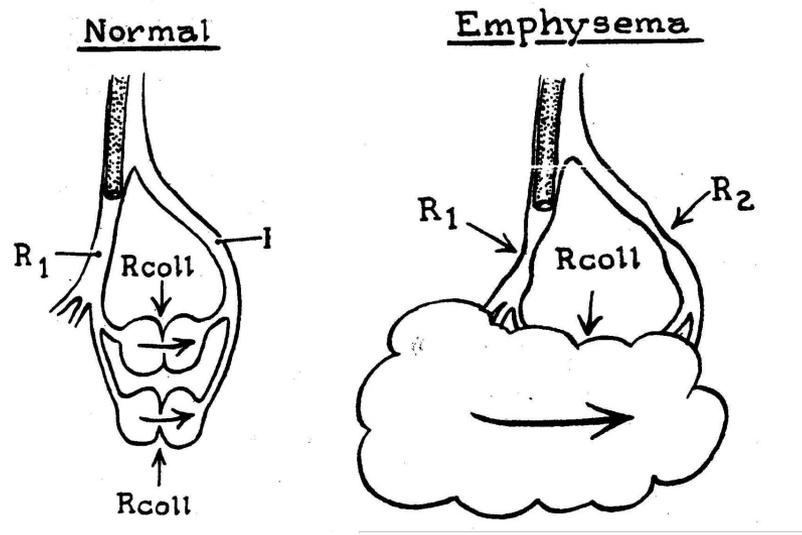


Basic Criteria

Variable	EBV (n=65)	SoC (n=32)
FEV ₁ %	29.8 ± 9.2	32.2 ± 8.4
RV %	249.4 ± 51.8	241.0 ± 41.4
6MWD (m)	282 ± 94	320 ± 92
SGRQ	64.3 ± 14.4	58.1 ± 13.3
BODE index	6.1 ± 1.68	5.6 ± 1.77

- + Emphysema on CT
- + Pulmonary rehabilitation
- + Optimum medical therapy

EBVs and Collateral Ventilation



No Collateral Ventilation (CV-)

Collateral Ventilation (CV+)

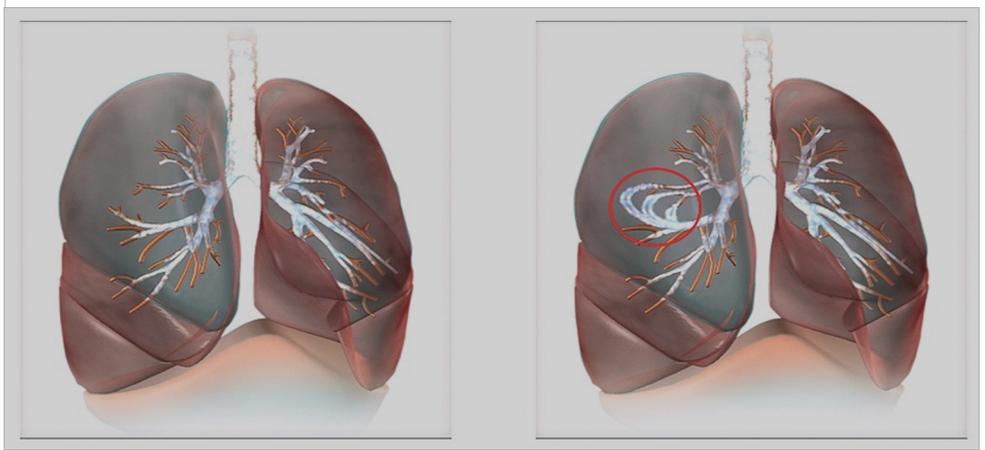


Table 2. Primary and Secondary Efficacy Outcomes in the Intention-to-Treat Population (Change from Baseline at 6 Months).*

Outcome	Endobronchial-Valve Therapy (N = 220)	Control (N = 101) <i>number (95% confidence interval)</i>	Between-Group Difference in Change from Baseline	P Value
Primary outcome				
FEV ₁				
Mean absolute percent change from baseline	4.3 (1.4 to 7.2)	-2.5 (-5.4 to 0.4)	6.8 (2.1 to 11.5)	
Mean change in value from baseline — ml	34.5 (10.8 to 58.3)	-25.4 (-48.3 to -2.6)	60.0 (21.5 to 98.4)	0.002
Distance on 6-min walk test†				
Median absolute percent change from baseline	2.5 (-1.1 to 6.1)	-3.2 (-8.9 to 2.4)	5.8 (0.5 to 11.2)	0.04
Median change from baseline — m	9.3 (-0.5 to 19.1)	-10.7 (-29.6 to 8.1)	19.1 (1.3 to 36.8)	0.02
Secondary outcome				
Mean change in score on SGRQ from baseline‡	-2.8 (-4.7 to -1.0)	0.6 (-1.8 to 3.0)	-3.4 (-6.7 to 0.2)	0.04
Mean change in score on Modified Medical Research Council dyspnea scale from baseline§	-0.1 (-0.21 to 0.09)	0.2 (0.01 to 0.37)	-0.3 (-0.50 to -0.01)	0.01

23.4%

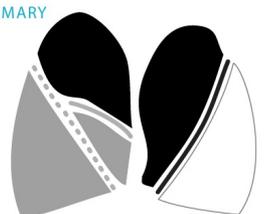
-6.6

Semi-Automated Fissure Analysis

StratX™ Lung Report

Patient ID 35-127-AJJ Upload Date 27 July 2016
Scan ID 0026671 Report Date 27 July 2016
CT Scan Date 16 February 2011 Scan Comments

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

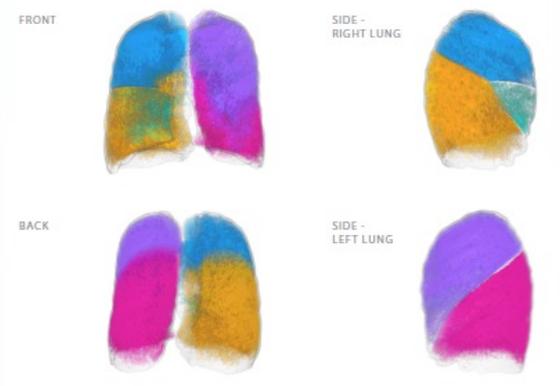
RESULTS

	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	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

Voxel Density Less Than -910 HU

Patient ID 31-102-G-5 Upload Date 27 July 2016
Scan ID 0003440 Report Date 27 July 2016
CT Scan Date 9 June 2010 Scan Comments

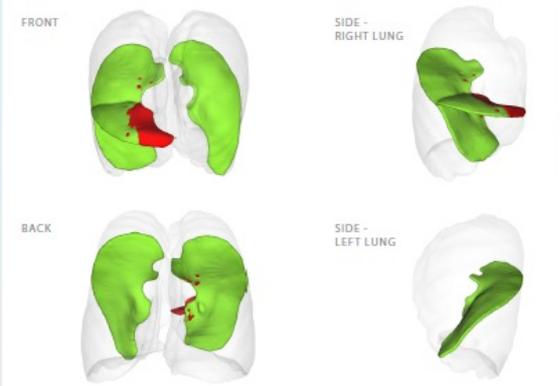
	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Voxel Density Less Than -910 HU	66	58	27	65	70	75



