Mr. D.H.

- 67 year old gentleman
- Carpenter. Self employed. Ceased work at the age of 60 years because of breathlessness.
- Smoker 90 pack years
- Ceased aged 60 yrs
- Intercurrent IHD. 2 coronary artery stents inserted 5 years ago
- Plavix

Respiratory Background

- Exercise tolerance 300m on the flat when he ceased work. Now 25-40m. Difficulty with one flight of stairs
- Some exertional wheeze and cough. No sputum
- 3 years ago, applied for disabled parking permit
- Therapy:

Tiotropium

Salmeterol, Fluticasone

Salbutamol prn

Respiratory Background

- Relevant Occupational factors
- Family History and Past History
- Co-morbidities – Hypertension, Gastro-oeosphageal Reflux, Peripheral vascular disease
- Ischaemic Heart Disease

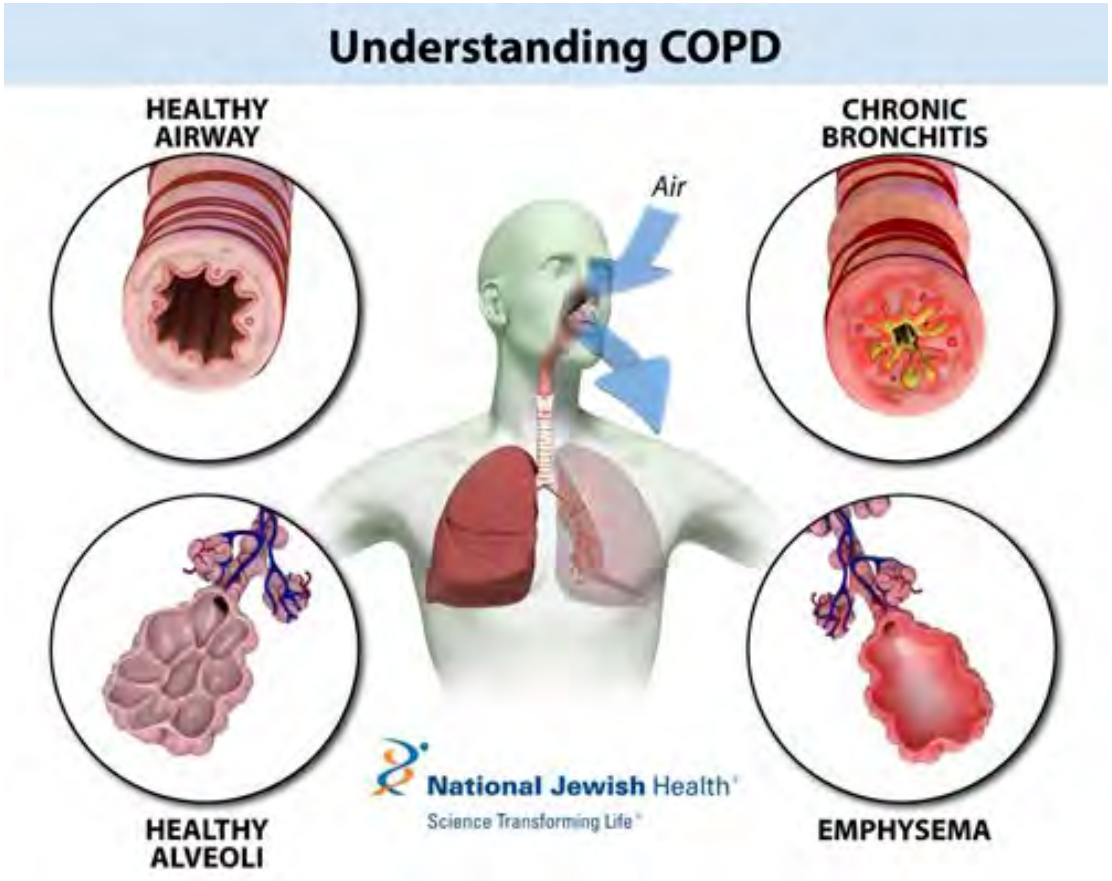
Examination

- Peripheral Signs
- Central signs
- Chest signs
- Co-morbidities / Pulmonary Hypertension / CVS signs

COPD

- Emphysema, Chronic Bronchitis, Bronchiolitis (Bronchiectasis)
- Inflammation induced by cigarette smoke is the major factor in pathogenesis. Open wood fires / air pollution. Genetic factors
- 6th leading cause of death World Wide
- Affects 2.3% of the population
- 7% of population over 60yrs
- 60,000 hospitalisations per year
- Of all major diseases, COPD presents the fastest increasing healthcare burden.

COPD – Airflow Limitation



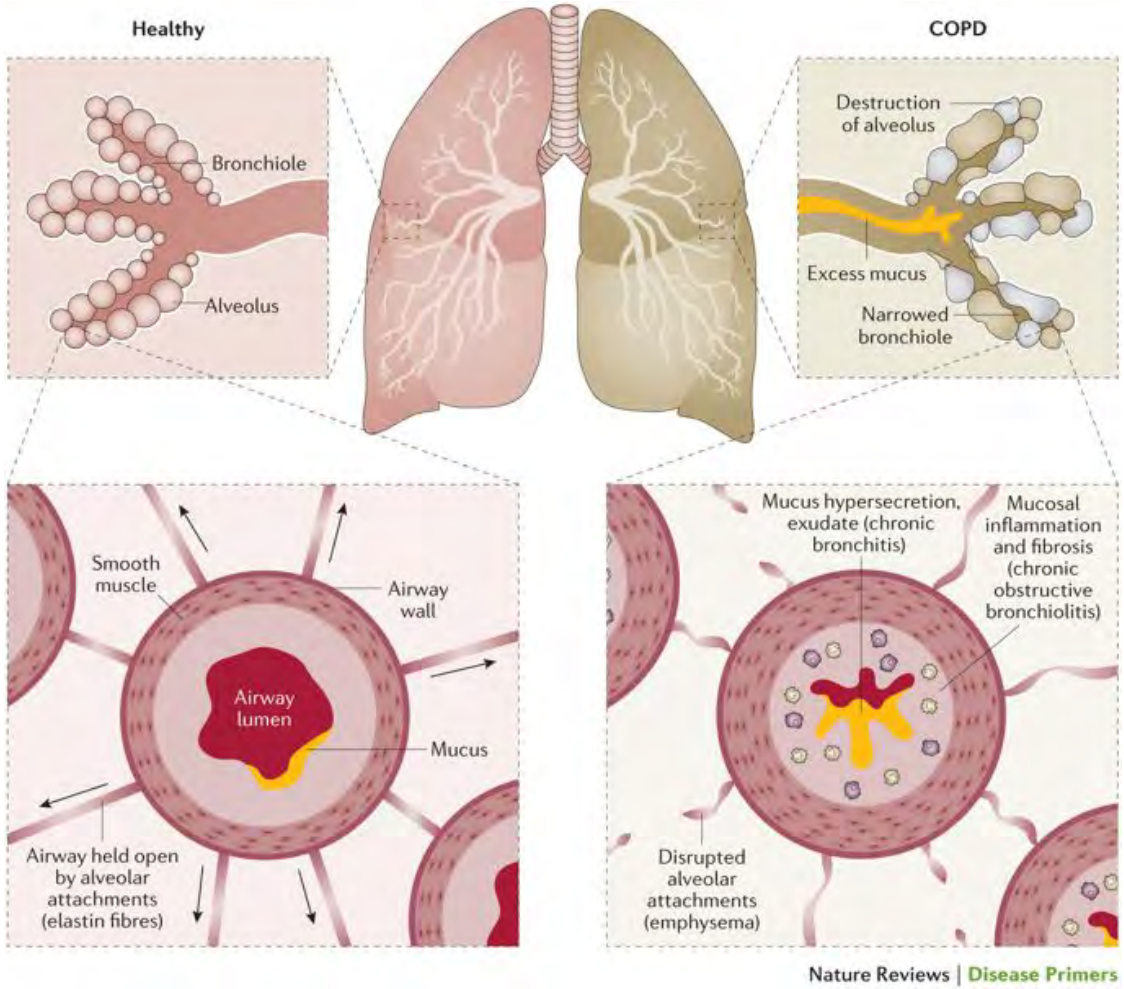
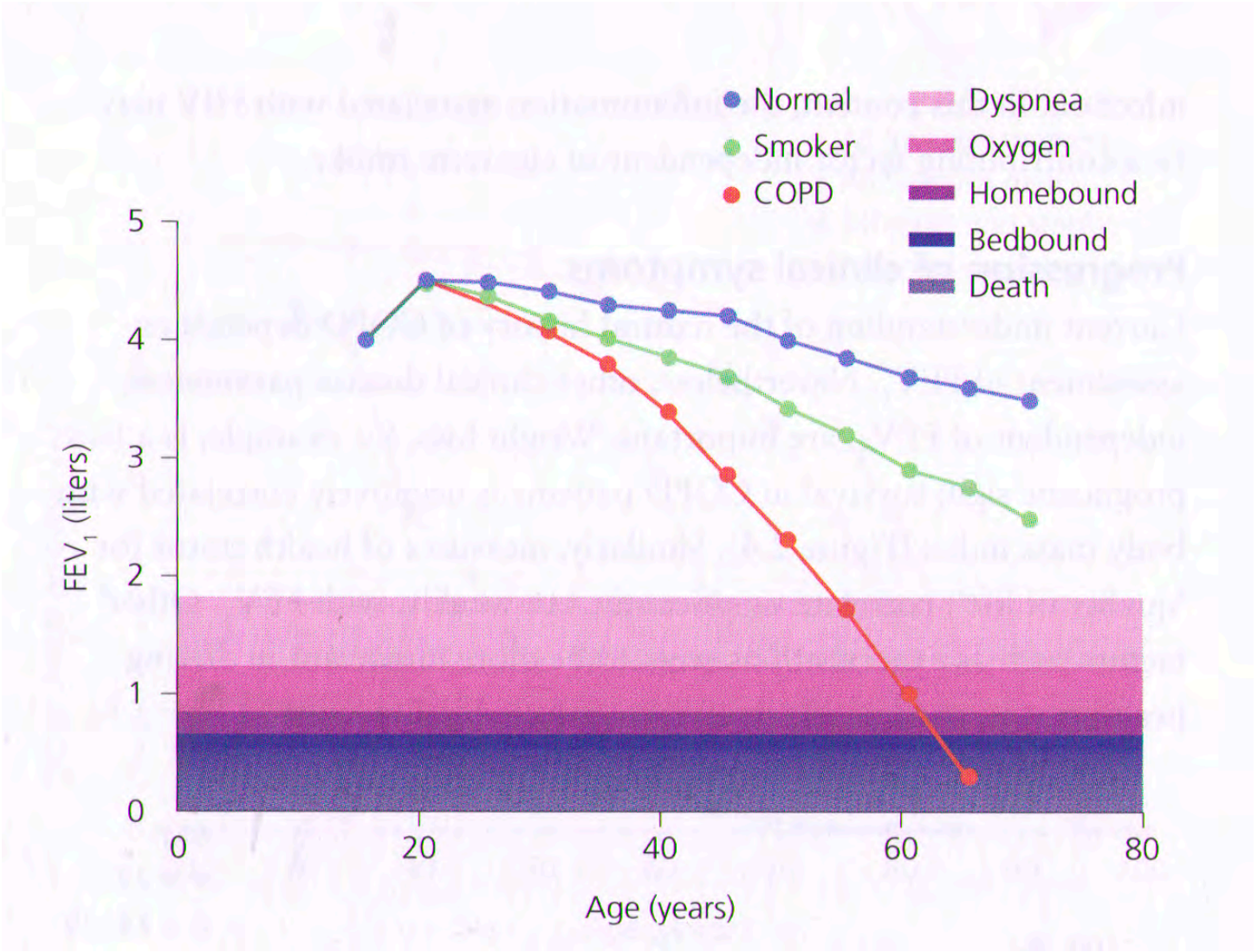


Table 2.1. Key indicators for considering a diagnosis of COPD	
Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is required to establish a diagnosis of COPD.	
Dyspnea that is:	Progressive over time. Characteristically worse with exercise. Persistent.
Chronic cough:	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic sputum production:	Any pattern of chronic sputum production may indicate COPD.
Recurrent lower respiratory tract infections	
History of risk factors:	Host factors (such as genetic factors, congenital/developmental abnormalities etc.). Tobacco smoke (including popular local preparations). Smoke from home cooking and heating fuels. Occupational dusts, vapors, fumes, gases and other chemicals.
Family history of COPD and/or childhood factors:	For example low birthweight, childhood respiratory infections etc.

Table 2.7. Differential diagnosis of COPD	
Diagnosis	**Suggestive Features**
COPD	Onset in mid-life. Symptoms slowly progressive. History of tobacco smoking or exposure to other types of smoke.
Asthma	Onset early in life (often childhood). Symptoms vary widely from day to day. Symptoms worse at night/early morning. Allergy, rhinitis, and/or eczema also present. Family history of asthma. Obesity coexistence.
Congestive Heart Failure	Chest X-ray shows dilated heart, pulmonary edema. Pulmonary function tests indicate volume restriction, not airflow limitation.
Bronchiectasis	Large volumes of purulent sputum. Commonly associated with bacterial infection. Chest X-ray/CT shows bronchial dilation, bronchial wall thickening.
Tuberculosis	Onset all ages. Chest X-ray shows lung infiltrate. Microbiological confirmation. High local prevalence of tuberculosis.
Obliterative Bronchiolitis	Onset at younger age, nonsmokers. May have history of rheumatoid arthritis or acute fume exposure. Seen after lung or bone marrow transplantation. CT on expiration shows hypodense areas.
Diffuse Panbronchiolitis	Predominantly seen in patients of Asian descent. Most patients are male and nonsmokers. Almost all have chronic sinusitis. Chest X-ray and HRCT show diffuse small centrilobular nodular opacities and hyperinflation.
These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in the developing world where other risk factors may be more important than cigarette smoking); asthma may develop in adult and even in elderly patients.	

Table 2.4. Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted



2 year mortality after first admission is 32%

COPD - Investigations

RESPIRATORY FUNCTION TESTS

SPIROMETRY

(Post-BD = 400ug Salbutamol via spacer unless otherwise indicated in comments)

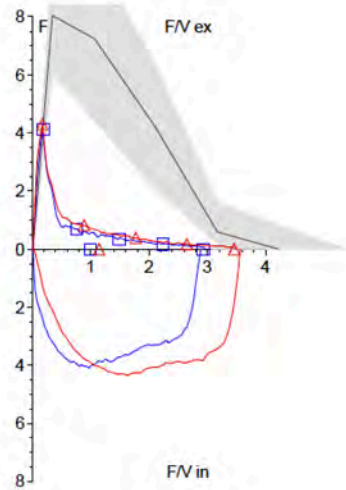
		Pre	Pre%...	Post	Post%...	%Change	Pred	Pred LL
FEV 1	L	0.98	31	1.14	36	16	3.14	2.22
FVC	L	2.92	69	3.45	82	18	4.22	3.08
FEV 1 % FVC	%	34	45	33	44	-2	75	61
MMEF 75/25	L/s	0.32	14	0.32	14	-1	2.26	0.91
PEF	L/s	4.13	51	4.29	53	4	8.04	6.05

LUNG VOLUMES

TLC	[L]	9.52	129				7.38	6.23
VC	[L]	3.22	75				4.29	3.37
IC	[L]	1.88	58				3.26	3.26
FRCpleth	[L]	7.64	200				3.82	2.83
ERV	[L]	1.33	129				1.03	1.03
RV	[L]	6.31	226				2.79	2.12
RV % TLC	[%]	66	153				43	34
sR 0.5	[kPa*s]	2.19						
R 0.5	[kPa/(L/s)]	0.27	89				0.30	0.30

GAS TRANSFER

DLCO_SB	[ml/(min*mmHg)]	7.92	29				27.26	20.33
DLCOcSB	[ml/(min*mmHg)]	7.81	29				27.26	20.33
VA_SB	[L]	5.25	73				7.23	7.23
KCO_SB	[ml/(min*mmHg*L)]	1.51	41				3.69	2.59
KCOc_SB	[ml/(min*mmHg*L)]	1.49	40				3.69	2.59
VIN_SB	[L]	3.48	81				4.29	3.37
Hb	[g(Hb)/100mL]	15.10						



INTERPRETATION

Severe airflow limitation with significant improvement in FVC after salbutamol. Moderate hyperinflation and gas trapping with reduced gas transfer c/w emphysema.

Prof Matthew Peters MD FRACP

(Physician 02.02.2017 06:26PM)

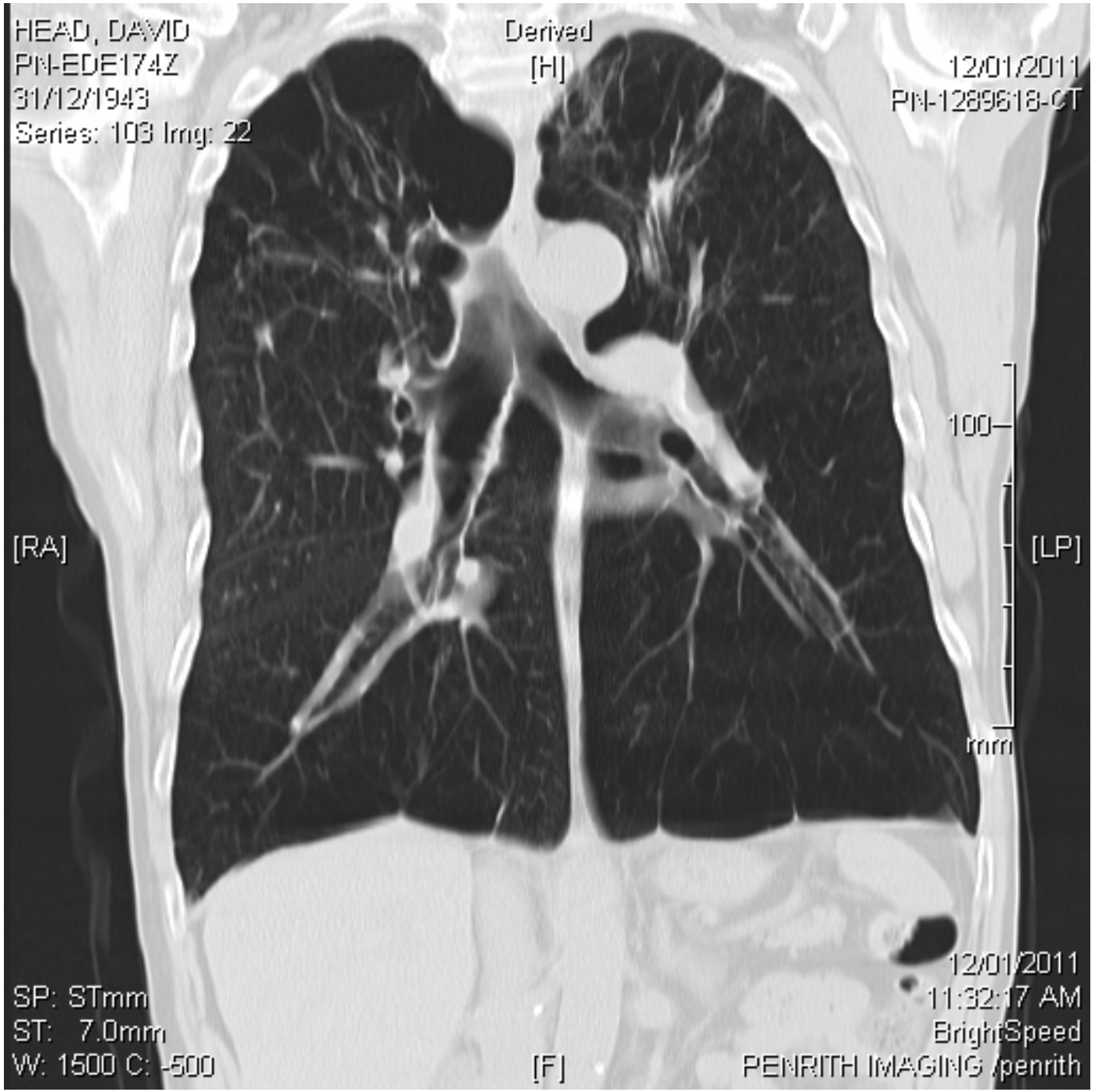
Tests meet ATS standards for acceptability & repeatability. Hb from pathology 28/1/17.

