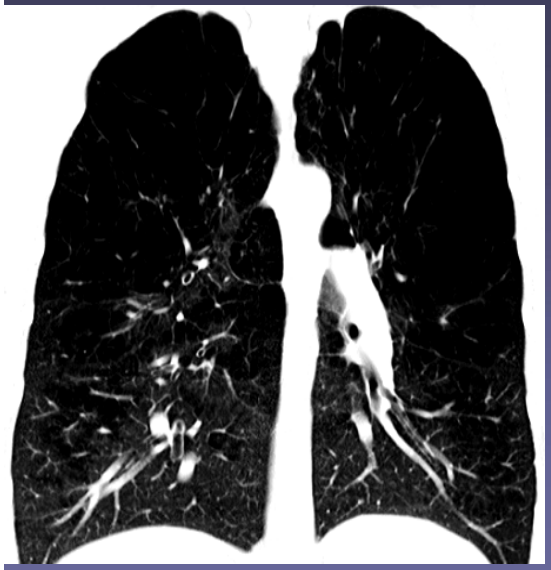


Βρογχοσκοπική μείωση όγκου στο Πνευμονικό Εμφύσημα

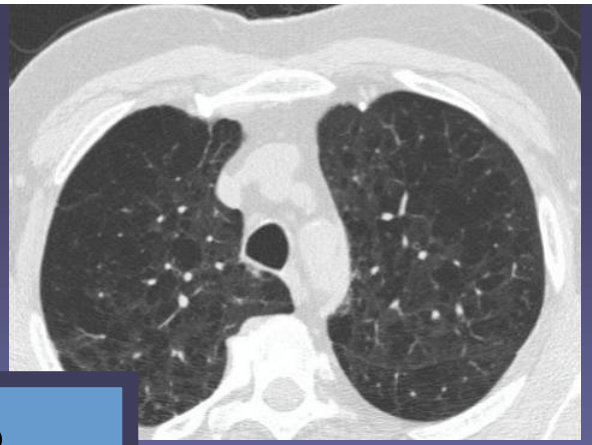
Γρ. Στρατάκος , Χ. Ζήσης

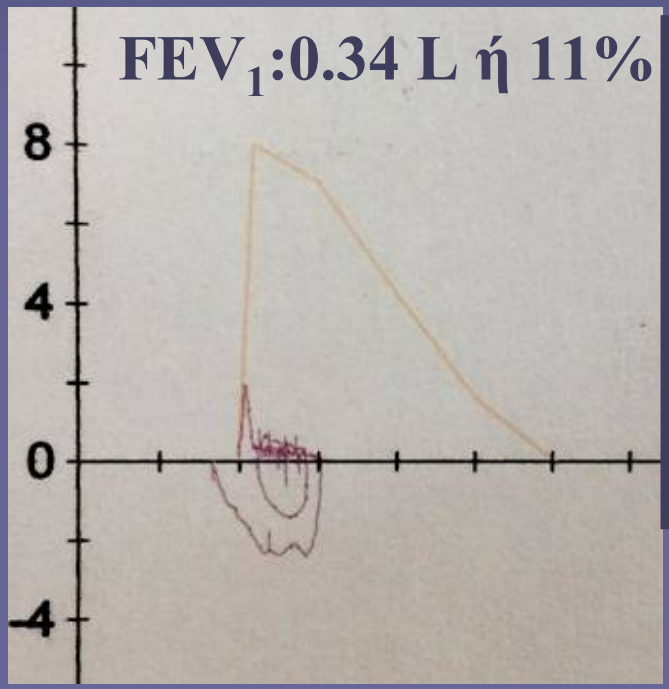
Α' Πνευμονολογική Κλινική ΕΚΠΑ

ΝΝΘΑ «Σωτηρία»

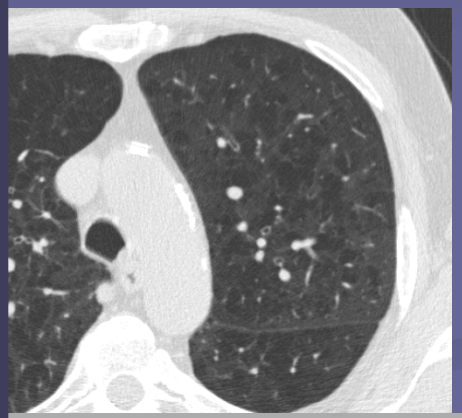
Χειρ/κη Κλινική Θώρακος- Ν. «Ευαγγελισμός»

♂, 65ετών, πρώην καπνιστής 50p.y.





SGRQ : 71,2
mMRC : 3
CAT score: 24
6mWT:106 m
Activity monitor: 574 steps



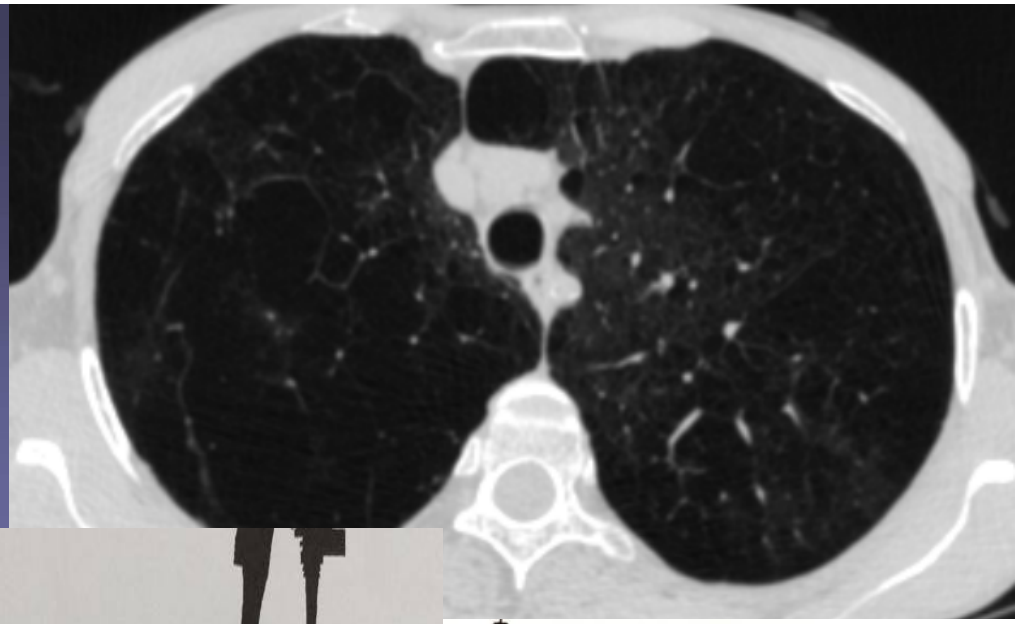
Lung Volumes

TLC	Liters	6.90	8.23	119
VC	Liters	4.23	1.05	[illegible]
RV	Liters	2.47	7.18	291
FRC PL	Liters	3.58	7.55	[illegible]
ERV	Liters	1.48	0.37	25
IC	Liters	2.96	0.68	23
RV/TLC	%	39	87	
Raw	kPa/L/sec	0.123	1.590	1296
Vtg	Liters		7.74	
sGaw	L/sec/kPa/L	2.27	0.08	4

Diffusion

DLCO	mmol/kPa.min	9.2	2.1	23
DL Adj	mmol/kPa.min	9.2	2.1	[illegible]
DLCO/VA	DLCO/L	1.33	0.75	57
DL/VA Adj	DLCO/L	1.33	0.75	57

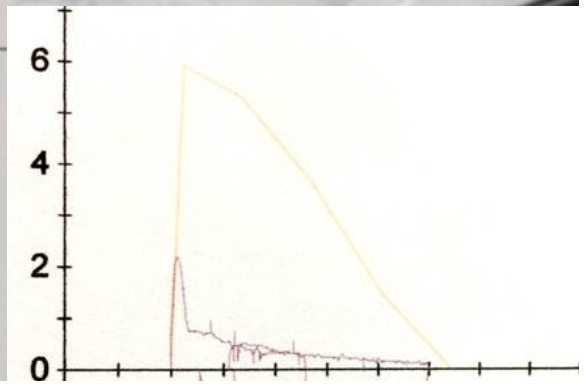
♀, 52ετών, πρώην καπνίστρια 40p.y.



ght(cm): 157
eight(kg): 38.0

Spirometry (BTPS)

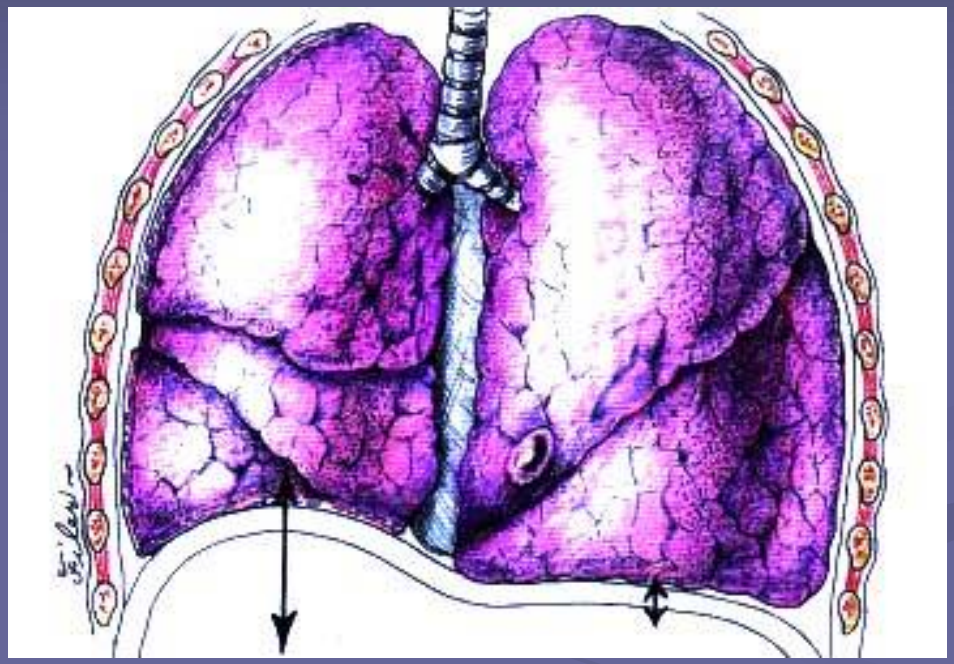
		PRED	PRE-RX BEST	%PRED
FVC	Liters	2.74	2.50	91
FEV1	Liters	2.33	0.64	27
FEV1/FVC	%	79	25	
FEF25-75%	L/sec	3.15	0.23	7
FEF75%	L/sec	1.48	0.17	11
FEF50%	L/sec	3.73	0.29	8
FEF25%	L/sec			
PEF	L/sec			
FIVC	Liters			
FEF/FIF50				



TLC	Liters	4.57	8.56	187
VC	Liters	2.71	1.95	72
RV	Liters	1.66	6.61	399
FRC PL	Liters	2.57	7.15	278
ERV	Liters	1.00	0.54	54
IC	Liters	1.99	1.41	71
RV/TLC	%	36	77	
Raw	kPa/L/sec	0.124	0.938	756
Vtg	Liters		7.30	
sGaw	L/sec/kPa/L	2.69	0.15	5

SGRQ : 40
mMRC : 3
CAT score: 24

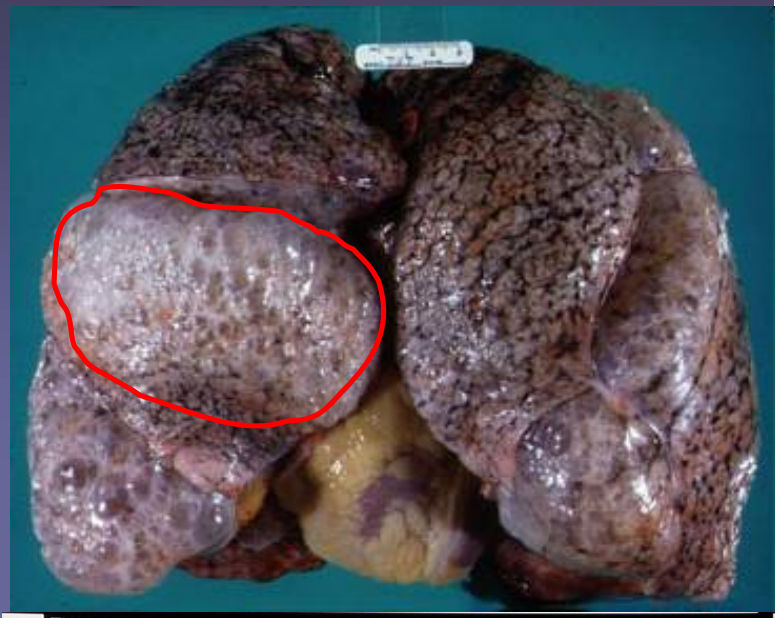
Χειρουργική αποκατάσταση της μηχανικής της αναπνοής

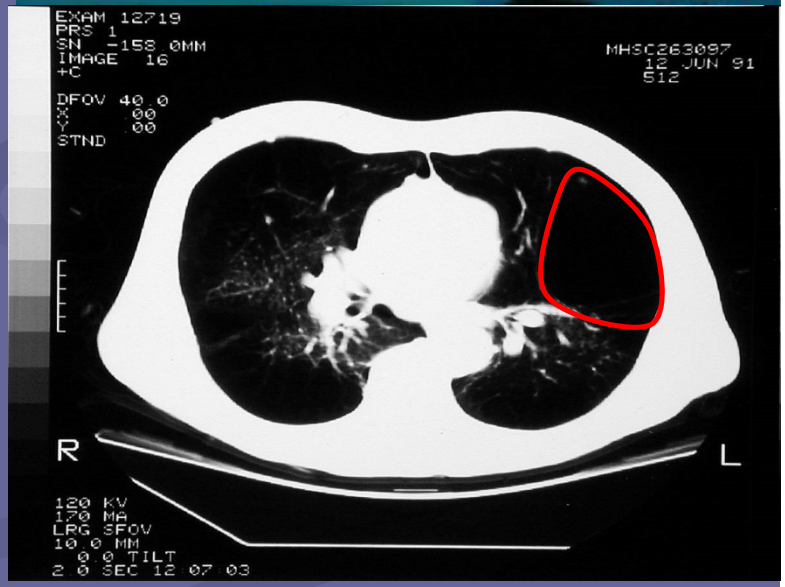


- **Bullectomy**
- **LVRS (Brantigan 1959) υψηλή περι-εγχειρητική νοσηρότητα θνητότητα**
- **Μεταμόσχευση πνεύμονα**

- **Η μείωση του συνολικού όγκου των υπερδιατεταμένων πνευμόνων:**

- Δημιουργεί ζωτικό χώρο μέσα στη θωρακική κοιλότητα για τον υπόλοιπο πνεύμονα να εκπτυχθεί και να λειτουργήσει καλύτερα κατά την εισπνοή
- Μειώνει την υπερδιάταση όπως εκφράζεται από το λόγο RV/TLC
- Αποκαθιστά τις μηχανικές ιδιότητες του αναπνευστικού συστήματος
- Θεωρητικά βελτιώνει τη δύσπνοια του ασθενούς και την αντοχή του στην άσκηση.





NETT 1998-2003
1218 pts randomized 1/1- 2003 results

High risk group: Homogeneous emphysema with FEV_1 or DLCO <20% present high risk of early mortality following **LVRS**.

Η μελέτη αναγνώρισε έναν φαινότυπο ασθενών με εμφύσημα άνω λοβών και αφετηριακά χαμηλή ικανότητα για άσκηση οι οποίοι παρουσίασαν:

- Βελτίωση της ικανότητας άσκησης
- Βελτίωση της ποιότητας ζωής (SGRQ)
- Αύξηση της επιβίωσης έναντι του control group

στα 2-5 έτη παρακολούθησης

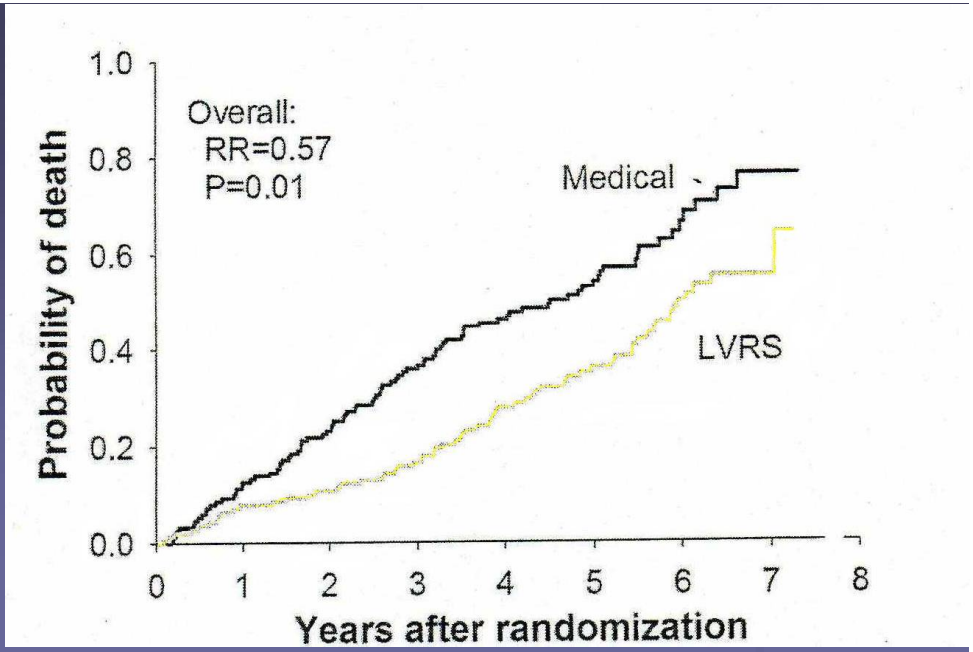


Table 3. Improvement in Exercise Capacity and Health-Related Quality of Life at 24 Months.*

Patients	Improvement in Exercise Capacity				Improvement in Health-Related Quality of Life			
	Surgery Group	Medical-Therapy Group	Odds Ratio	P Value	Surgery Group	Medical-Therapy Group	Odds Ratio	P Value
	no./total no. (%)				*no./total no. (%)*			
All patients	54/371 (15)	10/378 (3)	6.27	<0.001	121/371 (33)	34/378 (9)	4.90	<0.001
High-risk†	4/58 (7)	1/48 (2)	3.48	0.37	6/58 (10)	0/48	—	0.03
Other	50/313 (16)	9/330 (3)	6.78	<0.001	115/313 (37)	34/330 (10)	5.06	<0.001
Subgroups‡								
Predominantly upper-lobe emphysema								
Low exercise capacity	25/84 (30)	0/92	—	<0.001	40/84 (48)	9/92 (10)	8.38	<0.001
High exercise capacity	17/115 (15)	4/138 (3)	5.81	0.001	47/115 (41)	15/138 (11)	5.67	<0.001
Predominantly non–upper-lobe emphysema								
Low exercise capacity	6/49 (12)	3/41 (7)	1.77	0.50	18/49 (37)	3/41 (7)	7.35	0.001
High exercise capacity	2/65 (3)	2/59 (3)	0.90	1.00	10/65 (15)	7/59 (12)	1.35	0.61

N Engl J Med 2003;348:2059-73

Table 2. Mortality among All Patients and in Subgroups.*

Patients	90-Day Mortality			Total Mortality					
	Surgery Group	Medical-Therapy Group	P Value	Surgery Group		Medical-Therapy Group		Risk Ratio	P Value
	no. of deaths/total no. (% [95% CI])			*no. of deaths/ total no.*	*no. of deaths/ person-yr*	*no. of deaths/ total no.*	*no. of deaths/ person-yr*		
All patients	48/608 (7.9 [5.9–10.3])	8/610 (1.3 [0.6–2.6])	<0.001	157/608	0.11	160/610	0.11	1.01	0.90
High-risk†	20/70 (28.6 [18.4–40.6])	0/70 (0 [0–5.1])	<0.001	42/70	0.33	30/70	0.18	1.82	0.06
Other	28/538 (5.2 [3.5–7.4])	8/540 (1.5 [0.6–2.9])	0.001	115/538	0.09	130/540	0.10	0.89	0.31
Subgroups‡									
Patients with predominantly upper-lobe emphysema									
Low exercise capacity	4/139 (2.9 [0.8–7.2])	5/151 (3.3 [1.1–7.6])	1.00	26/139	0.07	51/151	0.15	0.47	0.005
High exercise capacity	6/206 (2.9 [1.1–6.2])	2/213 (0.9 [0.1–3.4])	0.17	34/206	0.07	39/213	0.07	0.98	0.70
Patients with predominantly non–upper-lobe emphysema									
Low exercise capacity	7/84 (8.3 [3.4–16.4])	0/65 (0 [0–5.5])	0.02	28/84	0.15	26/65	0.18	0.81	0.49
High exercise capacity	11/109 (10.1 [5.1–17.3])	1/111 (0.9 [0.02–4.9])	0.003	27/109	0.10	14/111	0.05	2.06	0.02

- **Περιεγχειρητική θνητότητα** (90 ημερών) 7,9% στην ομάδα του LVRS vs 1,3% controls.
- Σε FEV1 ≤20% και/ή διάχυση <20 % διαπιστώθηκε υψηλή περιεγχειρητική θνητότητα 30 ημερών (16%) και μικρό προβλεπόμενο όφελος από τη LVRS

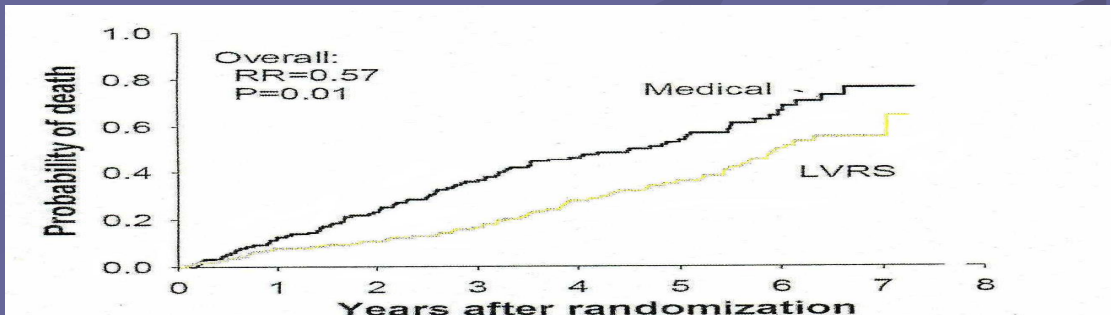
•**Διαφυγή αέρα:** Από τους 580 ασθενείς, οι 552 παρουσίαζαν διαφυγή αέρα στην παρακολούθηση 30 ημερών (μέσος όρος 7 ημέρες).
• **Άλλες επιπλοκές**: αρρυθμία (23.5%), πνευμονία (18,2%), επαναδιασώληνωση (21,8%), αποτυχία weaning (5,1%) κ.α.