Fissure Completeness

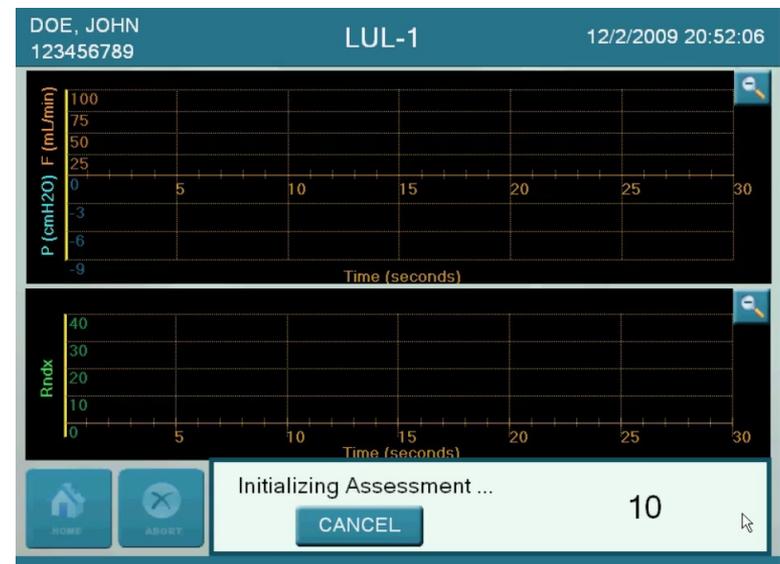
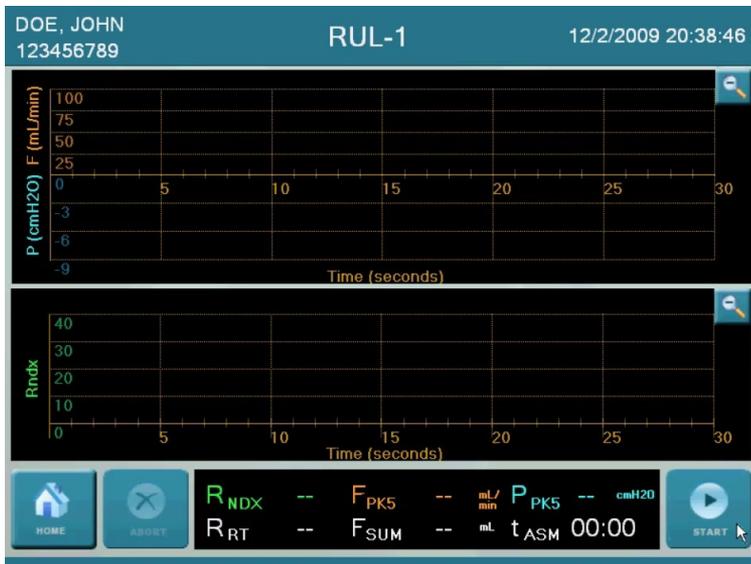
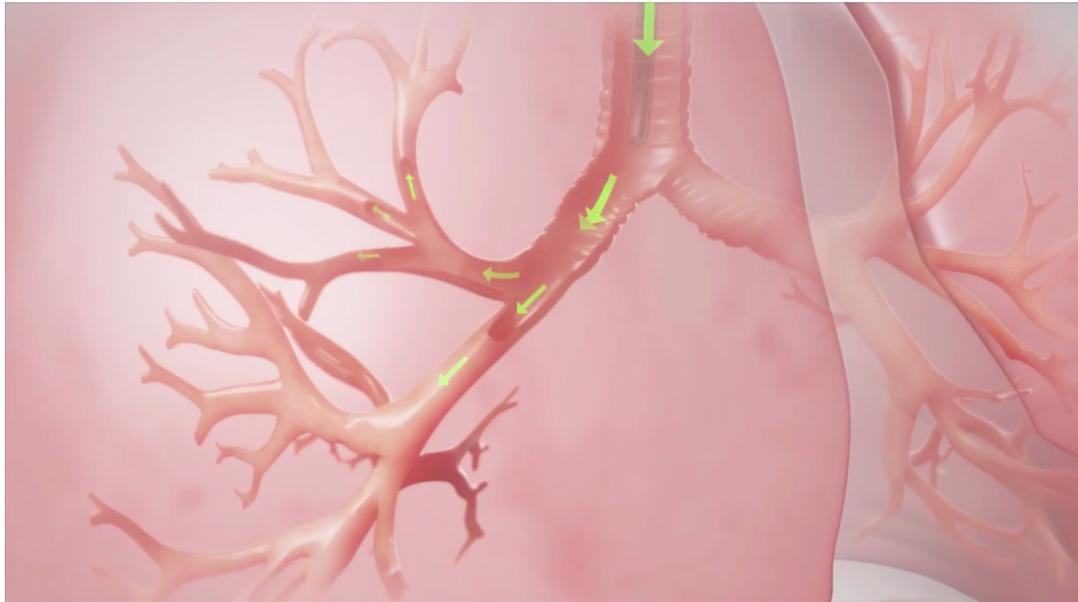
Patient ID 31-102-G-5 Upload Date 27 July 2016
Scan ID 0003440 Report Date 27 July 2016
CT Scan Date 9 June 2010 Scan Comments

	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	80.6	99.8	79.3	99.8	100	100



Disclaimer: Report contains quantitative assessment only and should not be construed as a complete radiological analysis.

Chartis Pulmonary Assessment System



QCT Assessment

SUMMARY



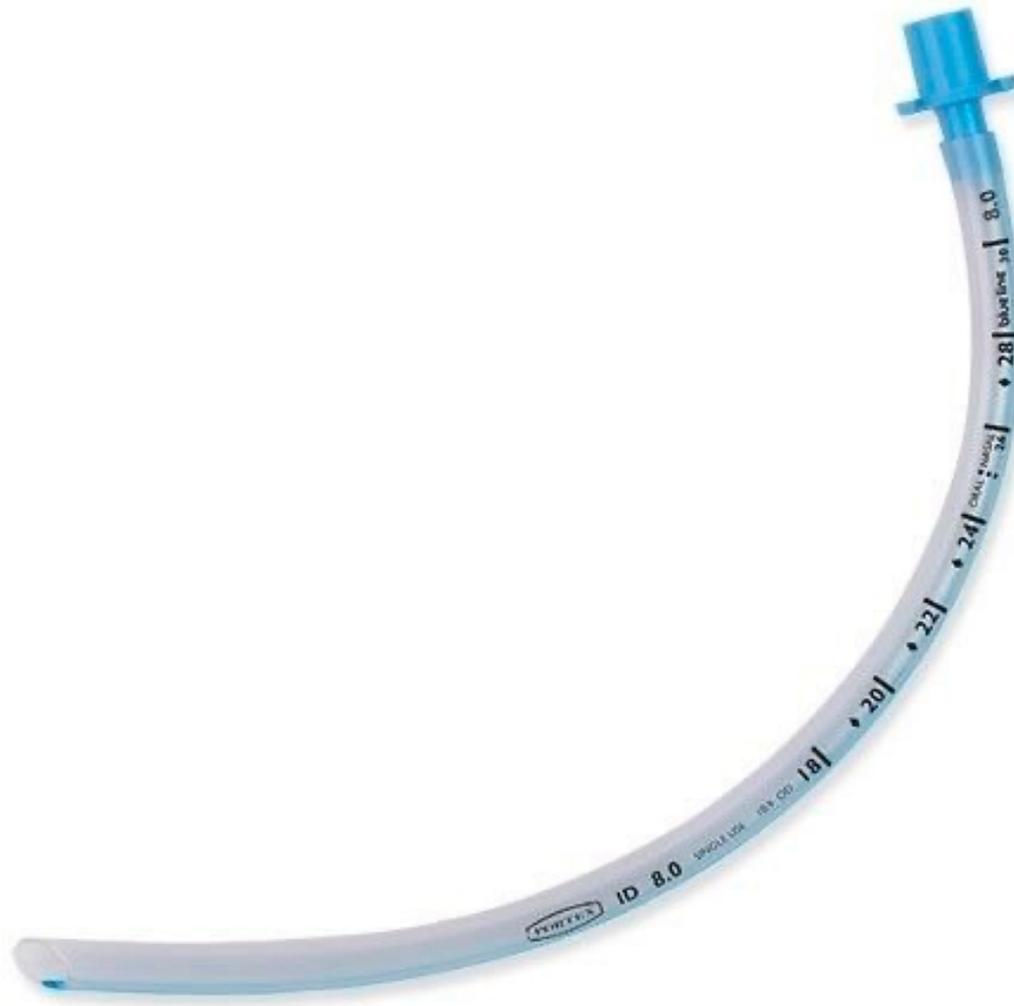
KEY

- >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	80.2	86.9	86.1	86.9	97.4	97.4
% Voxel Density Less Than -910 HU	76	68	46	49	62	33
% Voxel Density Less Than -950 HU	46	37	14	19	29	9
Inspiratory Volume (ml)	2208	3025	817	1404	2233	1624