Investigations

Detail	Value w/Units	Normal Range	Comment Ind
FIO2	21 %		
pH	7.48	7.36-7.44	
pO2	56 mmHg	80-100	
pCO2	34 mmHg	35-45	
O2 Saturation	89 %	95-99	
Bicarbonate	27 mmol/L	22-30	
Base Excess	3 mmol/L	-2-2	

Blood Gases	Gas Sample Type	Arterial

COPD Phenotypes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31/12/1943
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12/01/2011
PN-1289618-CT
100
mm
[RA]
[LP]
SP: STmm
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[F]
12/01/2011
11:32:17 AM
BrightSpeed
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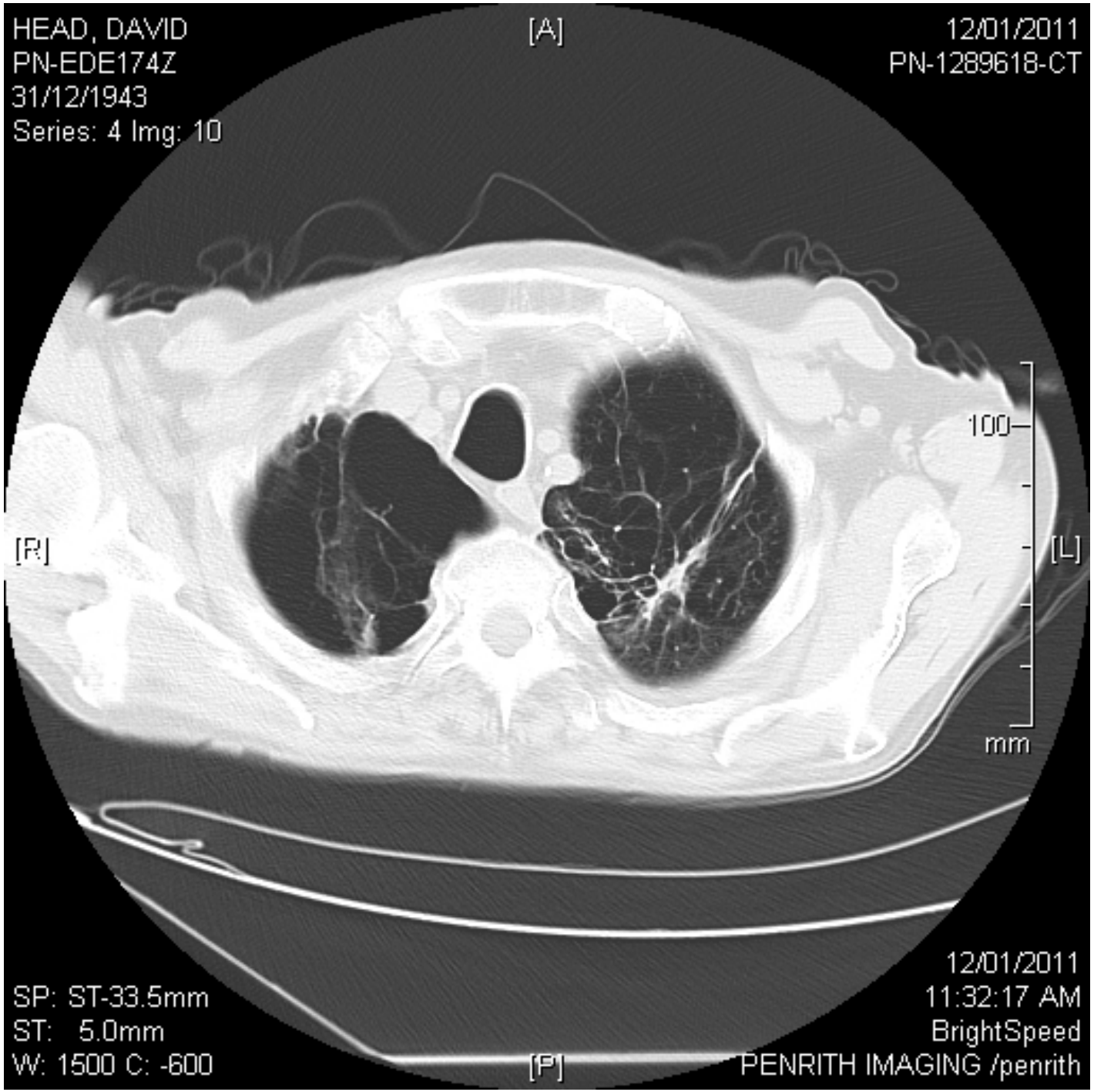
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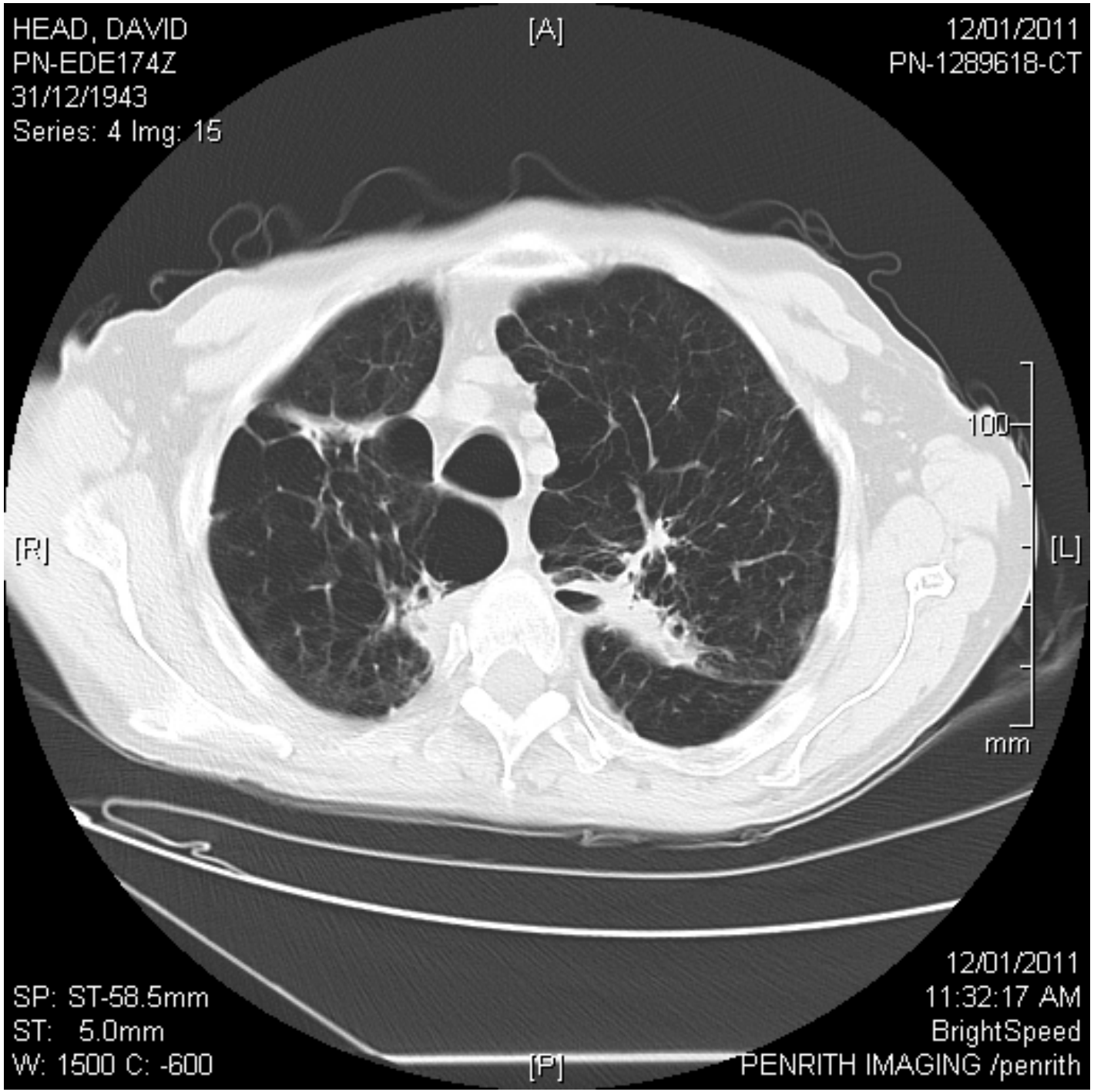
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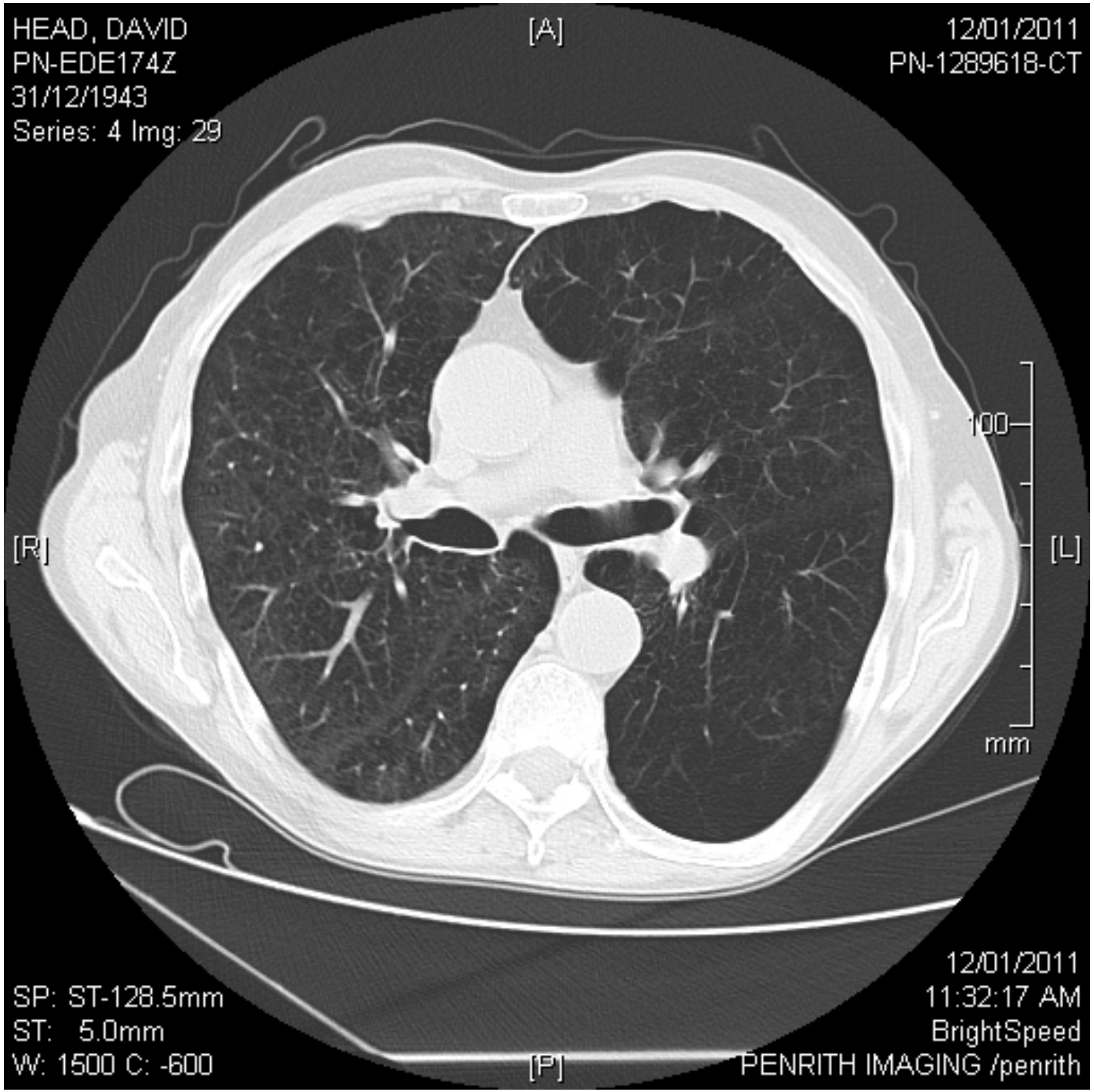
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[L]
mm
SP: ST-128.5mm
ST: 5.0mm
W: 1500 C: -600
[P]
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BrightSpeed
PENRITH IMAGING /penrith

COPD Management

- Smoking Cessation

- Medical therapy:

Long acting anti-cholinergics

Long acting Beta Agonists

Low dose Macrolides - anti-inflammatory agent

LTOT

Pulmonary Rehabilitation

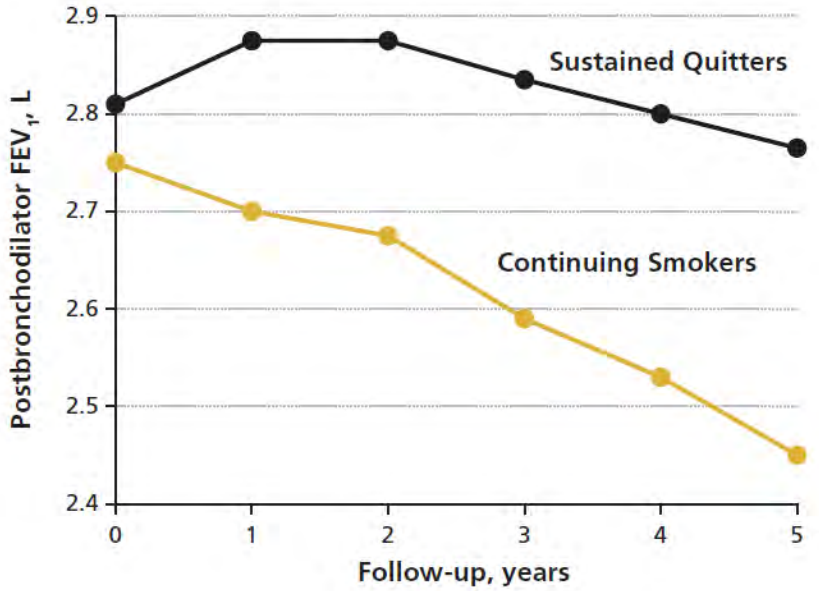
Ultra Long acting Beta Agonists

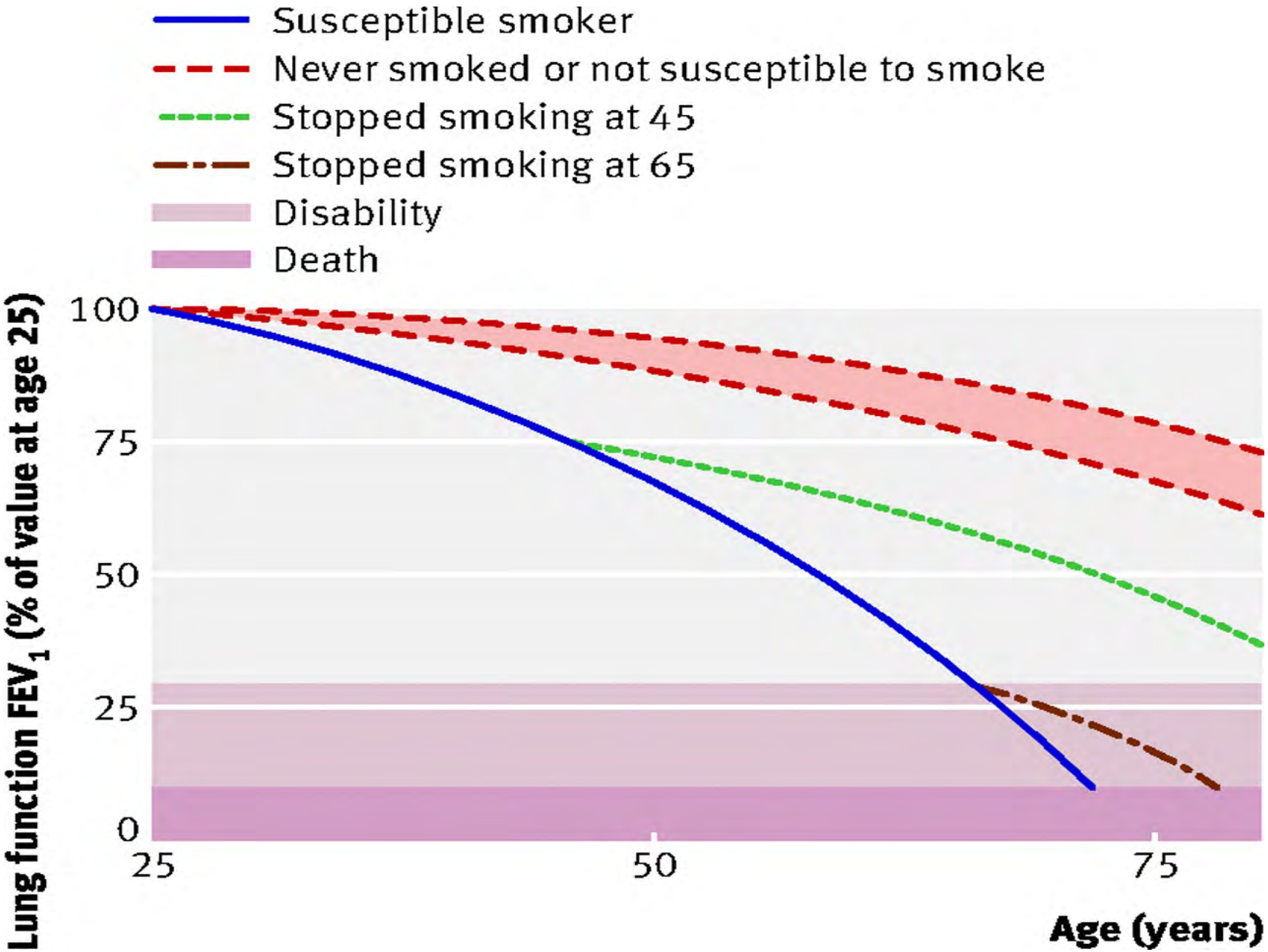
- Lung Volume Reduction

- Transplantation

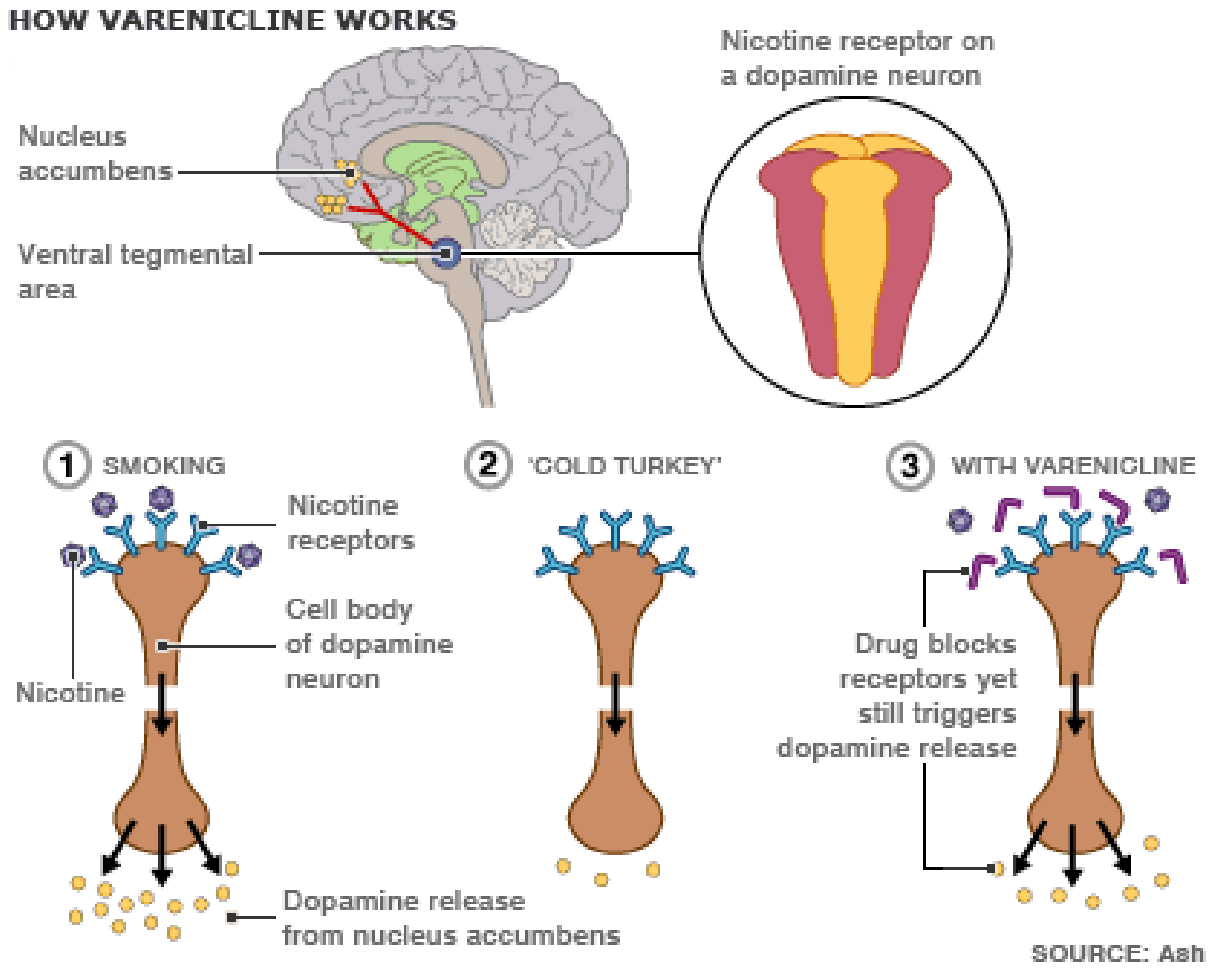
Smoking Cessation / Avoiding Inhaled Particulate Matter

Figure 1. Effect of quitting smoking on progression of airflow limitation in COPD.