N Engl J Med 2003;348:2059-73

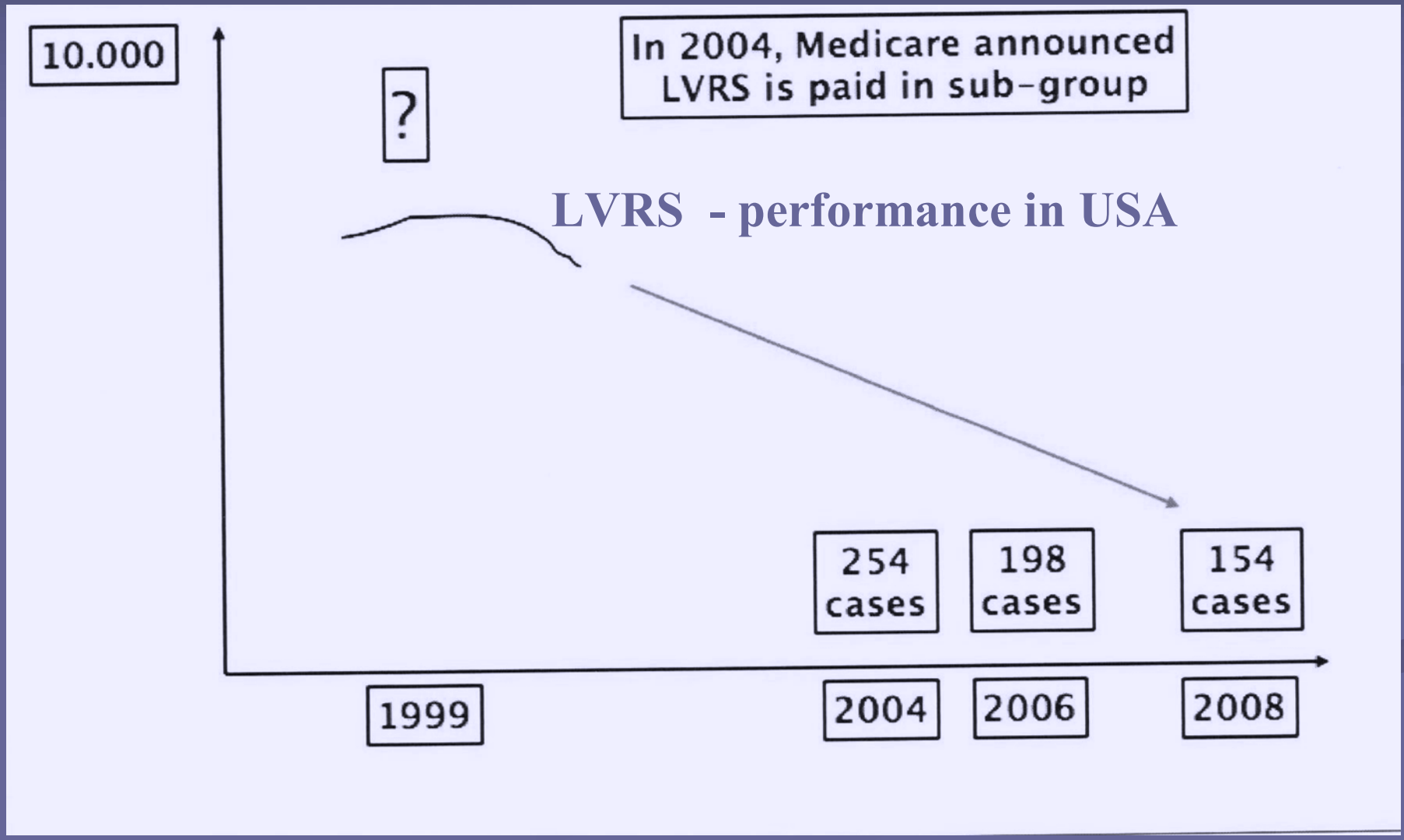
Μετά 8 έτη- 2006

- Ασθενείς με εμφύσημα άνω λοβών και χαμηλή αντοχή στην άσκηση είχαν σταθερό πλεονέκτημα στην επιβίωση (risk ratio 0.67, p=0.003), βελτιωμένη δυνατότητα άσκησης (p<0.001) και λιγότερα συμπτώματα (SGRQ) (p<0.001). **RECOMENDED**
- Εάν η αντοχή στην καρδιο-αναπνευστική κόπωση ήταν διατηρημένη προεγχειρητικά το πλεονέκτημα στην επιβίωση δεν ήταν σημαντικό αλλά υπήρχε βελτίωση λειτουργική (p<0.01) ποιότητας ζωής (SGRQ) (p<0.01). **PALLIATION**

Ann Thorac Surg 2006;82:431-3



Very few LVRS are performed in USA and even less in Europe. Why??



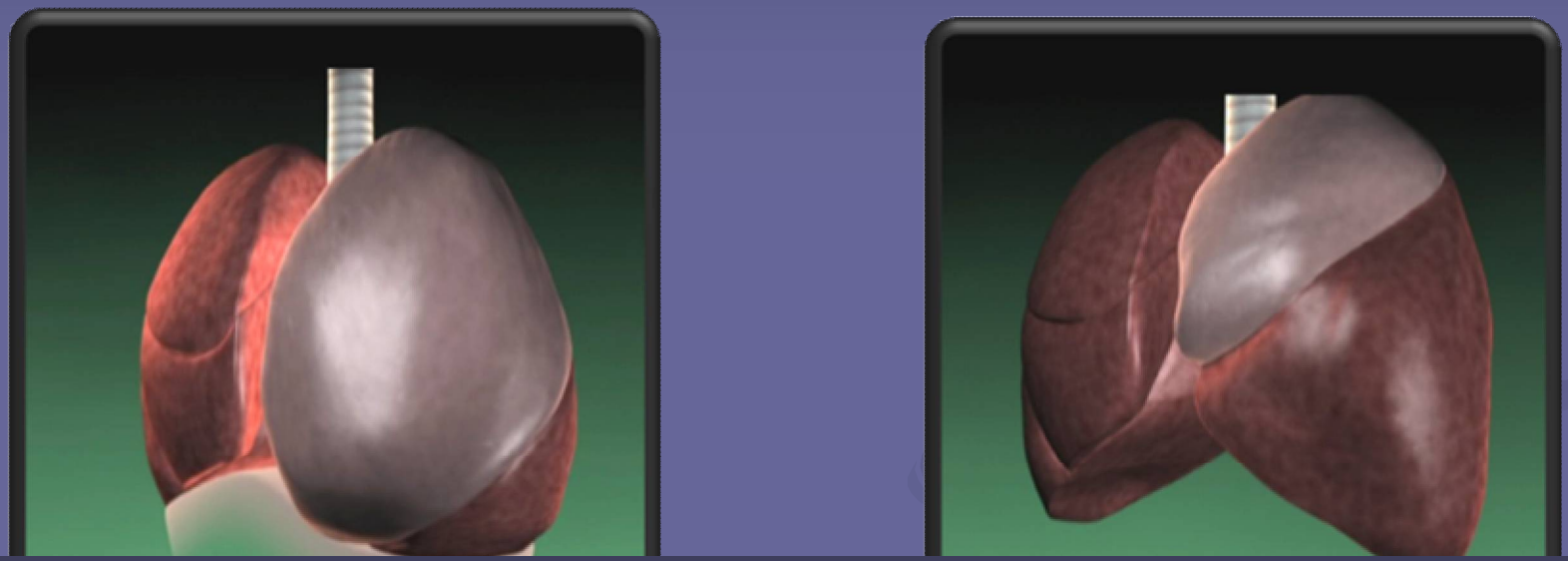
Ενδοσκοπική Μείωση όγκου??

- Θα μείωνε την περιεγχειρητική νοσηρότητα /θνητότητα και κόστος
- Θα αύξανε τις ενδείξεις σε μη χειρουργήσιμους ασθενείς
- Θα απέφευγε τον τραυματισμό και τη διαδικασία επούλωσης των αναπνευστικών μυών

Midline sternotomy→ VATS → Bronchoscopy

Mechanism of Action

Hyperinflated lung → → **Volume reduction and re-distribution of air**



Α. Τροποποίηση αεραγωγών και ροής

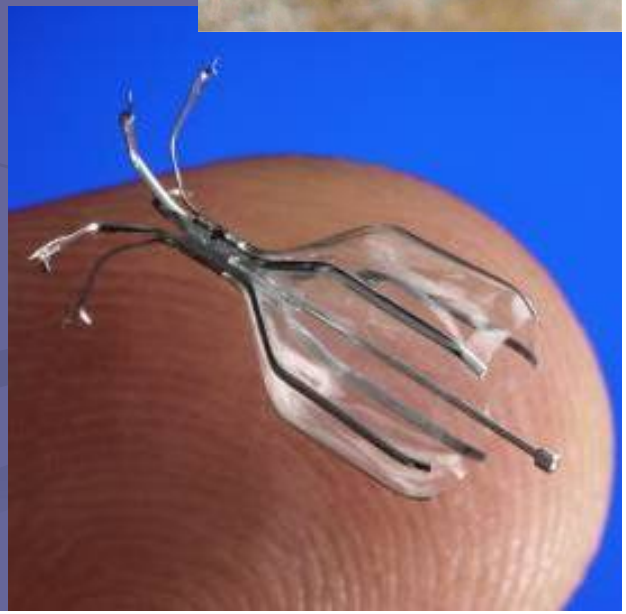
Β. Τροποποίηση πνευμονικού παρεγχύματος

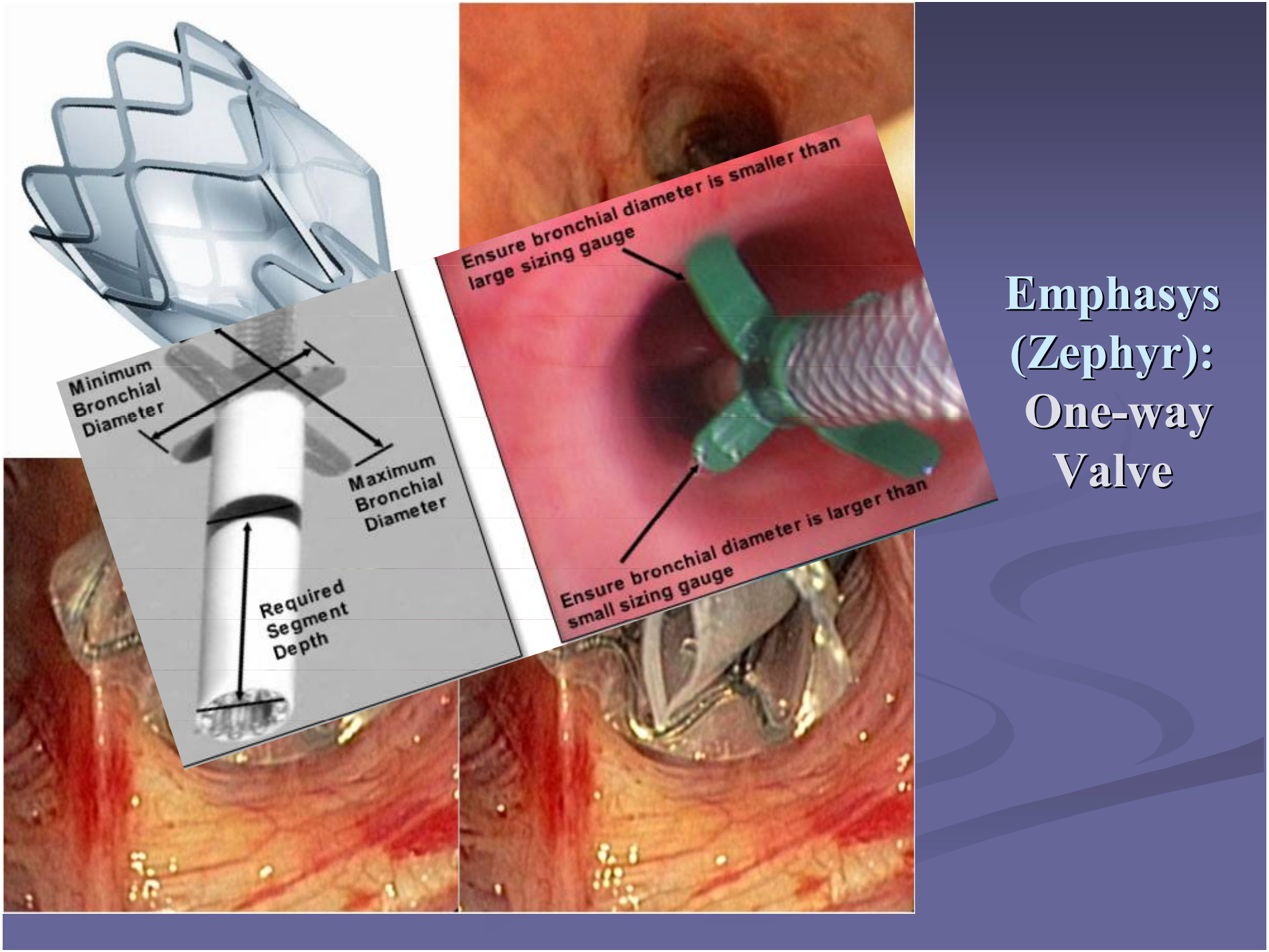
Endoscopic LVR

Α. Τροποποίηση αεραγωγών και ροής

Endobronchial valves

- Emphasis-Zephyr (Pulmonx): One-way Valve
- Spiration: Umbrella





Emphasys (Zephyr): One-way Valve

Zephyr valve - VENT Study:

- **Πολυκεντρική προοπτική μελέτη**

2 EBV:1 control

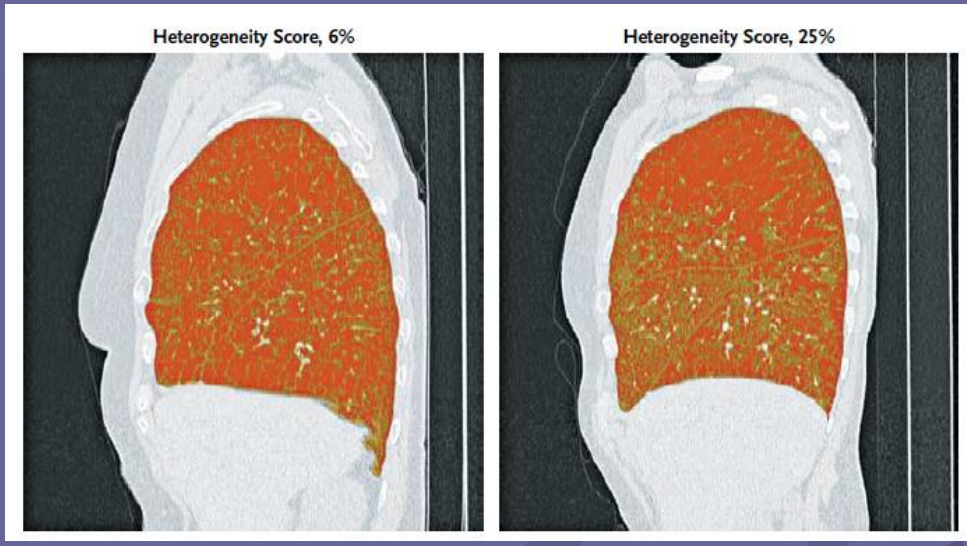
321ασθενείς (220 EBV vs 101 SMC).

Βέλτιστη φαρμακευτική αγωγή και πνευμονική αποκατάσταση πριν την επέμβαση για 8 εβδομάδες

Κριτήρια εισαγωγής/αποκλεισμού:

- Σοβαρό μη ομοιογενές εμφύσημα καθοριζόμενο από HRCT.
- FEV1 15-45%, TLC >100%, RV >150%, DLCO >20%
- Κλινικά σταθερός ασθενής (όχι σε παρόξυνση)
- PaCO2 <50 mmHg,
- Απουσία μεγάλων φυσαλίδων , ή ανεπάρκεια α1 αντιθρυψίνης

NEJM 2010;363:1233-44

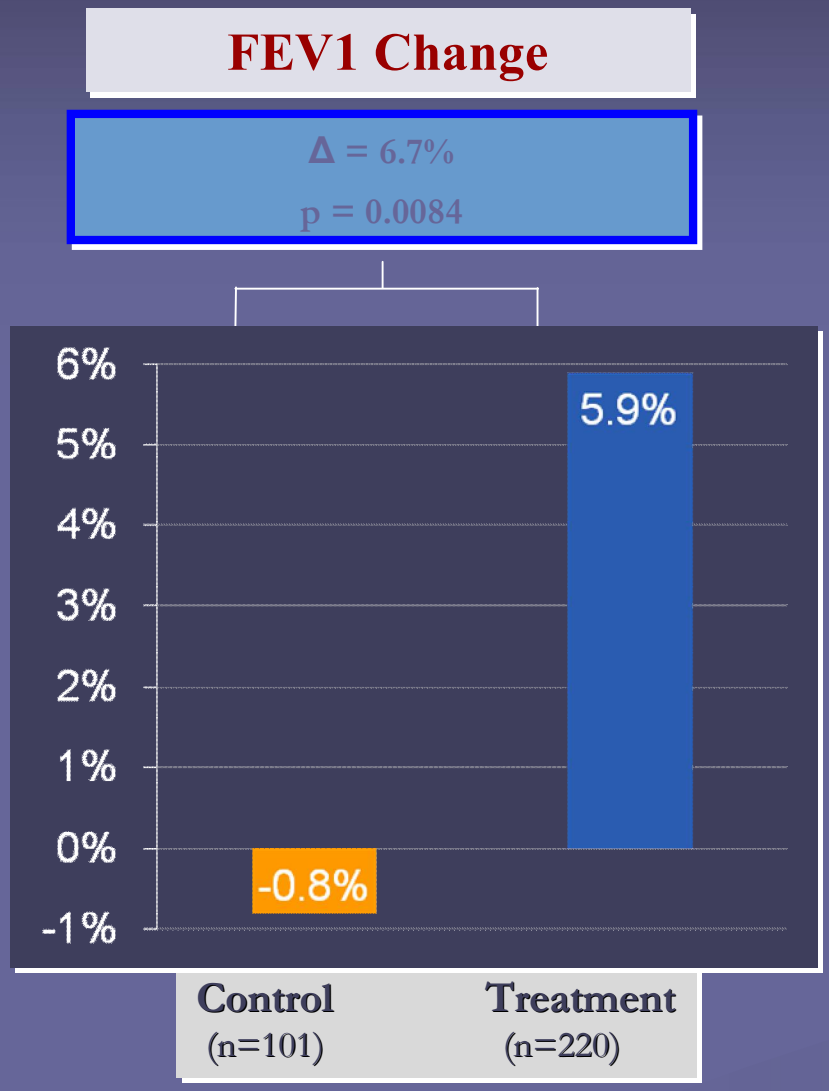


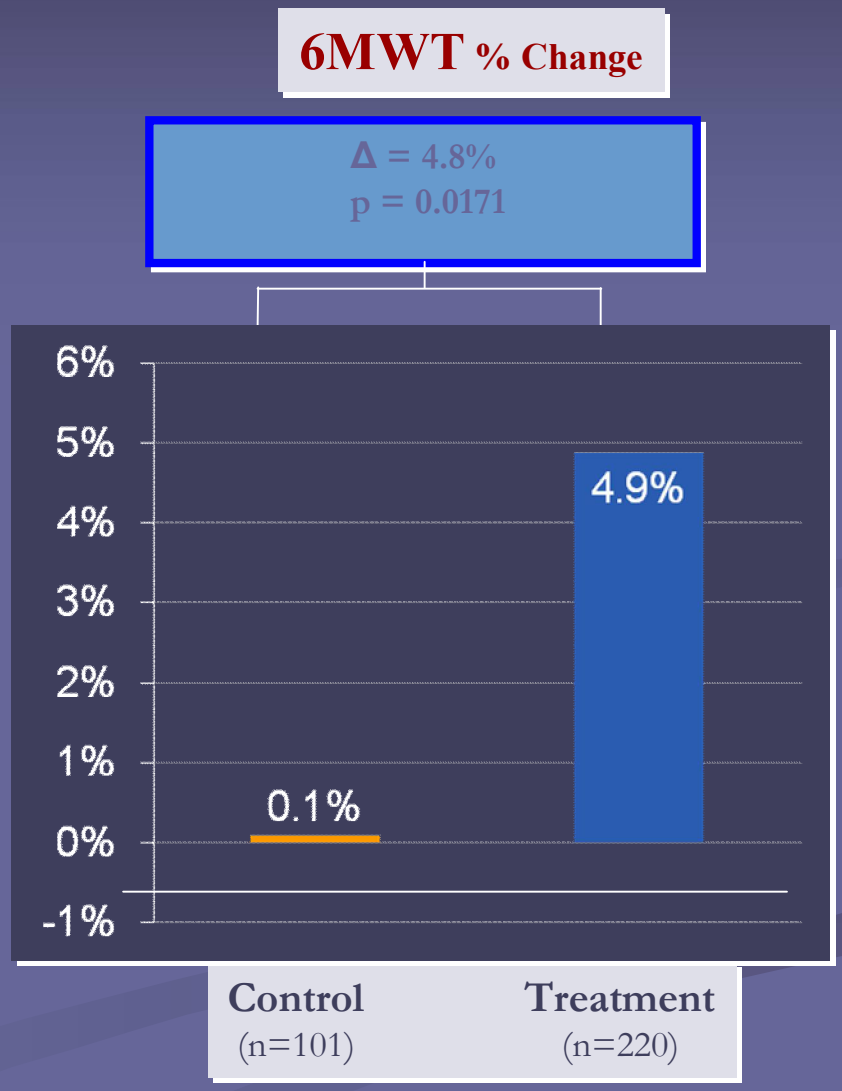
Διαφορά στο ποσοτικό score Εμφυσήματος: Ποσοστό pixels <-910 HU μεταξύ του λοβού-στόχου και του ετερόπλευρου λοβού-μη στόχου

Results-Complications in 6 and 12 months

	Primary Safety Endpoint 6 months			Additional Safety Analysis 12 months (cumulative)		
	Control n=101	EBV n=220	p value	Control n=101	EBV n=220	p value
Major Complication Composite (MCC)	1.1%	6.1%	0.0748	4.6%	10.4%	0.1724
Death	0.0%	2.8%	0.1867	3.5%	3.7%	1.0000
Empyema	0.0%	0.0%	----	0.0%	0.0%	----
Massive Hemoptysis	0.0%	0.5%	1.0000	0.0%	0.5%	1.0000
Distal Pneumonia	NA	1.4%	----	NA	4.2%	----
Pneumothorax/ air leak > 7 days	1.1%	1.4%	1.0000	1.2%	1.9%	1.0000
Resp. Failure ≥ 24 hours vent	1.1%	1.9%	1.0000	2.3%	2.8%	1.0000

Primary end points at 6 months





Sciurba , Ernst, Herth et al., A randomized Study of Endobronchial Valves for Advanced Emphysema. **N Engl J Med 2010;363:1233-44**.