ET Tube



Valves and Catheters



4.0-LP EBV



5.2 mm

4.0-7.0 mm

4.0 EBV



6.9 mm

4.0-7.0 mm

5.5-LP EBV



5.8 mm

5.5-8.5 mm

5.5 EBV

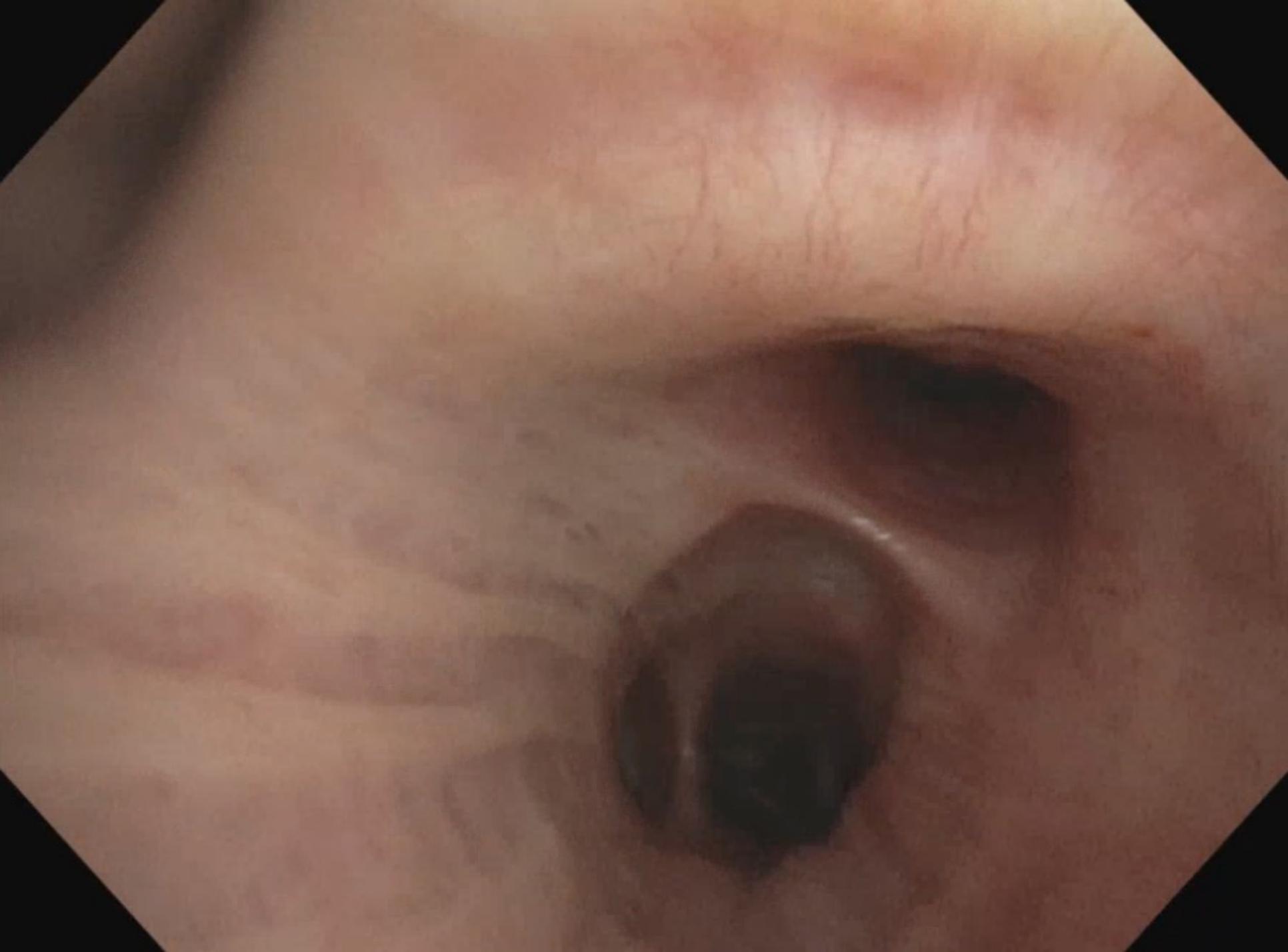


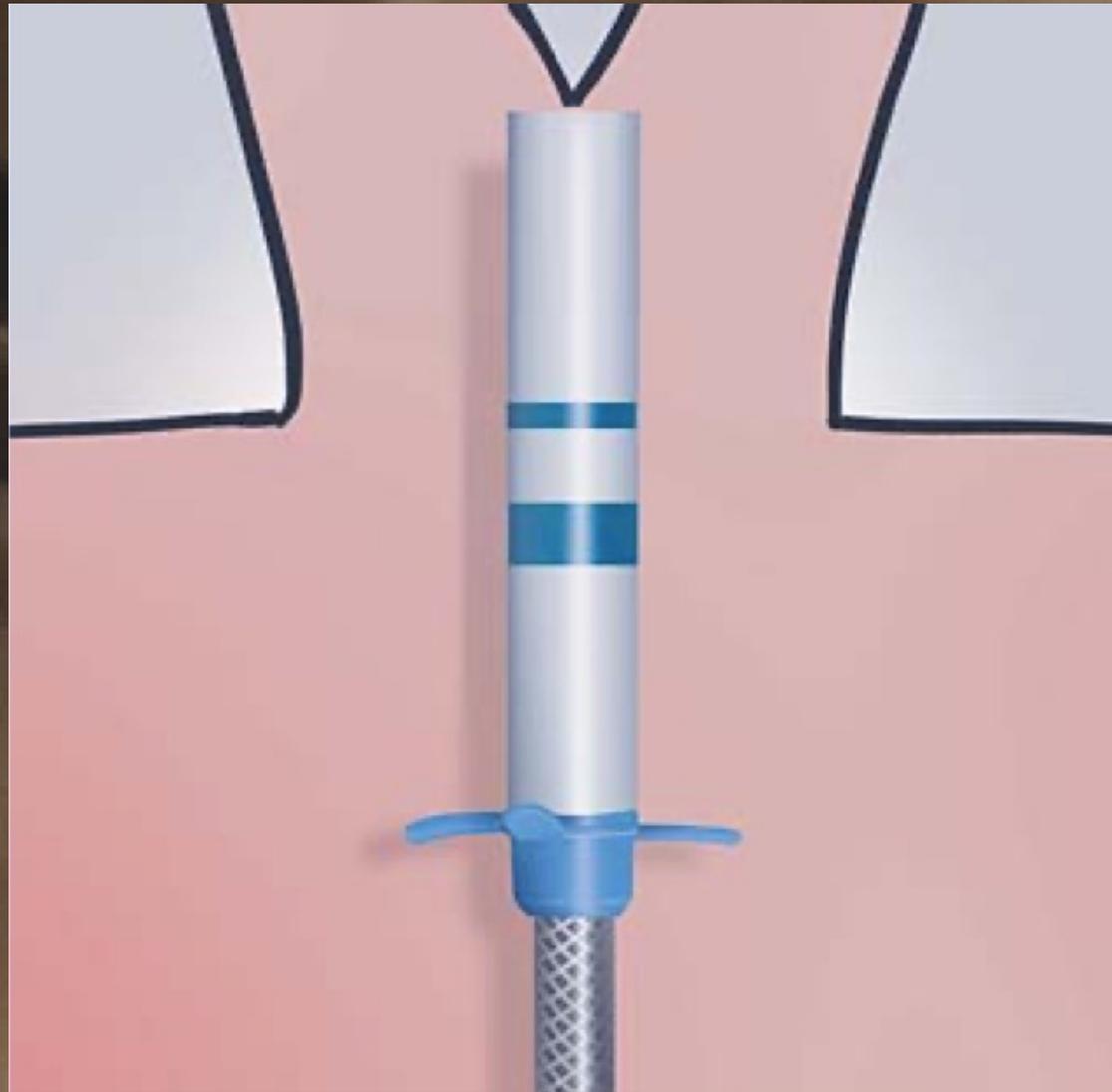
8.0 mm

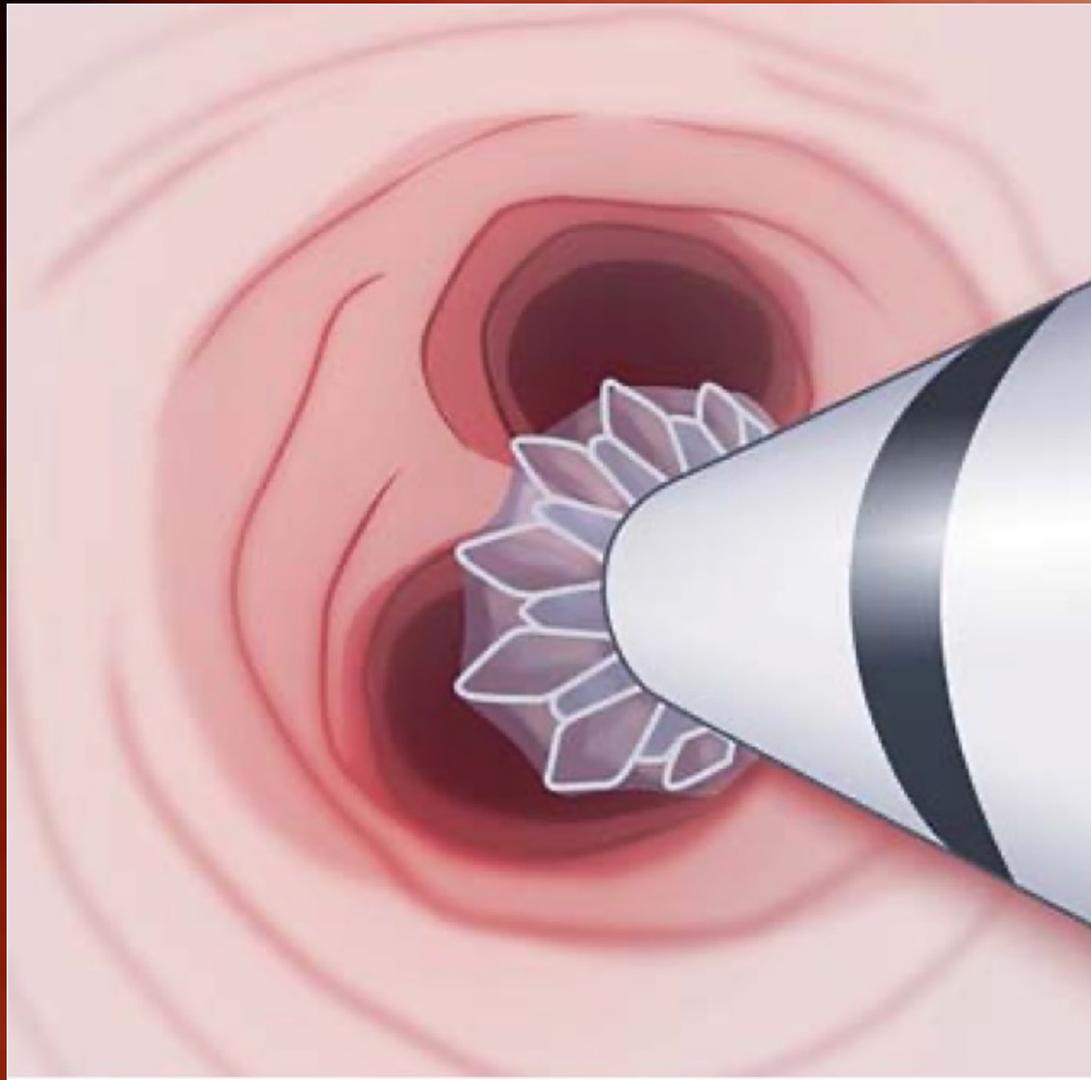
5.5-8.5 mm

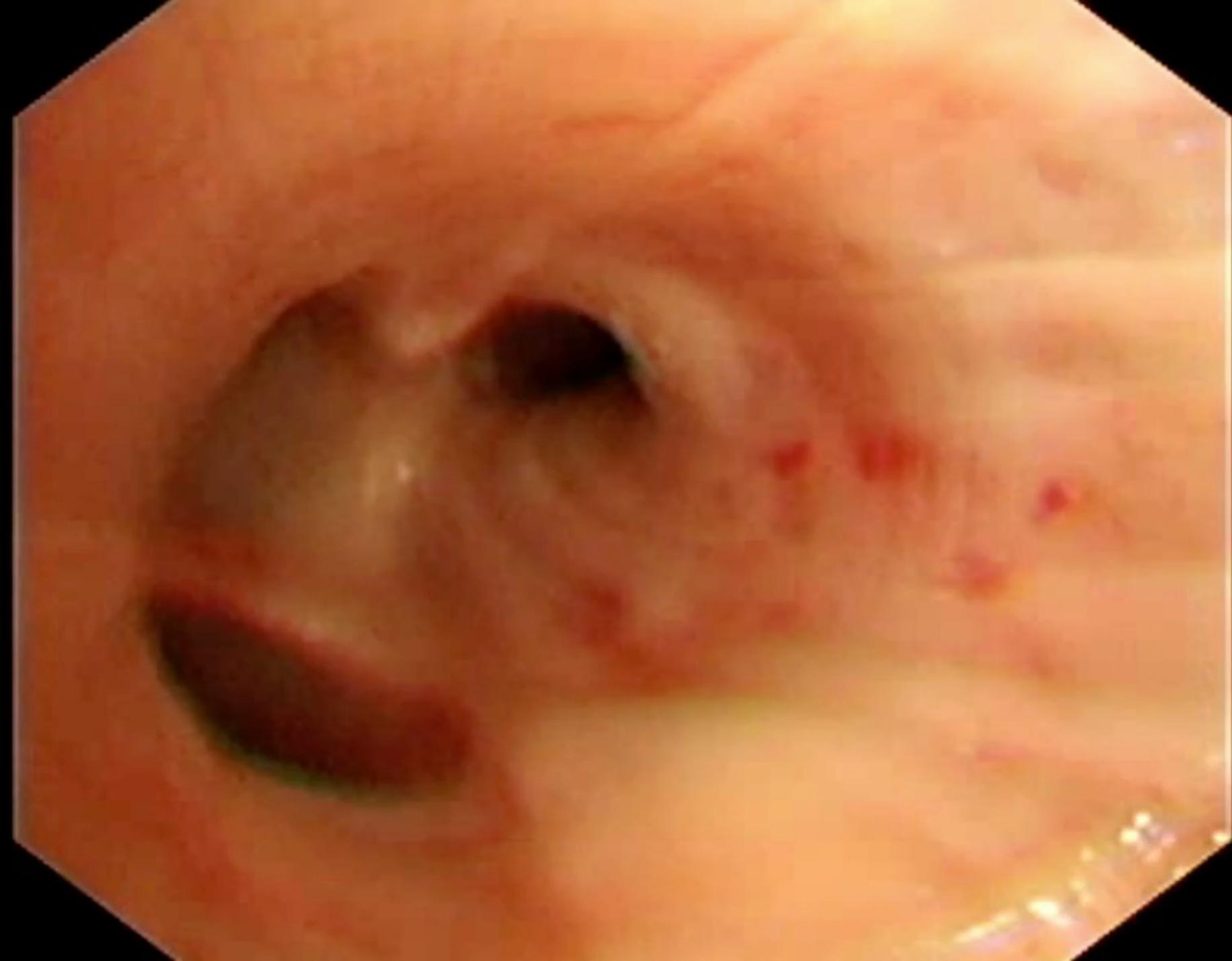
Sealing length

Airway diameter range









Important EBV Studies

- 2 single centre RCTs in heterogeneous disease
 - BeLieVeR HIFi (Lancet)
 - STELVIO (NEJM)
- 2 multicentre RCT in heterogeneous disease
 - TRANSFORM >10% heterogeneity¹
 - LIBERATE >15% heterogeneity²
- 1 multicentre RCT in homogeneous disease
 - IMPACT <10% heterogeneity³

EBV Multicentre RCT Outcomes

RCT	Sample size & Follow-up	Difference EBV vs Control Groups			
		FEV ₁ %	Residual Volume	6MWD	SGRQ