Susceptible smoker
Never smoked or not susceptible to smoke
Stopped smoking at 45
Stopped smoking at 65
Disability
Death
Lung function FEV1 (% of value at age 25)
100
75
50
25
0
25
50
75
Age (years)

Smoking Cessation / Avoiding Inhaled Particulate Matter



Champix

Partial Nicotine Agonist

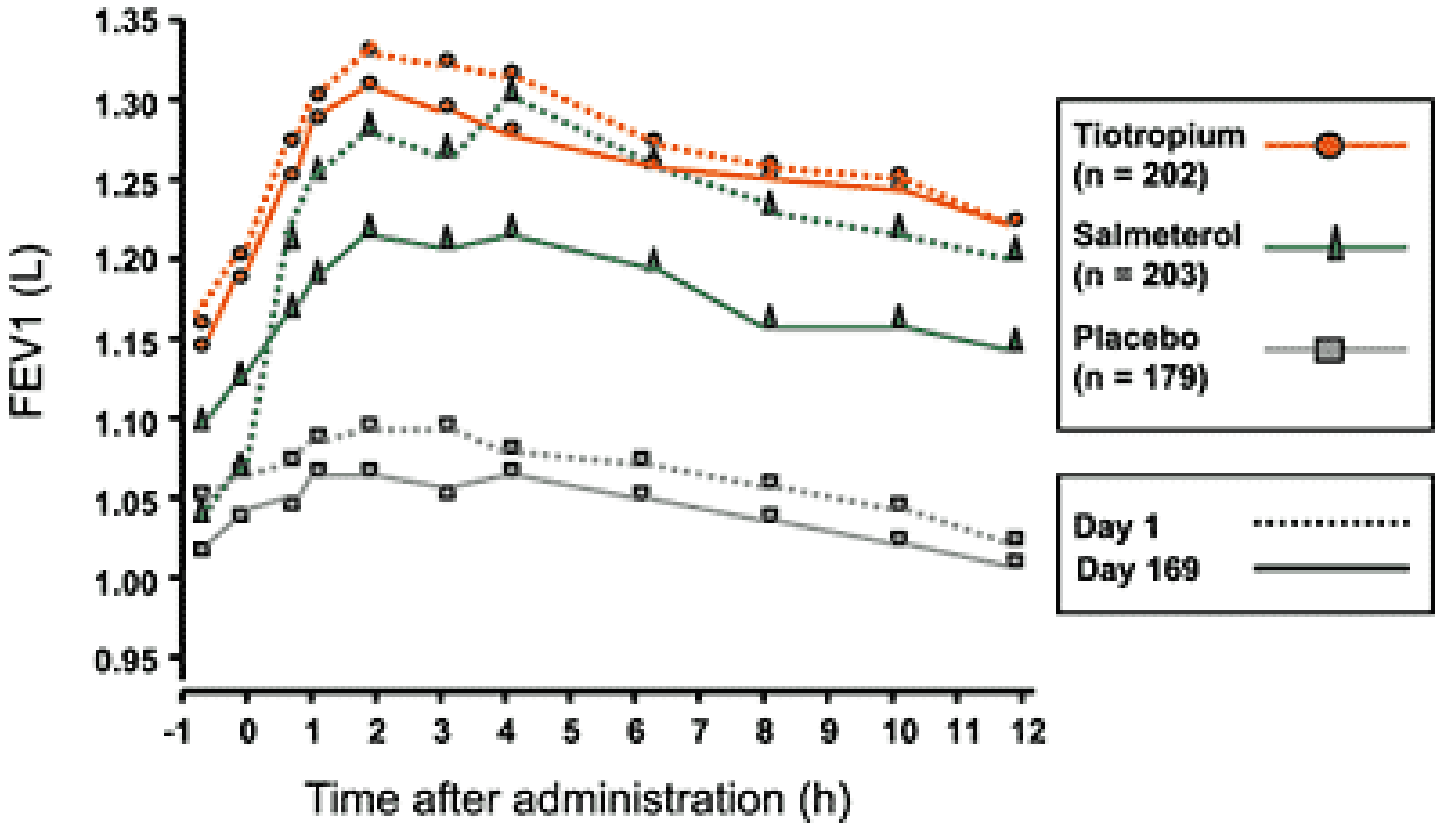
Smoking Cessation

- Champix – Smoking abstinence at 3 months (56%) greater than with NRT patches (43%).
- However, at 1 year the difference was no longer statistically significant (26% vs 20%, p=0.06).
- Adverse reactions

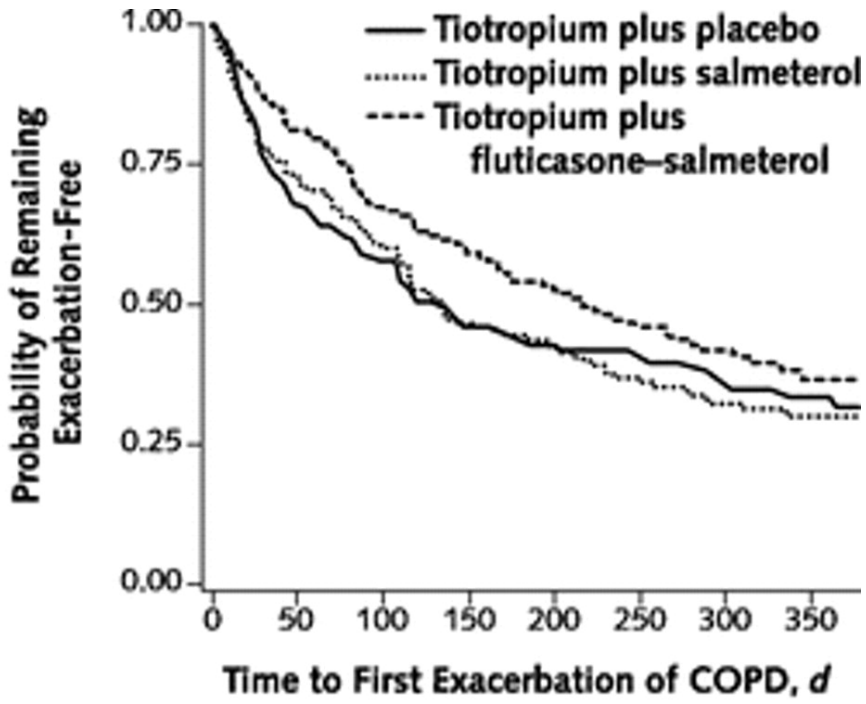
Smoking Cessation

- Nicotine Replacement Therapy
- Smoking Cessation Clinics – 23% Long term success
- Other – hypnotherapy / acupuncture

Long Acting Anticholinergics

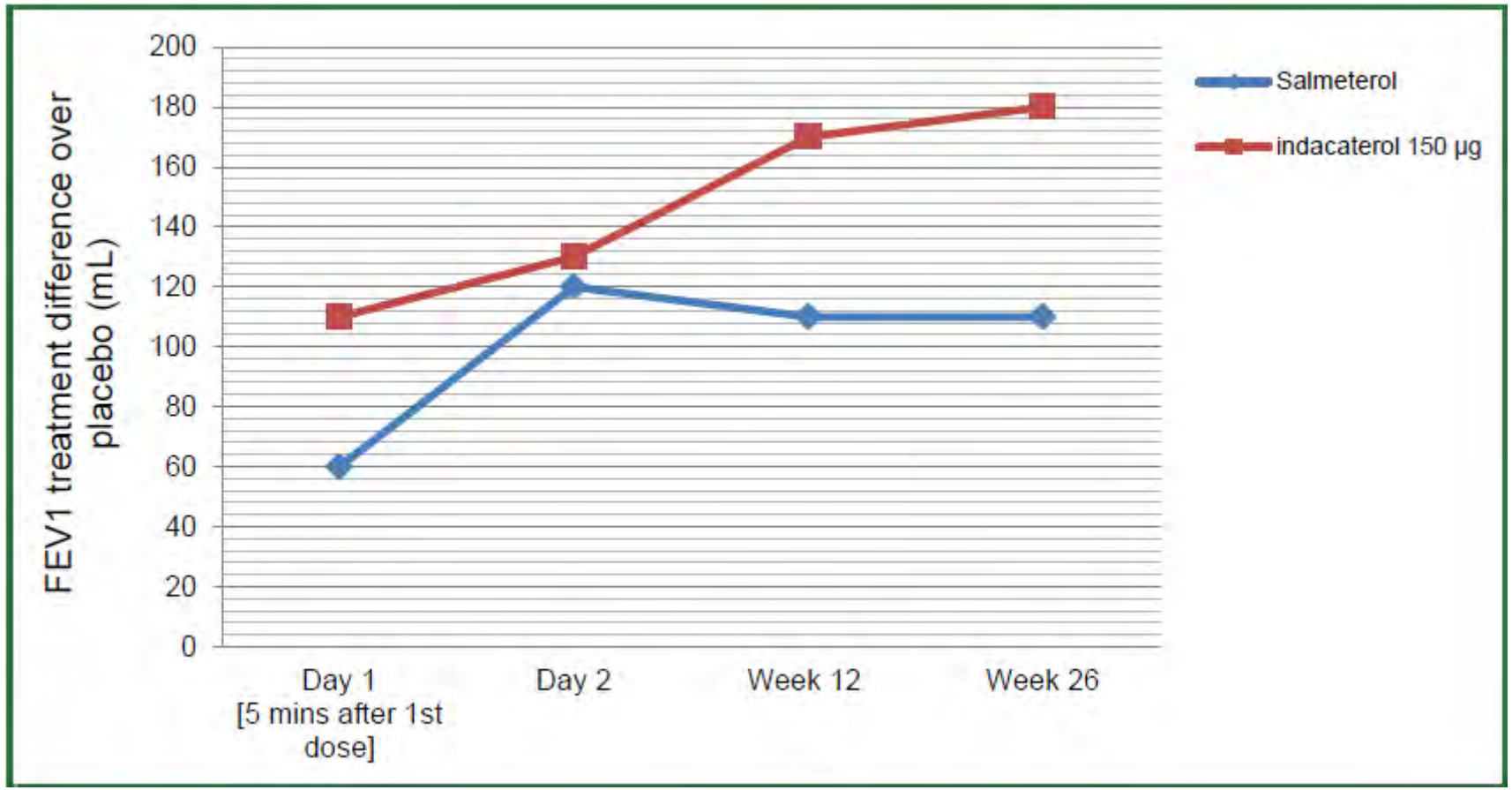


Long Acting Anticholinergics + long acting B agonists

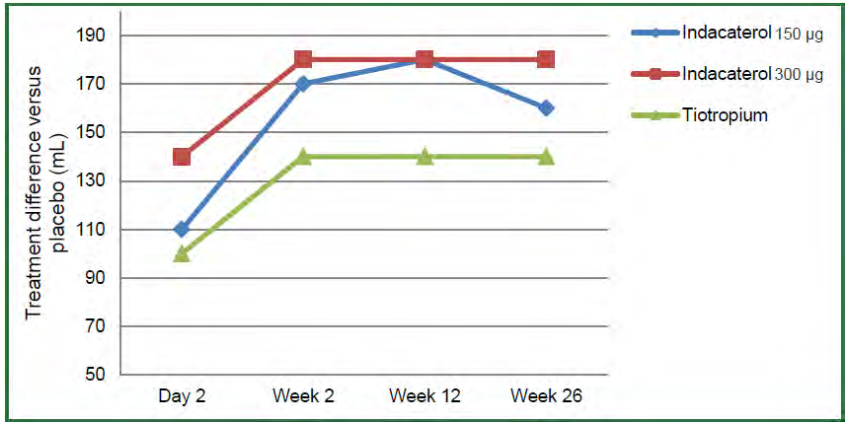


Patients at risk, *n*								
Tiotropium plus placebo	156	102	84	65	59	57	50	45
Tiotropium plus salmeterol	148	100	81	61	55	48	41	38
Tiotropium plus fluticasone–salmeterol	145	116	94	82	72	62	55	48

Ultra long acting B agonists



Long acting anticholinergics +Ultra long acting B agonists



Concurrent use of indacaterol plus tiotropium in patients with COPD provides superior bronchodilation compared with tiotropium alone: a randomised, double-blind comparison

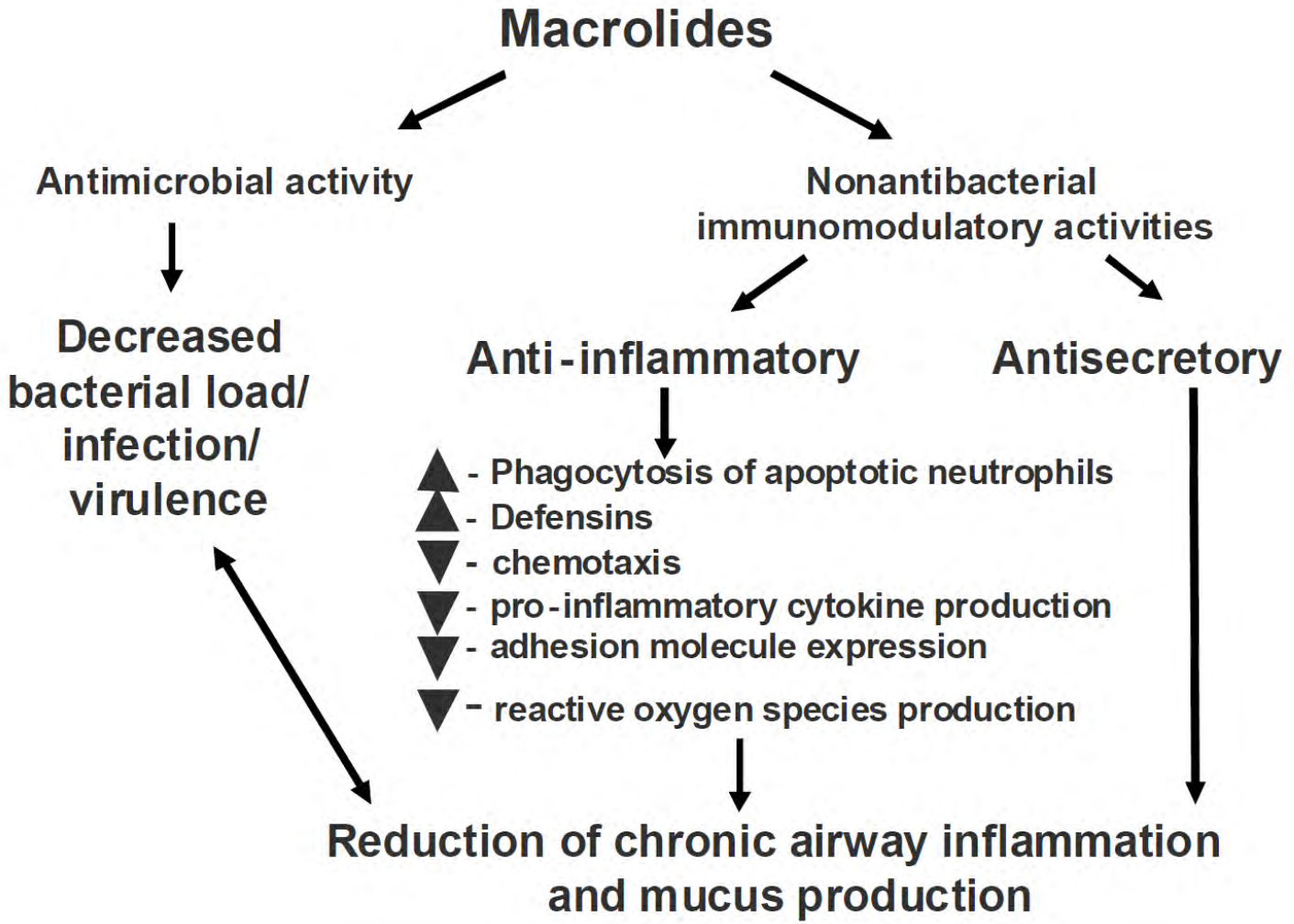
Donald A Mahler,[1,2] Anthony D'Urzo,[3] Eric D Bateman,[4] Serir A Özkan,[5] Tracy White,[6] Clare Peckitt,[7] Cheryl Lassen,[7] Benjamin Kramer,[6] on behalf of the INTRUST-1 and INTRUST-2 study investigators

Thorax 2012;**67**:781–788. doi:10.1136/thoraxjnl-2011-201140

Drug class	Inhaler medications	Indication	Comment
SABA	Salbutamol, terbutaline	Reliever	Useful in all severities for relief of symptoms. Rapid action, effect lasts 4-6 hrs.
SAMA	Ipratropium bromide	Reliever	Useful in all severities for relief of symptoms. Slower onset of relief than with SABA. Medication effect lasts 4-6 hours.
LAMA	Tiotropium bromide, glycopyrronium, aclidinium, umeclidinium	Reliever and preventer	Improves health status, symptoms, and effectiveness of pulmonary rehabilitation. Greater effect on exacerbations than LABA.
LABA	Salmeterol, indacaterol, eformoterol	Preventer and reliever	Medication effect lasts for >12 hours. Can be used in conjunction with as needed SABA with caution.
LABA/LAMA	Indacaterol/glycopyrronium, umeclidinium/vilanterol	Preventer and reliever	Combination therapy superior to monotherapy with either agent or ICS/LABA. May increase degree of bronchodilation than with either agent alone.
ICS	Fluticasone, budesonide, beclomethasone, ciclesonide	Anti-inflammatory preventer	Used in combination with LABA, LAMA, LABA/LABA bronchodilators. Associated with voice hoarseness, oral Candidiasis and increased risk of pneumonia.
ICS/LABA	Fluticasone/salmeterol, Budesonide/eformoterol, Fluticasone/vilanterol	Preventer and reliever	ICS/LABA superior to monotherapy with ICS or LABA alone. Use in severe disease or in asthma/COPD overlap syndrome

SAMA: short-acting antimuscarinic, SABA: short-acting beta2 agonist, LAMA: long-acting antimuscarinic, LABA: long-acting beta2 agonist, ICS: inhaled corticosteroid.

Macrolide Therapy in COPD



Macrolide Therapy in COPD

Martinez et al

Table 3 Effect of azithromycin prophylactic therapy in COPD patients at high risk of AECOPD and treatment failure

Outcome	Treatment group		p value
	Azithromycin (n = 54)	Control (n = 40)	
Exacerbations/year	187	249	<0.0001
Hospitalizations/year	22	45	<0.05

Long Term Oxygen Therapy

- NOTT and BHMRC studies
- Improved mortality and morbidity
- $paO_2 < 55$ mmHg / $paO_2 < 60$ mmHg with pul HT / polycythemia
- Intercurrent OSA/ Obesity Hypoventilation with some phenotype – need for nocturnal CPAP / oxygen

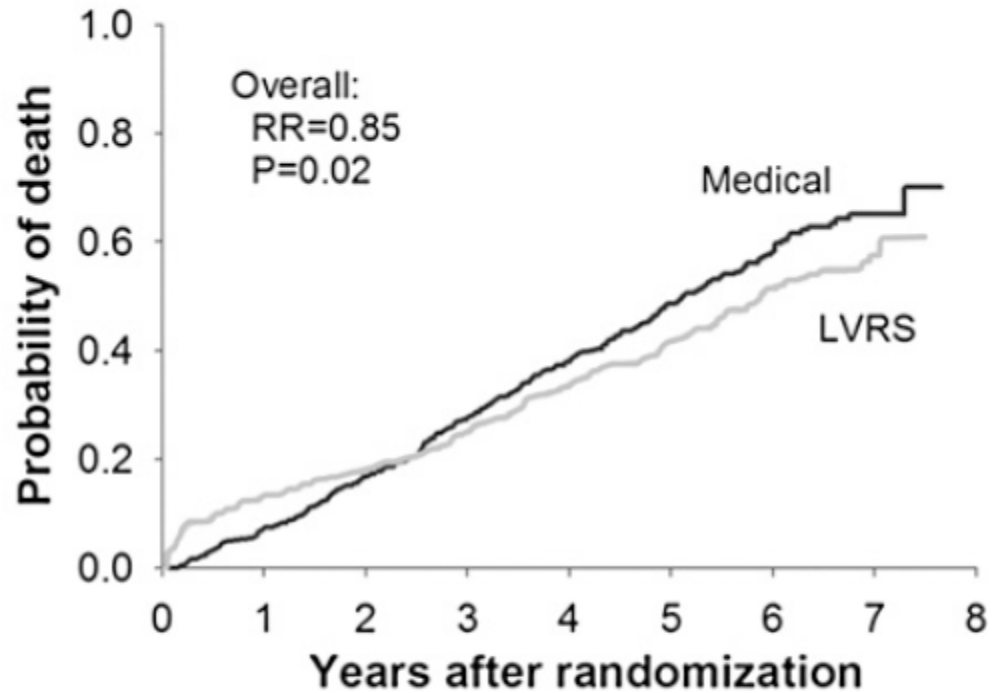
Pulmonary rehabilitation

- Improves exercise tolerance
- Improves symptoms and QOL. Improved gas exchange
- Reflected in improved 6 min walk / CAT scores and SQRQ
- No improvement in RFT
- Vital prior to ELVR

Lung Volume Reduction Surgery

- Improves lung function, QOL and mortality in selected pts with advanced COPD
- Rapid increase in bilateral LVRS procedures 1993-1997
- Tempered by initial mortality and morbidity of the procedure
- NETT Trial – 90 day mortality 7.9% (1.3% medical group)

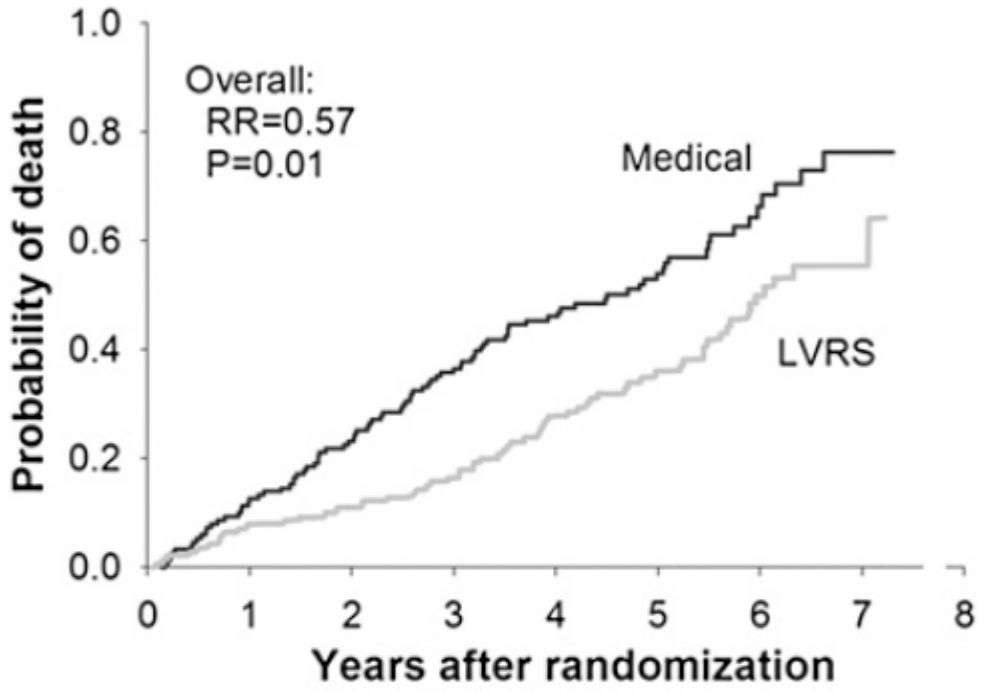
a.