Υπο-ανάλυση ομάδων ανάλογα με την ετερογένεια του εμφυσήματος στη HRCT και την πληρότητα της μεσολοβίου σχισμής

Table 4. Percent Changes in the FEV_1 and Distance on the 6-Minute Walk Test at 6 and 12 Months, According to Subgroup of Disease Severity.*

Subgroup and Outcome	Percent Change from Baseline at 6 Mo		Percent Change from Baseline at 12 Mo	
	Difference between EBV Group and Control Group	P Value†	Difference between EBV Group and Control Group	P Value†
	% (95% CI)		% (95% CI)	
High heterogeneity				
FEV_1	10.7 (3.5 to 17.9)	0.004	13.3 (5.7 to 20.9)	<0.001
Distance on 6-min walk test	12.4 (4.8 to 20.1)	0.002	7.1 (–0.8 to 14.9)	0.08
Low heterogeneity				
FEV_1	2.5 (–3.1 to 8.2)	0.38	1.5 (–4.7 to 7.6)	0.64
Distance on 6-min walk test	–1.0 (–6.4 to 8.4)	0.80	–0.6 (–6.4 to 7.7)	0.84
Complete fissure				
FEV_1	16.2 (8.8 to 23.8)	<0.001	17.9 (9.8 to 25.9)	<0.001
Distance on 6-min walk test	7.7 (–1.8 to 17.2)	0.14	3.9 (–4.0 to 11.8)	0.31
Incomplete fissure				
FEV_1	2.0 (–3.9 to 7.9)	0.51	2.8 (–3.8 to 9.4)	0.41
Distance on 6-min walk test	5.3 (–1.5 to 12.2)	0.13	4.5 (–2.7 to 11.8)	0.20

NEJM 2010;363:1233-44

Τι προβλέπει την αποτελεσματικότητα της BLVR με βαλβίδες? (European cohort of VENT 161 ασθενείς)

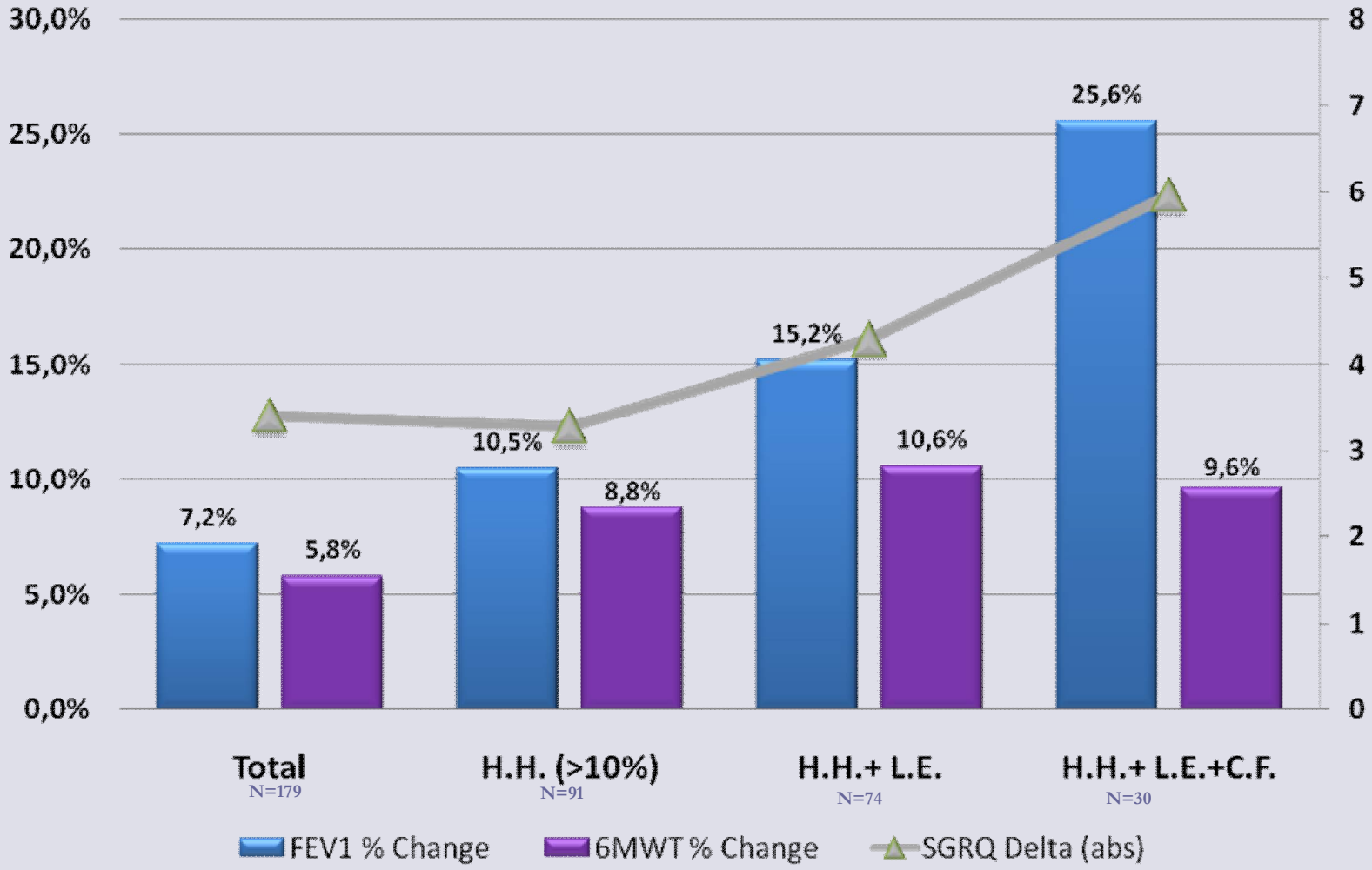
TABLE 3 Clinical effectiveness outcomes at 6 and 12 months in patients having computed tomography (CT) suggestive of complete fissure, with endobronchial valve (EBV) therapy patients stratified by CT assessment of lobar occlusion

	Complete fissure			
	Lobar occlusion	No lobar occlusion	p-value#	Controls
Patients n¶	20	17		19
Δ TLVR %+				
6 months	-80±0.30	-29±0.25	<0.0001	0±0.08
⩾55% reduction§	15 (79)	3 (18)	0.0002	0 (0)
Δ TLC L				
6 months	-0.5±0.7	-0.4±1.0	0.7	-0.2±0.5
12 months	-0.3±0.7	-0.2±1.2	0.6	-0.4±0.7
Δ FEV_1 %				
6 months	26±24	6±12	0.004	3±14
12 months	28±32	2±10	0.005	-2±22
⩾15% improved	12 (67)	1 (8)	0.002	1 (6)
Δ cycle ergometry workload W				
6 months	8±15	0±14	0.10	-3±7
12 months	6±16	5±10	0.9	-2±9
⩾10 W improved	8 (44)	3 (27)	0.4	1 (7)
Δ 6MWD %				
6 months	22±38	-2±19	0.03	19±54
12 months	22±40	0±20	0.06	10±44
⩾35 m improved	10 (56)	3 (25)	0.1	6 (38)

Eur Respir J 2012; 39: 1334–1342

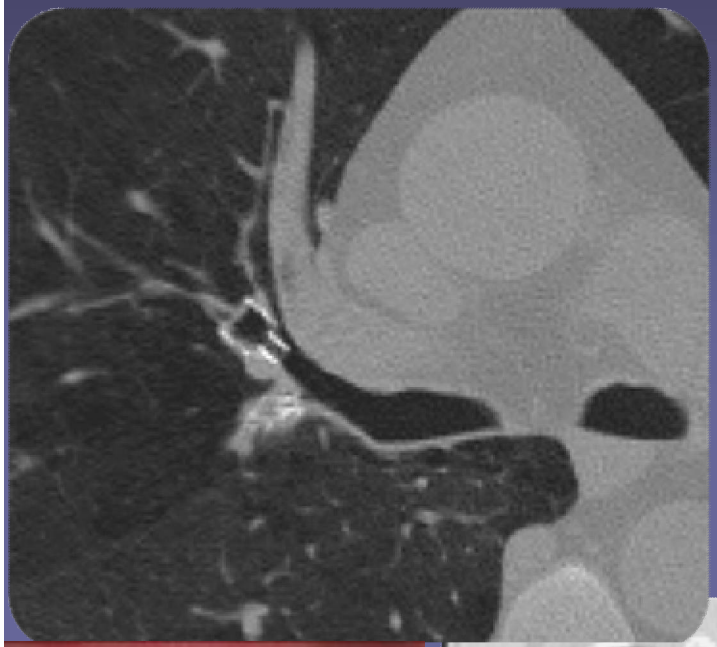
VENT Responder Summary

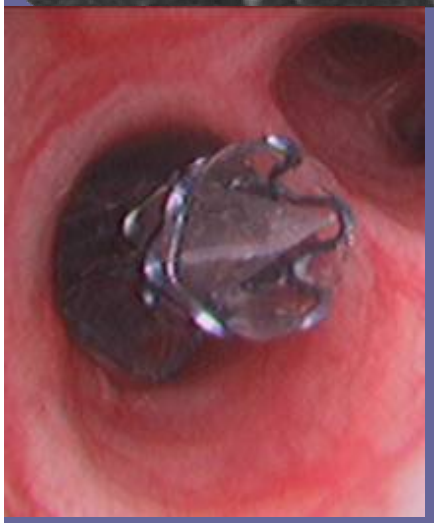
(Delta Treatment & Control @ 6mons)

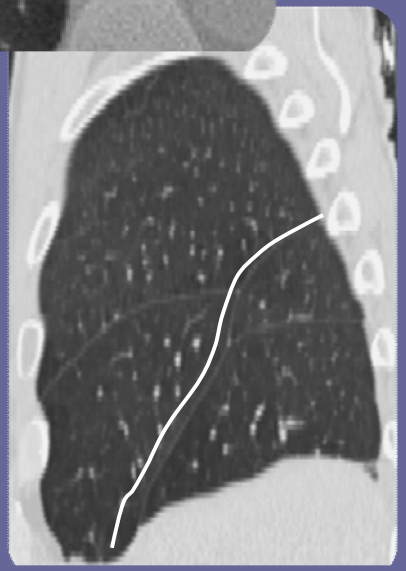


H.H. – High Heterogeneity, L.E. – Lobar Exclusion Achieved, C.F. – Low Collateral Flow

Predictor Analysis – Παράγοντες που επηρεάζουν το αποτέλεσμα



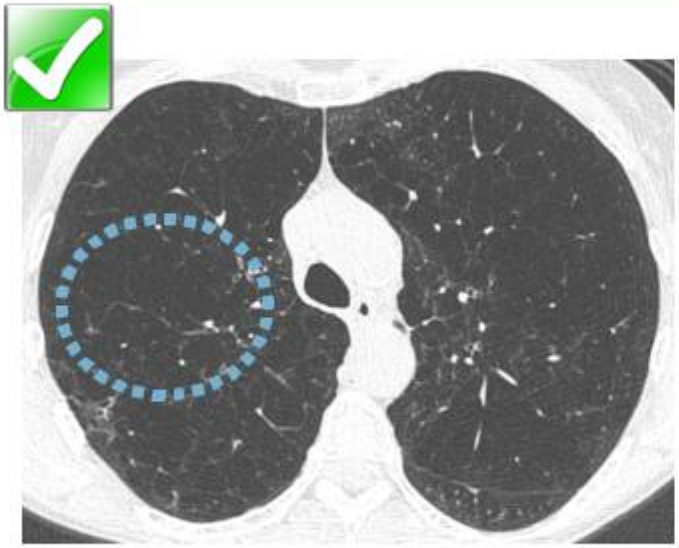


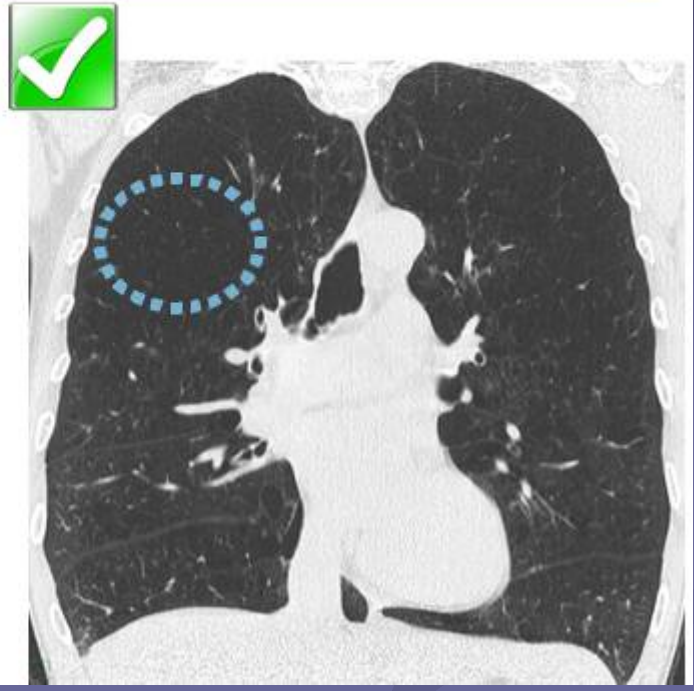


- **Πλήρης αποκλεισμός ΌΛΩΝ των αεραγωγών που οδηγούν στο λοβό στόχο.**
- **Πλήρεις μεσολόβιοι**
- Ασυνέχεια των μεσολοβίων σχισμών ή αποτυχία πλήρους απόφραξης των λοβών στόχων μείωνε την πιθανότητα αποτελεσματικής θεραπείας.

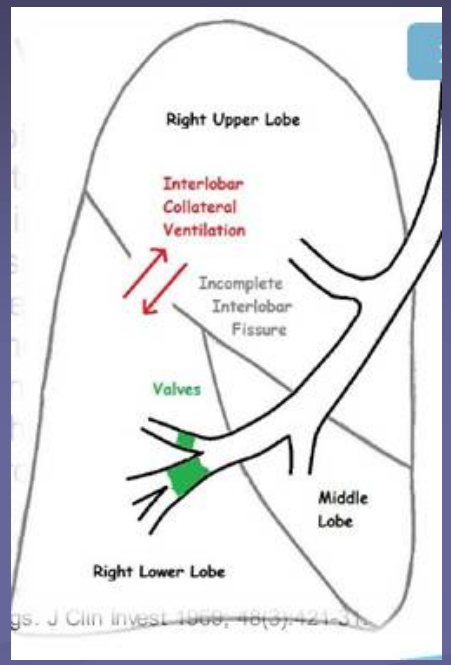
Good candidate for EBV therapy

pulmonX Interventional Pulmonology

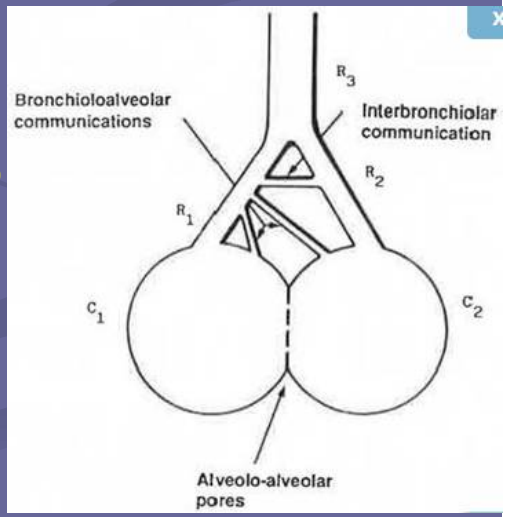




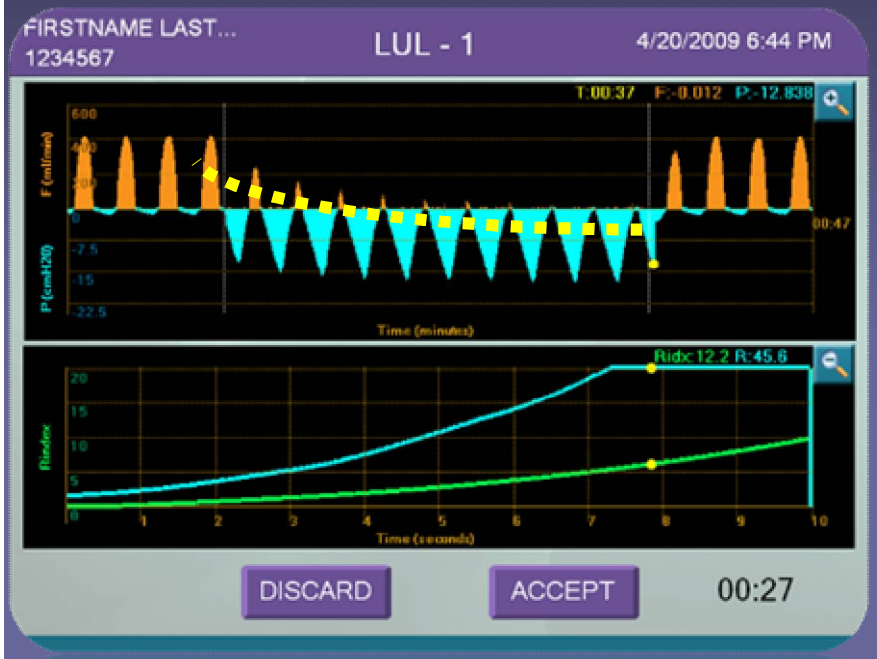
Picture and data courtesy: Department of Radiology, Otto-Wagner Spital Vienna, Dr. Arschang Valipour



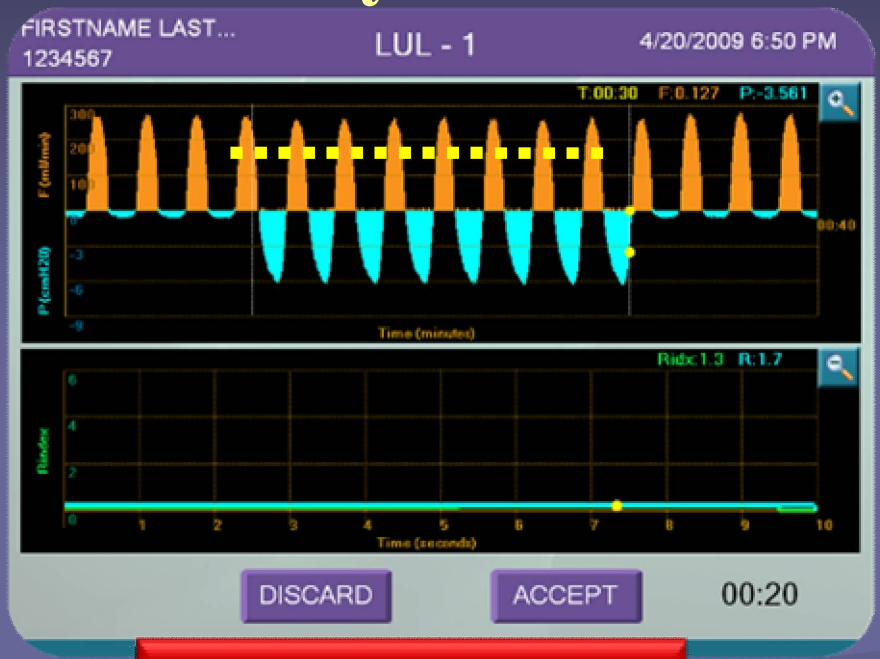
- **Ετερογένεια στους άνω λοβούς**
- **Πλήρης απομόνωση όλων των στομίων του λοβού στόχου.**
- **Πλήρεις μεσολόβιοι (όχι παράπλευρος αερισμός)**



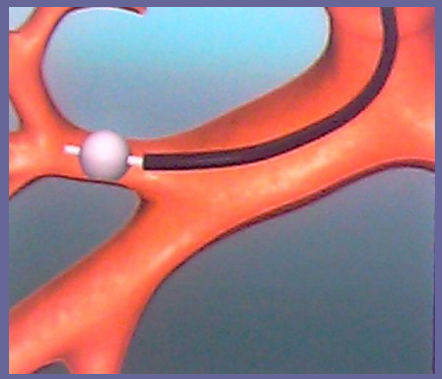
Chartis CV Assessment System

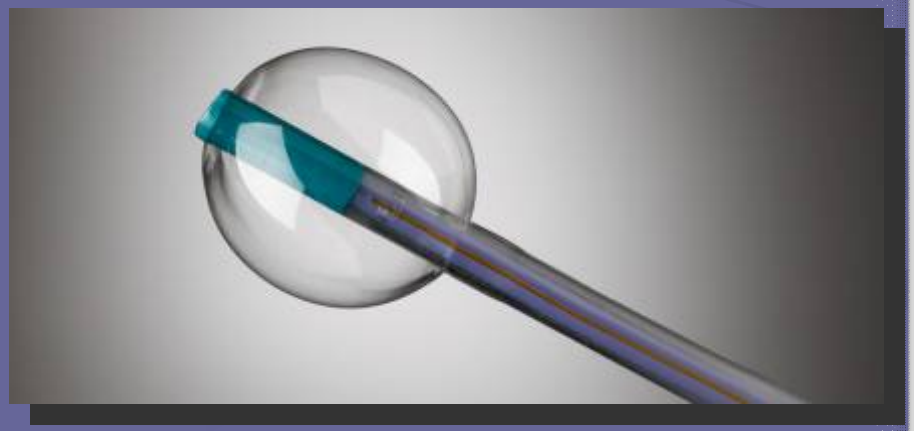


No collateral ventilation



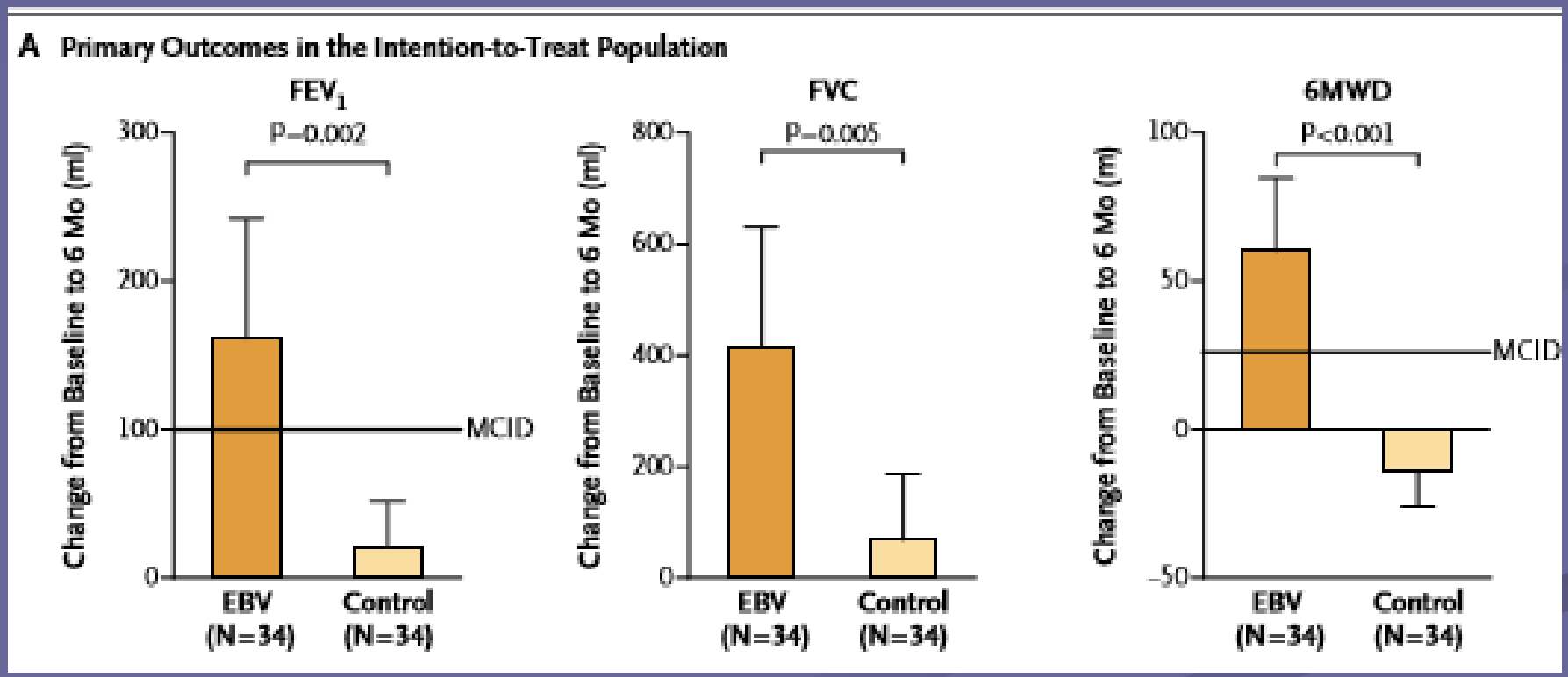
Collateral ventilation





Stelvio Study:

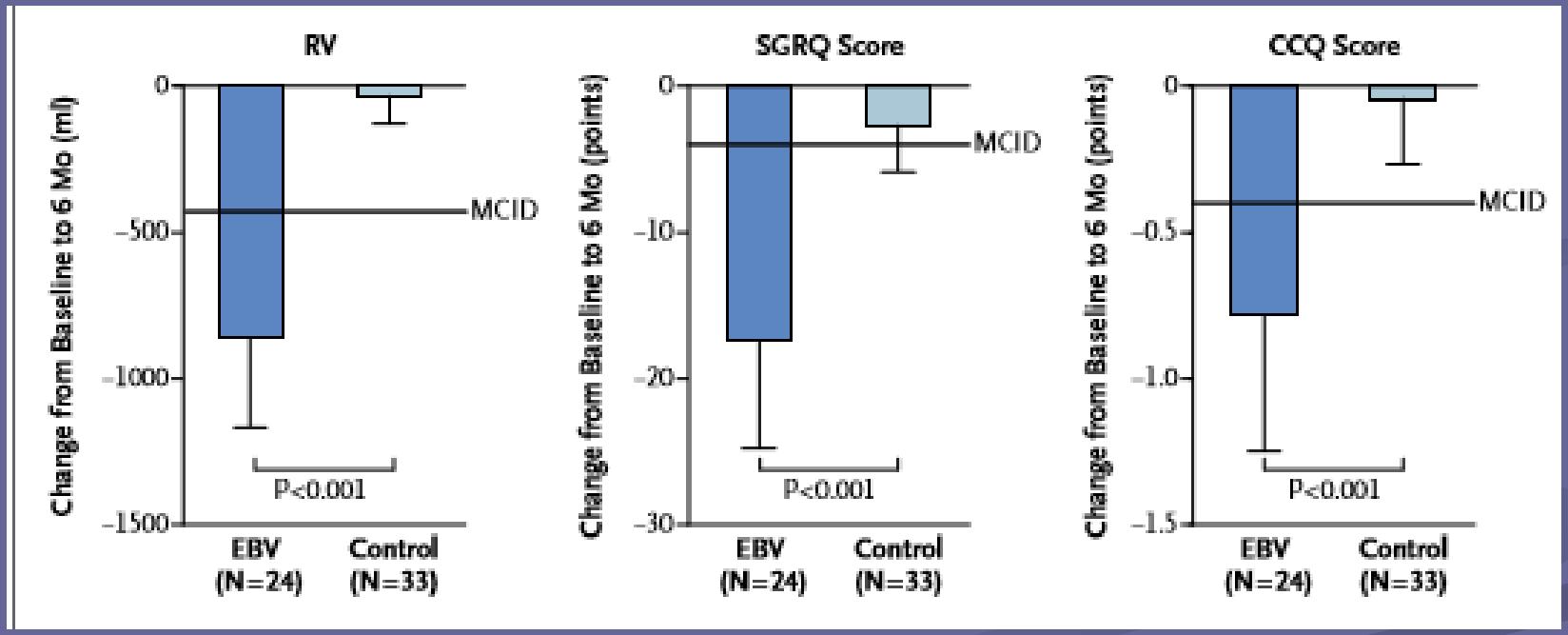
Τυχαιοποιημένη μελέτη, 84 ασθενείς με ετερογένεια εμφυσήματος και απουσία παράπλευρου αερισμού στον λοβό-στόχο.