LVRS – NETT Trial ¹	n=290 6 months	27.6%	-	42 m	-13.4 pts
IMPACT ²	n=93 6 months	16.3%	-0.48L	28 m	- 7.5 pts
TRANSFORM ³	n=97 6 months	29.3%	-0.67L	79 m	- 6.5 pts
LIBERATE ⁴	n=190 12 months	17.9%	-0.52L	39 m	-7.1 pts

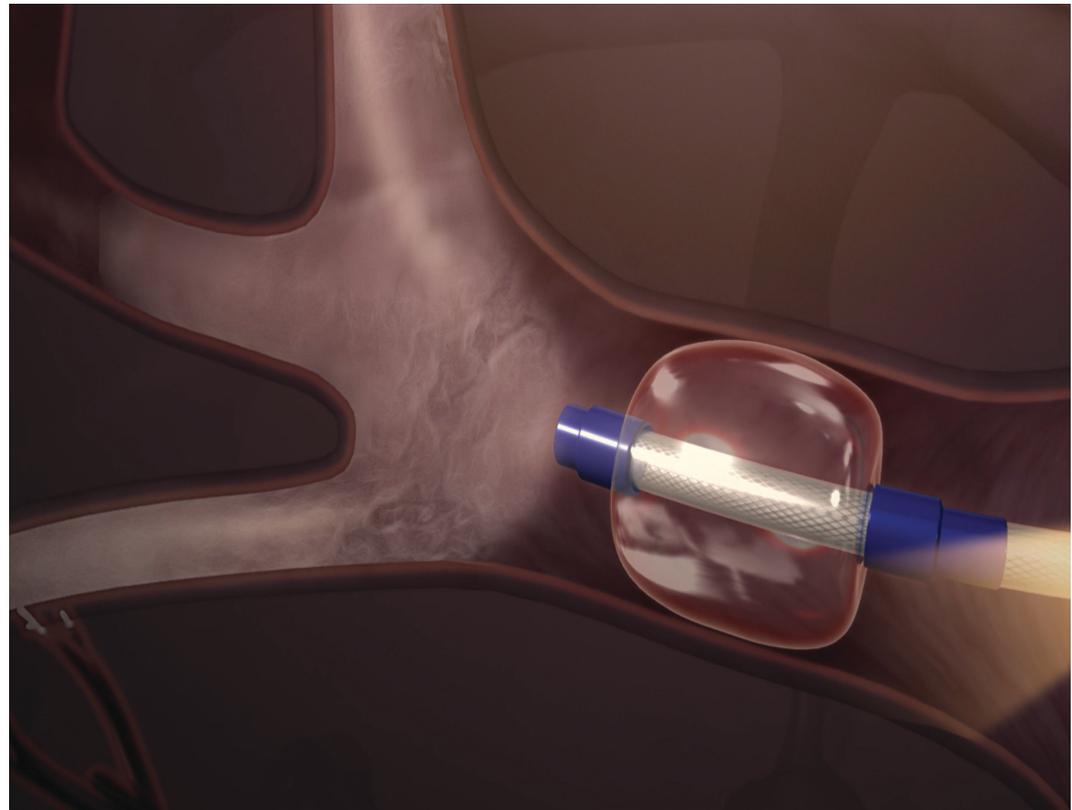
Adverse Events

Respiratory Adverse Events during follow-up						
Adverse Event	TRANSFORM EBV (n=65) (% subjects)	TRANSFORM SoC (n=32) (% subjects)	LIBERATE EBV (n=128) (% subjects)	LIBERATE SoC (n=62) (% subjects)	IMPACT EBV (n=43) (% subjects)	IMPACT SoC (n=50) (% subjects)
Pneumothorax	20 (29.2%)	0	46 (34.4%)	0	12 (27.9%)	0
COPD exacerbation	7 (9.2%)	3 (6.3%)	38 (30.8%)	22 (35.4%)	25 (47.2%)	13 (25.5%)
Pneumonia	6 (9.2%)	1 (3.1%)	8 (6.3%)	5 (8.1%)	0	4 (2%)
Haemoptysis	1 (1.5%)	0	4 (3.1%)	0	0	0
Death	1 (1.5%)	0	5 (3.9%)	1 (1.6%)	0	2 (4%)