No. at risk								
LVRS	608	526	496	454	352	227	122	29
Medical	610	564	507	441	335	210	99	29
Probability of death								
LVRS		0.13	0.18	0.25	0.34	0.42	0.52	0.57
Medical		0.08	0.17	0.28	0.38	0.49	0.58	0.65
Ratio		1.79	1.09	0.91	0.89	0.86	0.89	0.88
P		0.001	0.48	0.35	0.15	0.02	0.05	0.06

N Engl J Med 2003;348:2059-73.

C.

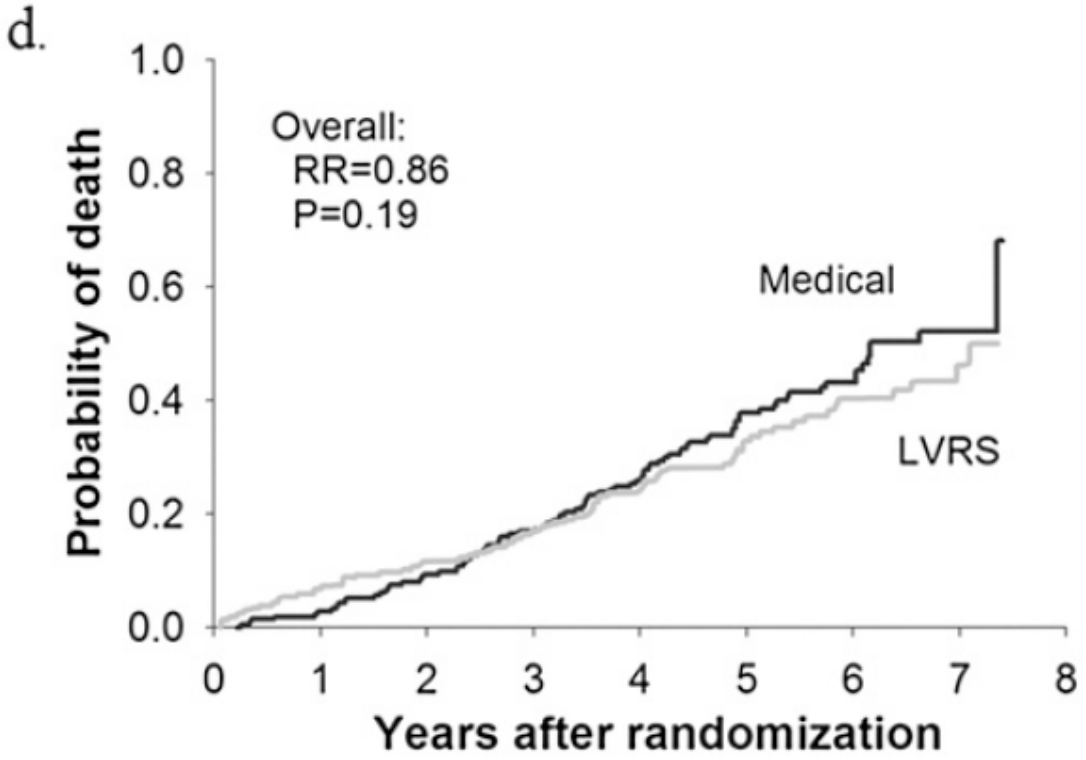


No. at risk								
LVRS	139	127	123	115	88	57	32	6
Medical	151	131	115	95	70	47	16	4

Probability of death							
LVRS	0.09	0.12	0.17	0.28	0.36	0.52	0.55
Medical	0.13	0.24	0.37	0.47	0.54	0.66	0.76
Ratio	0.65	0.48	0.47	0.59	0.67	0.78	0.72
P	0.20	0.01	<0.001	0.001	0.003	0.04	0.006

Upper Lobe Predominant Disease – Low Exercise Capacity

N Engl J Med 2003;348:2059-73.



No.at risk								
LVRS	206	191	181	170	136	80	52	17
Medical	213	206	192	176	143	92	55	17
Probability of death								
LVRS		0.07	0.12	0.17	0.25	0.33	0.40	0.46
Medical		0.03	0.10	0.17	0.26	0.38	0.43	0.52
Ratio		2.21	1.23	1.01	0.94	0.87	0.94	0.89
P		0.07	0.46	0.98	0.71	0.32	0.61	0.39

Upper Lobe Predominant Disease – High Exercise Capacity

N Engl J Med 2003;348:2059-73.

Bronchoscopic LVRS

- Endobronchial Valves
- Coils
- Glue
- Steam
- Targeted Lung Denervation
- Electroporation

INTERVENTIONAL THERAPY IN STABLE COPD

LUNG VOLUME REDUCTION SURGERY

- Lung volume reduction surgery improves survival in severe emphysema patients with an upper–lobe emphysema and low post–rehabilitation exercise capacity **(Evidence A)**.

BULLECTOMY

- In selected patients bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance **(Evidence C)**.

TRANSPLANTATION

- In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity **(Evidence C)**.

BRONCHOSCOPIC INTERVENTIONS

- In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improves exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves **(Evidence B)**; Lung coils **(Evidence B)**; Vapor ablation **(Evidence B)**.

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

2019 REPORT

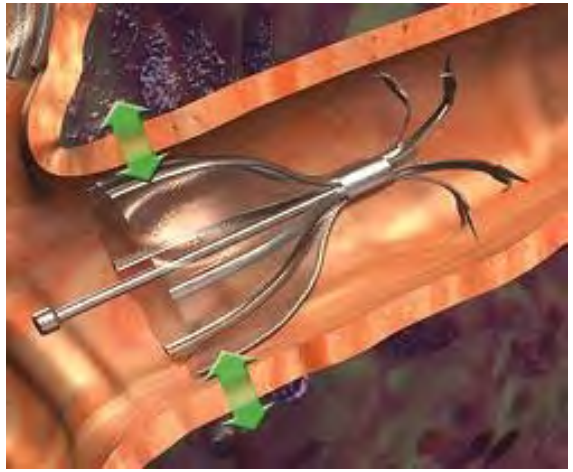
<table>
<tr><td>LVRS</td><td></td><td>LVRS</td><td></td><td rowspan="8">Consider lung transplant</td></tr>
<tr><td>Valves</td><td>Valves</td><td></td><td></td></tr>
<tr><td>Vapor (UL)</td><td rowspan="2">Vapor</td><td>Vapor (UL)</td><td rowspan="2">Vapor</td></tr>
<tr><td>Vapor (LL)</td><td>Vapor (LL)</td></tr>
<tr><td>Coils (RV>200%, RV/TLC>0.58, LAA>20%,no bronchitis)</td><td>Coils (RV>200%, RV/TLC>0.58, LAA>20%,no bronchitis)</td><td>Coils (RV>200%, RV/TLC>0.58, LAA>20%,no bronchitis)</td><td>Coils (RV>200%, RV/TLC>0.58, LAA>20%,no bronchitis)</td></tr>
<tr><td>Foam</td><td>Foam</td><td>Foam</td><td>Foam</td></tr>
<tr><td>Heterogeneous</td><td>Homogeneous</td><td>Heterogeneous</td><td>Homogeneous</td></tr>
<tr><td colspan="2">FI complete (QCT)/chartis negative</td><td colspan="2">FI incomplete (QCT)/chartis positive</td><td></td></tr>
<tr><td colspan="5">Emphysema optimal Rx
FEV1 <50% and RV >175%, RV/TLC >0.58, 6 MWT 150–450 m</td></tr>
<tr><td colspan="5">Optimal pharmacological and non-pharmacological treatments
Smoking cessation, optimal diet, vaccination
Pulmonary rehabilitation
Consider long-term oxygen therapy, non-invasive ventilation

☐ Approved ☐ RCTs have been completed, at least within registries
■ Clinical trials in progress</td></tr>
</table>

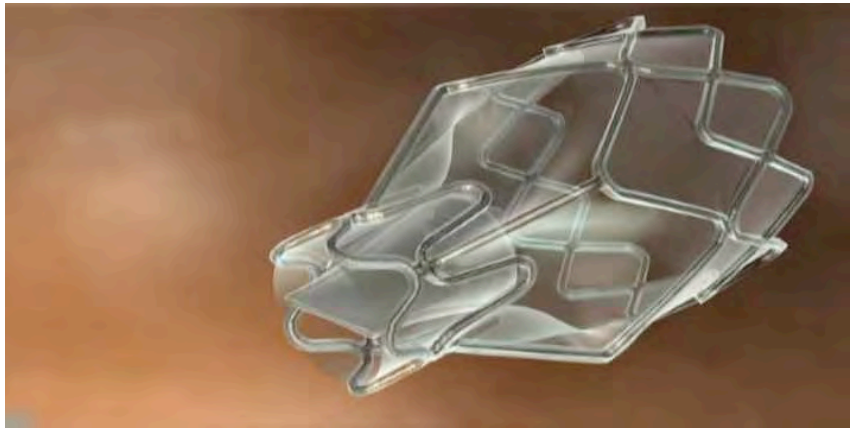
Felix J.F. Herth, Dirk-Jan Slebos, Gerard J. Criner, Arschang Valipour, Frank Sciurba, Pallav L. Shah

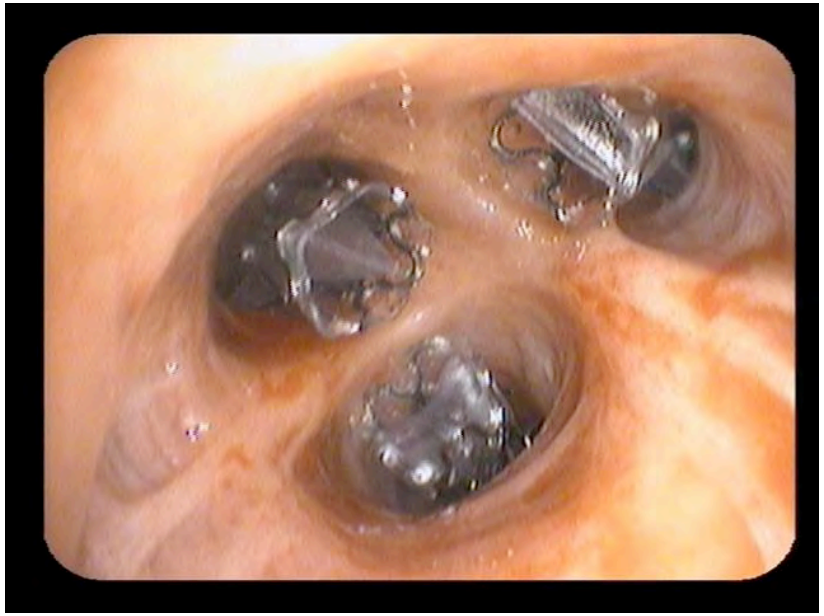
ELVR Expert Panel Recommendations. Respiration, 5th March 2019.

Olympus IBV



Pulmonx Zephyr EBV





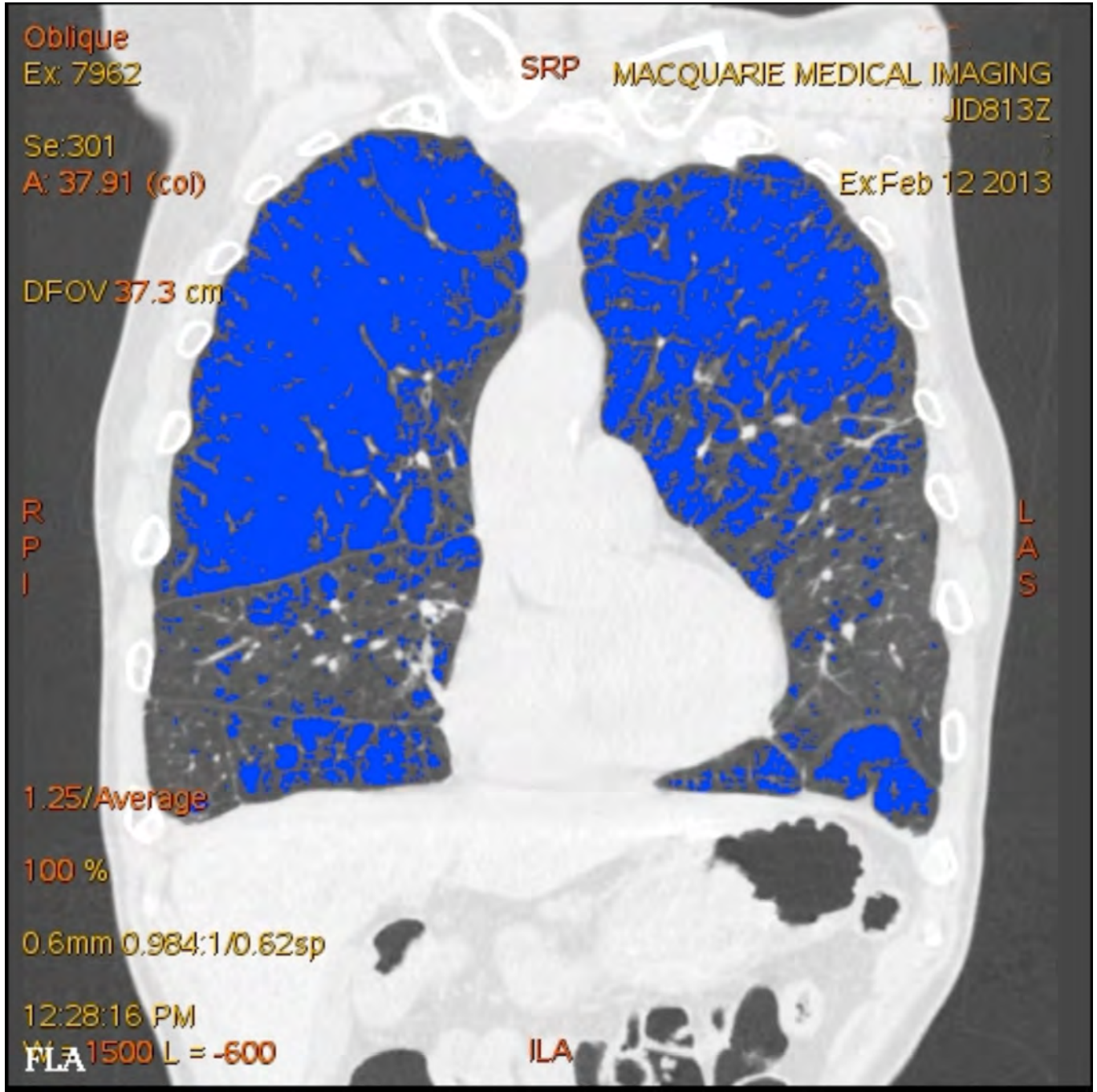
Indications for ELVR with valves

- COPD FEV1: 20–45% RV>175%
- 6MWT > 100-500m
- Stabilised on Medical Therapy, undertaken pulmonary rehabilitation
- Heterogenous disease ?
- Absence of collateral ventilation

	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%

Table 2. Mean Change from Baseline to 6 Months of Follow-up in Primary Efficacy Outcomes in the Intention-to-Treat Population.*

Variable	EBV Group (N=34)	Control Group (N=34)	Between-Group Difference	P Value
Change in FEV_1				
Milliliters (95% CI)	161 (80 to 242)	21 (–9 to 52)	140 (55 to 225)	0.002
Percentage (95% CI)	20.9 (11.1 to 30.7)	3.1 (–0.4 to 6.6)	17.8 (7.6 to 28.0)	0.001
Response rate — %	59	24	—	0.003
Change in FVC				
Milliliters (95% CI)	416 (201 to 631)	69 (–50 to 187)	347 (107 to 588)	0.005
Percentage (95% CI)	18.3 (9.3 to 27.3)	4.0 (–0.7 to 8.6)	14.4 (4.4 to 24.3)	0.005
Change in distance on 6-min walk test				
Meters (95% CI)	60 (35 to 85)	–14 (–25 to –3)	74 (47 to 100)	<0.001
Percentage (95% CI)	19.6 (10.4 to 28.9)	–3.6 (–6.9 to –0.4)	23.3 (13.6 to 32.9)	<0.001
Response rate — %	59	6	—	<0.001


Oblique
Ex: 7962
SRP
MACQUARIE MEDICAL IMAGING
JID813Z
Se:301
A: 37.91 (col)
Ex:Feb 12 2013
DFOV 37.3 cm
R
P
I
L
A
S
1.25/Average
100 %
0.6mm 0.984:1/0.62sp
12:28:16 PM
W: 1500 L = -600
ILA
FLA