N Engl J Med 2015;373:2325-35

Stelvio Study:

Τυχαιοποιημένη μελέτη, 84 ασθενείς με ετερογένεια εμφυσήματος και απουσία παράπλευρου αερισμού στον λοβό-στόχο.

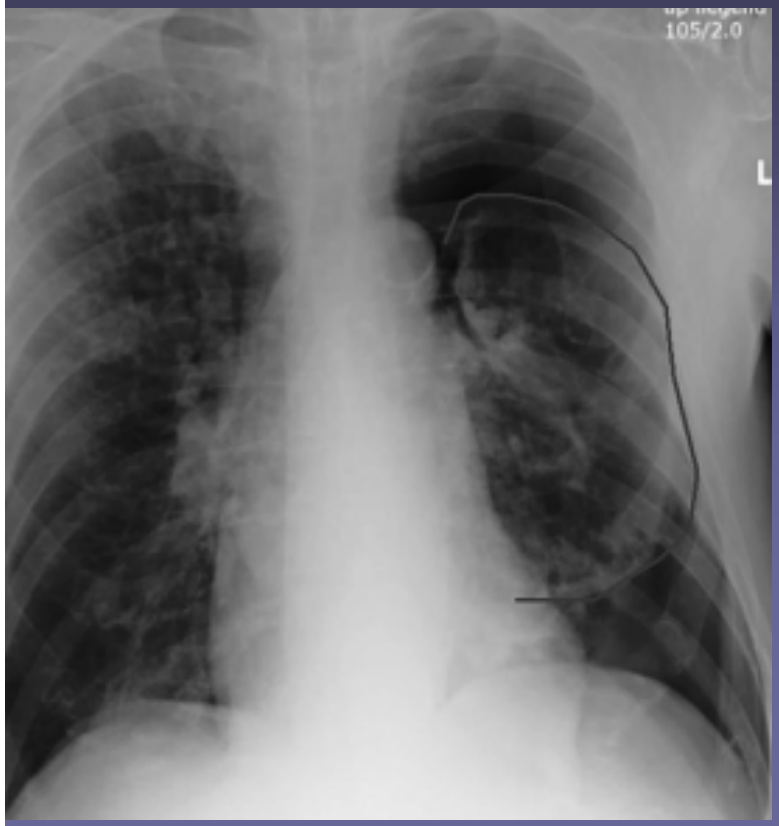


N Engl J Med 2015;373:2325-35

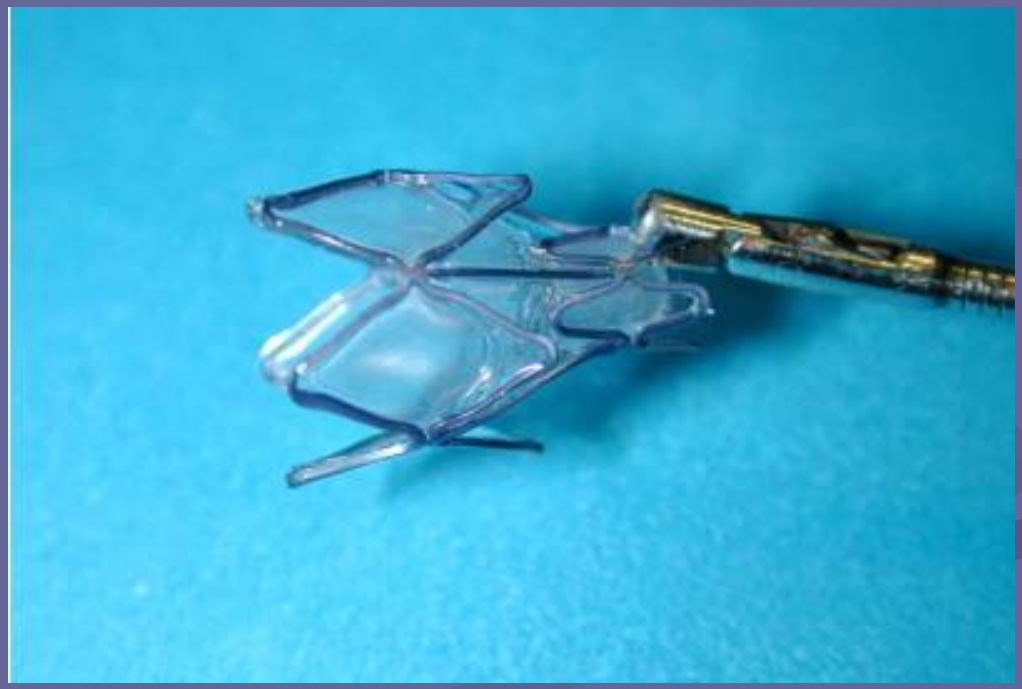
Table 3. Serious Adverse Events during 6 Months of Follow-up.*

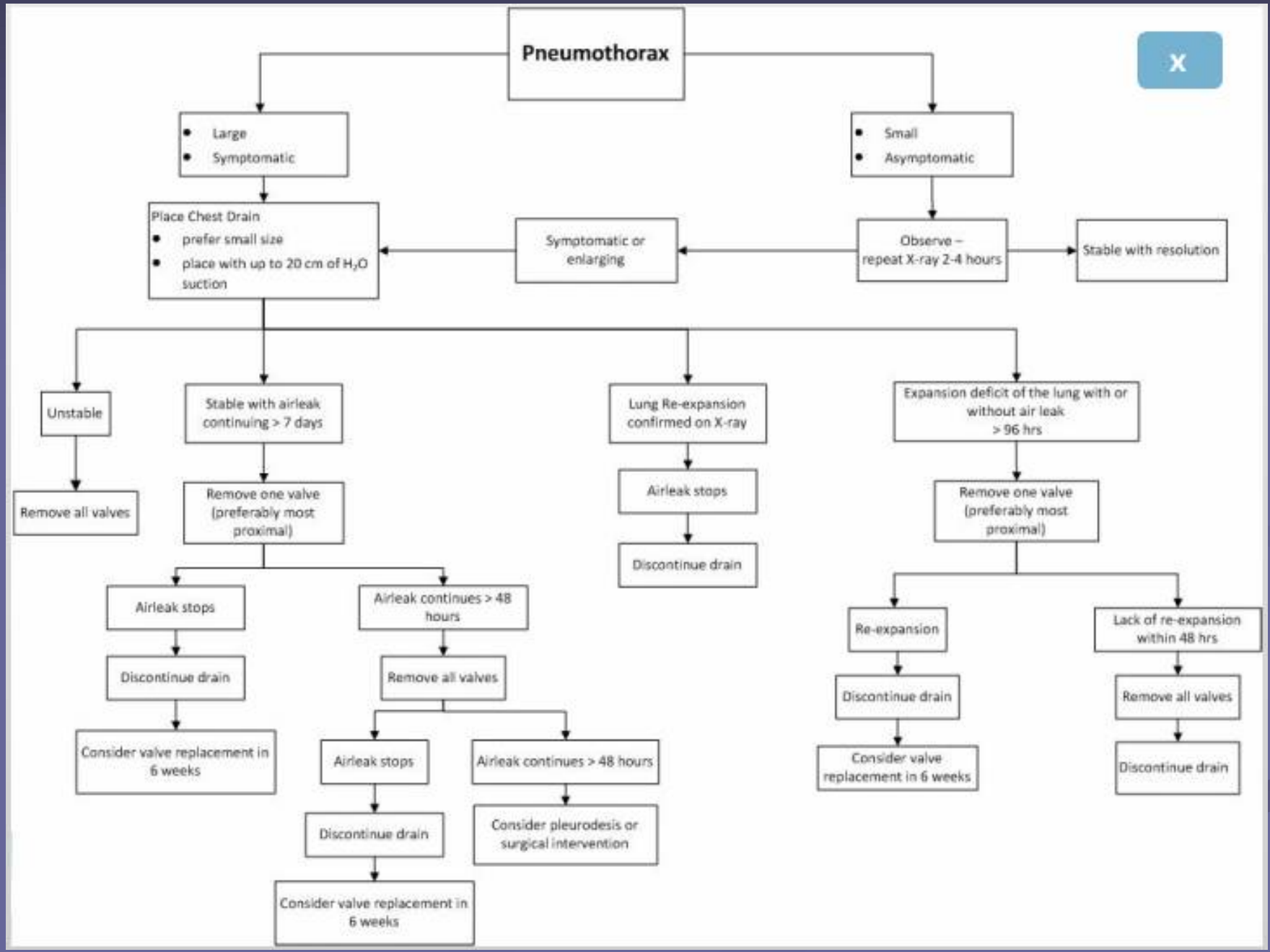
Event	EBV Group (N=34)	Control Group (N=34)	P Value†
	no. (%)		
Total no. of serious events	23	5	<0.001
Pulmonary events			
Death	1 (3)‡	0	1.00
COPD exacerbation with hospitalization	4 (12)	2 (6)	0.67
Pneumonia	2 (6)	1 (3)	1.00
Pneumothorax	6 (18)	0	0.02
Resolved ≤14 days after onset, without drainage	1 (3)	0	1.00
Resolved ≤14 days after onset, with drainage	2 (6)	0	0.49
Required temporary valve removal	1 (3)§	NA	NA
Required permanent valve removal because of recurrent pneumothorax	1 (3)	NA	NA
Required permanent valve removal, after temporary removal and reimplantation, because of recurrent pneumothorax	1 (3)	NA	NA
Other EBV-related events requiring permanent removal of all valves			
Torsion of the bronchus	2 (6)¶	NA	NA
Pneumonia distal to valve	1 (3)‖	NA	NA
Increased sputum, dyspnea, or coughing without patient-perceived treatment benefit	2 (6)	NA	NA
Other EBV-related events requiring valve replacement			
Valve migration	2 (6)	NA	NA
Valve expectoration	0	NA	NA
Valve dislocation due to formation of granulation tissue	1 (3)	NA	NA
Increased sputum, dyspnea, or coughing	1 (3)	NA	NA
Stroke	1 (3)	2 (6)	1.00

N Engl J Med 2015;373:2325-35



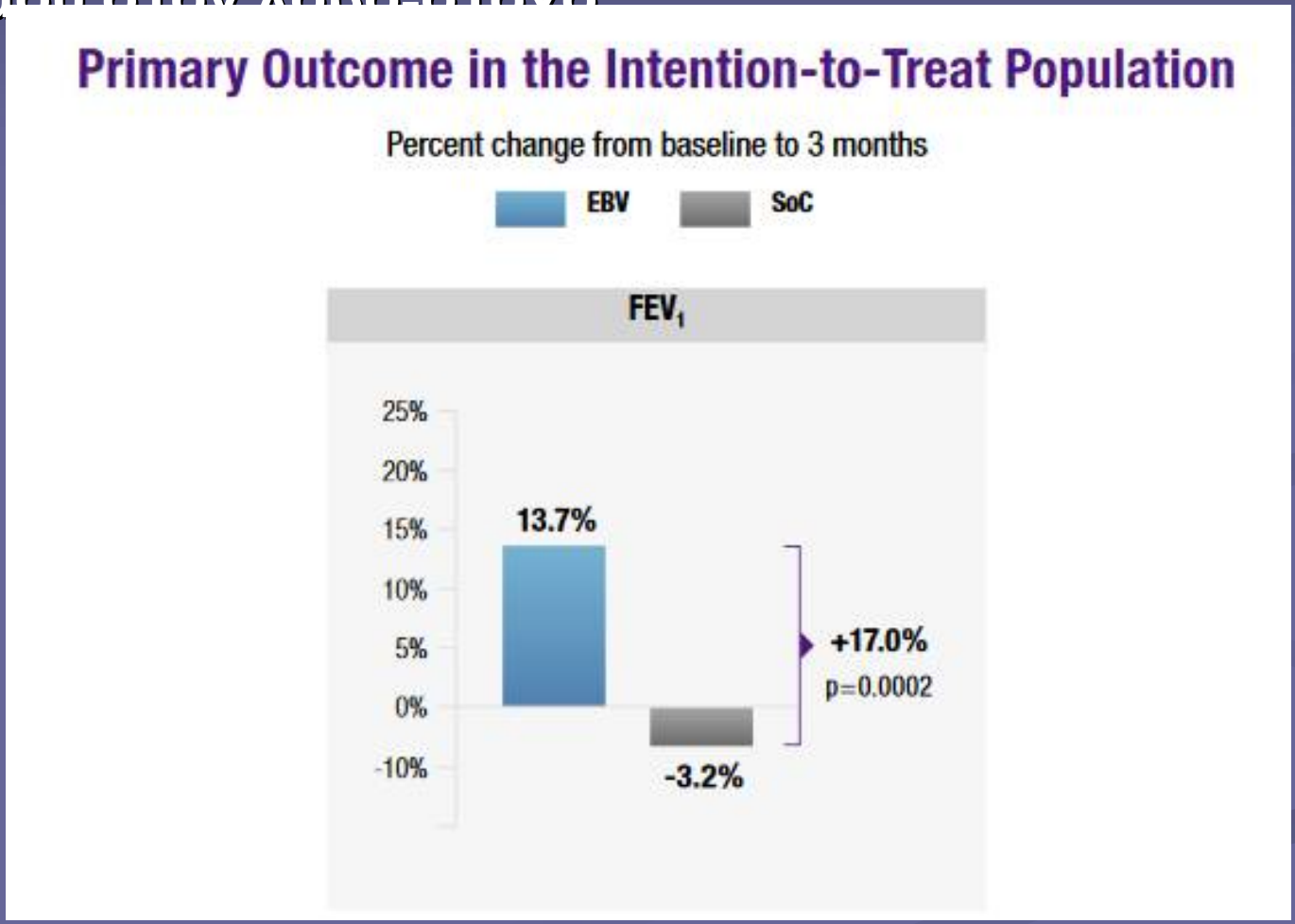
If persistent pneumothorax occurs……..




Pneumothorax
X
Large
Symptomatic
Small
Asymptomatic
Place Chest Drain
prefer small size
place with up to 20 cm of H_2O suction
Symptomatic or enlarging
Observe – repeat X-ray 2-4 hours
Stable with resolution
Unstable
Remove all valves
Stable with airleak continuing > 7 days
Remove one valve (preferably most proximal)
Airleak stops
Discontinue drain
Consider valve replacement in 6 weeks
Airleak continues > 48 hours
Remove all valves
Airleak stops
Discontinue drain
Consider valve replacement in 6 weeks
Airleak continues > 48 hours
Consider pleurodesis or surgical intervention
Lung Re-expansion confirmed on X-ray
Airleak stops
Discontinue drain
Expansion deficit of the lung with or without air leak > 96 hrs
Remove one valve (preferably most proximal)
Re-expansion
Discontinue drain
Consider valve replacement in 6 weeks
Lack of re-expansion within 48 hrs
Remove all valves
Discontinue drain

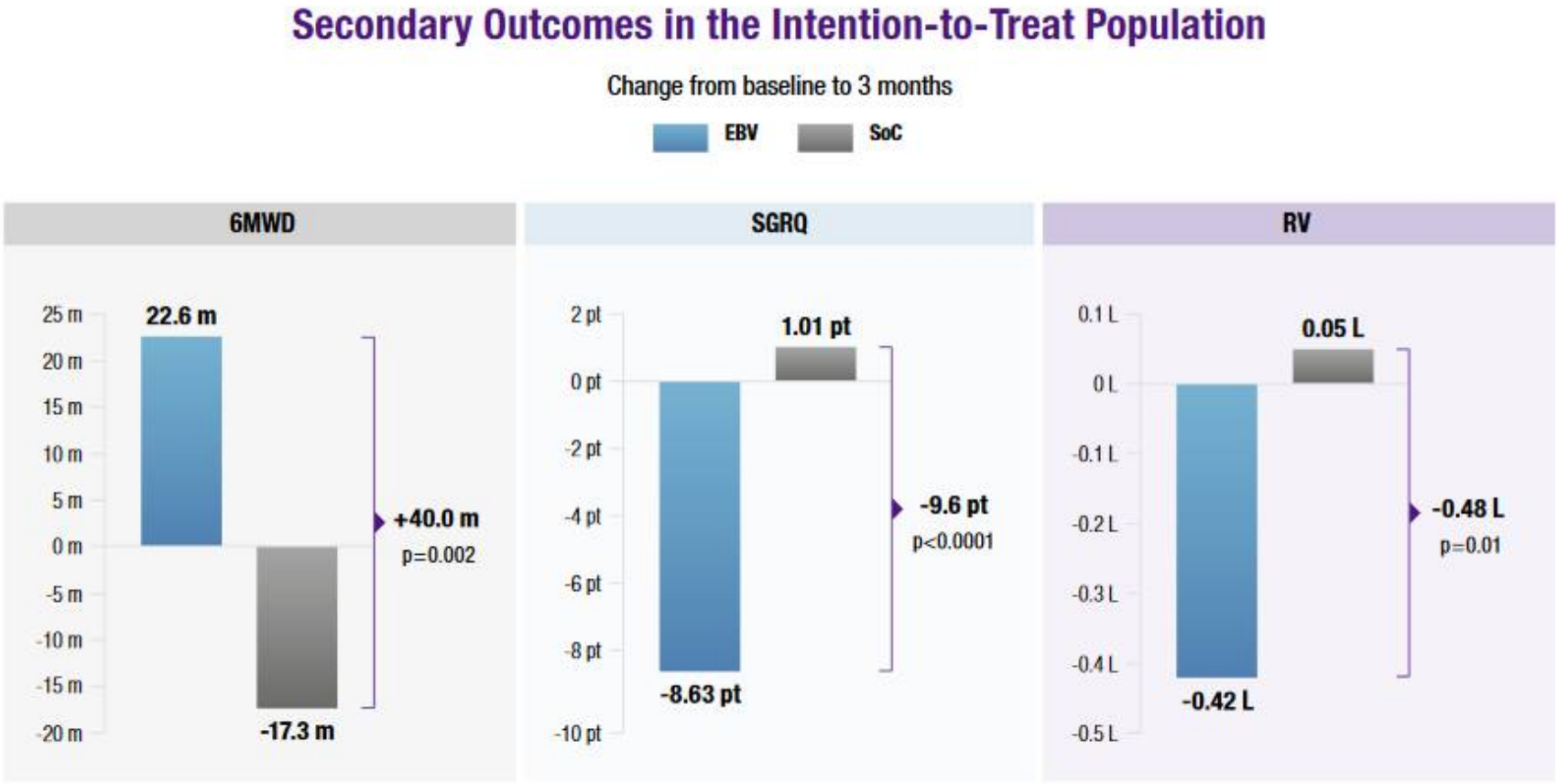
ΟΜΟΙΟΓΕΝΕΣ ΕΜΦΥΣΗΜΑ: IMPACT Study

Τυχαιοποιημένη μελέτη, 93 ασθενείς με σοβαρο, ομοιογενές εμφύσημα και απουσία παράπλευρου αερισμού στον λοβό-στόχο



Valipour A, et al. Am J Respir Crit Care Med. 2016.

IMPACT Study:



Valipour A, et al. Am J Respir Crit Care Med. 2016.

ANAMENETAI: LIBERATE trial: RCT 190 patients enrolled, 2:1

PULMONX COMPLETES ENROLLMENT IN U.S. PIVOTAL TRIAL OF ZEPHYR® ENDOBRONCHIAL VALVE

Redwood City, Calif. – October 5, 2016 – Pulmonx, a leader in interventional pulmonology, today announced completion of enrollment in its pivotal IDE study – the LIBERATE Trial – a randomized, controlled, multi-center study of the Zephyr® Endobronchial Valve (EBV) in patients with severe emphysema, a form of chronic obstructive pulmonary disease (COPD). Results from the LIBERATE Trial will support approval of the device for use in the U.S.

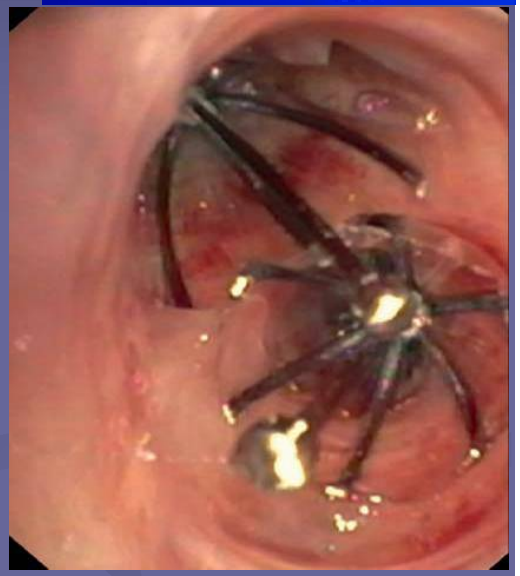
Zephyr EBVs are tiny, minimally-invasive, one-way valves placed in select airways of the lungs to occlude diseased regions and reduce lung hyperinflation. As a result, the remaining healthier regions may function more efficiently, enabling better breathing and an improved quality of life for patients.

The LIBERATE Trial enrolled 190 patients at 24 centers to evaluate the safety and effectiveness of the Zephyr EBV versus optimal medical management, with patients randomized 2:1 Zephyr EBV versus control. The primary outcome to be evaluated at one year is Forced Expiratory Volume in one second (FEV_1, an objective measure of breathing function). Secondary outcomes are volume reduction of the treated lobe of the lung, the Six Minute Walk Distance (6MWD, a measure of exercise tolerance) and the St. George's Respiratory Questionnaire (SGRQ, a measure of quality of life).

"The Zephyr EBV is the most studied endoscopic lung volume reduction device globally and is considered first-line therapy by leading physicians outside of the U.S.," said Pulmonx Chief Executive Officer Glen French. "Completing enrollment in this important trial moves us one step closer to making this proven treatment available to U.S. patients who have few options today."

pulmonX®

Spiration Intrabronchial Valves (IBV) - Inferior Results



Multicenter pilot study of a bronchial valve for treatment of severe emphysema

91 pts, 609 valves . 57% 12m response rate.