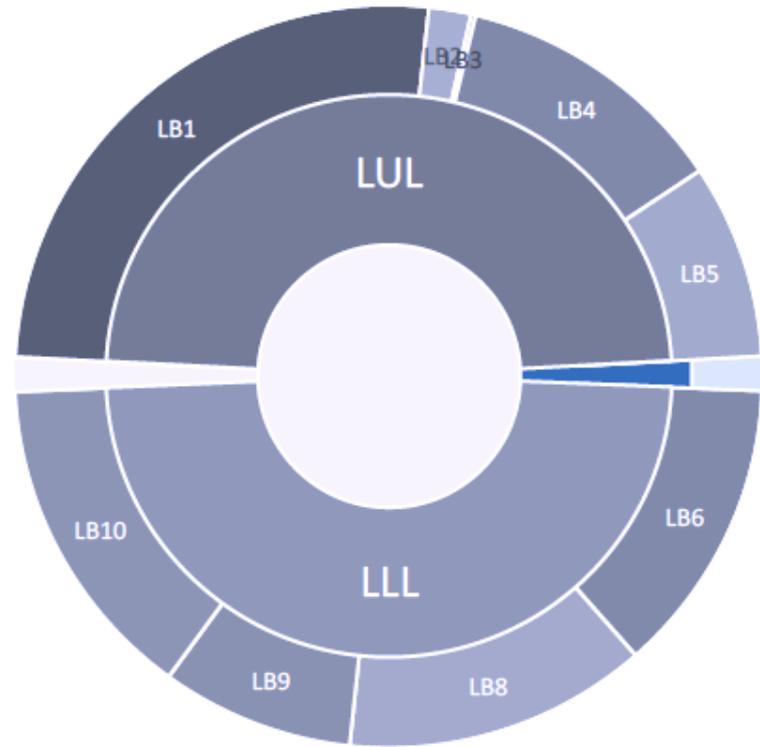
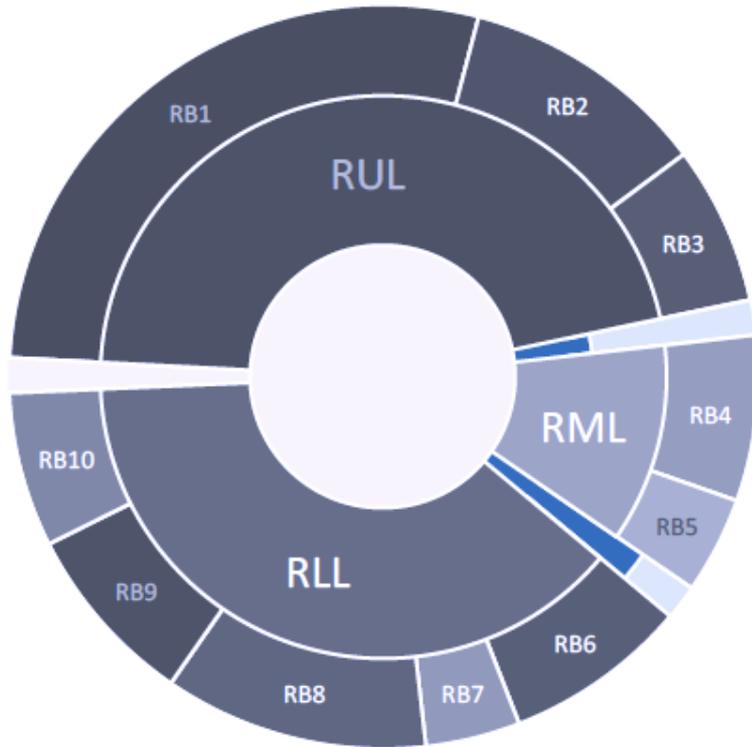
- 75/236 subjects had a pneumothorax (31.8%)
- 0.30 vs 0.26 exacerbations per subject at trial end
- 0.06 vs 0.07 pneumonias per subject at trial end
- 2.5% vs 2.1% deaths at trial end

Thermal Vapor Ablation

- Use of energy from steam to induce thermal injury
- Independent of collateral ventilation
- Quick and simple procedure
- Requires dedicated CT analysis
- Usually 1 night admission only