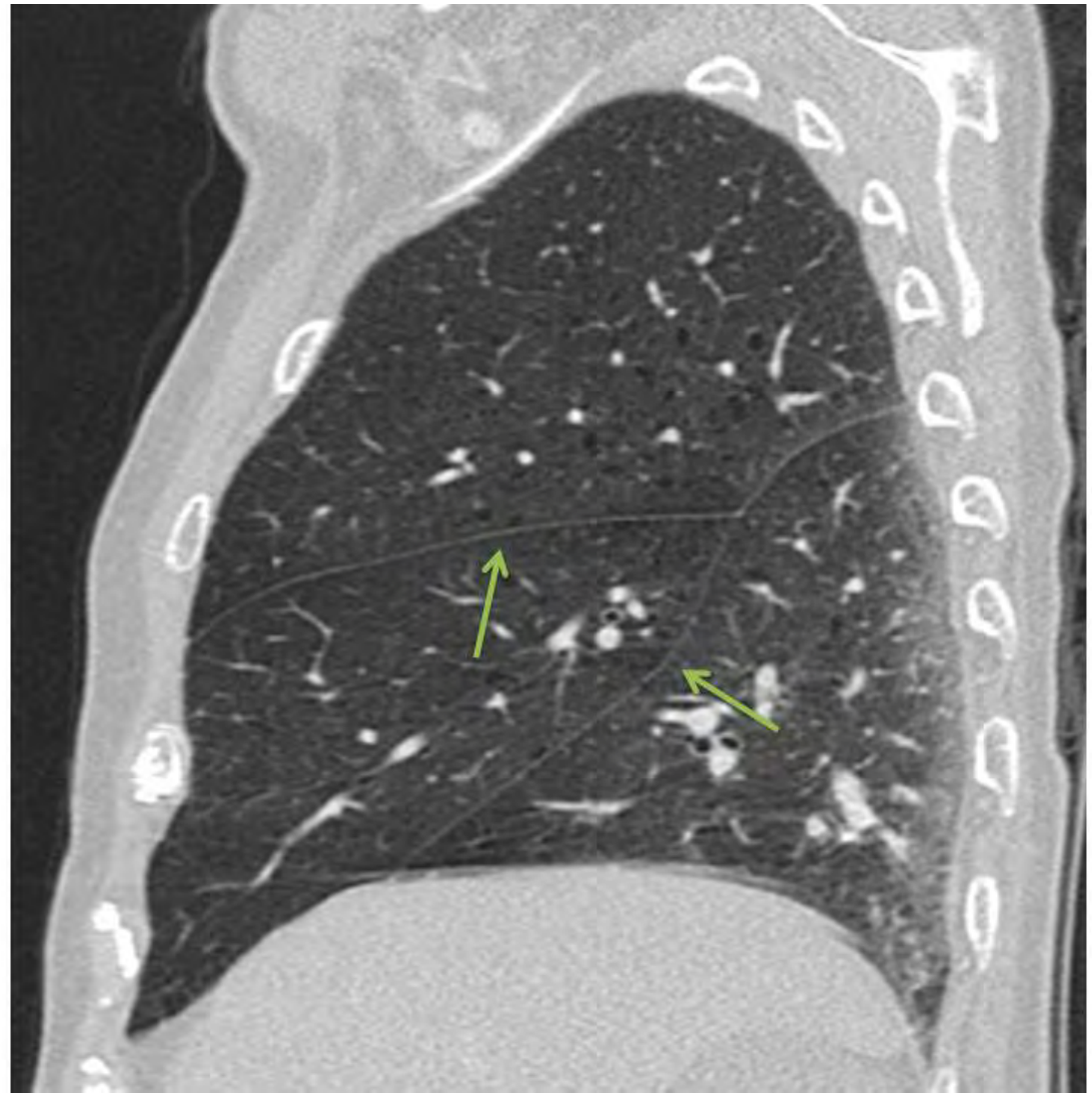
SUMMARY

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

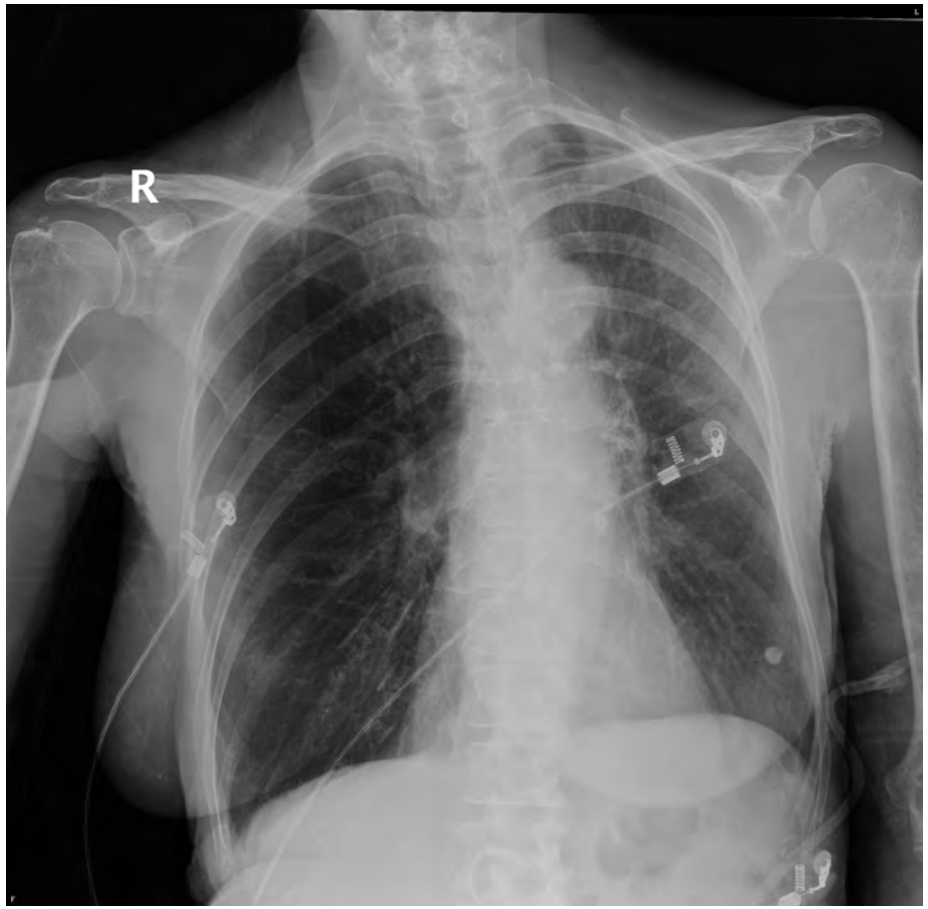
RESULTS

	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	53.8	100.0	57.2	100.0	100.0	100.0
% Voxel Density Less Than -910 HU	54	52	38	43	55	41
% Voxel Density Less Than -950 HU	31	29	14	24	31	17
Inspiratory Volume (ml)	1238	1367	129	1042	1168	1194



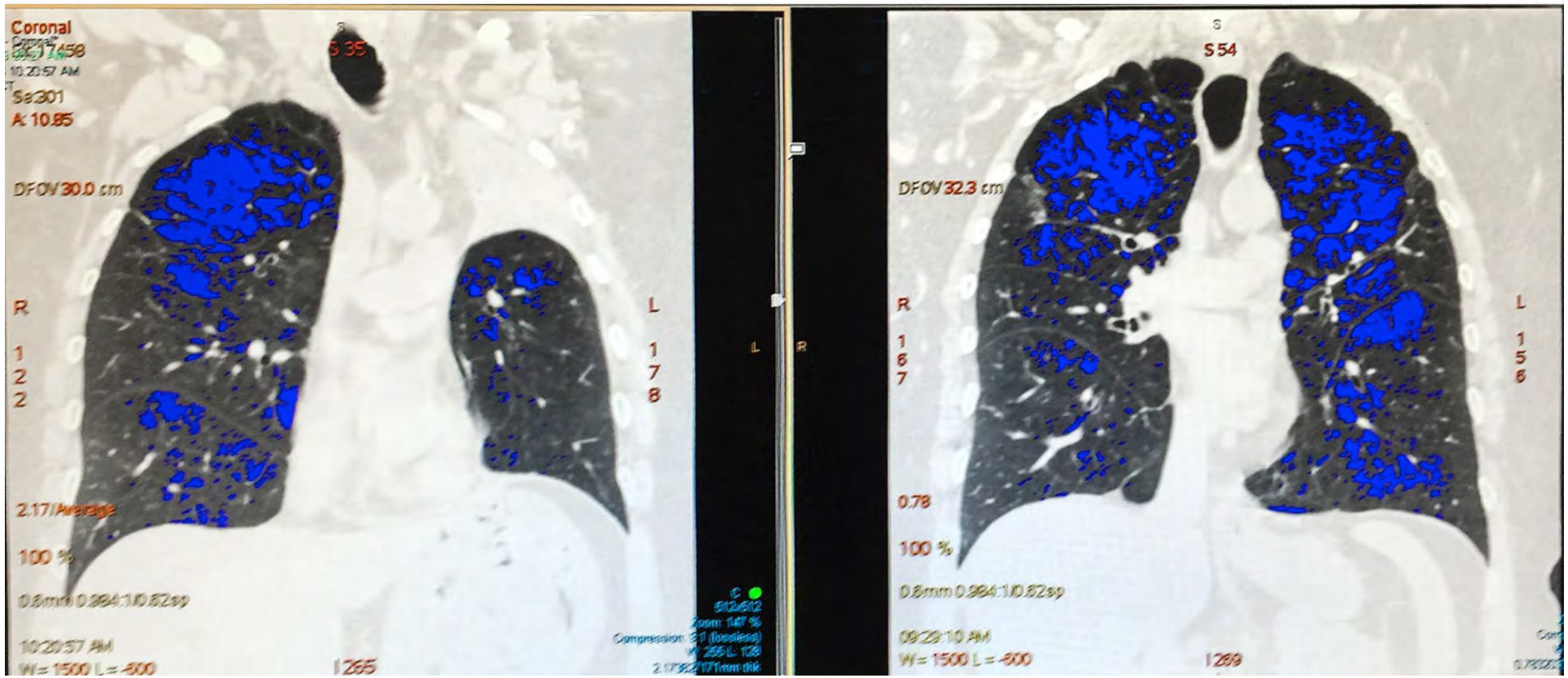
Fissure Analysis

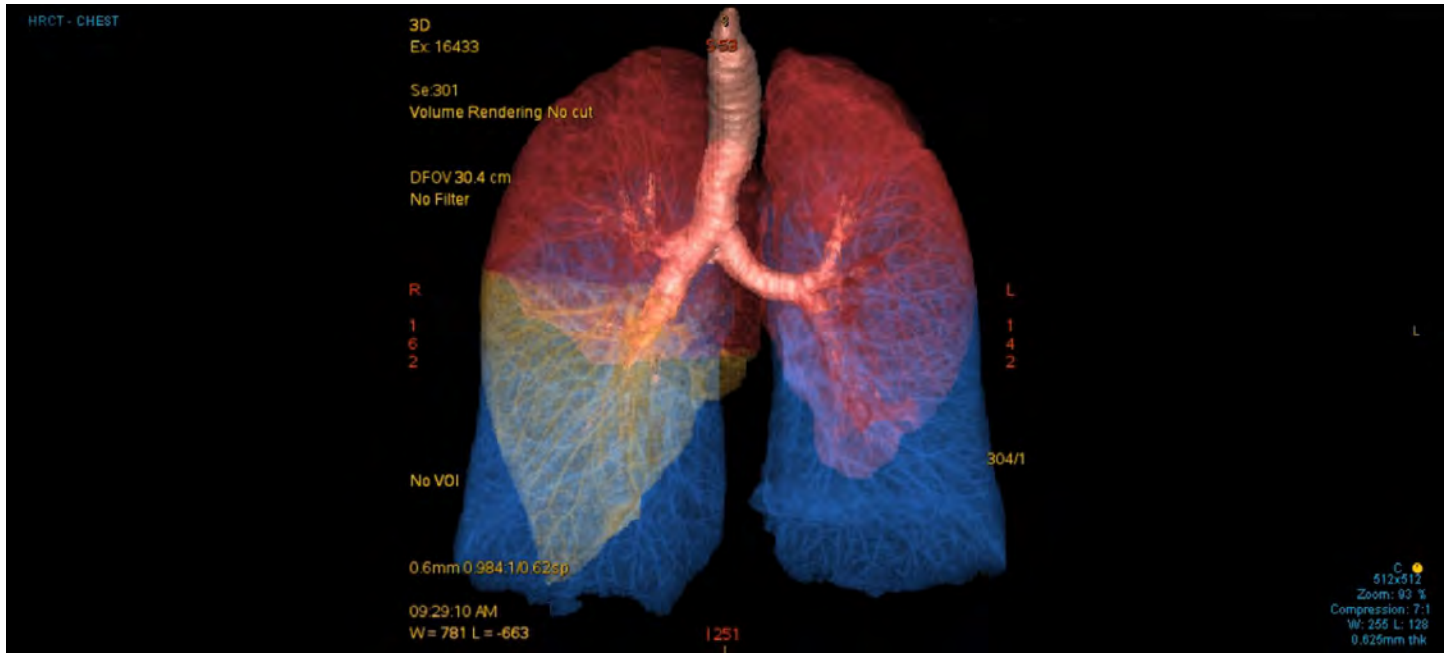
- Fissure > 95% complete – Proceed with ELVR if other criteria are met.
- Fissure 80-95% complete – Perform CHARTIS
- Fissure < 80% complete – not suitable for ELVR with endobronchial valves

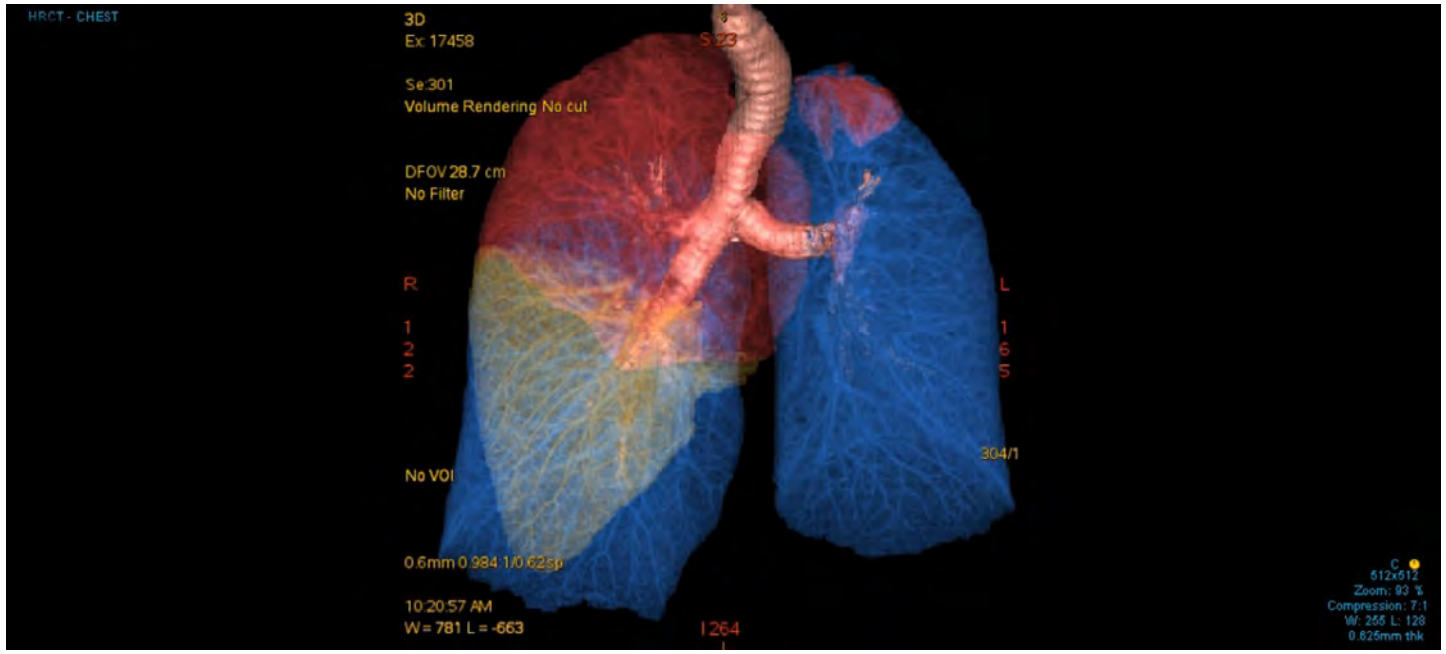


Immediate Post-op

Day 3 Post-op


Coronal
S 35
Se:301
A: 10.85
DFOV 30.0 cm
R
122
L
178
2.17/Average
100 %
0.8mm 0.984:1/0.82sp
10:20:57 AM
W = 1500 L = -600
I 265
S 54
DFOV 32.3 cm
R
167
L
156
0.78
100 %
0.8mm 0.984:1/0.82sp
09:29:10 AM
W = 1500 L = -600
I 269


HRCT - CHEST
3D
Ex: 16433
Se:301
Volume Rendering No cut
DFOV 30.4 cm
No Filter
R
1
6
2
L
1
4
2
No VOI
304/1
0.6mm 0.984:1/0.62sp
09:29:10 AM
W = 781 L = -663
I 251
C
512x512
Zoom: 93 %
Compression: 7:1
W: 255 L: 128
0.625mm thk


HRCT - CHEST
3D
Ex: 17458
Se:301
Volume Rendering No cut
DFOV 28.7 cm
No Filter
R
1
2
2
L
1
6
5
No VOI
304/1
0.6mm 0.984:1/0.62sp
10:20:57 AM
W = 781 L = -663
I 264
C
512x512
Zoom: 93 %
Compression: 7:1
W: 255 L: 128
0.625mm thk

RESPIRATORY FUNCTION TESTS

SPIROMETRY

(Post-BD = 400ug Salbutamol via spacer unless otherwise indicated in comments)

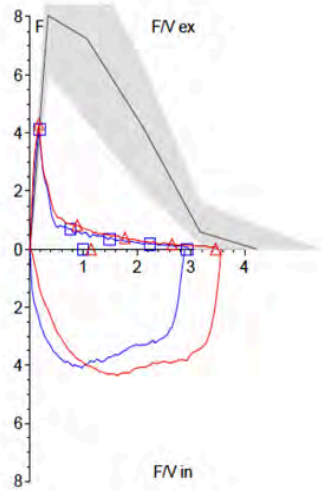
		Pre	Pre%...	Post	Post%...	%Change	Pred	Pred LL
FEV 1	L	0.98	31	1.14	36	16	3.14	2.22
FVC	L	2.92	69	3.45	82	18	4.22	3.08
FEV 1 % FVC	%	34	45	33	44	-2	75	61
MMEF 75/25	L/s	0.32	14	0.32	14	-1	2.26	0.91
PEF	L/s	4.13	51	4.29	53	4	8.04	6.05

LUNG VOLUMES

TLC	[L]	9.52	129				7.38	6.23
VC	[L]	3.22	75				4.29	3.37
IC	[L]	1.88	58				3.26	3.26
FRCpleth	[L]	7.64	200				3.82	2.83
ERV	[L]	1.33	129				1.03	1.03
RV	[L]	6.31	226				2.79	2.12
RV % TLC	[%]	66	153				43	34
sR 0.5	[kPa*s]	2.19						
R 0.5	[kPa/(L/s)]	0.27	89				0.30	0.30

GAS TRANSFER

DLCO_SB	[ml/(min*mmHg)]	7.92	29				27.26	20.33
DLCOcSB	[ml/(min*mmHg)]	7.81	29				27.26	20.33
VA_SB	[L]	5.25	73				7.23	7.23
KCO_SB	[ml/(min*mmHg*L)]	1.51	41				3.69	2.59
KCOc_SB	[ml/(min*mmHg*L)]	1.49	40				3.69	2.59
VIN_SB	[L]	3.48	81				4.29	3.37
Hb	[g(Hb)/100mL]	15.10						



INTERPRETATION

Severe airflow limitation with significant improvement in FVC after salbutamol. Moderate hyperinflation and gas trapping with reduced gas transfer c/w emphysema.

Prof Matthew Peters MD FRACP

(Physician 02.02.2017 06:26PM)

Tests meet ATS standards for acceptability & repeatability. Hb from pathology 28/1/17.

RESPIRATORY FUNCTION TESTS

SPIROMETRY

(Post-BD = 400ug Salbutamol via spacer unless otherwise indicated in comments)

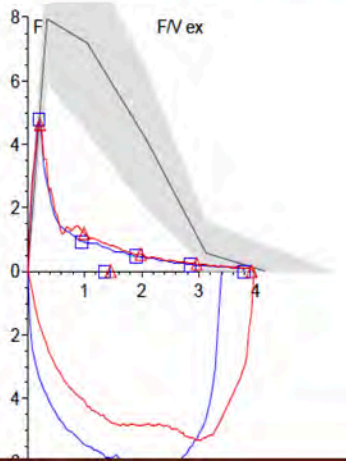
		Pre	Pre%...	Post	Post%...	%Change	Pred	Pred LL
FEV 1	L	1.34	44	1.45	47	8	3.08	2.16
FVC	L	3.79	91	3.92	94	3	4.16	3.02
FEV 1 % FVC	%	35	47	37	50	5	75	60
MMEF 75/25	L/s	0.42	19	0.46	21	8	2.19	0.86
PEF	L/s	4.78	60	4.62	58	-3	7.95	5.96

LUNG VOLUMES

TLC	[L]	9.53	129				7.38	6.23
VC	[L]	3.78	89				4.24	3.31
IC	[L]	2.50	77				3.23	3.23
FRCpleth	[L]	7.03	183				3.84	2.85
ERV	[L]	1.28	128				1.00	1.00
RV	[L]	5.75	203				2.84	2.16
RV % TLC	[%]	60	137				44	35
sR 0.5	[kPa*s]	1.63						
R 0.5	[kPa/(L/s)]	0.21	71				0.30	0.30

GAS TRANSFER

DLCO_SB	[ml/(min*mmHg)]	7.78	29				26.87	19.94
DLCOcSB	[ml/(min*mmHg)]	7.80	29				26.87	19.94
VA_SB	[L]	5.86	81				7.23	7.23
KCO_SB	[ml/(min*mmHg*L)]	1.33	36				3.64	2.54
KCOc_SB	[ml/(min*mmHg*L)]	1.33	37				3.64	2.54
VIN_SB	[L]	3.68	87				4.24	3.31
Hb	[g(Hb)/dL]	14.50						



INTERPRETATION

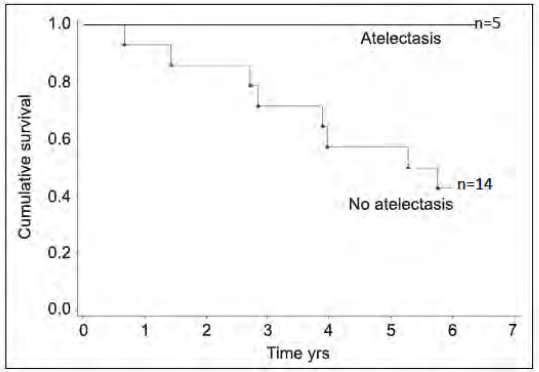
FVC is marginally higher than June and FEV1 is improved over pre-ELVR tests. Lung volumes show stable reduction in RV. Stable diffusng capacity.

Prof Matthew Peters MD FRACP

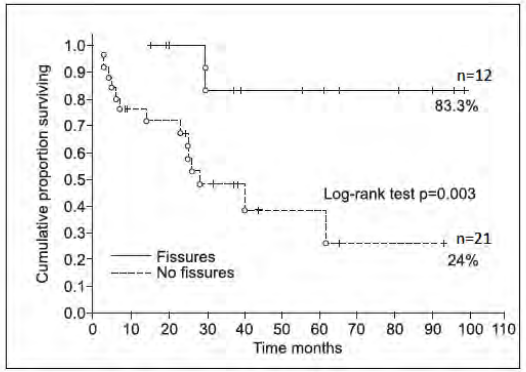
(Physician 04.10.2018 18:40:22)

Symbicort and Spiolto taken approx 2.5hrs prior. Tests meet ATS standards for acceptability and repeatability. Hb taken from previous test.