Significant improvement in SGRQ. 12% PTX

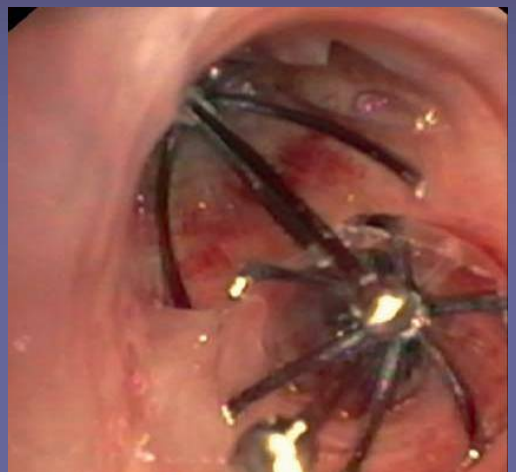
Sterman DH et al. Respiration 2010;79:222-233

37 vs 36 pts. Bilateral upper lobe treatment with bronchial valves without complete lobar occlusion was safe but not effective in the majority of patients.

ERJ 2012;39:1319-1325

Inferior Results

Spiration Intrabronchial Valves (IBV)



Multicentre European study for the treatment of advanced emphysema with bronchial valves

Eur Respir J 2012; 39: 1319–1325

ve for

treatment of severe emphysema. **Respiration 2010;79:222-233**

91 pts, 609 valves

37 vs 36 pts. Bilateral upper lobe treatment with bronchial valves without complete lobar occlusion was safe but not effective in the majority of patients.

- improvement in SGRQ: 12 % vs 1 %

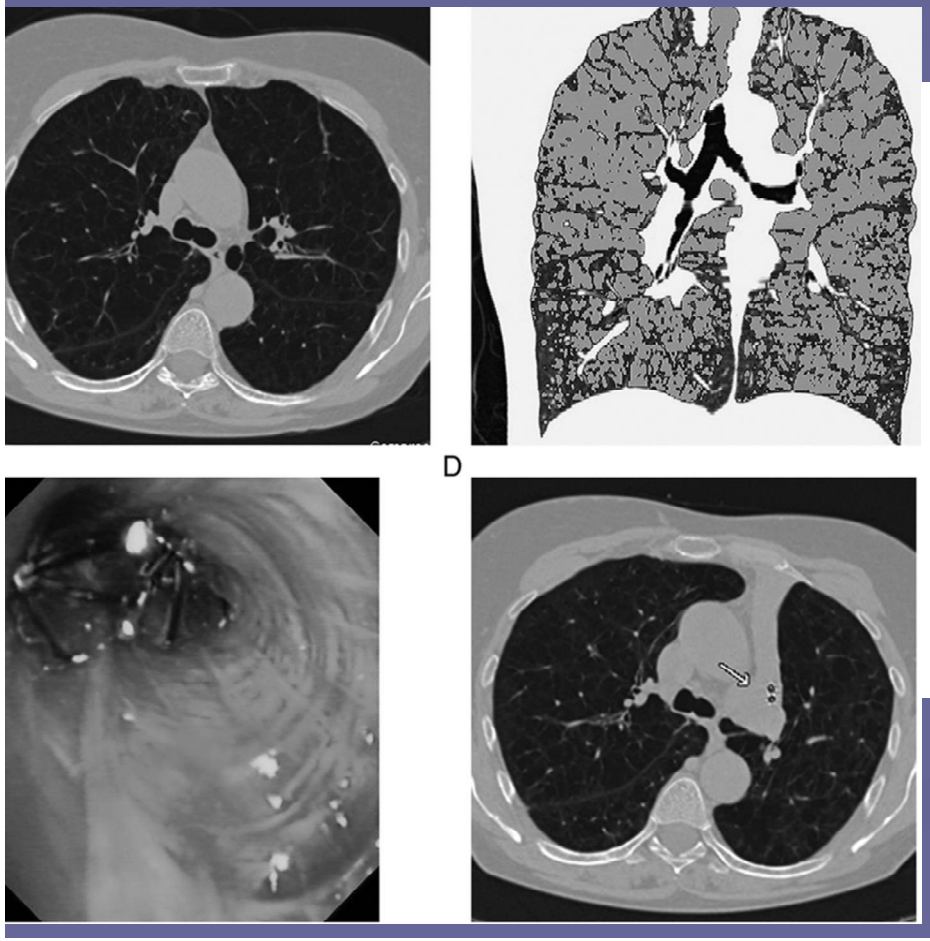
CHEST

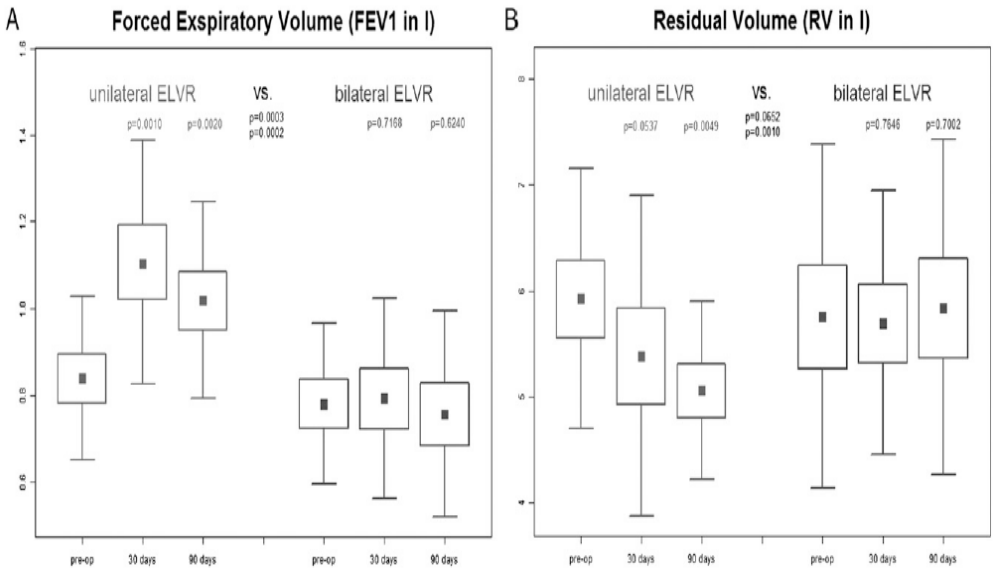
Chest. 2012;142(4):900-908. doi:10.1378/chest.11-2886

COPD

Complete Unilateral vs Partial Bilateral Endoscopic Lung Volume Reduction in Patients With Bilateral Lung Emphysema

Ralf Eberhardt, MD; Daniela Gompelmann, MD; Maren Schuhmann, MD; Hannah Reinhardt, MD; Armin Ernst, MD, FCCP; Claus P. Heussel, MD; and Felix J. F. Herth, MD, FCCP





Overview of the principal ELVR studies*

	Study	Study design	Patient population	Time point	ΔFEV$_1$	Δ6-MWT	ΔSGRQ	ΔTLVR
Valves	Sciurba et al. 2010: „VENT" (9)	Randomized, controlled	Treatment group (n = 214)	6 months	4,3%	9,3 m	−2,8 pts	–
	Herth et al. 2012: „Euro-VENT" (10)	Randomized, controlled	Treatment group (n = 111)	6 months	7 ± 20%	15 ± 91 m	−5 ± 14 pts	–
			Subgroup with complete fissure, complete lobar occlusion (n = 20)		26 ± 24%	22 ± 38%	−10 ± 15 pts	80%
	Herth et al. 2013: „Chartis-Study" (20)	Prospective, noncontrolled	CV negative (n = 51)	1 month	16 ± 22%	24 ± 57 m	−10 ± 13 pts	56%
			CV positive (n = 29)		1 ± 15%	10 ± 57 m	−5 ± 15 pts	6%
	Eberhardt et al. 2012: „Complete unilateral vs. partial bilateral" (23)	Prospective, randomized, noncontrolled	Complete unilateral occlusion (n = 11)	3 months	21 ± 11%	49 ± 53 m	−12 ± 11 pts	–
			Partial bilateral occlusion (n = 11)		−3 ± 15%	−52 ± 81 m	2 ± 9 pts	–
	Ninane et al. 2012: „Multicenter European study" (11)	Randomized, controlled	Partial occlusion (n = 37)	3 months	−90 mL	7 m	−4 pts	7%

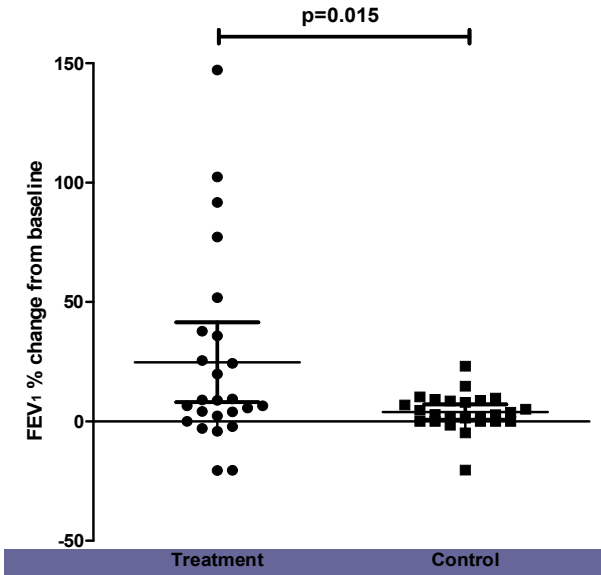
pulmonX
Interventional Pulmonology

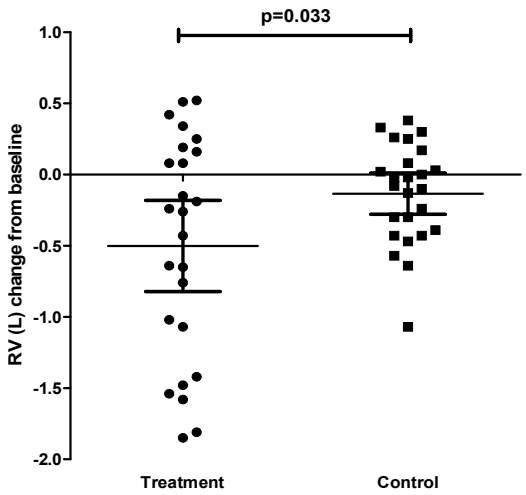
Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (BeLieVeR-HIFi)*

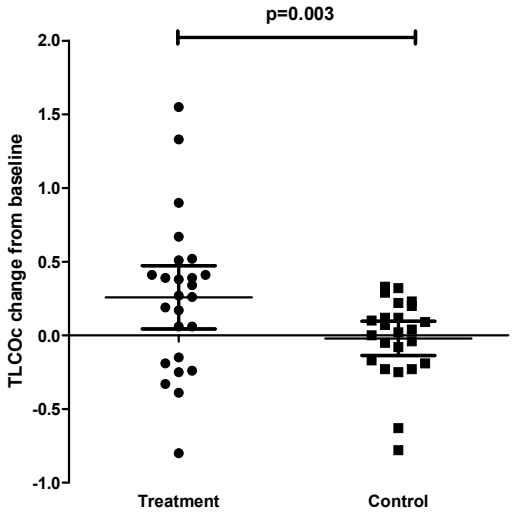
Claire Davey[1], Zaid Zoumot[1], William McNulty[1], Simon Jordan[1], Denis Carr[1], Michael Rubens[1], David Hansell[1], Michael Polkey[1], Pallav Shah[1], Nicholas Hopkinson[1]

Lung function outcomes

Mean (95% CI)	EBV Zephyr® (n=23)	Control (n=24)	Between group diff	p value
% change in FEV_1	24.8 (8.0-41.5)	3.9 (0.7-7.1)	20.9 (4.3-37.5)	0.01
change in RV (L)	-0.5 (-0.8, -0.2)	-0.1 (-0.3-0.0)	-0.4 (-0.7-0.0)	0.03
change in TLCO	3.1 (0.6-5.6)	0.3 (-1.1-1.7)	2.8 (0.3-5.6)	0.05







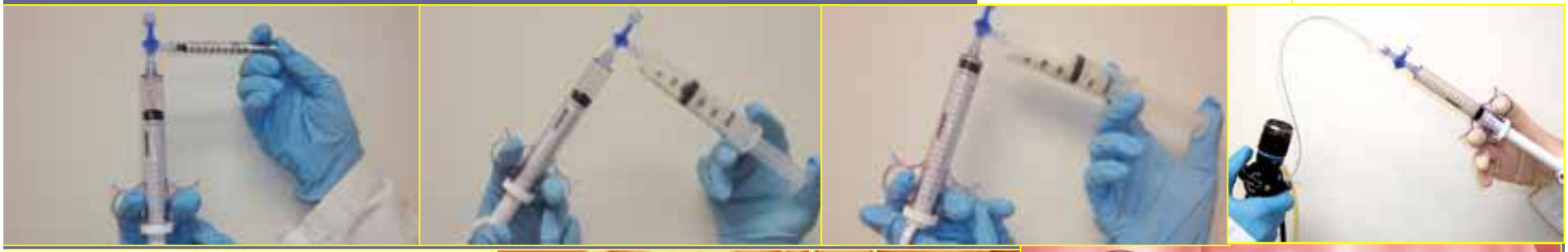
Β. Τροποποίηση πνευμ. παρεγχύματος : 1. Polymer sealant LVR

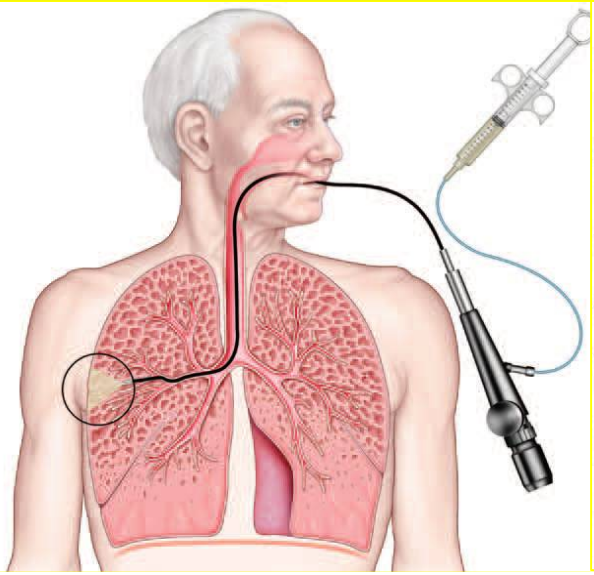
Aeriseal® system

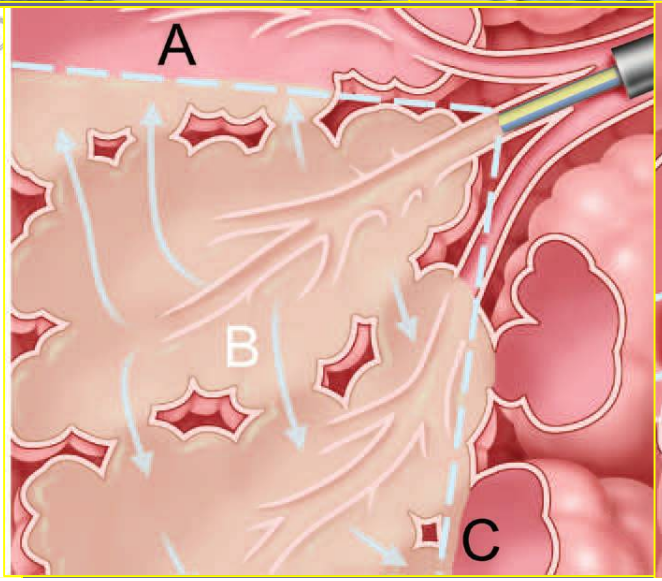
(συνθετικός πολυμερικός αφρός)

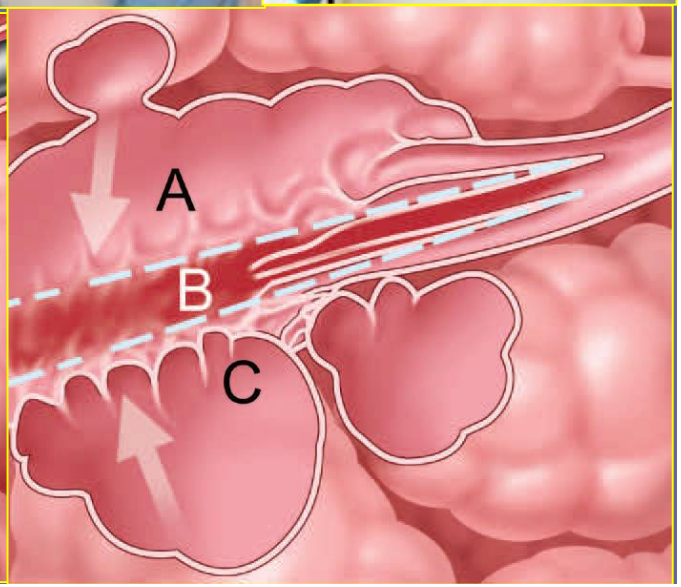
Πολυμερίζεται in situ σε 60 sec.

Προκαλεί ικανοποιητική ατελεκτασία ανεξαρτήτως παράπλευρου αερισμού









Published data:

Treatment escalation study Herth et al Expert Rev Med Devices. 2011	25 ULP, no control	• Decrease in hyperinflation (RV/TLC Δ=-7.4 ± 10.3%) • Improvement in spirometry parameters at 6 months : • FEV_1 +15.9 ± 22.6% • FVC +24.1 ± 22.7%) • SGRQ -9.9 ± 15.3 units • MRC -1.0 ± 1.04 units	Flu like syndrome/C OPD exacerbation
Herth et al, Respiration 2011	25 ULP, no control	GOLD stage III- optimal response: •ΔRV/TLC –7.4 ± 10.3% •ΔFEV1 +15.9 ± 22.6% •ΔFVC +24.1 ± 22.7% •6MWD improved 28.7 ± 59.6 m •MRCD score –1.0 ± 1.04 units. •SGRQ score improved –9.9 ± 15.3 units.	Gold IV not so good response
Single session bilateral treatment study CHEST 2012	20 ULP and homogeneous, no control	• RV/TLC -6.1 ± 15.5% • ΔFEV_1 31 ± 32,7%, • ΔFVC 13,8 ± 19,4%) • SGRQ -11.2 ± 12.7 U • MRC score (-0.5 ± 0.78U).	

Respiration

Respiration 2011;82:36–45
DOI: 10.1159/000322649

Received: July 20, 2010
Accepted after revision: November 7, 2010
Published online: January 11, 2011

Treatment of Advanced Emphysema with Emphysematous Lung Sealant (AeriSeal®)

F.J.F. Herth[a] D. Gompelmann[a] F. Stanzel[b] R. Bonnet[c] J. Behr[d] B. Schmidt[e]
H. Magnussen[f] A. Ernst[a, g] R. Eberhardt[a]

- In the cohort of 25 pts with inhomogeneous emphysema, patients with **GOLD stage III had better response** in 3 months follow up: (ΔRV/TLC –7.4 ± 10.3%, ΔFEV1 +15.9 ± 22.6% και ΔFVC +24.1 ± 22.7%).
- 6MWD increased by 28.7 ± 59.6 m, MRCD score by –1.0 ± 1.04, SGRQ score by –9.9 ± 15.3 units. GOLD stage IV pts did not improve as much.

CHEST

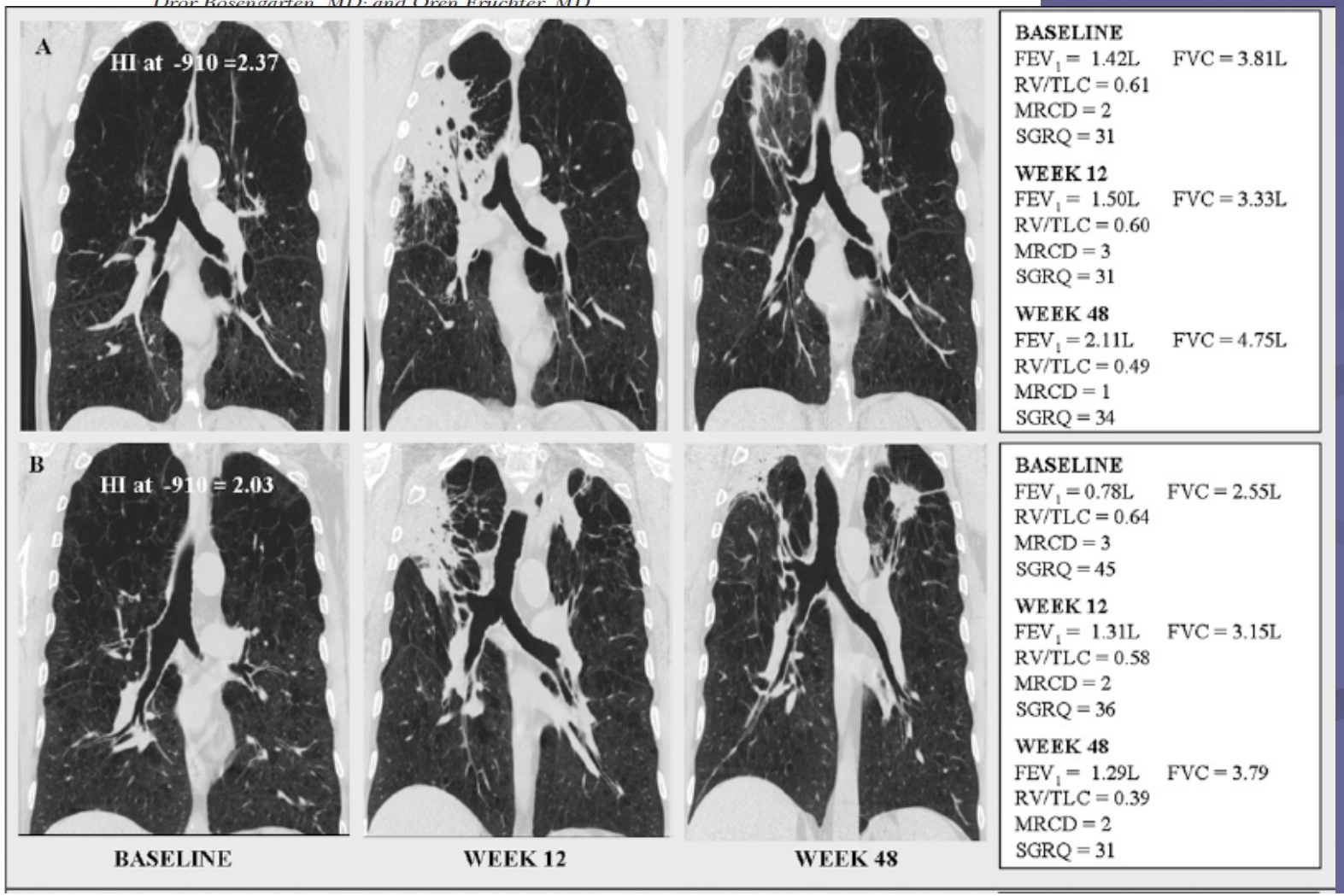
Original Research

COPD

Bilateral Endoscopic Sealant Lung Volume Reduction Therapy for Advanced Emphysema

Mordechai R. Kramer, MD, FCCP; Yael Refaely, MD; Nimrod Maimon, MD; Dror Rosengarten, MD; and Oren Fruchter, MD