Lung Segment Treatment Overview

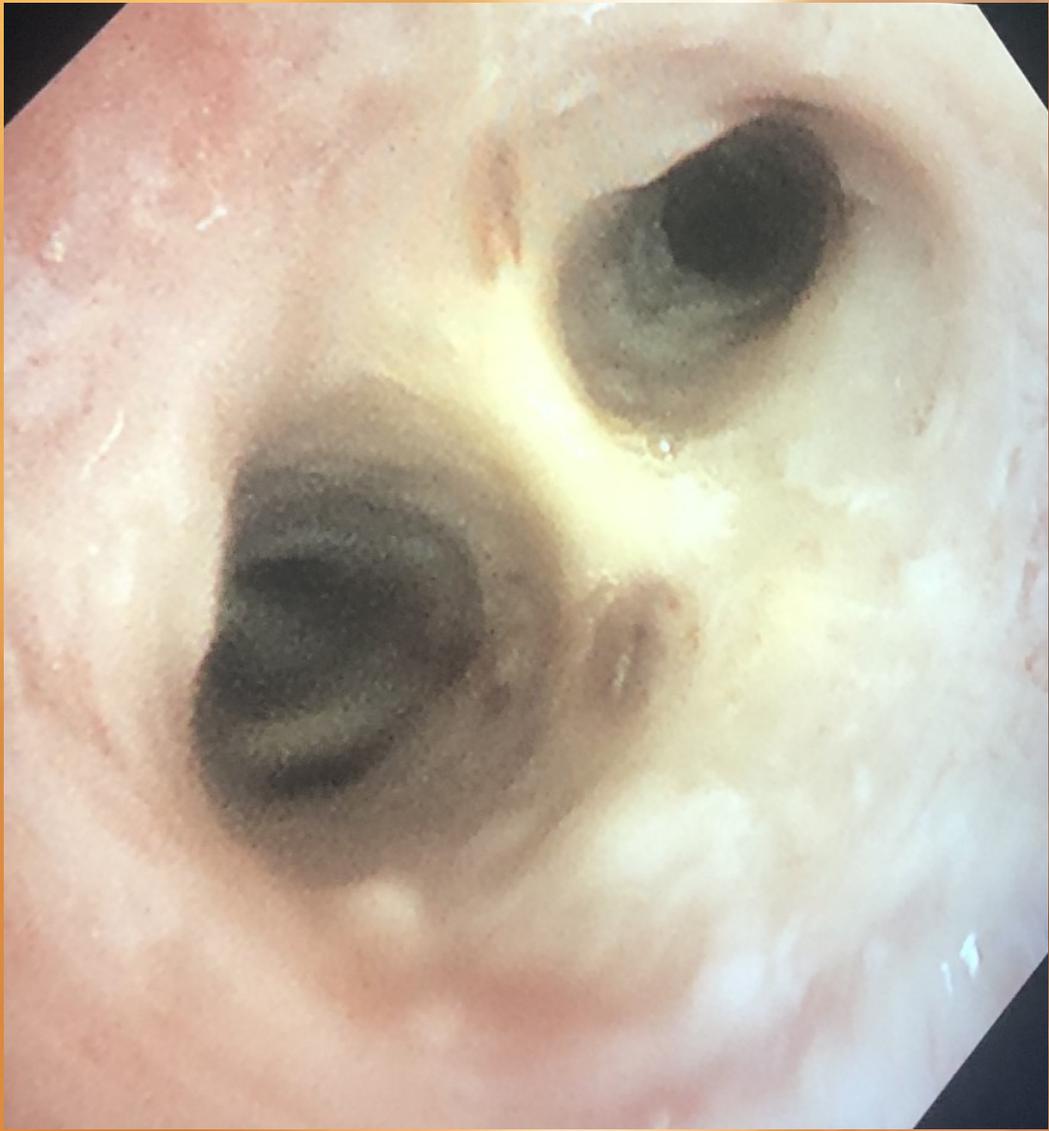


Legend

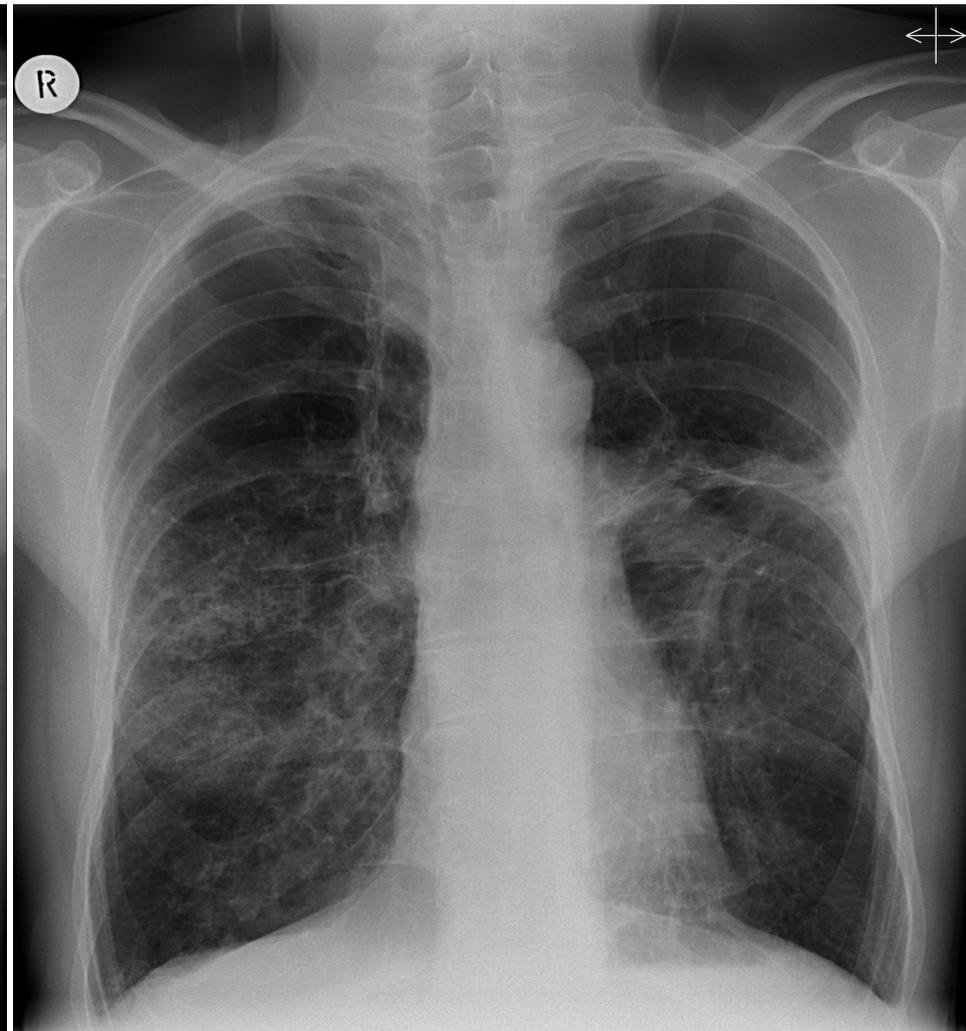
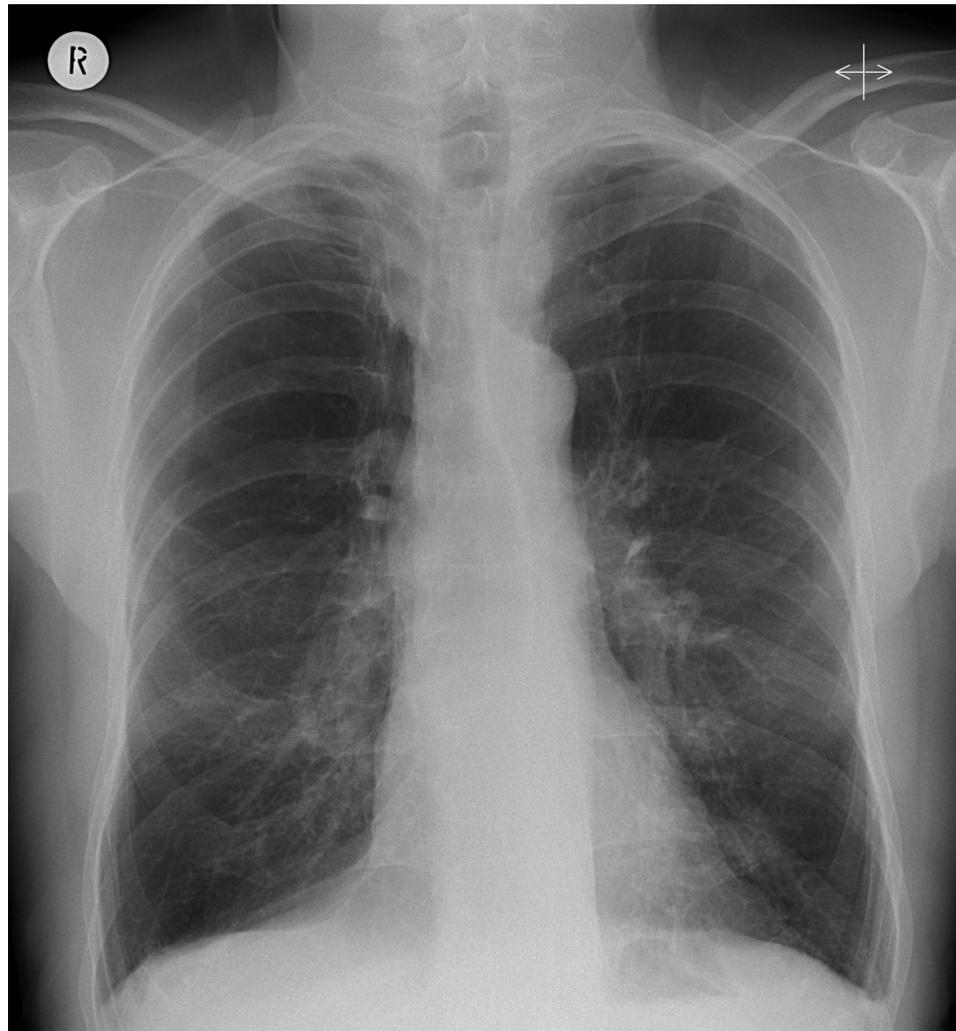
Fissure Integrity: % Complete

Disease Severity: 0 > 70 %

Relative Volume: Represented by relative size of region shape



Treatment Effect



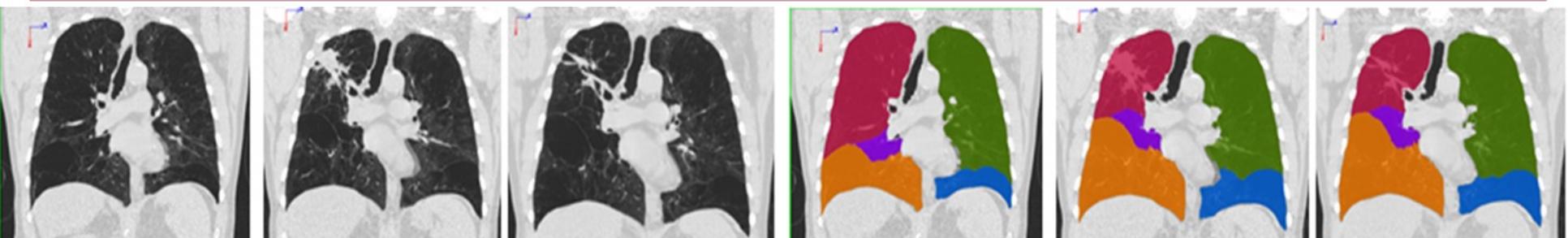
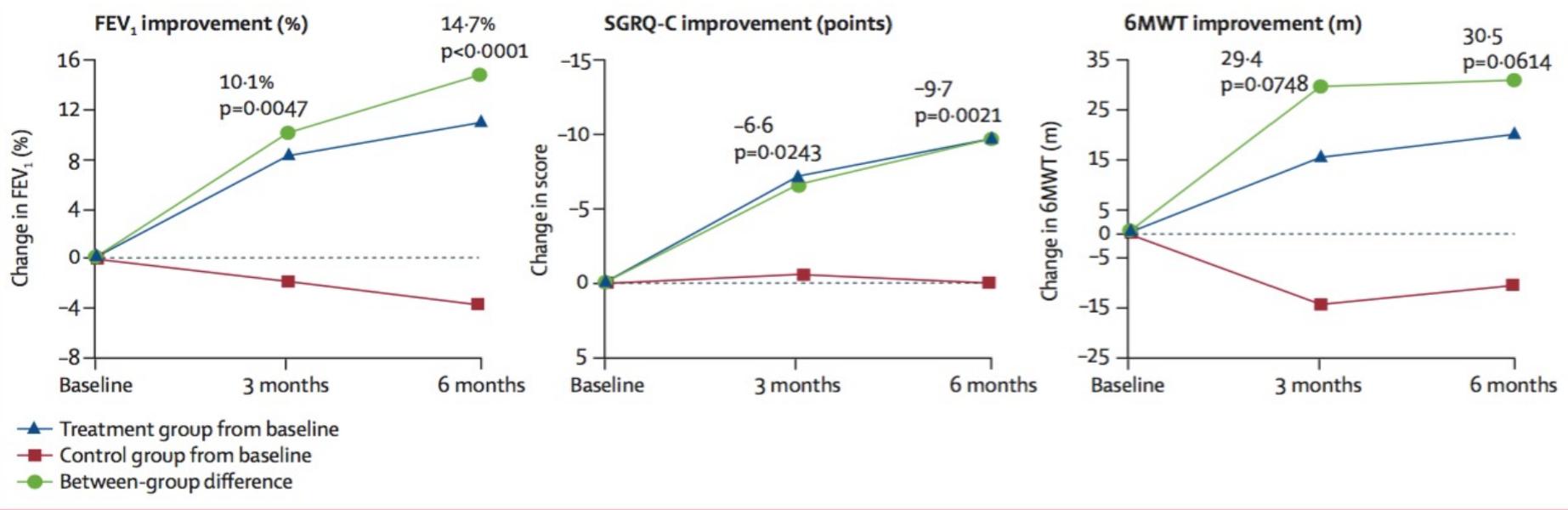
Thermal Vapor Ablation

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, Anshang Vaidya, Pallavi L Shah, Ralf Eberhardt, Christian Grah, Jim Egan, Joachim H Ficker, Manfred Wagner, Christian Witt, Uta Liebers, Peter Hopkins, Wolfgang Geslerich, Martin Phillips, Franz Stanzel, William H McNulty, Christoph Petermann, Greg Snell, Daniela Gompelmann



Thermal Vapor Ablation

- BTVA causes an unpredictable inflammatory response
- Anything from mild to very severe
- Be vigilant for delayed inflammatory reaction

- No real consensus on steroid dosing
- Expert statement - 0.5mg/kg tapering for 2–4 weeks plus ≥ 14 days antibiotics
- Further week of steroids and antibiotics to take home

- Research into lower lobe and ‘whole lung’ treatments

LVR Evidence Summary

RCT	Sample size & Follow-up	Difference EBV vs Control Groups			
		FEV ₁ %	Residual Volume	6MWD	SGRQ
LVRS – NETT Trial ¹	n=290 6 months	27.6%	-	42 m	-13.4 pts
BeLieVeR HIFi ²	n=50 3 months	20.9%	-0.18L	33m	-5.1 pts
STELVIO ³	n=68 6 months	17.8%	-0.83L	74 m	- 14.7 pts
IMPACT ³	n=93 6 months	16.3%	-0.48L	28 m	- 7.5 pts
TRANSFORM ⁵	n=97 6 months	29.3%	-0.67L	79 m	- 6.5 pts
LIBERATE ⁶	n=190 12 months	17.9%	-0.52L	39 m	-7.1 pts
STEP-UP ⁷	n=70 12 months	14.7%	-0.30L	31 m	-9.7 pts