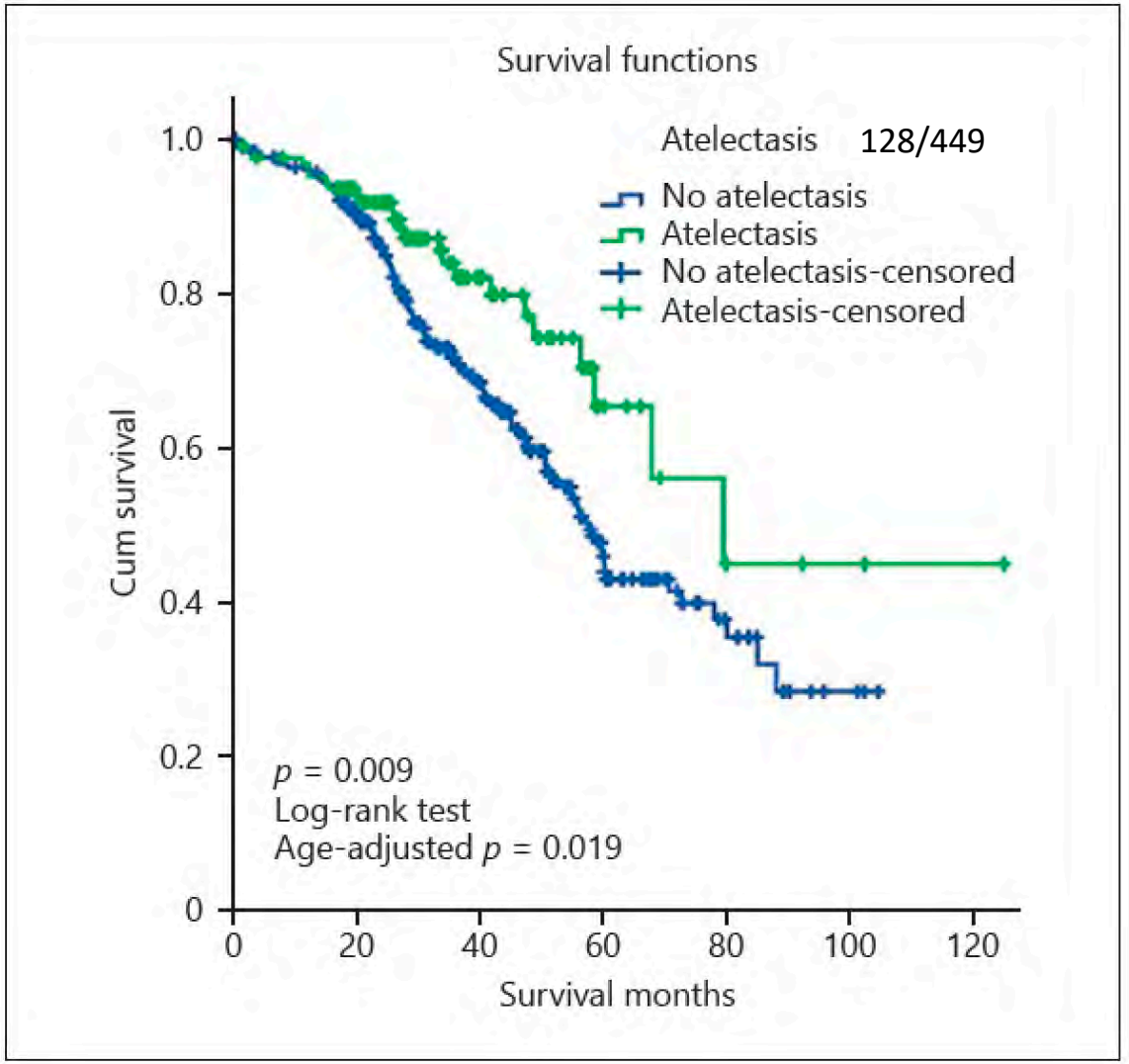
Clinical Response + Targeted atelectasis



Hopkinson et al., Eur Respir J, 2011



Venuta et al., Eur Respir J, 2012



128/449

Respiration 2019;97:145–152
DOI: 10.1159/000492274

Gompelmann et al.

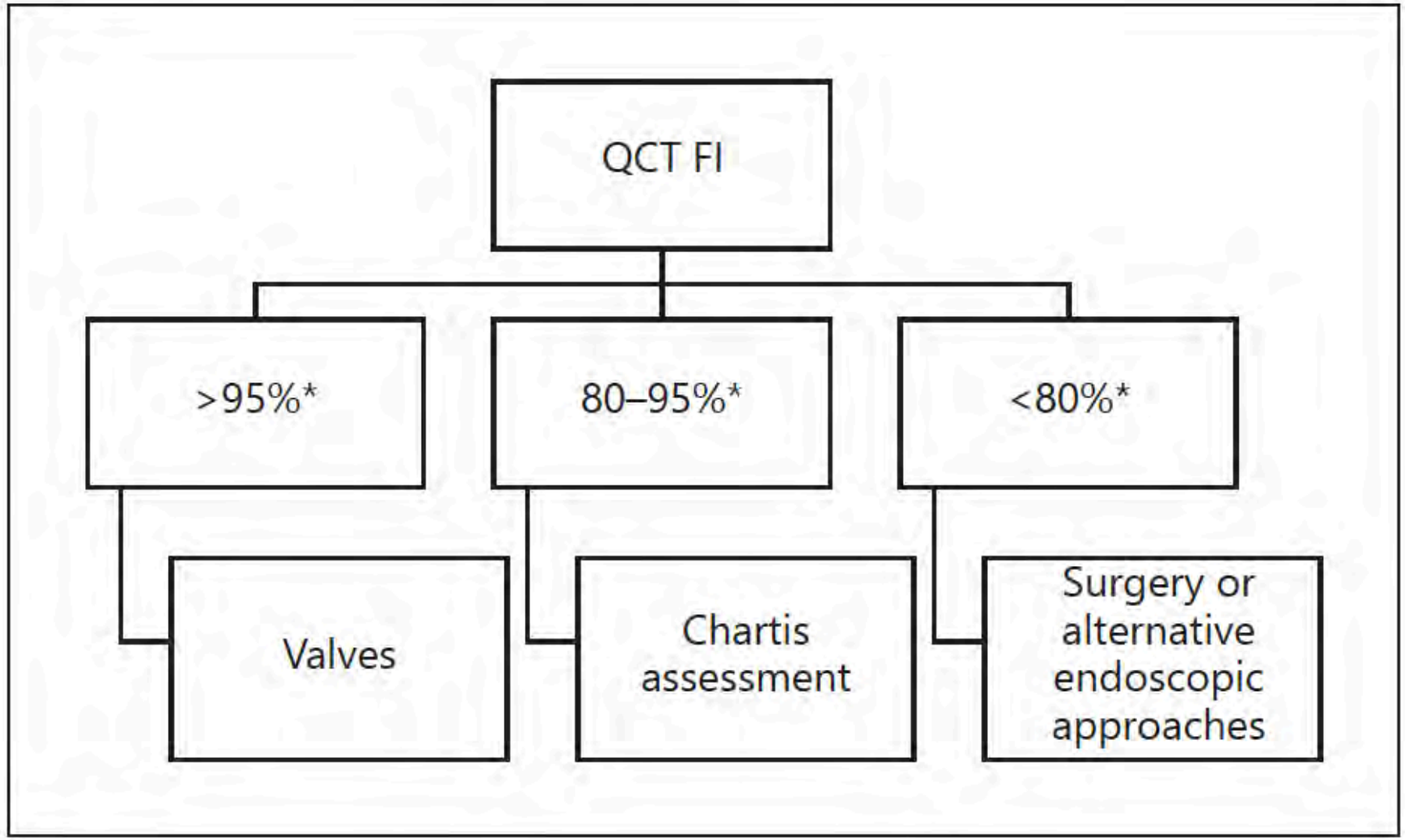
	Study	Study design	Patient population	Time point	ΔFEV$_1$	Δ6-MWT	ΔSGRQ	ΔTLVR
Valves	Sciurba et al. 2010: „VENT" (9)	Randomized, controlled	Treatment group (n = 214)	6 months	4,3%	9,3 m	−2,8 pts	–
	Herth et al. 2012: „Euro-VENT" (10)	Randomized, controlled	Treatment group (n = 111)	6 months	7 ± 20%	15 ± 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%

Mechanism of Action

- Volume Loss, deflation of targeted lobe
- Ventilation / Perfusion Matching
- Reduction of Pulmonary Pressures / Pul HT
- Changes in small airways / lung mechanics (as assessed by FOT)

ELVR – Learning Curve

- Patient Selection
- Interventional MDT
- Risk and Management of Pneumothorax
- Need for ELVR follow up and revision

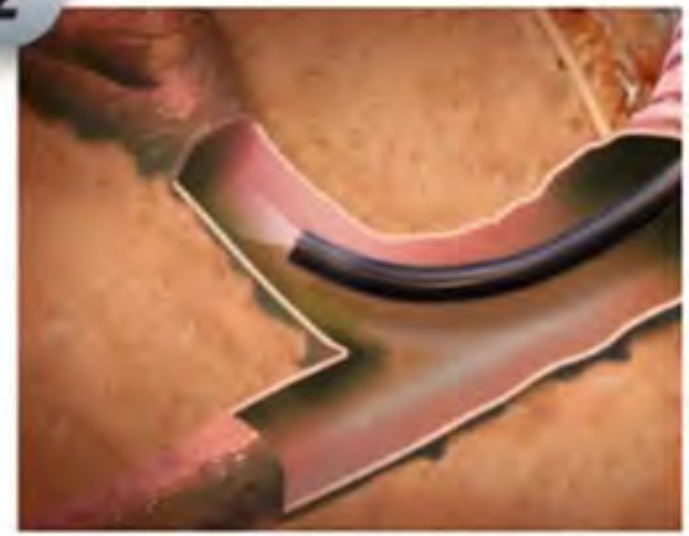

QCT FI
>95%*
80–95%*
<80%*
Valves
Chartis assessment
Surgery or alternative endoscopic approaches

Thermal Vapour Ablation

1

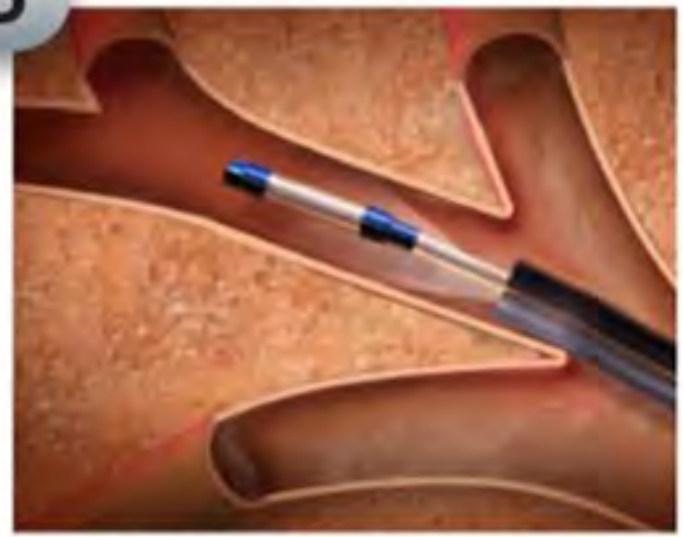
IP3 identifies airway targets for procedure

2



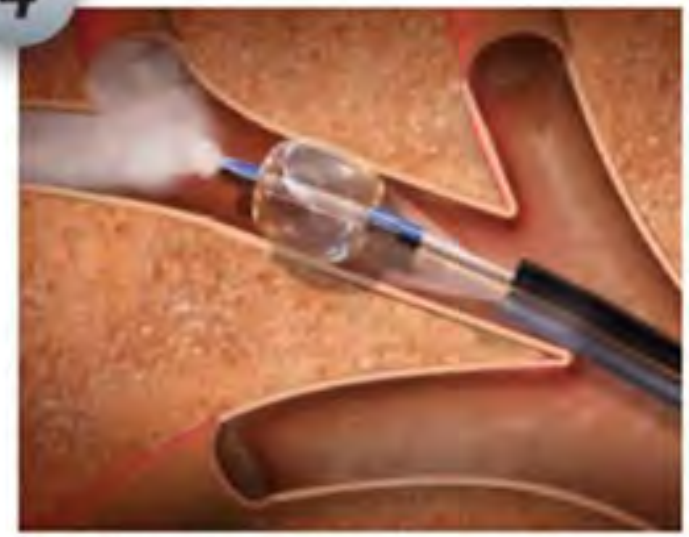
Bronchoscope is inserted into target segment airway

3



InterVapor catheter is placed into position

4



Occlusion balloon is inflated and heated water vapor is delivered

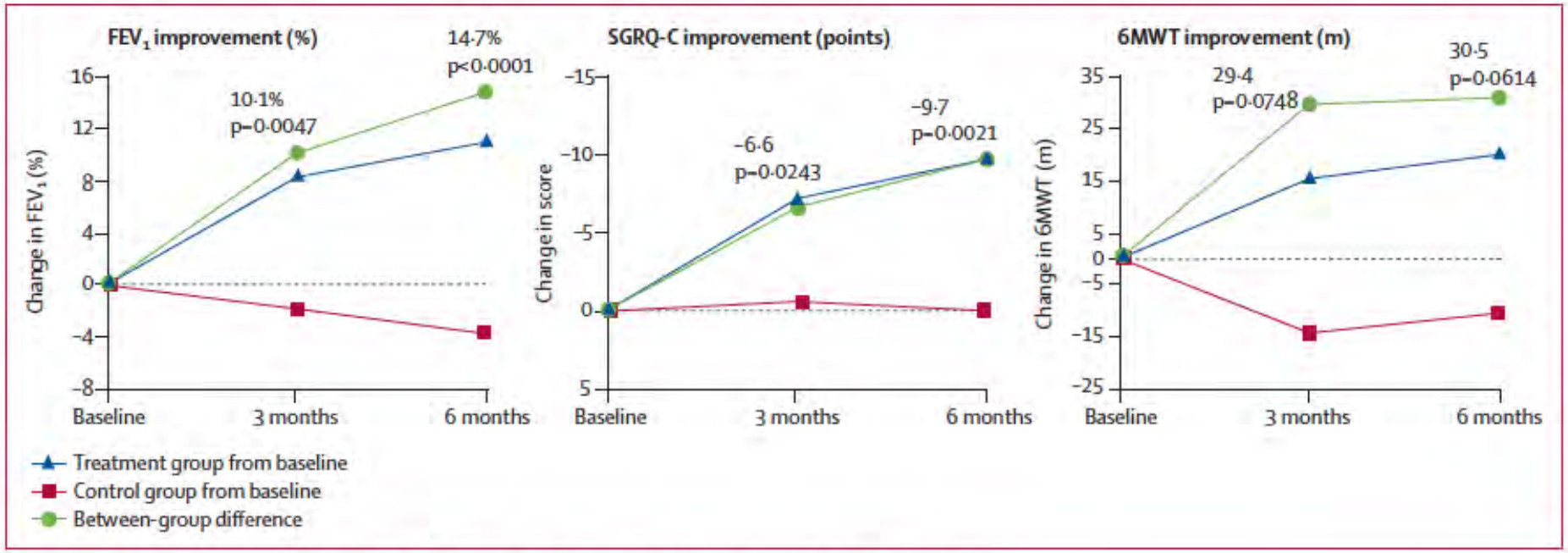


***Figure 3*: Endpoints for pulmonary function, quality of life, and exercise tolerance in each trial group**
FEV_1=forced expiratory volume in 1 s. SGRQ=St George's Respiratory Questionnaire. 6MWT=6-min walk test.

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

Lancet Respir Med 2016; 4: 185–93

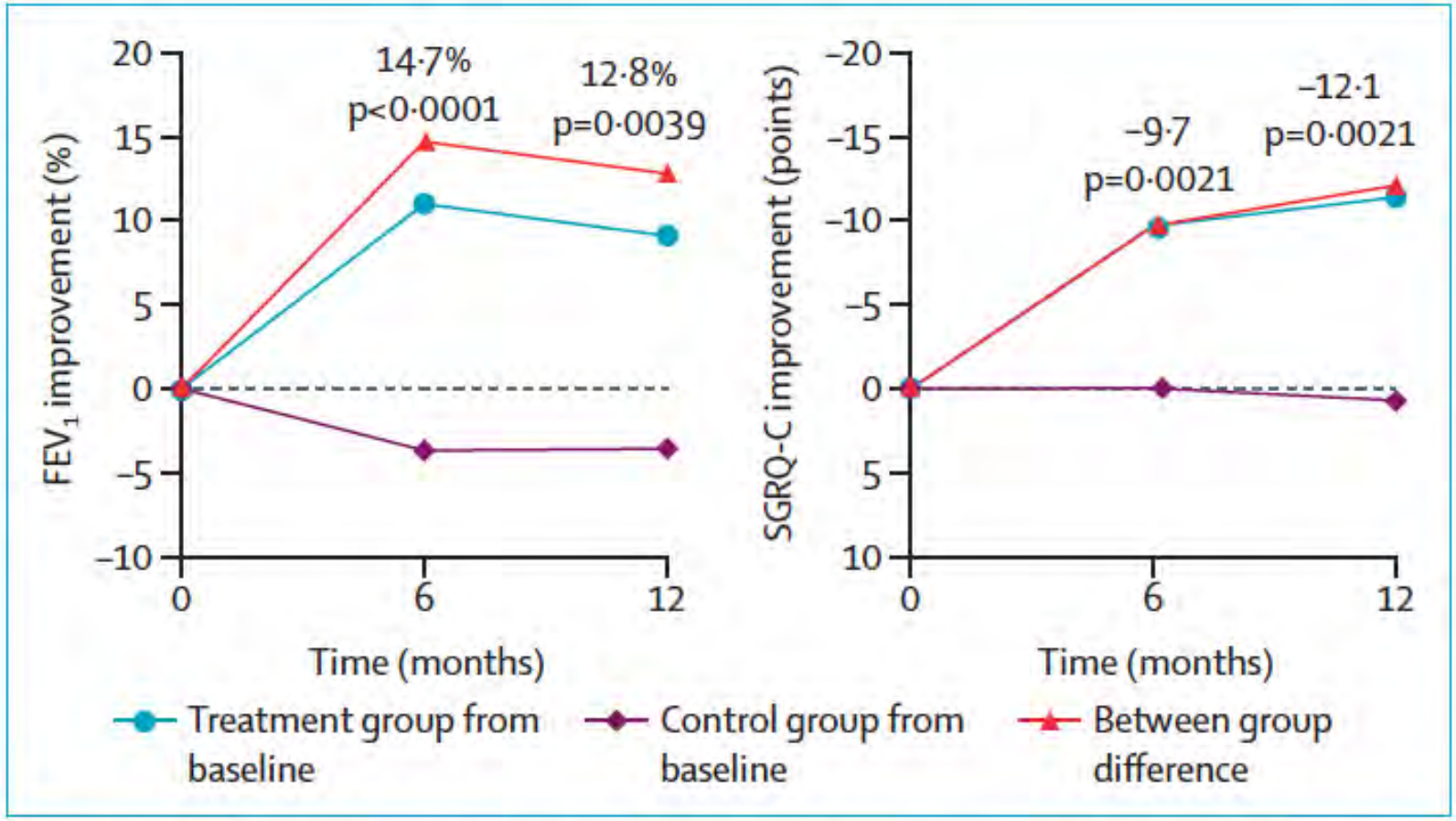


Figure: **Primary endpoint efficacy measures at 6 months and 12 months after vapour ablation**

p values calculated with two-sample t test. Full statistical plan previously reported.[1,3] FEV_1=forced expiratory volume in 1 s. SGRQ-C=Saint George's respiratory questionnaire for COPD.

	Treatment group (n=45)			Control group (n=24)
	After treatment session 1	After treatment session 2	0–180 days of treatment (overall)*	0–180 days of randomisation (overall)
COPD exacerbation	6 (13%)	6 (15%)	11 (24%)	1 (4%)
Pneumonia or pneumonitis	6 (13%)	3 (8%)	8 (18%)	2 (8%)
Pneumothorax	0	1 (3%)	1 (2%)	0
Requiring surgery	0	0	0	0
Requiring chest tube(s)	0	0	0	0
Haemoptysis	0	1 (3%)	1 (2%)	0
Death	1 (2%)	0	1 (2%)	0
Any serious respiratory adverse event	10 (22%)	9 (23%)	16 (36%)	3 (13%)

Data are n (%). *180 days after treatment session 1 or 90 days after treatment session 2.