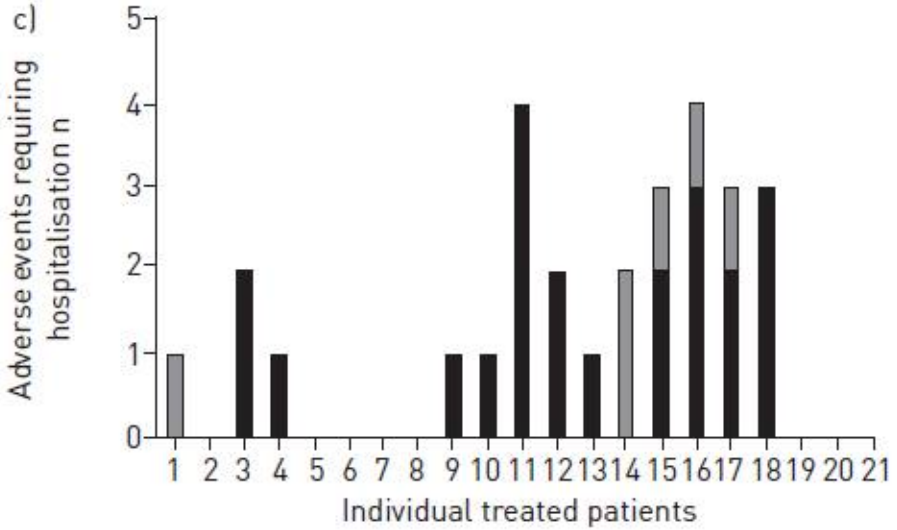
CHEST 2012; 142(5):1111–1117

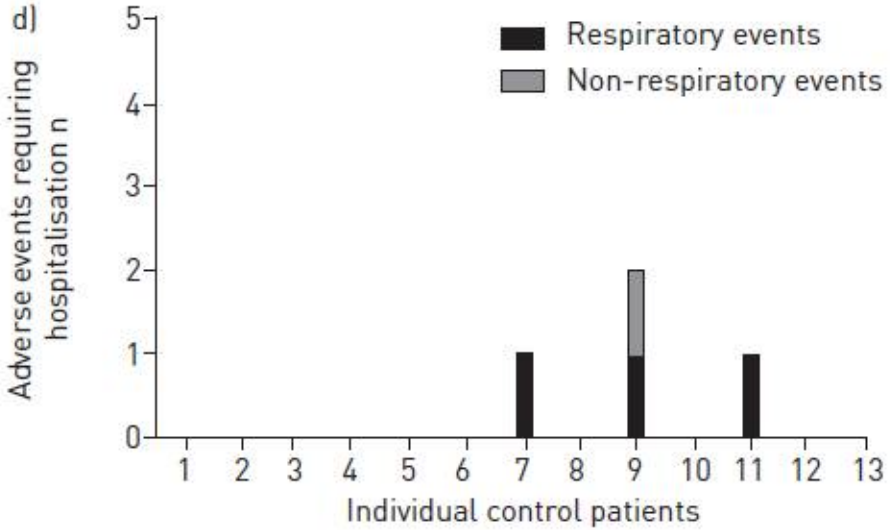


Eur Respir J. 2015 Apr 2. [Epub ahead of print]

ASPIRE

A randomised trial of lung sealant *versus* medical therapy for advanced emphysema





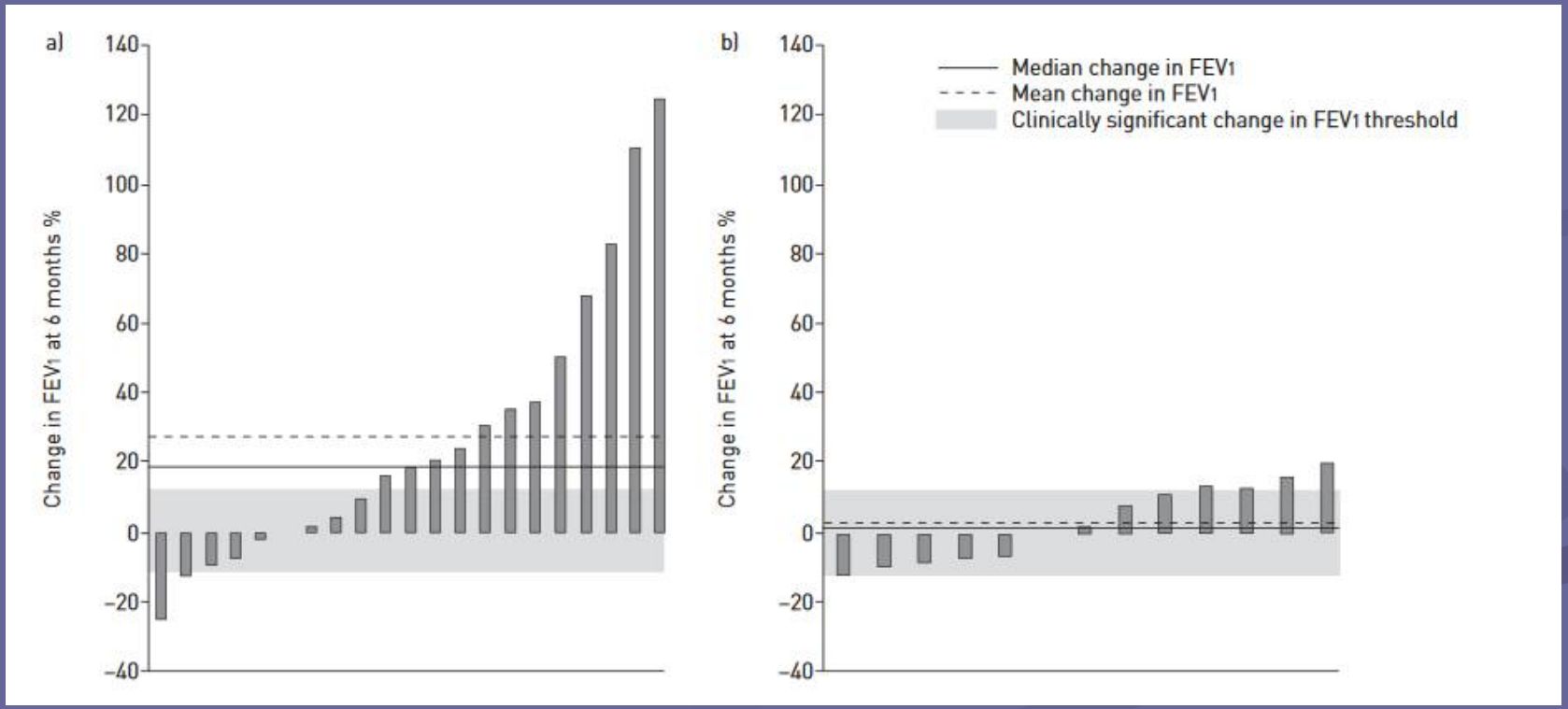
Δ from baseline	6m Treatment G	6m Control G	p
FEV1(% ; mL)	26±42 %; 174±317mL	3±11; 31±145	0.03
SGRQ(U)	-13±15	-3±6	0.02
MRCD(U)	-0.6±1.2	-0.5±0.7	0.61
6MWT(m)	16±52	-17±46	0.08

Subjects n
FEV1#
SGRQ¶
mMRC+
6MWD§

Data are p
George's R
6-min walki
FEV1 from b
[25]; §: MCID 26 m increase from baseline [27].

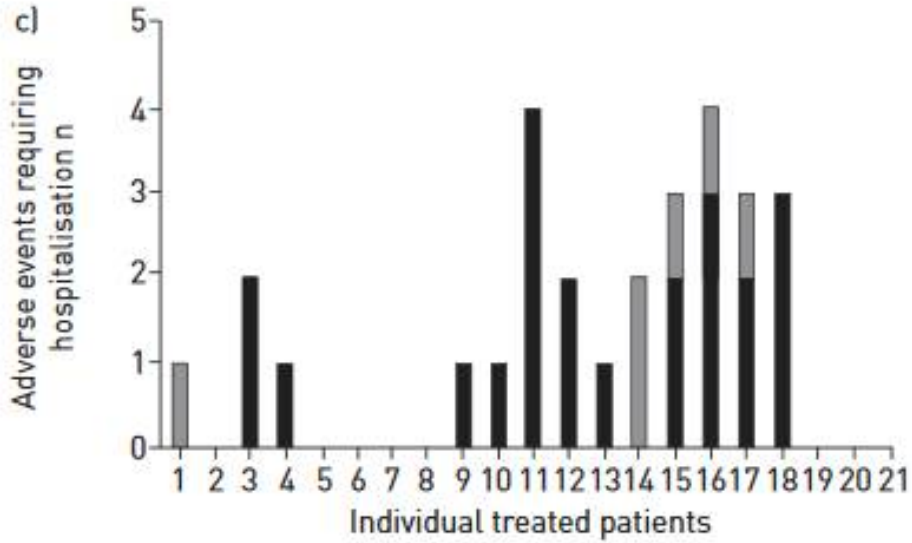
ASPIRE

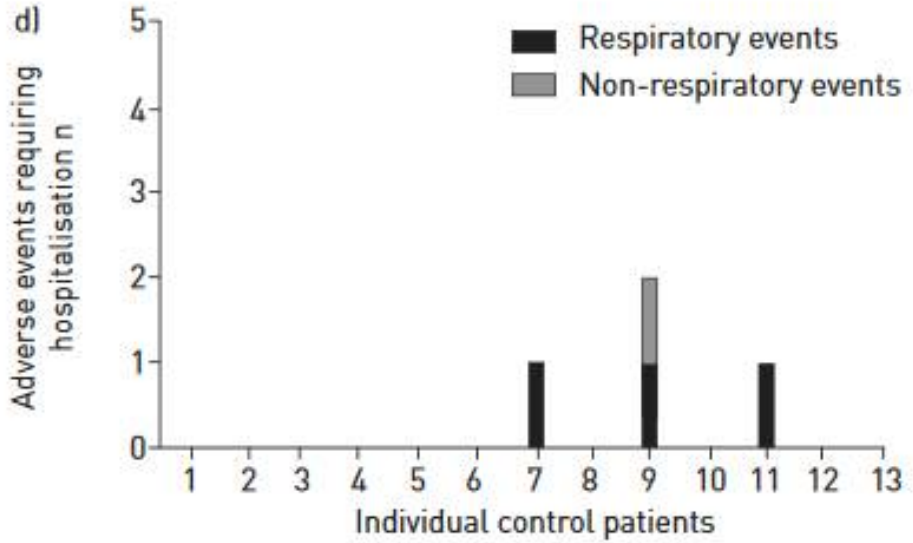
- 61 ασθενείς με σοβαρό εμφύσημα ανω λοβών
- Τυχαιοποιημένοι σε Aeriseal ή συντηρητική αγωγή
- Endoints: Change in FEV_1 (18.9% vs 1.3%) , SGRQ (-12 vs 0) , 6MWT improvement (31m vs -22m), mMRC (NS)
- >50% of treated patients had a MCID in FEV_1 at 6 months *versus* 15% of control patients



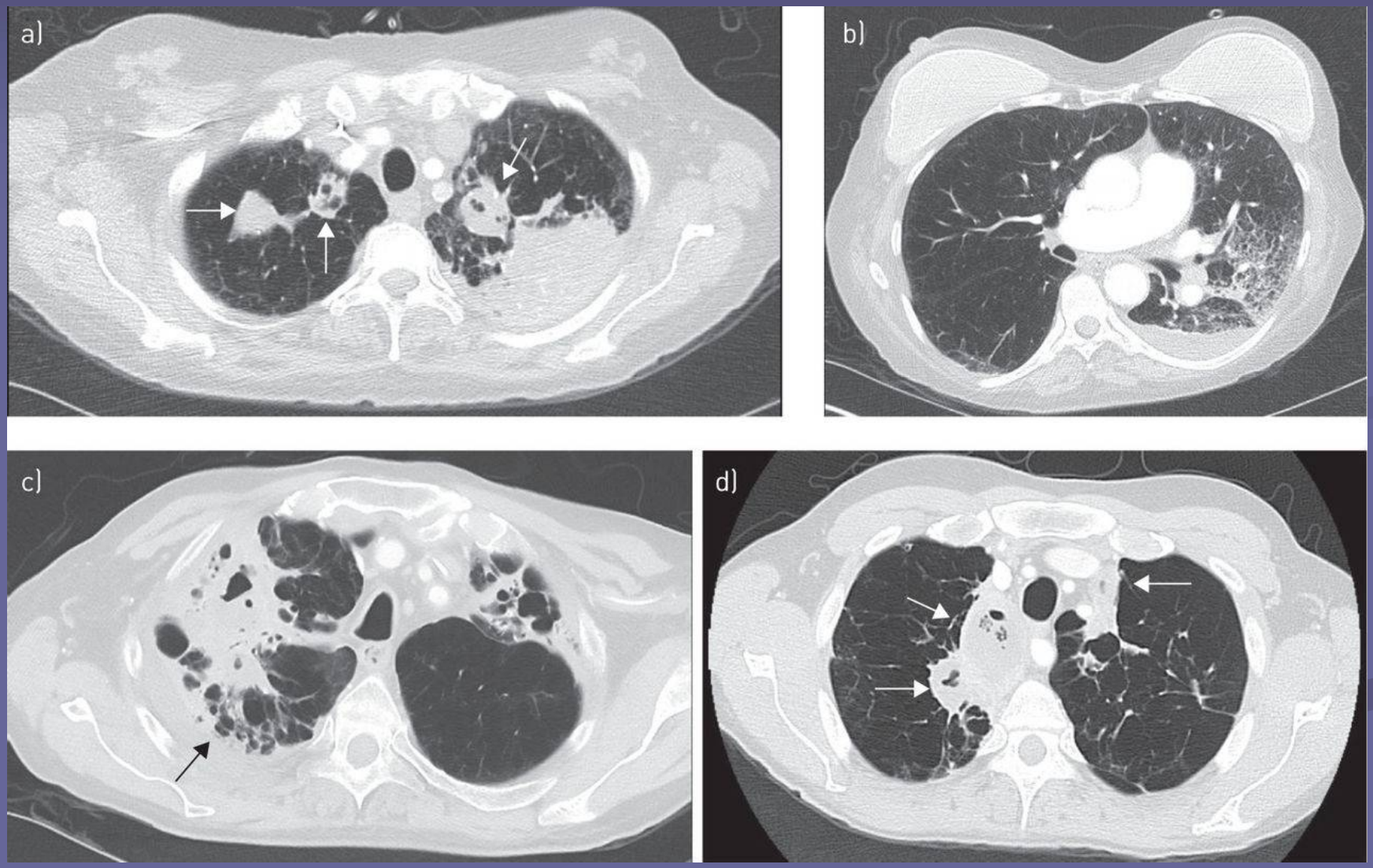
European Respiratory Journal 2015 46: 651-662

- 44% of treated patients experienced adverse events requiring hospitalisation (2.5-fold more than control, p=0.01), with two deaths in the treated cohort.
- Treatment responders tended to be those experiencing respiratory adverse events.
- Treatment-associated pulmonary complications, including pulmonary infiltrate, pleural effusion and possible lung abscess.





European Respiratory Journal 2015 46: 651-662


a)
b)
c)
d)

Products in Development

To improve the lives of patients suffering from lung disease, Pulmonx remains focused on developing life-changing, cost-effective technologies.

AeriSeal® System – Coming Soon

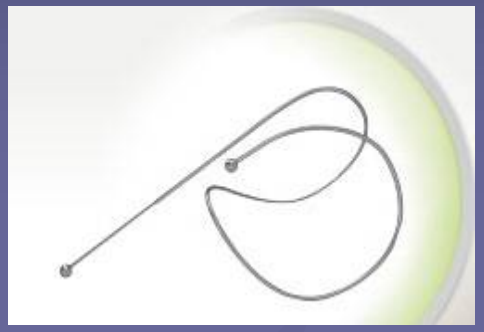
The AeriSeal treatment uses a polymeric foam to block diseased regions in the lung to achieve volume reduction and improve breathing function. The treatment is designed for patients with emphysema and is independent of collateral ventilation. AeriSeal received CE Mark approval at the end of 2015. Pulmonx is continuing to develop the post-market surveillance protocols and expects to be re-introducing the technology in 2017.

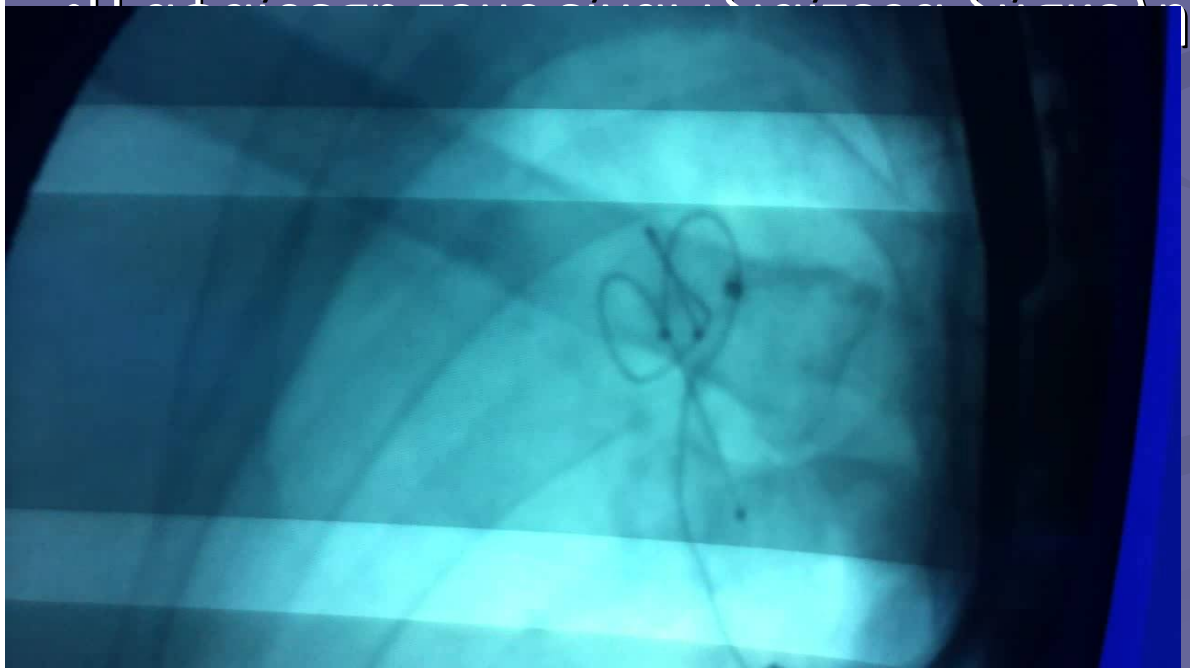
pulmonX®

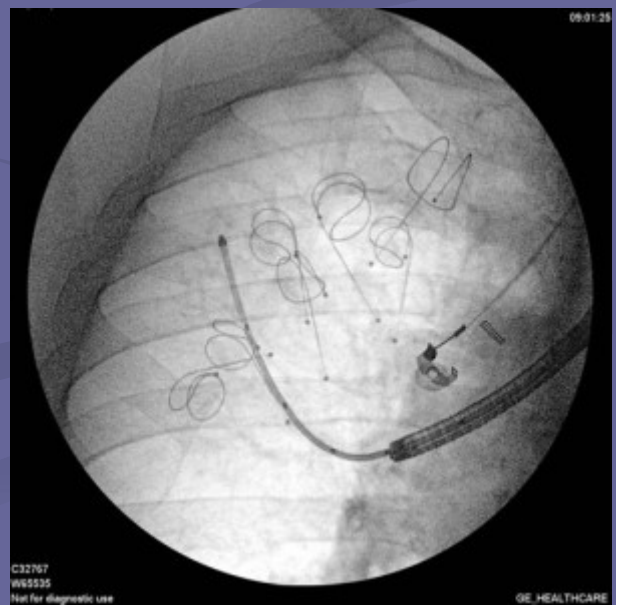
Β. Τροποποίηση πνευμ. παρεγχύματος :

2. Ενδοβρογχικά Ελάσματα από nitinol– Pneum RX®

- Τοποθέτηση υπό ακτινοσκοπικό έλεγχο
- Δεν επηρεάζονται από τον παράπλευρο αερισμό καθώς συμπιέζουν το παρέγχυμα
- 10 ελάσματα ανά λοβό για μείωση όγκου
- Δεν προτείνονται σε μεγάλη καταστροφή παρεγχύματος

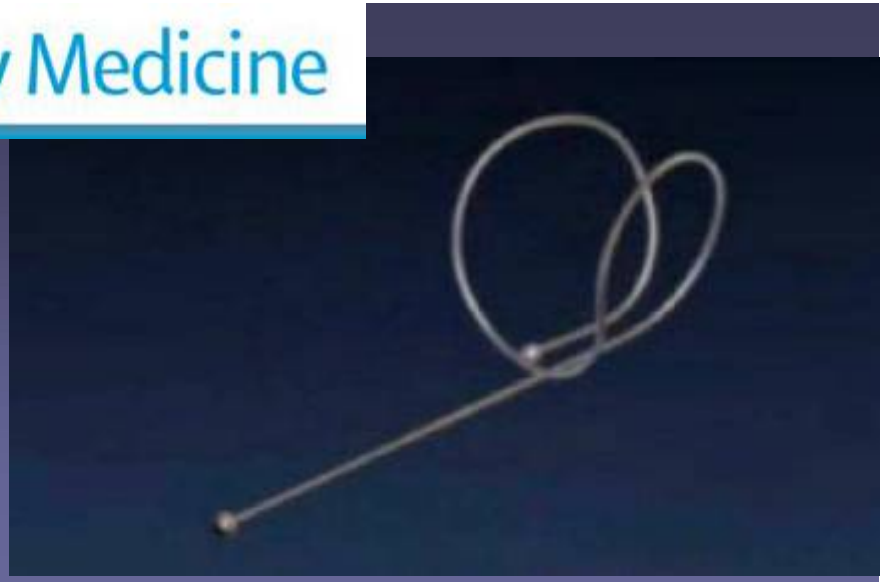






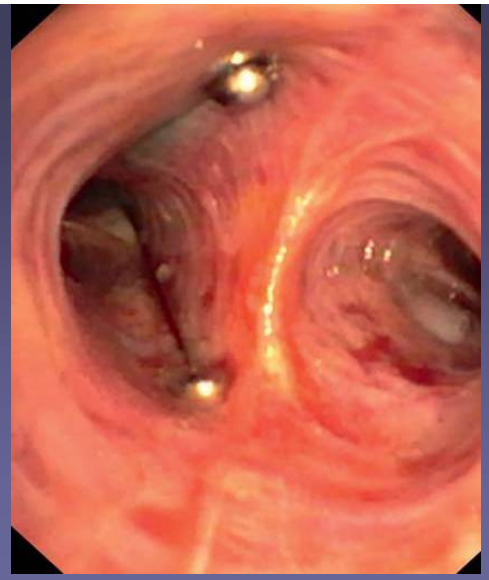
THE LANCET Respiratory Medicine

Shah PL, et al. RESET trial.
Lancet Respir.Med. 2013; ***1: 233–40.***



22 vs 23 pts randomised for coils vs medical tx.
SGRQ response at 90 days after final treatment was greater in the treatment group (**between-group difference -8·36 points p=0·04**).
FEV1, RV and 6 MWT improvement of the LVRC group was also significantly greater than in the CG.
No between-group difference in serious adverse events

Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial.
G. Deslee, K.Klooster, M. Hetzel et al.
Thorax 2014;69:980-986



Sixty patients (60.9 ± 7.5 years, FEV1 30.2 ± 6.3% pred, were bronchoscopically treated with coils (55 bilateral, 5 unilateral), with a median of 10 (range 5–15) coils per lobe.