Surgical and endoscopic interventions that reduce lung volume for emphysema: a systemic review and meta-analysis



Wouter H van Geffen, Dirk-Jan Slebos, Felix J Herth, Samuel V Kemp, Walter Weder, Pallav L Shah

AeriSeal[®] System

- Originally developed as a LVR product in isolation
- RCT halted as ran out of money – promising but high AE rate¹
- Problems with toxicity – linked to glutaraldehyde
- Acquired by PulmonX and repurposed for fissure closure²
- Smaller doses, product tweaks



AeriSeal Foam Components Vials



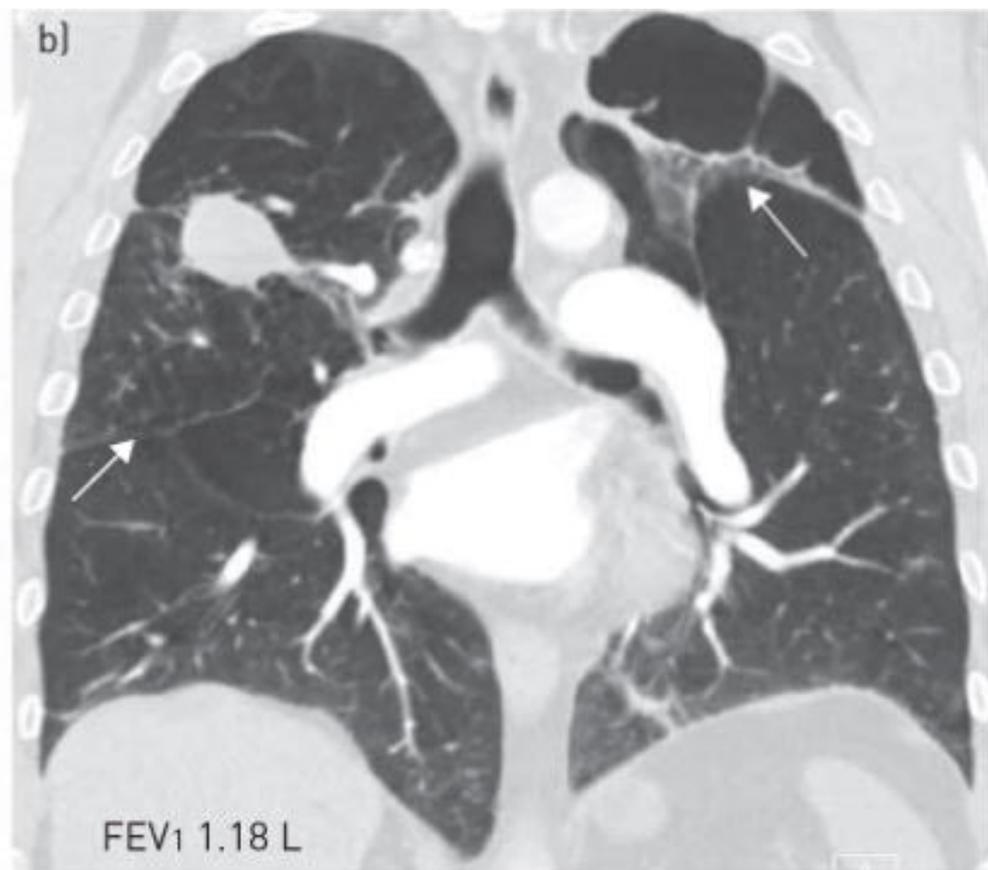
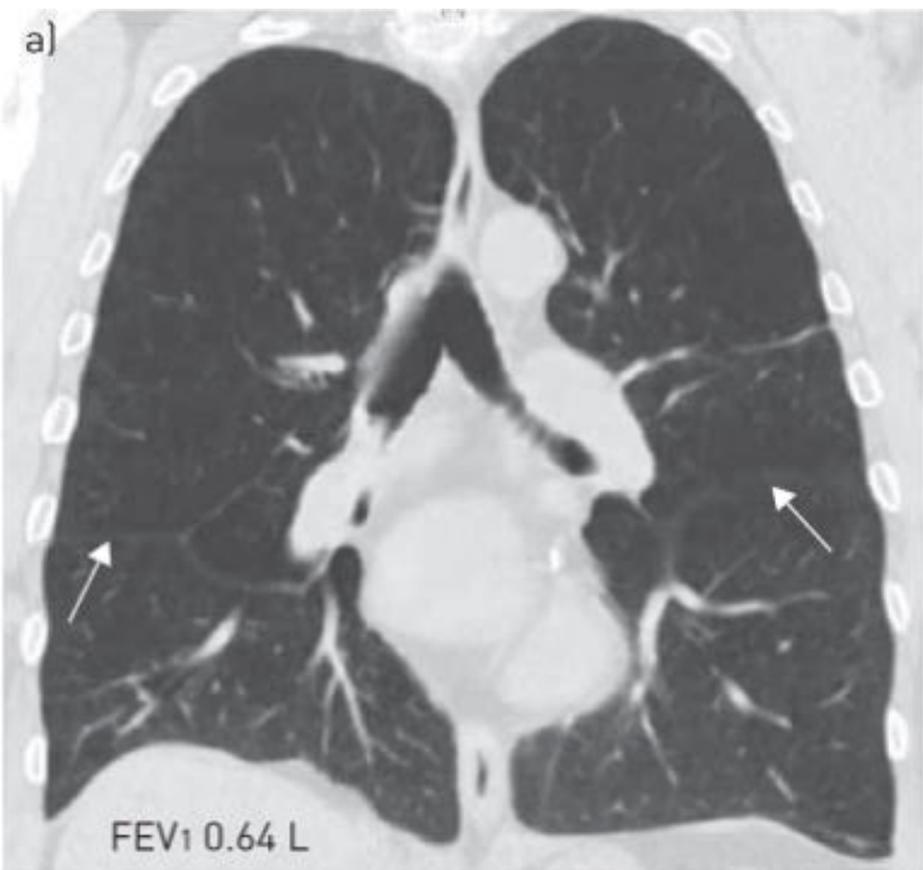
AeriSeal Balloon Catheter



Accessories Kit

1. Come CE, et al. Eur Respir J. 2015 Sep;46(3):651-62.

2. Ing A, et al. J Bronchology Interv Pulmonol. 2020 Jan;27(1):e14-e16.



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CONVERT Trial

Open-label, single-arm, prospective study (140 Subjects)

1. Evaluate the utility of AeriSeal System to occlude collateral channels in a target lobe to convert it from CV+ve to CV-ve.
2. Perform BLVR with Zephyr valves in the lobe successfully converted from CV+ve to CV-ve.

Two-Stage approach

1. AeriSeal Treatment for fissure closure – assess @ 45 days
2. Zephyr valves to cause volume reduction – assess @ 45 days

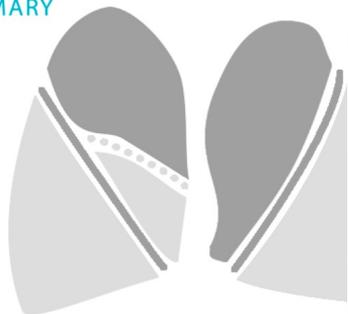
Data out to 12 months post-Zephyr Valve treatment

Fissure Gap Analysis

StratX™ Lung Report

Patient ID CVT-212-001-V1 Upload Date
Scan ID 996706 Report Date
CT Scan Date May 5, 2021 Scan Comments

SUMMARY



RESULTS

	RIGHT LUNG		
	RUL	RUL+RML	RLL
% Fissure Completeness	56.3	88.6	71.2
% Voxel Density Less Than -910 HU	68	64	64
% Voxel Density Less Than -950 HU	35	30	30
Inspiratory Volume (ml)	1741	2419	641

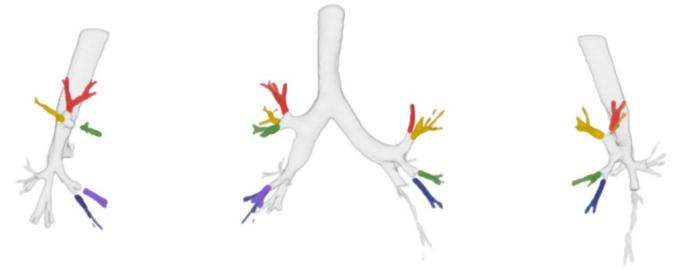
Fissure Targeting Report

Patient ID CVT-212-001-V1 Upload Date May 12, 2021
Scan ID 996706 Report Date June 3, 2021
CT Scan Date May 5, 2021 Scan Comments None

LEFT LUNG – Target Fissure Completeness 86.1%

	LB1+2	LB3	LB4	LB5	LB6	LB7+8	LB9	LB10	LB+	LB++
Volume (ml)	517	628	553	264	-	-	-	-	208	-
% Lobar Fissure Gap within Segment	0.0	0.0	0.9	99.1	-	-	-	-	0.0	-