Table 6: **Serious adverse events and hospital admissions**

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

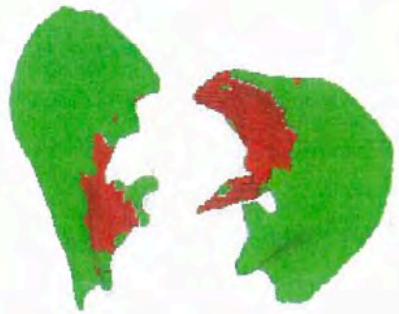
Lancet Respir Med 2016; 4: 185–93

	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	63.5	79.8	87.4	79.8	81.3	81.3

FRONT

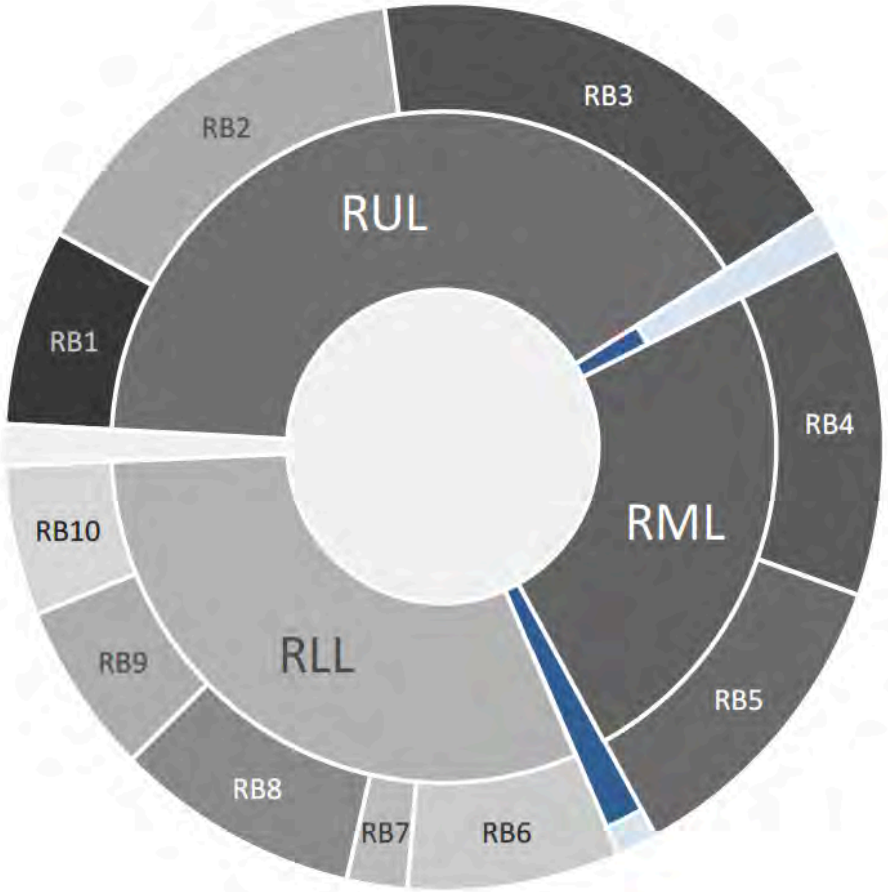
SIDE - RIGHT LUNG

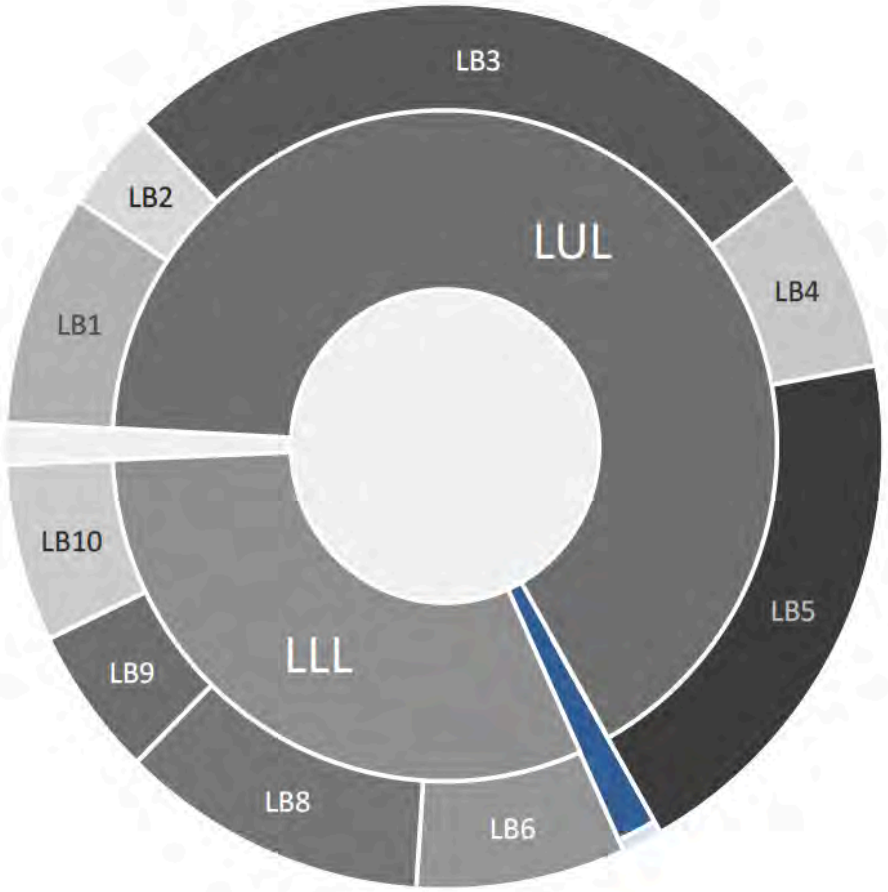
BACK



SIDE - LEFT LUNG

Lung Segment Treatment Overview





Legend

Fissure Integrity: % Complete

Disease Severity: 0 > 70 %

Relative Volume: Represented by relative size of region shape

Lung Segment Treatment Details

	RB1	RB2	RB3	LB1	LB2	LB3	LB1+2	
%-950 (Disease Severity)	57 %	25 %	49 %	23 %	11 %	48 %	19 %	Percent of voxels with density < -950 HU by QCT analysis (>40% equivalent to TAR <11%)
HI (Disease heterogeneity)	2.6	1.1	2.2	0.7	0.3	1.5	0.6	Segmental heterogeneity index: %-950 of segment / %-950 of ipsilateral lobe
Segment volume (ml)	310	642	792	321	138	1 014	459	Absolute volume of tissue and air
Percent of lobe	18 %	37 %	45 %	13 %	6 %	41 %	18 %	Relative volume with respect to lobe
Available for treatment?	✓	x	✓	x	x	✓	x	Based on volume and HI
Treat additional segment?	•RB3		•RB1					One of the listed segments may be treated in the same procedure

Fissure Integrity Right Oblique Horizontal	26 %

	RB4	RB5	LB4	LB5	
%-950 (Disease Severity)	47 %	43 %	16 %	56 %	Percent of voxels with density < -950 HU by QCT analysis (>40% equivalent to TAR <11%)
HI (Disease heterogeneity)	1.1	1.0	0.5	1.7	Segmental heterogeneity index: %-950 of segment / %-950 of ipsilateral lobe
Segment volume (ml)	554	502	274	746	Absolute volume of tissue and air
Percent of lobe	52 %	48 %	11 %	30 %	Relative volume with respect to lobe
Available for treatment?	x	x	x	x	Based on volume and HI
Treat additional segment?					One of the listed segments may be treated in the same procedure

Fissure Integrity Right Oblique	91 %

Fissure Integrity Left Oblique	96 %

	RB6	RB7	RB8	RB9	RB10	LB6	LB8	LB9	LB10	
%-950 (Disease Severity)	16 %	20 %	34 %	24 %	12 %	31 %	39 %	41 %	15 %	Percent of voxels with density < -950 HU by QCT analysis (>40% equivalent to TAR <11%)
HI (Disease heterogeneity)	0.4	0.5	0.8	0.6	0.3	0.7	1.0	1.0	0.4	Segmental heterogeneity index: %-950 of segment / %-950 of ipsilateral lobe
Segment volume (ml)	339	97	390	272	236	291	429	207	245	Absolute volume of tissue and air
Percent of lobe	25 %	7 %	29 %	20 %	18 %	25 %	37 %	18 %	21 %	Relative volume with respect to lobe
Available for treatment?	x	x	x	x	x	x	x	x	x	Based on volume and HI
Treat additional segment?										One of the listed segments may be treated in the same procedure

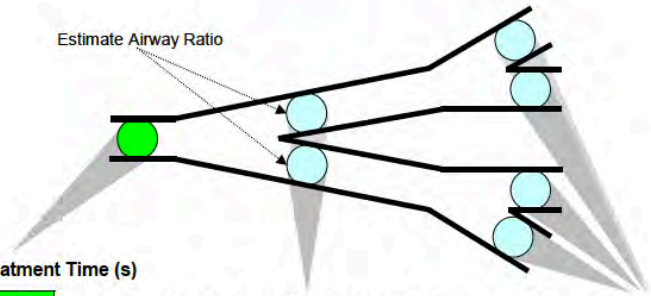
Note: NA = Not analyzable. HI = Heterogeneity Index. QCT = Quantitative Computed Tomography. HU = Hounsfield Unit. TAR = Tissue-to-Air Ratio

InterVapor ID: H7009JC46

Right Upper Lobe Segment: RB1

Segment volume:	310 ml	Target vapor dose:	8.5 cal/g
Segment mass:	24 g	Vapor dose lower limit:	7.5 cal/g
Percent of lobe:	18 %	Vapor dose upper limit:	8.5 cal/g
Emphysema (%-950):	57 %		

Preferred treatment location: Segmental Level



Segment Treatment Time (s)

5.6
8.5 cal/g

Sub-Segment Treatment Time (s)

50 %	50 %
3.3	3.3
8.5 cal/g	8.5 cal/g
33 %	67 %
DNT	4.1
11.1 cal/g	8.5 cal/g
25 %	75 %
DNT	4.4
14.9 cal/g	8.5 cal/g

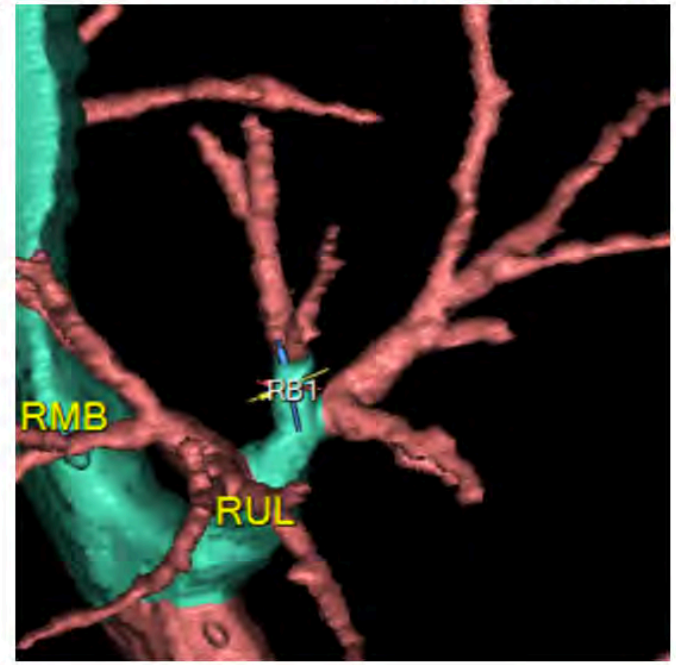
Sub-Sub-Segment Time (s)

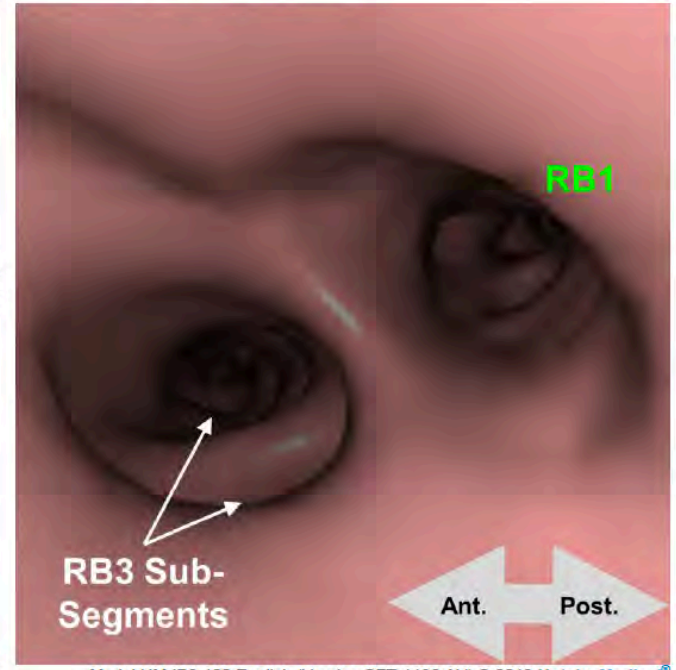
See Sub-Sub-Segments Table

Note: DNT = Do Not Treat

Comments:

None





AeriSeal – Foam Polymer

Foam Polymer

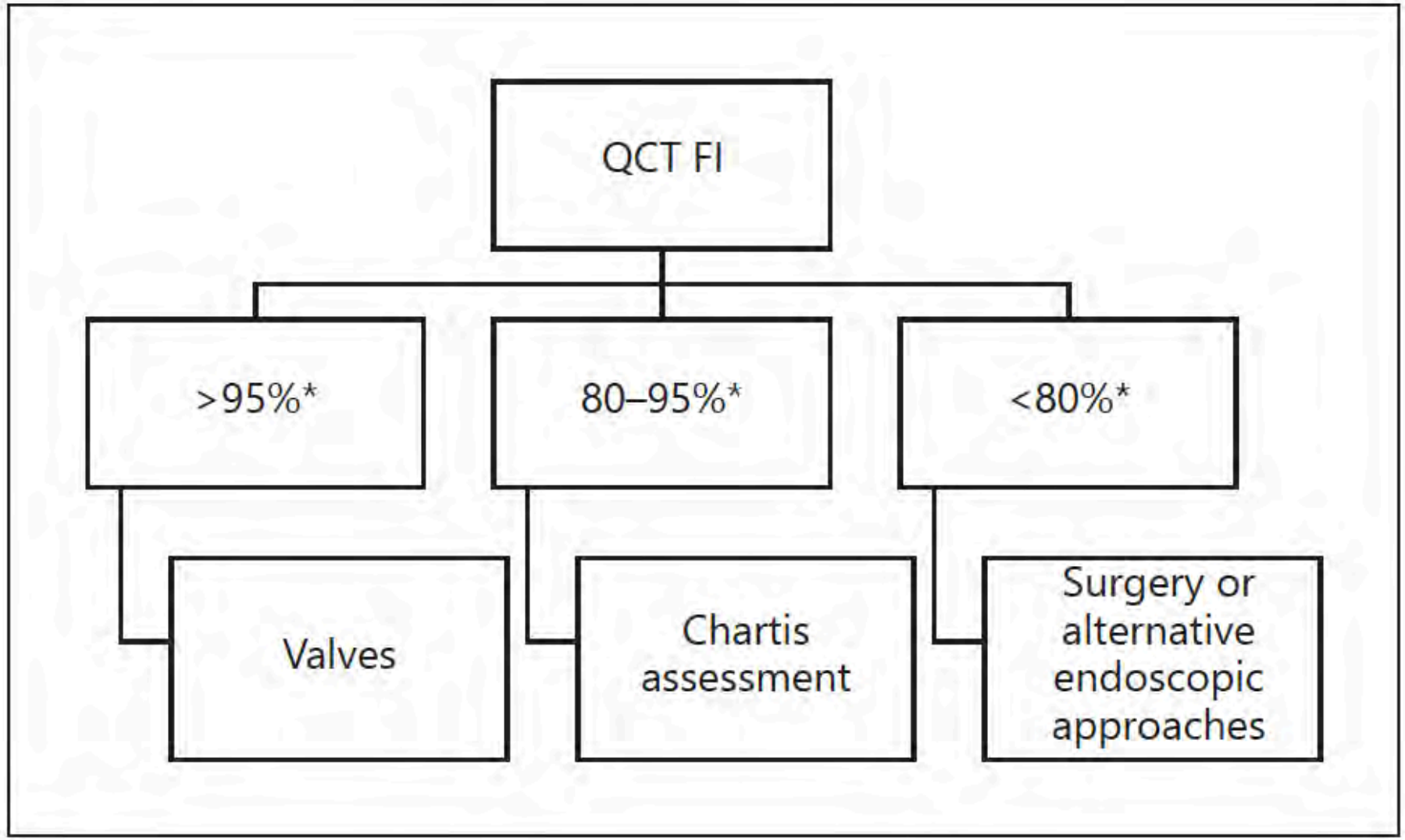
- Synthetic Foam Polymer. Aeris Therapeutics
- 2 parts – aeration of foam is critical

A single sub-segmental AeriSeal® System treatment consists of up to 20 mL of Foam Sealant

- 15 mL of air
- 4.5 mL of Solution A containing 2.1% (w/v) aminated **polyvinyl alcohol** [aPVA] and
- 0.5 mL of Solution B containing 1.25% (w/v) of **glutaraldehyde** [GA]

AeriSeal

- Administered bronchoscopically via a sealed balloon catheter
- Sealant obstructs small airways and collateral channels, as well as at alveolar level
- Promotes atelectasis, remodelling reducing hyperinflation


QCT FI
>95%*
80–95%*
<80%*
Valves
Chartis assessment
Surgery or alternative endoscopic approaches

StratX™ Lung Report

pulmonX

Patient ID		Upload Date	Sept. 9, 2018
Scan ID		Report Date	Sept. 11, 2018
CT Scan Date	Aug. 24, 2018	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	84.6	83.3	98.6	83.3	83.2	83.2
% Voxel Density Less Than -910 HU	59	57	52	46	56	45
% Voxel Density Less Than -950 HU	40	38	31	27	37	28
Inspiratory Volume (ml)	1858	2422	564	1750	1906	1945

VQDI = V/Vol X P/Vol

	Ventilation %	Perfusion %	Vol %	V/Vol	P/Vol	VQDI
RUL	26	22	23	1.13	0.96	1.08
RML	9	8	8	1.13	1.00	1.13
RLL	21	24	21	1.00	1.14	1.14
LUL	19	17	24	0.79	0.71	0.56
LLL	25	29	24	1.04	1.21	1.26

IRACRR VENTILATION Transaxials **IRACRR VENTILATION MIP**

	RIGHT				LEFT		
	RUL	RML	RLL	Total	LUL	LLL	Total
Counts kcts	26% 4891	9% 1607	21% 3942	56% 10440	19% 3437	25% 4675	44% 8113
Volume ml	23% 1827	8% 624	21% 1692	52% 4143	24% 1884	24% 1939	48% 3823

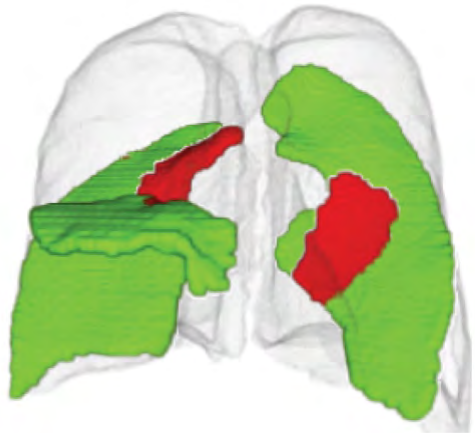
IRACRR VENTILATION
Lobar Distribution

IRACRR PERFUSION Transaxials **IRACRR PERFUSION MIP**

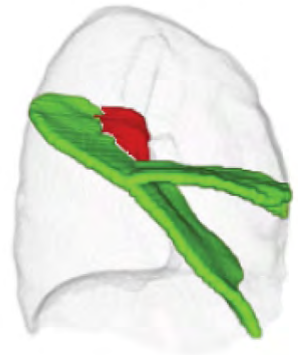
	RIGHT				LEFT		
	RUL	RML	RLL	Total	LUL	LLL	Total
Counts kcts	22% 20459	8% 7072	24% 22162	54% 49693	17% 15524	29% 26820	46% 42344
Volume ml	23% 1833	8% 627	21% 1678	52% 4138	24% 1874	24% 1947	48% 3821