	6 Months Overall group (N=58)	6 Months 12-month follow-up group (N=34)	12 Months 12-month follow-up group (N=34)
FEV_1, L	+0.11±0.20 (n=54, p<0.001)	+0.12±0.28 (n=33, p=0.021)	+0.11±0.30 (n=34, p=0.037)
FEV_1, % pred (% change)	+15.36±26.68 (n=54, p<0.001)	+17.81±31.71 (n=33, p=0.003)	+16.04±35.54 (n=34, p=0.017)
FVC, L	+0.20±0.53 (n=54, p=0.008)	+0.33±0.57 (n=33, p=0.002)	+0.28±0.45 (n=34, p=0.001)
RV, L	−0.65±0.90 (n=58, p<0.001)	−0.80±1.03 (n=34, p<0.001)	−0.71±0.81 (n=34, p<0.001)
RV, % pred (% change)	−11.31±15.25 (n=58, p<0.001)	−14.38±15.42 (n=34, p<0.001)	−13.75±12.65 (n=34, p<0.001)
RV/TLC	−4.51±12.19 (n=58, p=0.007)	−6.06±8.58 (n=34, p<0.001)	−3.12±15.59 (n=34, p=0.245)
6MWD, m	+29.7±74.1 (n=56, p=0.004)	+42.4±73.5 (n=34, p=0.002)	+51.4±76.1 (n=32, p=0.003)
SGRQ, points	−12.1±12.9 (n=56, p<0.001)	−10.4±15.8 (n=33, p<0.001)	−11.1±13.3 (n=32, p<0.001)
mMRC, points	−0.6±1.2 (n=58, p<0.001)	0.8±0.9 (n=34, p<0.001)	−0.7±0.8 (n=34, p<0.001)

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

Pallav L Shah, Zaid Zoumot, Suveer Singh, Stephen R Bicknell, Ewen T Ross, John Quiring, Nicholas S Hopkinson, Samuel V Kemp, for the RESET trial Study Group

Summary

Background Few treatment options exist for patients with severe emphysema. We assessed the clinical benefits and safety of lung volume reduction coils (LVRCs) for the treatment of patients with severe emphysema with hyperinflation.

Methods In a randomised study, we recruited patients with severe emphysema (aged ≥35 years) from three centres in the UK. Using a computer-generated randomisation sequence, we randomly allocated patients in a one-to-one ratio (block sizes of four and stratified by centre) to either LVRC treatment (treatment group) or best medical care (usual care group). The primary endpoint was the difference in response in the St George's Respiratory Questionnaire (SGRQ) between treatment and usual care groups at 90 days after final treatment (by intention-to-treat analysis). The trial is registered with ClinicalTrials.gov, number NCT01334307.

Findings Between Jan 27, 2010, to Oct 25, 2011, we recruited and randomly allocated 47 patients: 23 to treatment and 24 to usual care (23 patients in each group were included in the intention-to-treat analysis). SGRQ response at 90 days after final treatment was greater in the treatment group than it was in the usual care group (between-group difference in change from baseline −8·36 points [95% CI −16·24 to −0·47]; p=0·04). We detected no between-group difference in serious adverse events.

Interpretation Our findings suggest that treatment with endobronchial coils can improve quality of life for patients with severe emphysema and hyperinflation.

Published Online
April 23, 2013
http://dx.doi.org/10.1016/S2213-2600(13)70047-X

See Online/Comment
http://dx.doi.org/10.1016/S2213-2600(13)70051-1

The National Institute for Health Research Respiratory Biomedical Research Unit, Royal Brompton, Harefield NHS Foundation Trust, and Imperial College, London, UK (P L Shah MD, Z Zoumot MBBS, N S Hopkinson PhD, S V Kemp MBBS); **Chelsea and Westminster Hospital, London, UK** (P L Shah, Z Zoumot, S Singh PhD, S V Kemp); **Gartnavel General Hospital, Glasgow, UK** (S R Bicknell MD, E T Ross MD); **and QST Consultations Ltd, Allendale**

Shah PL, et al. RESET trial: randomized, 22 pts vs 23 controls

	Treatment	Usual care	Between group difference in change from baseline	P value
Primary outcome				
SGRQ	-8.11(-13.83 to -2.39)	0.25 (-5.58 to 6.07)	-8.36 (-16.24 to -0.47)	0.04
Secondary outcome				
TLC (L)	-0.24 (-0.38 to -0.10)	-0.13 (-0.27 to 0.01)	-0.11 (-0.29 to 0.07)	0.22
RV (L)	-0.51 (-0.73 to -0.30)	-0.20 (-0.42 to 0.02)	-0.31 (-0.59 to -0.04)	0.03
6 MWT	51.15 (27.65 to 74.66)	-12.39 (-36.61 to 11.83)	63.55 (32.57 to 94.53)	<0.001
%change in FEV1	14.19 (6.84 to 21.55)	3.57 (-4.02 to 11.17)	10.62 (1.12 to 20.12)	0.03
mMRC	-0.24 (-0.57 to 0.09)	-0.09 (-0.44 to 0.26)	-0.15 (-0.60 to 0.30)	0.5

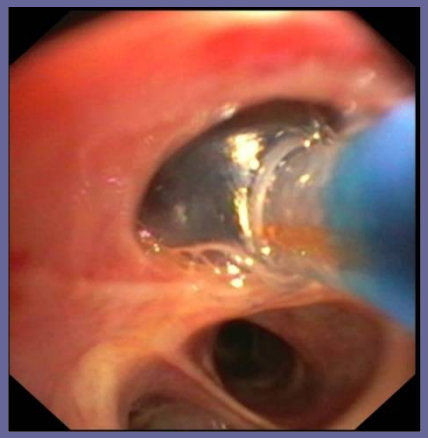
No between-group difference in serious adverse events

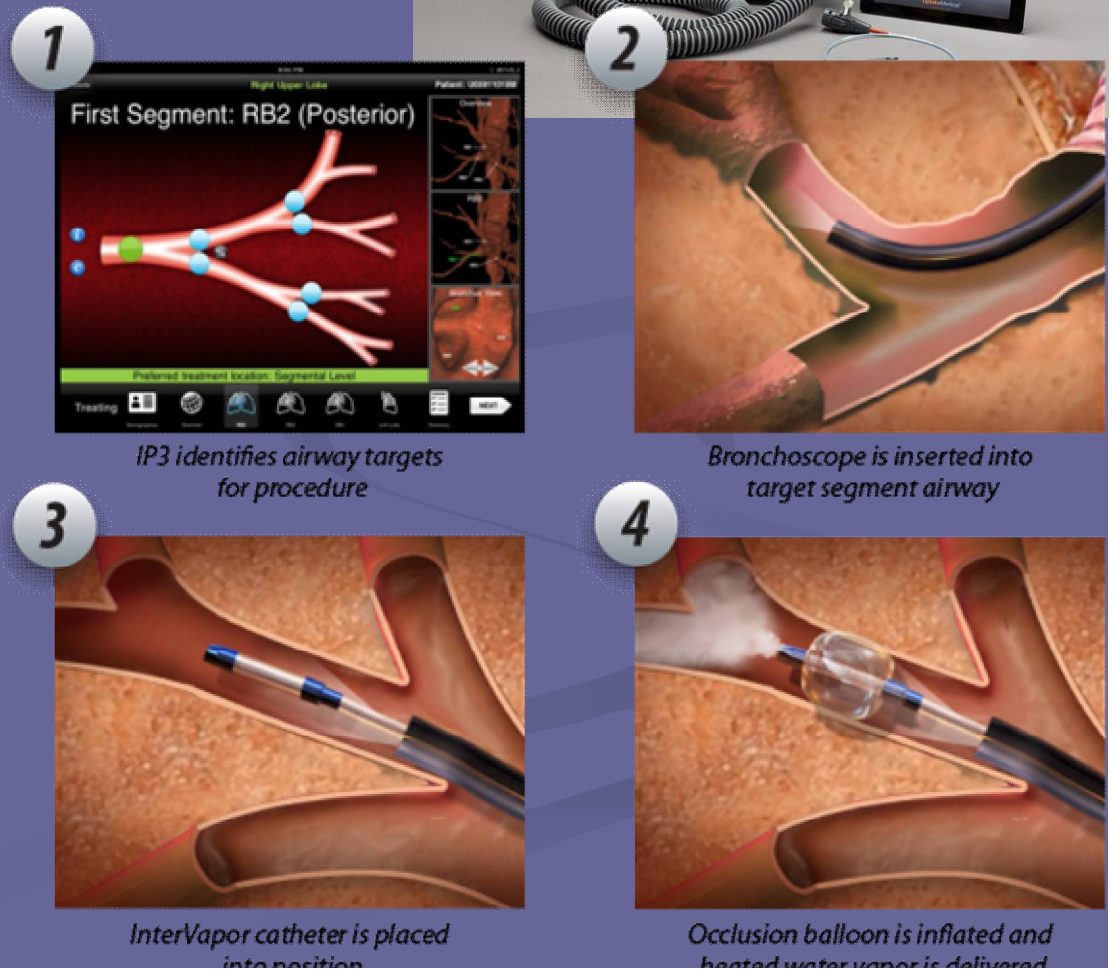
Lancet Respir.Med. 2013; 1: 233–40.

Β. Τροποποίηση πνευμ. παρεγχύματος :

3. Bronchoscopic Thermal Vapor Ablation InterVapor® System

- **Διοχετευση ατμού** (5-10 cal/gr) **με καθετήρα στα επιλεγμένα τμήματα**
- **Θερμική βλάβη που προκαλεί ουλοποίηση και ατελεκτασία**
- **Δεν επηρεάζεται από παράπλευρο αερισμό**





IP3 identifies airway targets for procedure

Bronchoscope is inserted into target segment airway

InterVapor catheter is placed into position

Occlusion balloon is inflated and heated water vapor is delivered

Vapor Ablation in the Presence of Incomplete Fissures: 12-Month Results from the STEP-UP Randomized Controlled Study

ULP- E, 45 patients treated, 24 control, One upper lobe per session

	Bronchoscopic vapour ablation group	Control group	Difference between groups (95% CI)	p value
FEV_1 (mL)	70·5 (SD 179·9)	−32·2 (SD 114·3)	102·6 (30·5 to 174·8)	0·0060
FVC (mL)	110·2 (SD 395·4)	−128·3 (SD 409·2)	238·5 (28·6 to 448·3)	0·0269
Residual volume (mL)	−159·1 (SD 572·4)	78·3 (SD 470·0)	−237·4 (−499·2 to 24·5)	0·0747
FRC (mL)	−163·6 (SD 564·5)	82·6 (SD 417·4)	−246·2 (−490·0 to −2·5)	0·0477
6MWT (m)	8·8 (SD 66·5)	5·1 (SD 73·4)	3·6 (−33·3 to 40·6)	0·8442

FEV_1=forced expiratory volume in 1 s. FVC=forced vital capacity. FRC=functional residual capacity. 6MWT=6 min walk test.

Table: Change in secondary endpoint measures at 12 months after vapour ablation

Shah et al, Lancet Resp Med 2016

Lung Volume Reduction with Vapor Ablation in the Presence of Incomplete Fissures: 12-Month Results from the STEP-UP Randomized Controlled Study

- 78% of treated patients were found to have 1 or more incomplete fissures adjacent to a treated lobe and were considered to be CV+

Table 1. Results for primary efficacy endpoints for patients with incomplete fissures

	Bronchoscopic vapor ablation group	Control group	Difference between groups (95% CI)	*p* value
Patients with incomplete fissures, *n*	35	19		
Δ FEV_1, %				
3 months	7.9	–1.2	9.1 (0.1 to 18.1)	0.0056
6 months	7.6	–3.4	10.9 (3.6 to 18.4	0.0024
12 months	9.2	–5.4	14.6 (3.1 to 26.7)	0.0137
Δ SGRQ-C (points)				
3 months	–7.7	–2.2	–5.5 (0.5 to –11.5)	0.0697
6 months	–6.8	–0.6	–6.1 (1.3 to –13.7)	0.1089
12 months	–9.4	–1.0	–8.4 (0.7 to –17.5)	0.0712

Respiration 2016;92:397–403

Table 3. SAEs and hospital admissions

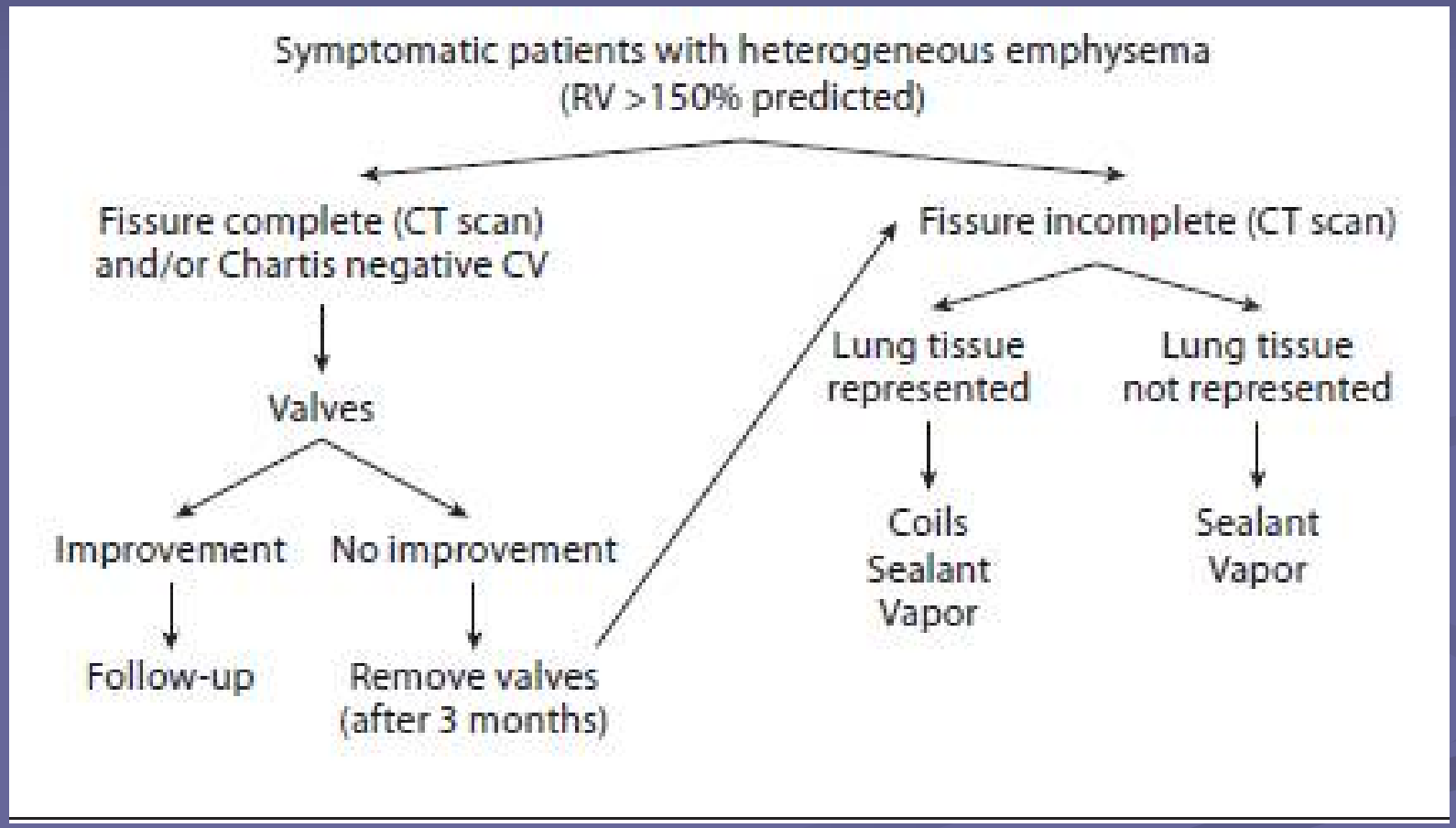
	Treatment group (n = 35)		Control group (n = 19)	
	0–180 days after treatment[1]	181–365 days after treatment[1]	0–180 days after randomization	181–365 days after randomization
COPD exacerbation	3 (9)	0	1 (5)	2 (11)
Pneumonia or pneumonitis	8 (23)	0	1 (5)	1 (5)
Pneumothorax	1[2] (3)	0	0	0
Hemoptysis	0	0	0	0
Death	1 (3)	0	0	0
Any respiratory SAE	9 (26)	0	2 (11)	3 (16)

Respiration 2016;92:397–403

Novel Modalities and Agents in Bronchoscopic Lung Volume Reduction

Grigoris Stratakos[1,*], Philip Emmanouil[1] and Stefano Gasparini[2]

Curr Drug Targets. 2013 Feb 1;14(2):253-61.



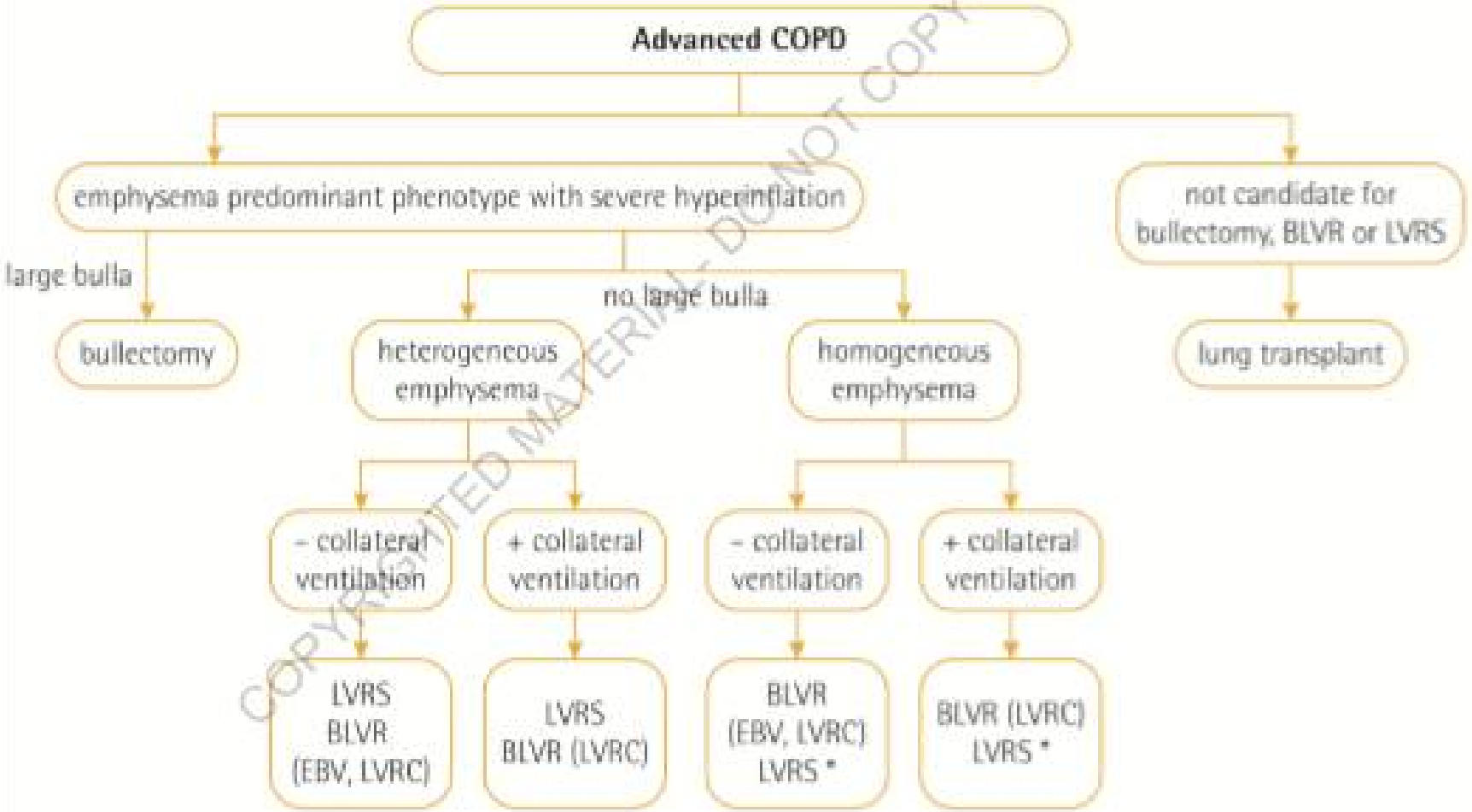
Respiration 2012;84:250–263

Intervention bronchoscopy and surgery

- Lung volume reduction surgery should be considered in selected patients with upper-lobe emphysema **(Evidence A)**.
- Bronchoscopic lung volume reduction interventions may be considered in selected patients with advanced emphysema **(Evidence B)**.
- In selected patients with a large bulla surgical bullectomy may be considered **(Evidence C)**.
- In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidate for lung volume reduction) lung transplantation may be considered for referral with at least one of the following: (1) history of hospitalization for exacerbation associated with acute hypercapnia (Pco_2 > 50 mm Hg); (2) pulmonary hypertension and/or cor pulmonale, despite oxygen therapy; or (3) FEV_1 < 20% and either DLCO < 20% or homogenous distribution of emphysema **(Evidence C)**.

GOLD guidelines 2017

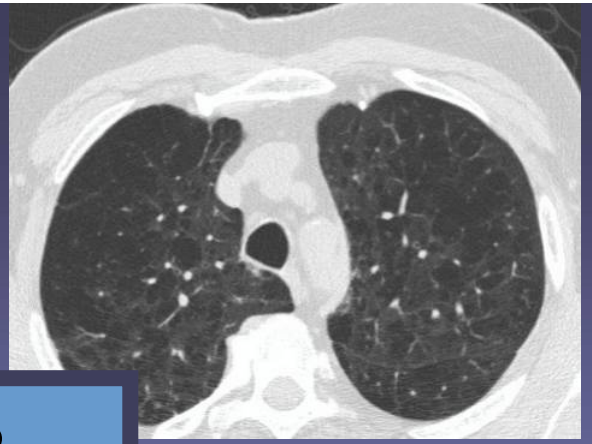
Overview of various therapies used to treat patients with COPD and emphysema worldwide. Note that all therapies are not approved for clinical care in all countries. Additionally, the effects of BLVR on survival or other long term outcomes or comparison to LVRS are unknown.

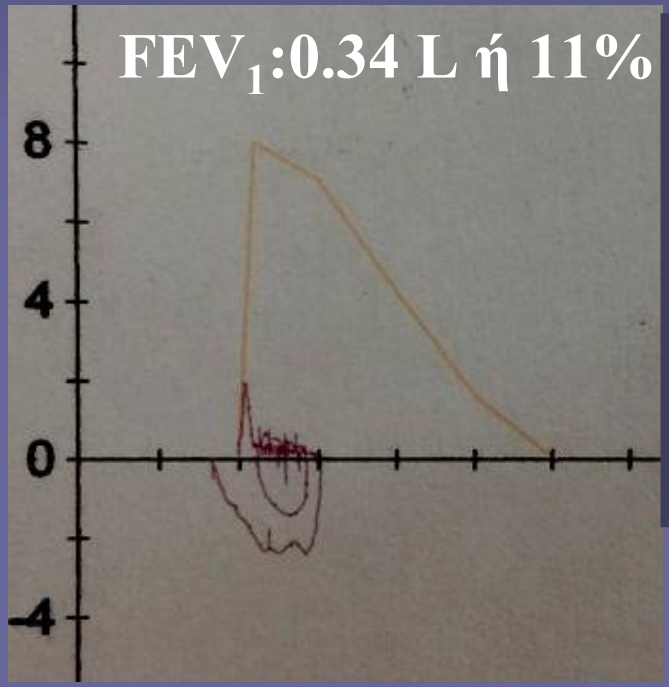


Definition of Abbreviations: BLVR, Bronchoscopic Lung Volume Reduction, EBV, endobronchial Valve, LVRS, Lung volume reduction surgery, LVRC, Lung volume reduction coil

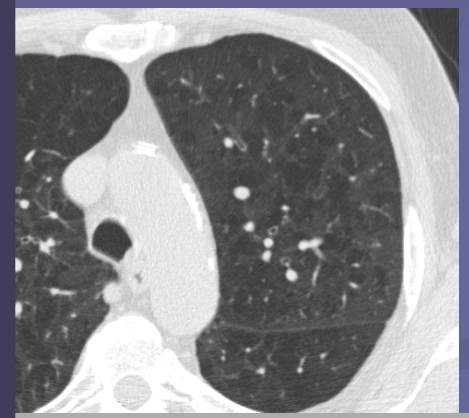
*at some but not all centers

♂, 65ετών, πρώην καπνιστής 50p.y.