Side — Right Lung Front Side — Left Lung



RIGHT LUNG – Target Fissure Completeness 88.6%

	RB1	RB2	RB3	RB4	RB5	RB6	RB7	RB8	RB9	RB10	RB+ RB++
Volume (ml)	716	390	636	433	245	-	-	-	-	-	-
% Lobar Fissure Gap within Segment	0.0	81.4	0.0	18.6	0.0	-	-	-	-	-	-

Fissure Targeting Report

Patient ID CVT-212-001-V1 Upload Date May 12, 2021
Scan ID 996706 Report Date June 3, 2021
CT Scan Date May 5, 2021 Scan Comments None

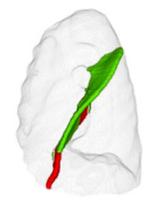
LEFT LUNG

L	RML	RLL	LUL	LLL
71.2	88.6	71.2	86.1	86.1

SIDE - RIGHT LUNG

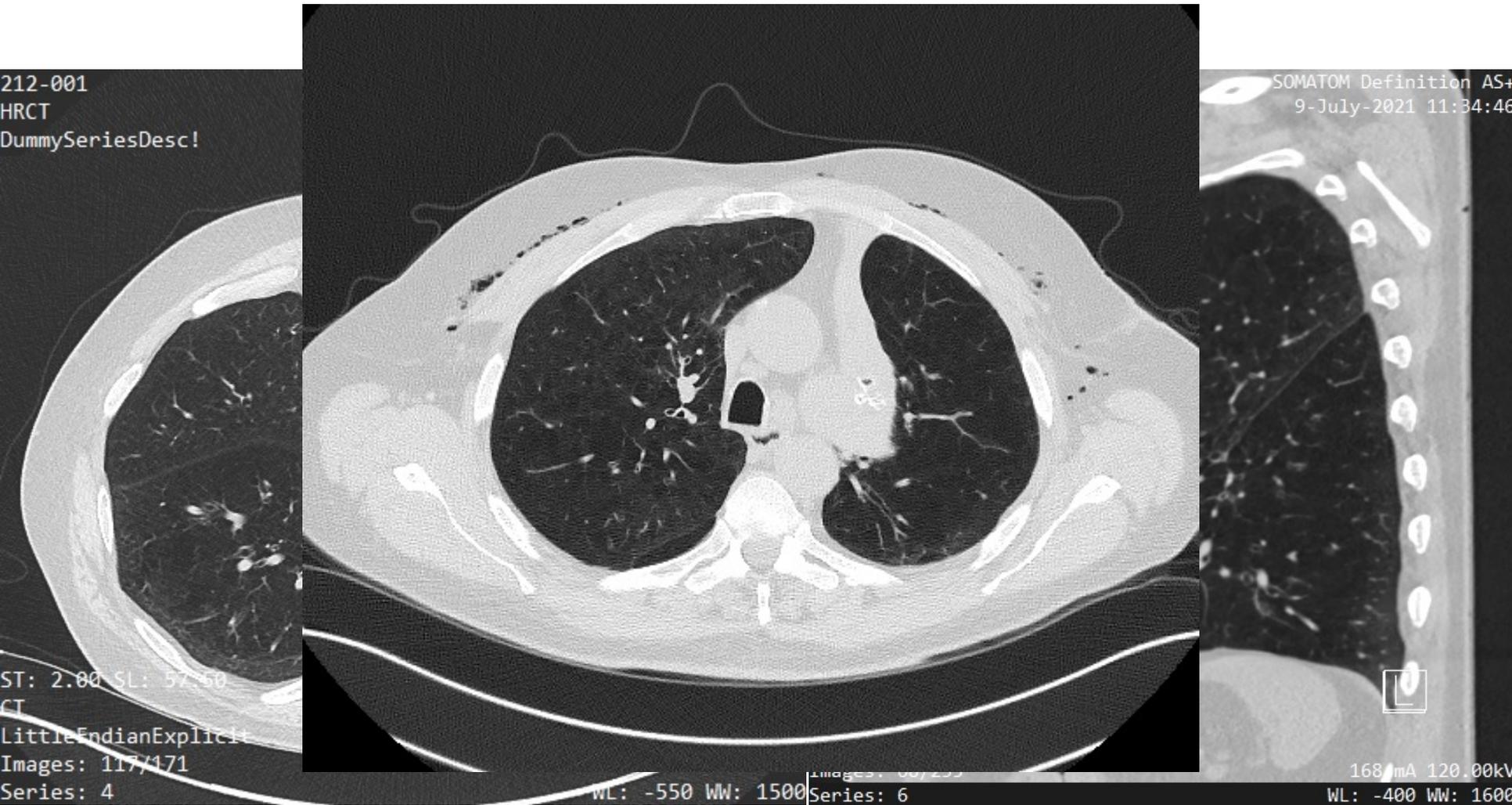


SIDE - LEFT LUNG



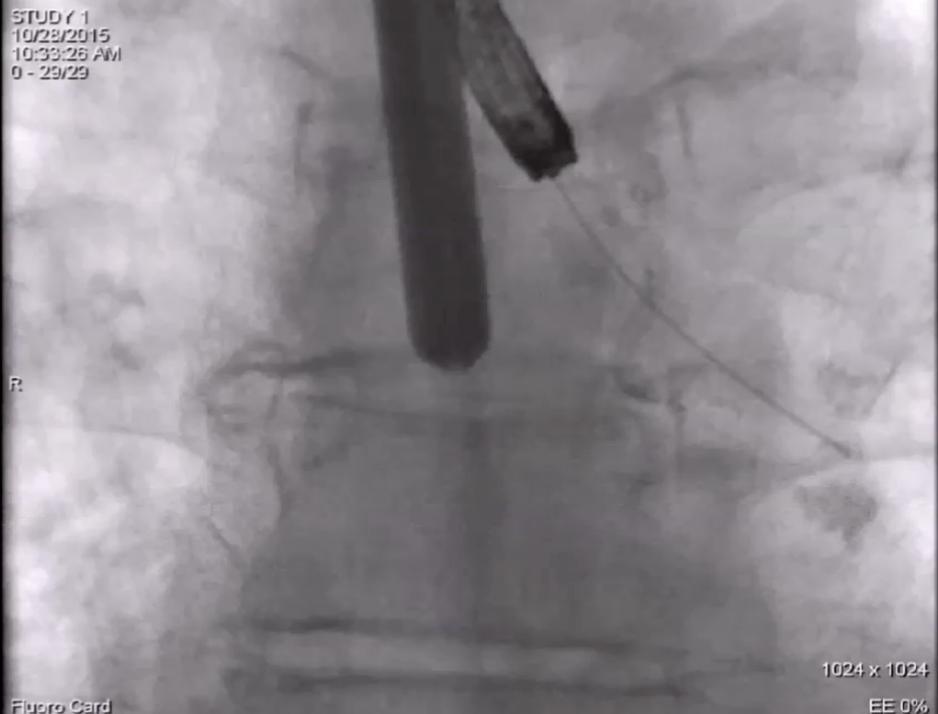


Post-Treatment CT





STUDY 1
10/28/2015
10:33:26 AM
0 - 29/29



R

Fluoro Card

1024 x 1024

EE 0%

XOD00030

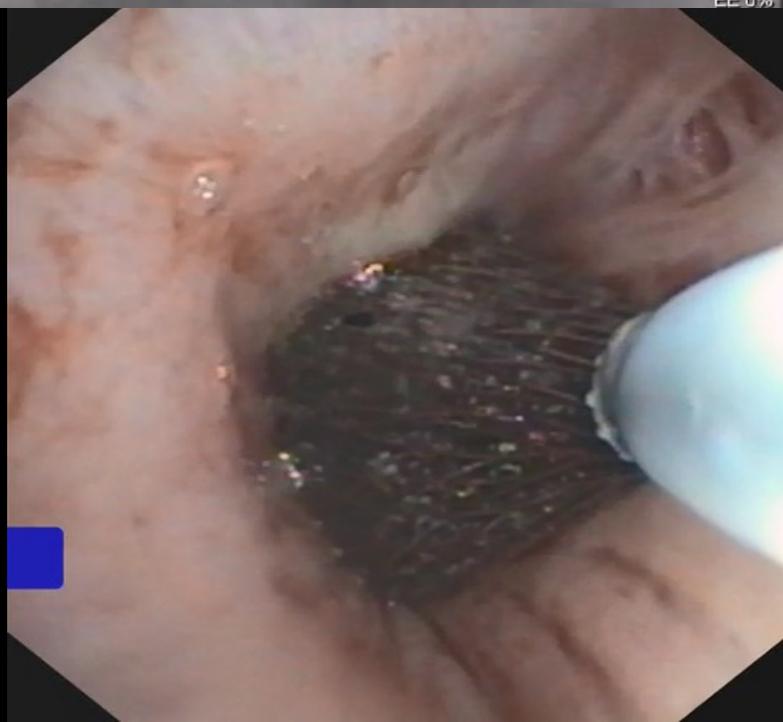
40861

08/20/2014

11:51:30

Cr:N Et:A1

Media: ■■■■



Start of Dose
0 seconds

An End to COPD Nihilism?

- Suite of available techniques for LVR
 - Broader indications
 - New techniques
 - More research on predictors of response needed
- Airways disease interventions showing some promise
 - Neuronal ablation
 - Epithelial regeneration
- Potential for: personalised approach to treatment
combination treatments

Questions?



Excellent health statistics - smokers are less likely to die of age related illnesses.'