SGRQ : 71,2
mMRC : 3
CAT score: 24
6mWT:106 m
Activity monitor: 574 steps

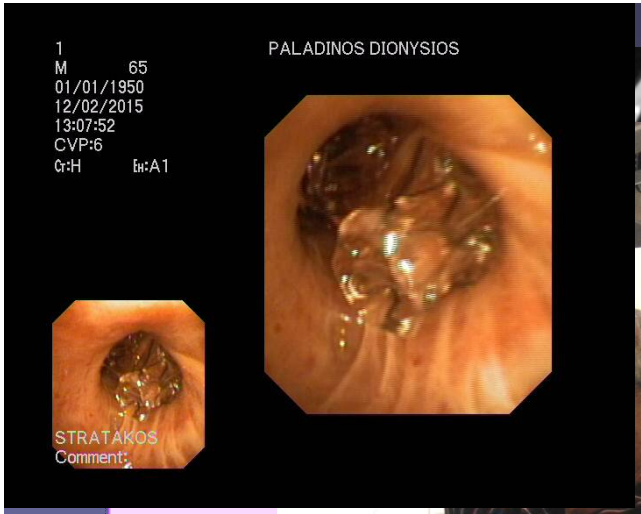


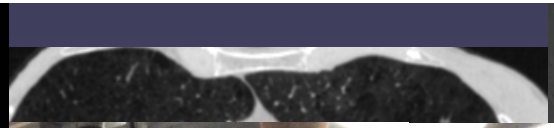
Lung Volumes

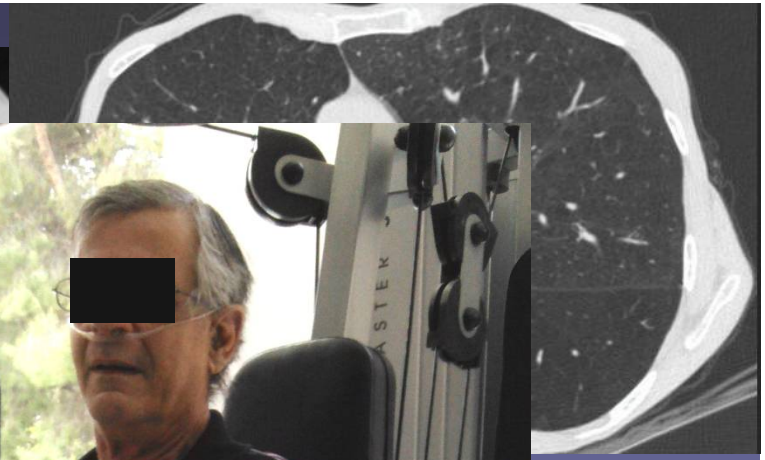
TLC	Liters	6.90	8.23	119
VC	Liters	4.23	1.05	25
RV	Liters	2.47	7.18	291
FRC PL	Liters	3.58	7.55	211
ERV	Liters	1.48	0.37	25
IC	Liters	2.96	0.68	23
RV/TLC	%	39	87	
Raw	kPa/L/sec	0.123	1.590	1296
Vtg	Liters		7.74	
sGaw	L/sec/kPa/L	2.27	0.08	4

Diffusion

DLCO	mmol/kPa.min	9.2	2.1	23
DL Adj	mmol/kPa.min	9.2	2.1	23
DLCO/VA	DLCO/L	1.33	0.75	57
DL/VA Adj	DLCO/L	1.33	0.75	57

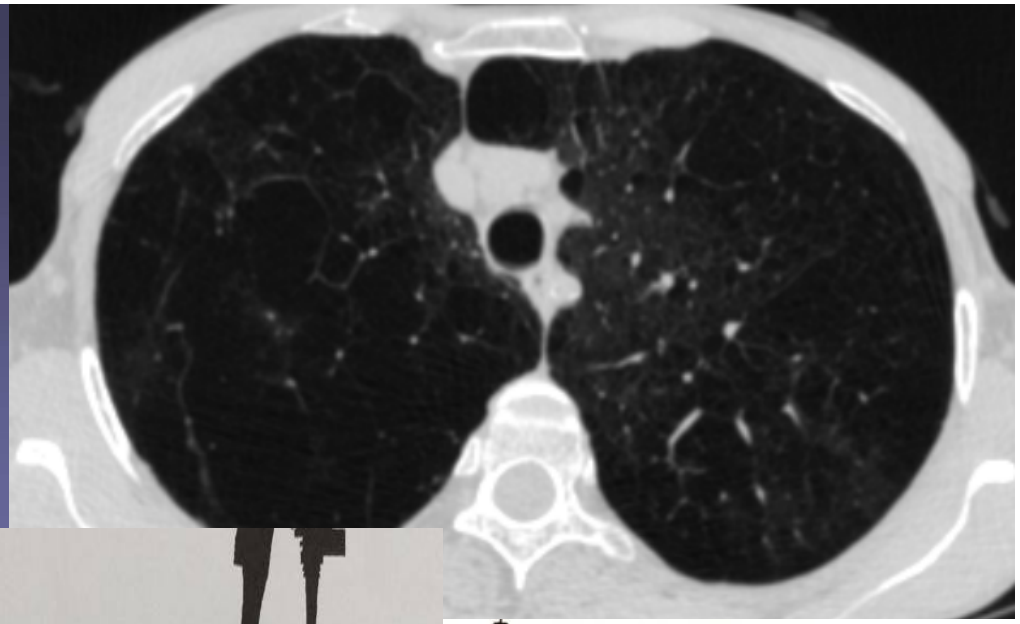






FEV1		
TLC		
RV		
6mW		
SGRQ		
mMR		
Act. Monitor	374 steps	1050 steps

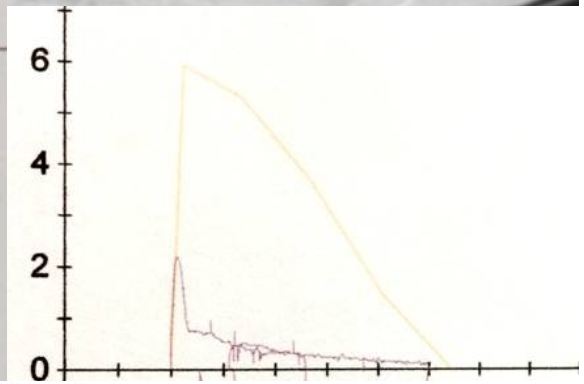
♀, 52ετών, πρώην καπνίστρια 40p.y.



ght(cm): 157
eight(kg): 38.0

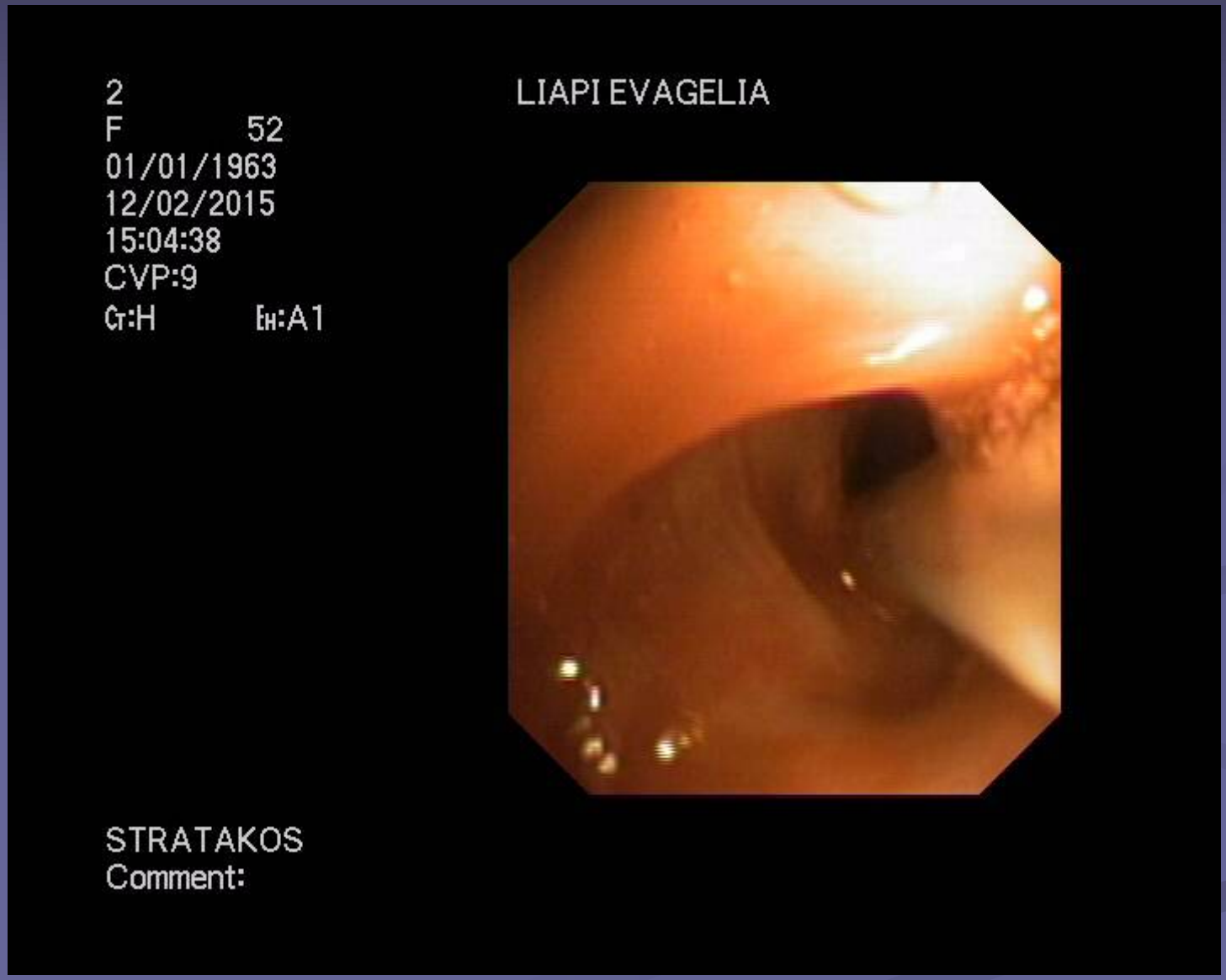
Spirometry (BTPS)

		PRED	PRE-RX BEST	%PRED
FVC	Liters	2.74	2.50	91
FEV1	Liters	2.33	0.64	27
FEV1/FVC	%	79	25	
FEF25-75%	L/sec	3.15	0.23	7
FEF75%	L/sec	1.48	0.17	11
FEF50%	L/sec	3.73	0.29	8
FEF25%	L/sec			
PEF	L/sec			
FIVC	Liters			
FEF/FIF50				



TLC	Liters	4.57	8.56	187
VC	Liters	2.71	1.95	72
RV	Liters	1.66	6.61	399
FRC PL	Liters	2.57	7.15	278
ERV	Liters	1.00	0.54	54
IC	Liters	1.99	1.41	71
RV/TLC	%	36	77	
Raw	kPa/L/sec	0.124	0.938	756
Vtg	Liters		7.30	
sGaw	L/sec/kPa/L	2.69	0.15	5

SGRQ : 40
mMRC : 3
CAT score: 24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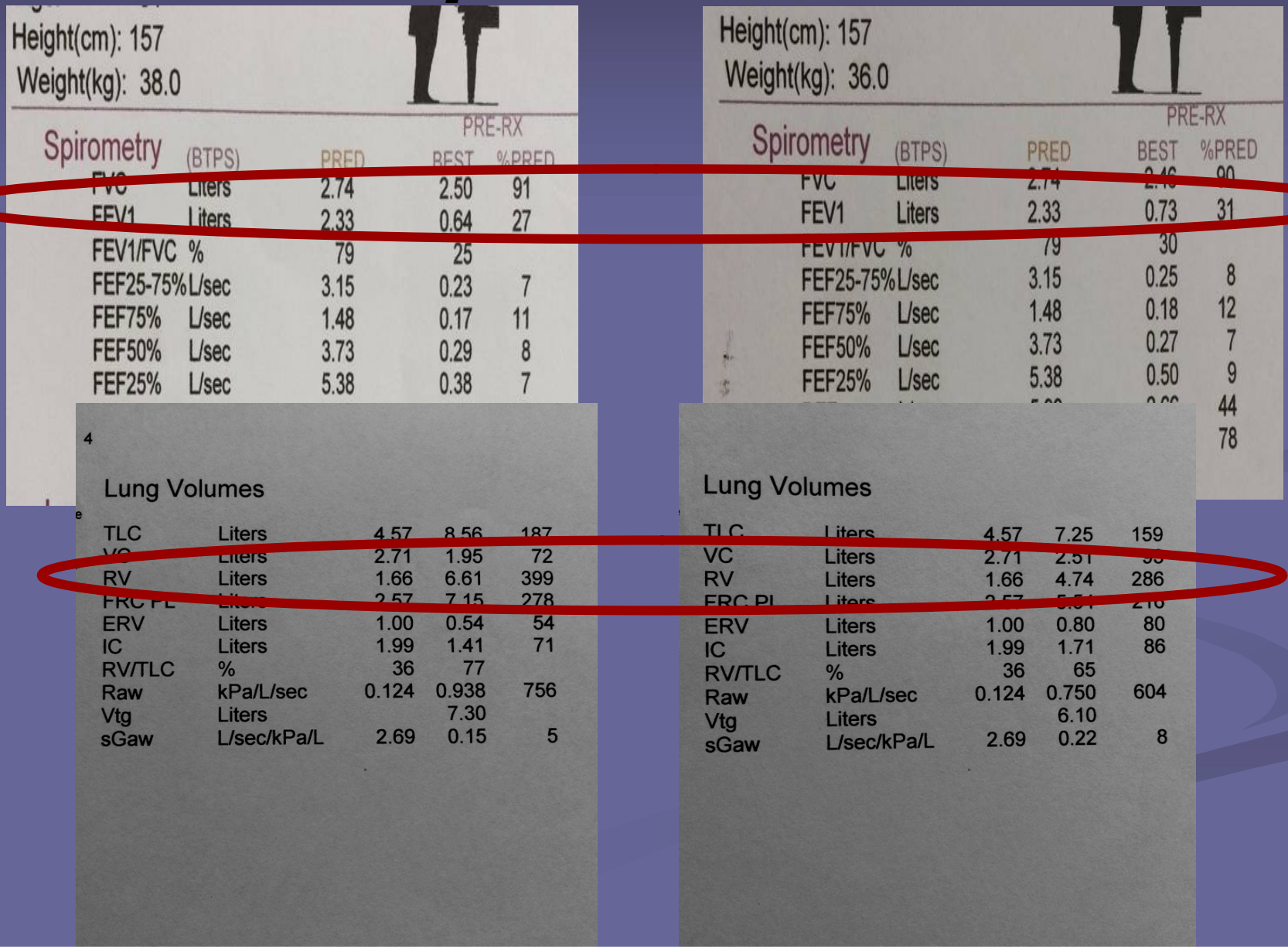


Height(cm): 157
Weight(kg): 38.0

Spirometry

	(BTPS)	PRED	PRE-RX BEST	%PRED
FVC	Liters	2.74	2.50	91
FEV1	Liters	2.33	0.64	27
FEV1/FVC	%	79	25	
FEF25-75%	L/sec	3.15	0.23	7
FEF75%	L/sec	1.48	0.17	11
FEF50%	L/sec	3.73	0.29	8
FEF25%	L/sec	5.38	0.38	7

Lung Volumes

TLC	Liters	4.57	8.56	187
VC	Liters	2.71	1.95	72
RV	Liters	1.66	6.61	399
FRC PL	Liters	2.57	7.15	278
ERV	Liters	1.00	0.54	54
IC	Liters	1.99	1.41	71
RV/TLC	%	36	77	
Raw	kPa/L/sec	0.124	0.938	756
Vtg	Liters		7.30	
sGaw	L/sec/kPa/L	2.69	0.15	5

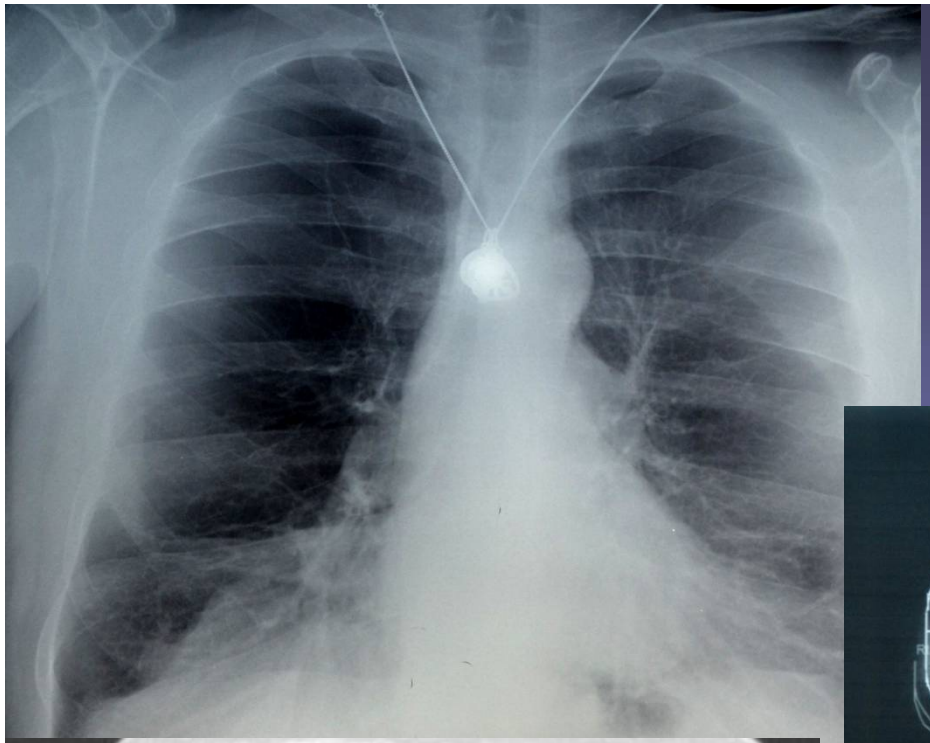
Height(cm): 157
Weight(kg): 36.0

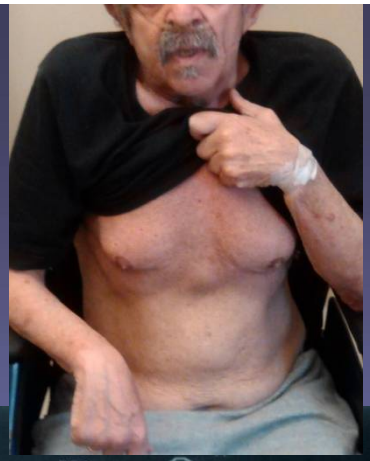
Spirometry

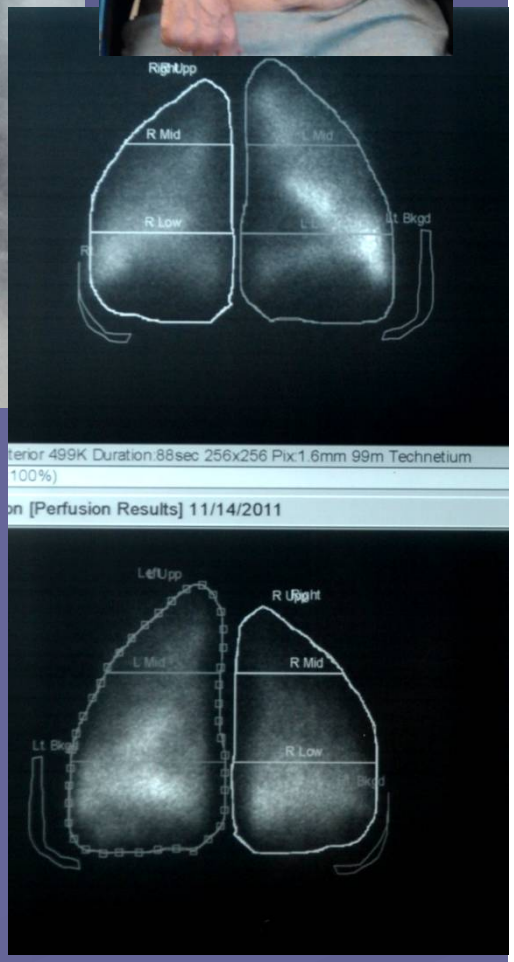
	(BTPS)	PRED	PRE-RX BEST	%PRED
FVC	Liters	2.74	2.46	90
FEV1	Liters	2.33	0.73	31
FEV1/FVC	%	79	30	
FEF25-75%	L/sec	3.15	0.25	8
FEF75%	L/sec	1.48	0.18	12
FEF50%	L/sec	3.73	0.27	7
FEF25%	L/sec	5.38	0.50	9
				44
				78

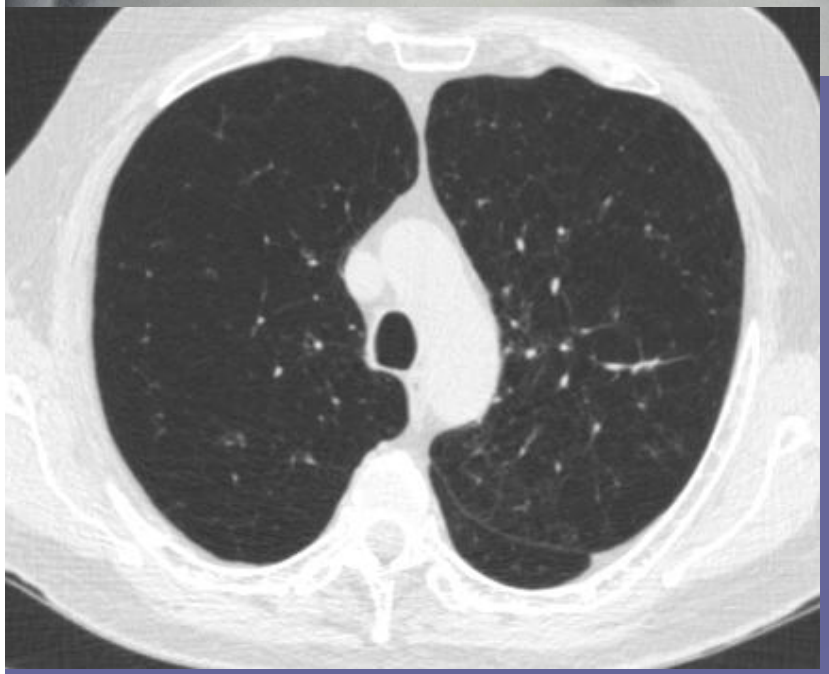
Lung Volumes

TLC	Liters	4.57	7.25	159
VC	Liters	2.71	2.51	93
RV	Liters	1.66	4.74	286
FRC PL	Liters	2.57	5.54	216
ERV	Liters	1.00	0.80	80
IC	Liters	1.99	1.71	86
RV/TLC	%	36	65	
Raw	kPa/L/sec	0.124	0.750	604
Vtg	Liters		6.10	
sGaw	L/sec/kPa/L	2.69	0.22	8









Perfusion

Posterior

(Counts)	Left	Right
Upper	029K	008K
Middle	108K	067K
Lower	130K	112K
Total	267K	188K

(% Ratios)	Left	Right
Upper	6.37	1.77
Middle	23.67	14.83
Lower	28.70	24.66
Total	58.74	41.26

Anterior

(Counts)	Left	Right
Upper	050K	015K
Middle	125K	086K
Lower	082K	067K
Total	257K	167K

(% Ratios)	Left	Right
Upper	11.78	3.46
Middle	29.45	20.19
Lower	19.36	15.76
Total	60.59	39.41

Geometric Mean

(Counts)	Left	Right
Upper	038K	011K
Middle	113K	076K
Lower	099K	084K
Total	250K	172K

(% Ratios)	Left	Right
Upper	8.98	2.66
Middle	26.77	18.10
Lower	23.51	19.98
Total	59.26	40.74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