IRACRR PERFUSION
Lobar Distribution

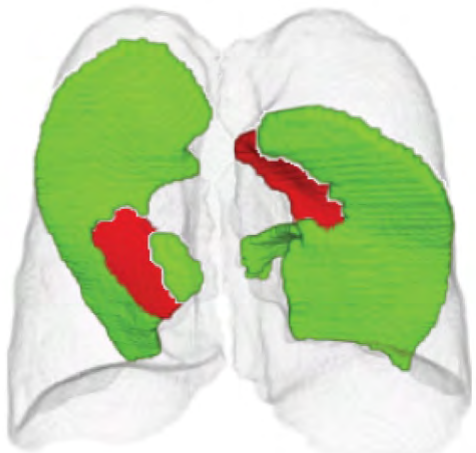
FRONT



SIDE -
RIGHT LUNG

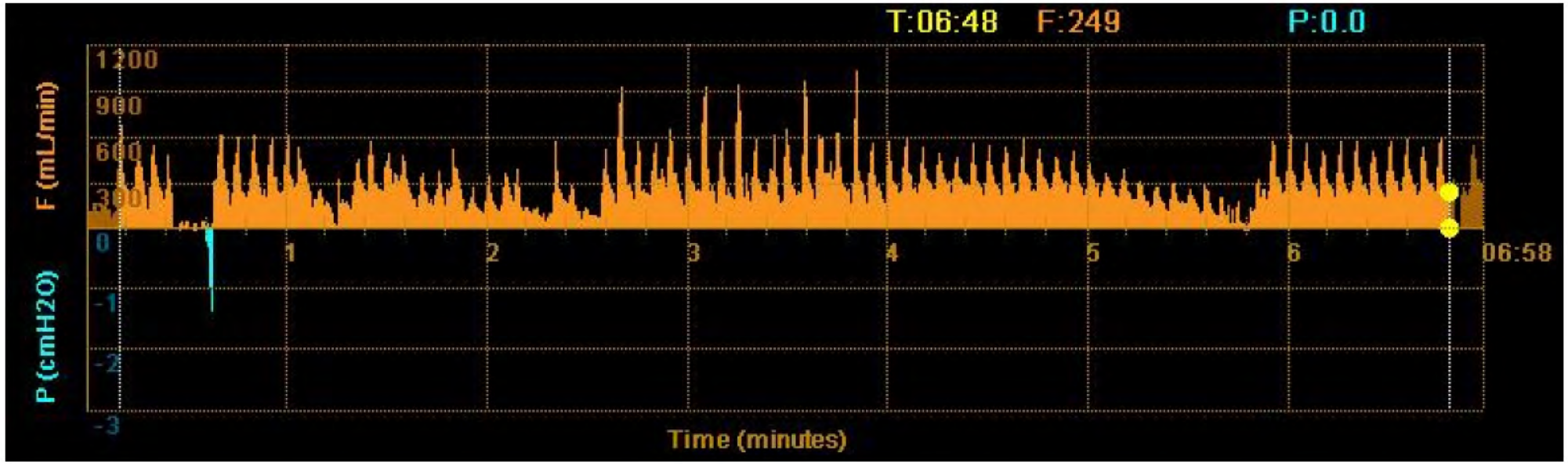


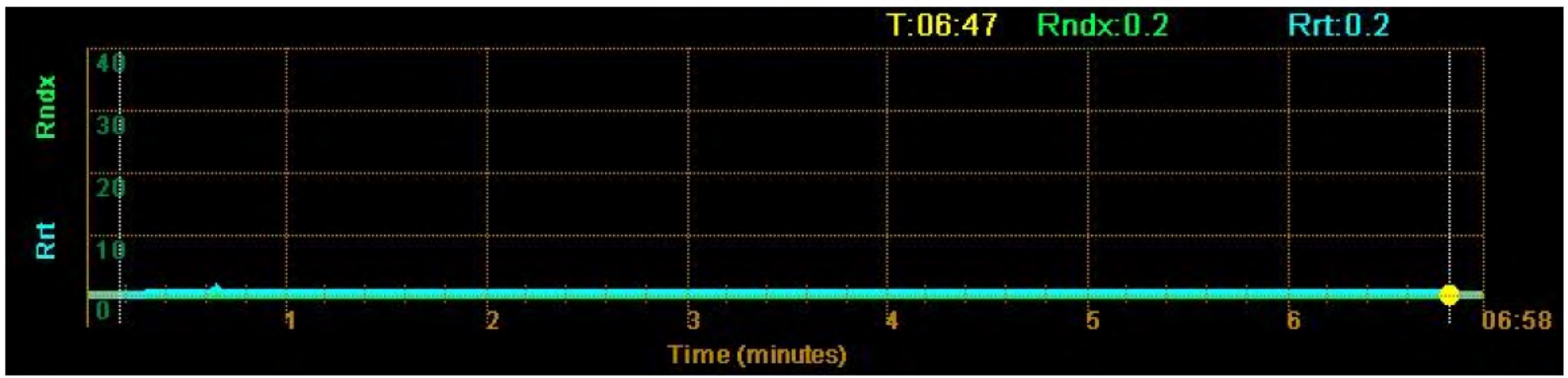
BACK

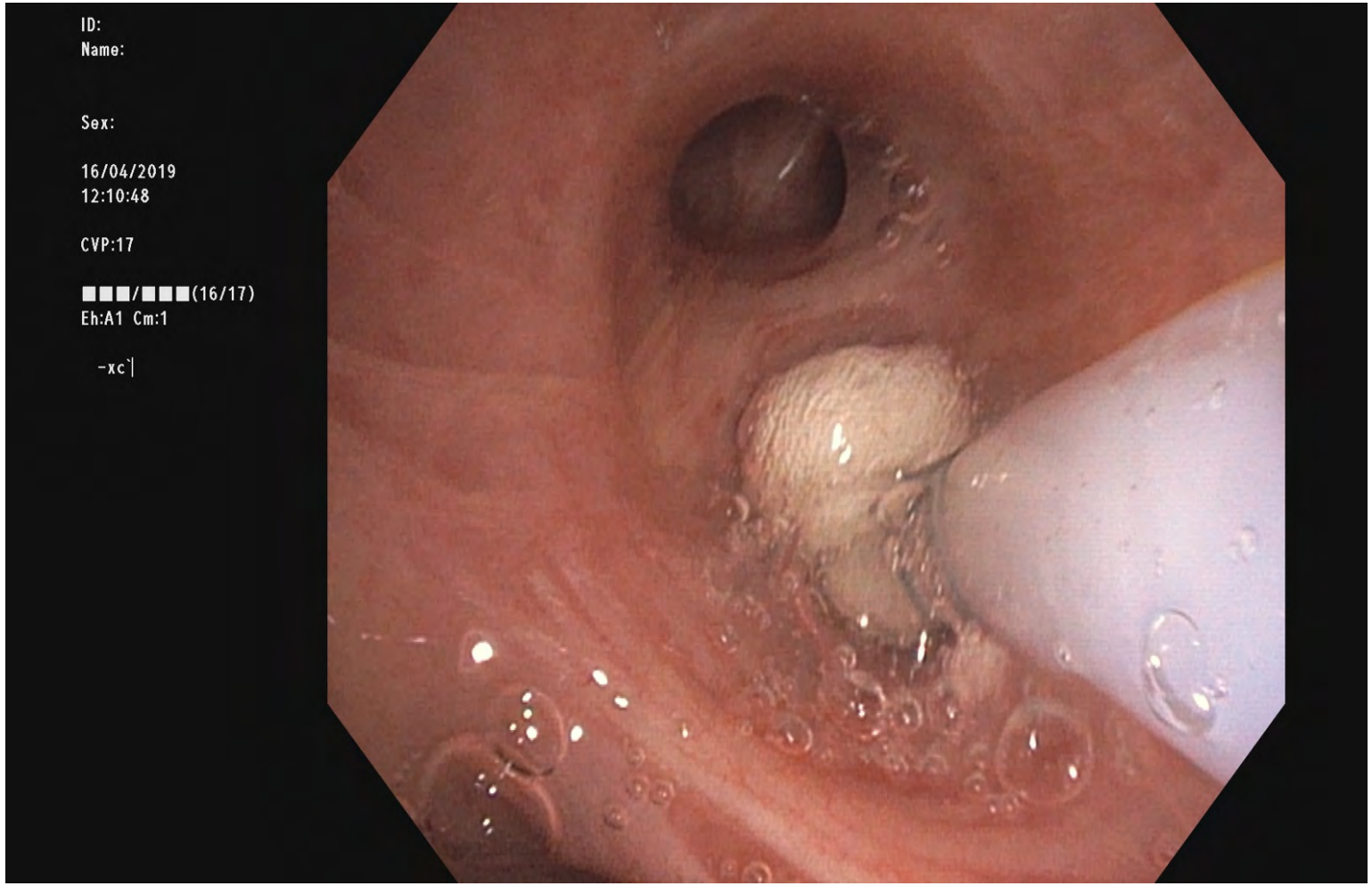


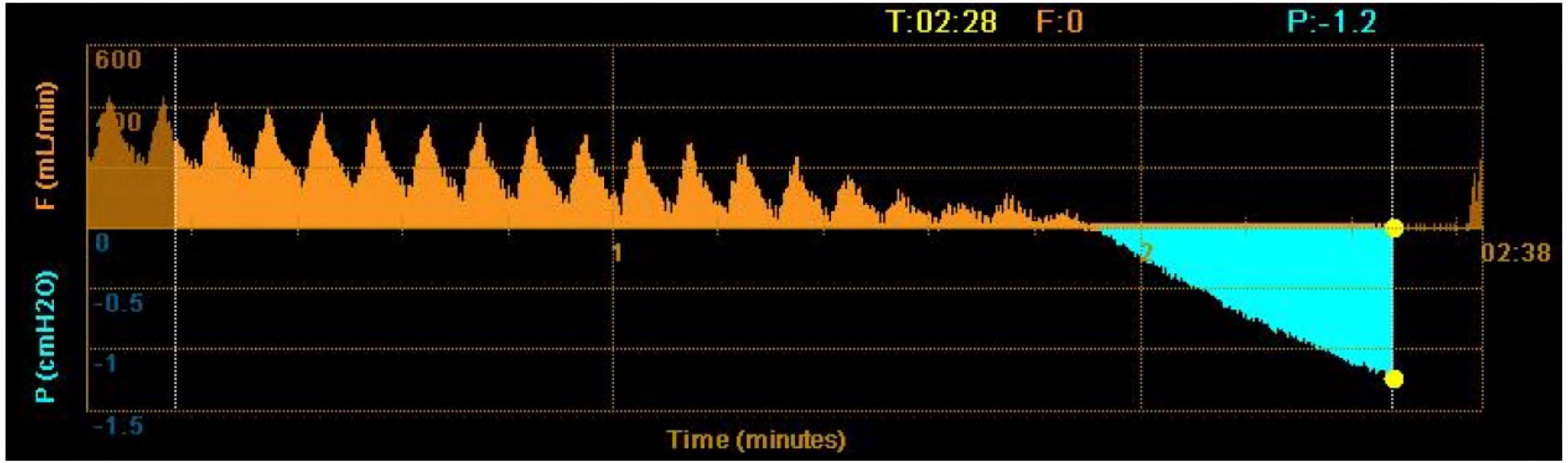
SIDE -
LEFT LUNG

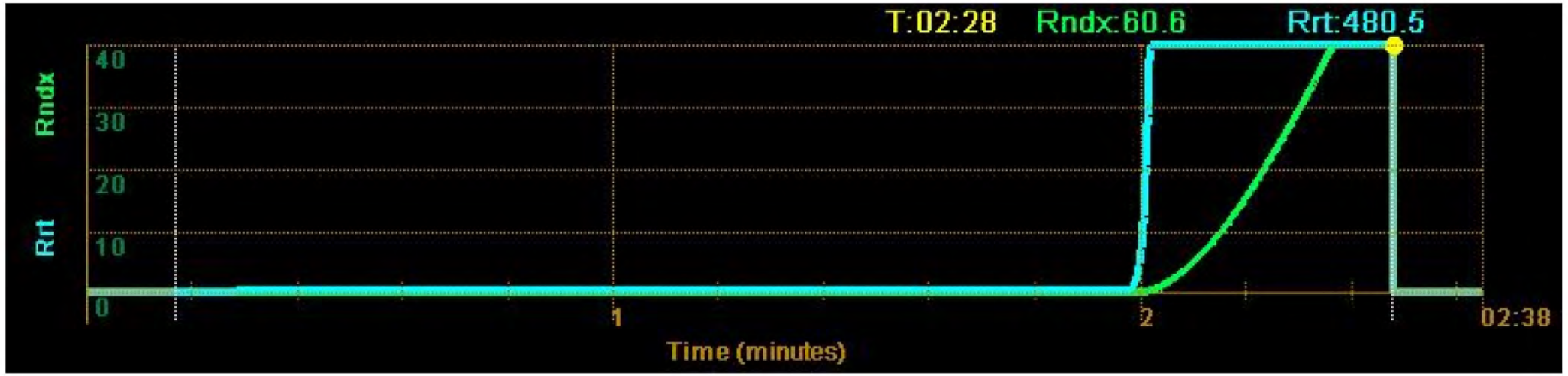
Segment	Segmental Volume (ml)	% of gap covered by segment
LB1+2	804.8	0
LB3	678.9	0
LB4	102.8	49.7
LB5	322.2	50.3

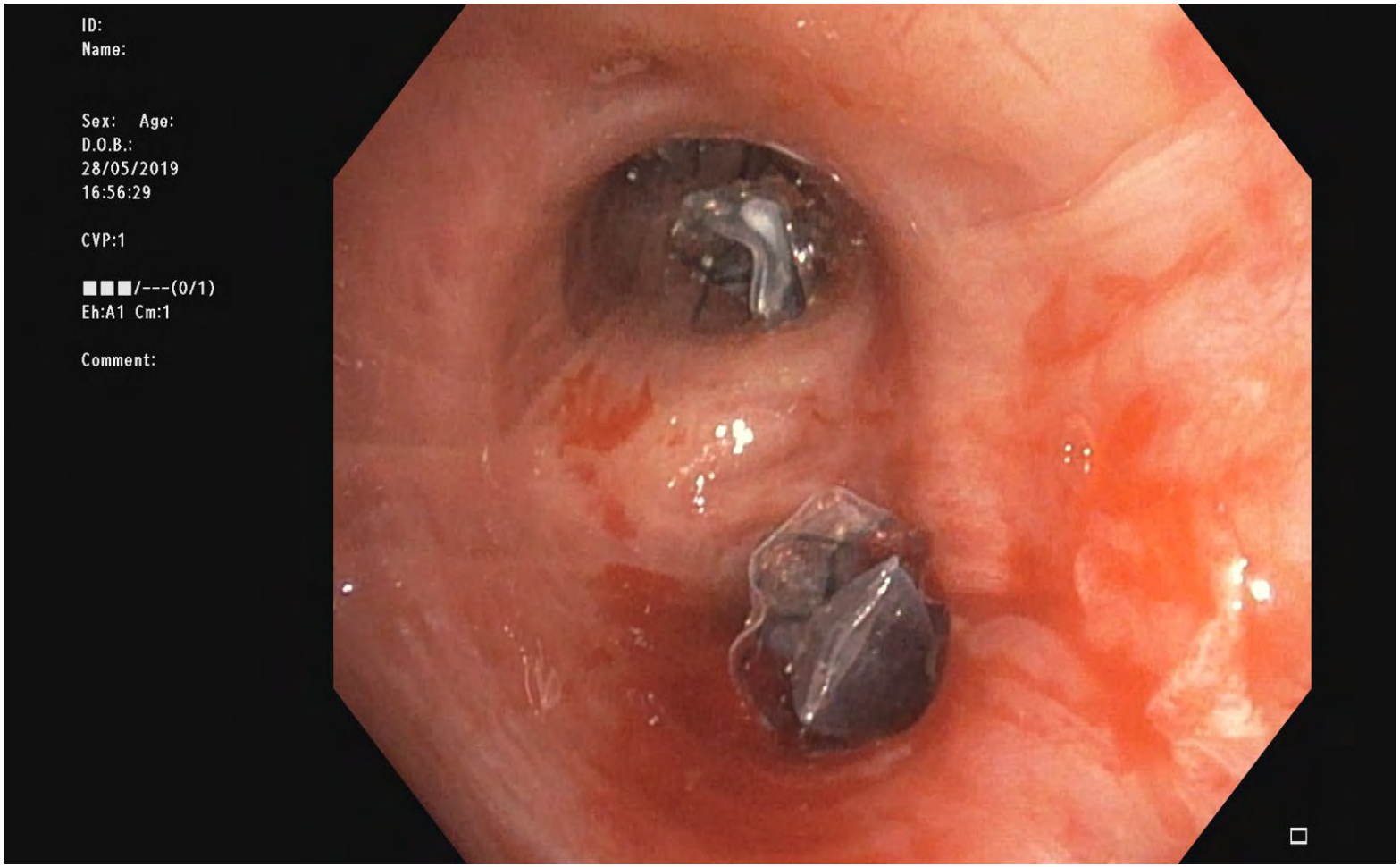

T:06:48
F:249
P:0.0
F (mL/min)
1200
900
600
300
P (cmH2O)
0
-1
-2
-3
1
2
3
4
5
6
06:58
Time (minutes)


T:06:47
Rndx:0.2
Rrt:0.2
Rndx
Rrt
40
30
20
10
0
1
2
3
4
5
6
06:58
Time (minutes)


ID:
Name:
Sex:
16/04/2019
12:10:48
CVP:17
■■■/■■■(16/17)
Eh:A1 Cm:1
-xc`


T:02:28
F:0
P:-1.2
600
F (mL/min)
0
-0.5
-1
P (cmH2O)
-1.5
1
2
02:38
Time (minutes)

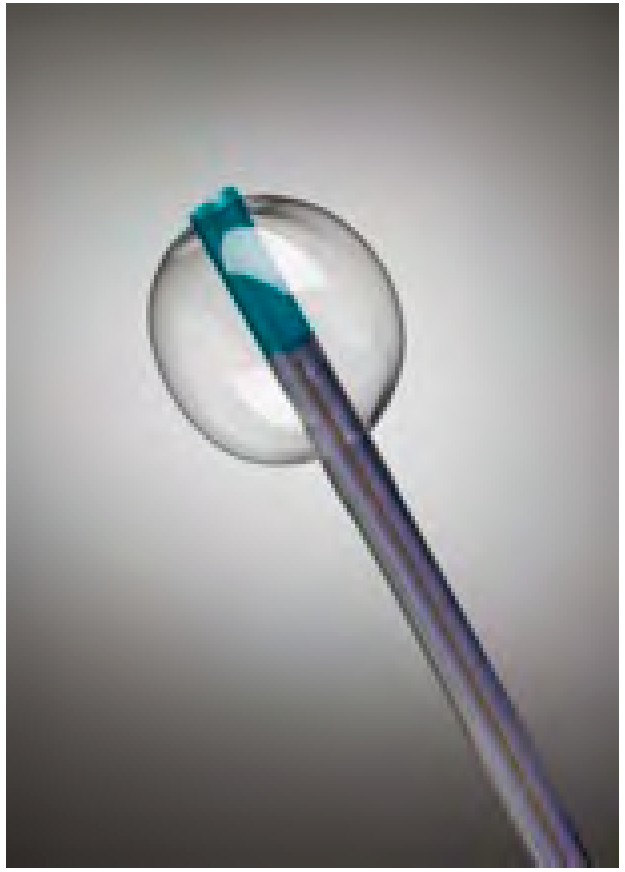

T:02:28
Rndx:60.6
Rrt:480.5
40
30
20
10
0
Rndx
Rrt
1
2
02:38
Time (minutes)

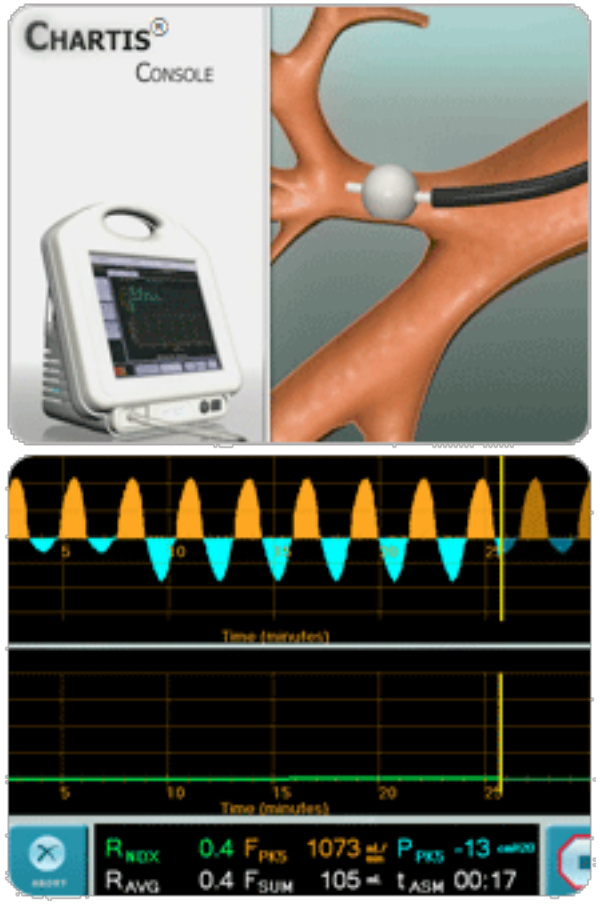

ID:
Name:
Sex: Age:
D.O.B.:
28/05/2019
16:56:29
CVP:1
■■■/---(0/1)
Eh:A1 Cm:1
Comment:


Se: 16/04/2019 12:00:05 PM
R
L
Se: 28/05/2019 4:08:36 PM
S
R

Measurement		Spiro			Body			Diff SB			
Parameter		FEV1	FVC	FEV1%F	TLC	FRCpl	RV	DLCO_S	KCO_SB	VA_SB	DLCOcS
Date	Medication	(L)	(L)	(%)	(L)	(L)	(L)	(m...	(m...	(L)	(m...
9/08/2017		1.27	3.59	35	9.45	7.17	5.77	14.95	2.19	6.83	15.22
9/08/2017		1.12	3.53	32							
20/11/2017		1.17	3.44	34	9.25	7.30	5.88	13.92	2.16	6.44	14.13
20/11/2017	Salbutamol	1.19	3.32	36							
20/08/2018		0.83	3.26	26	9.65	7.95	6.76	12.67	1.81	7.01	12.63
20/08/2018	Salbutamol	0.98	3.54	28							
14/06/2019		1.26	4.03	31				14.72	2.16	6.82	15.31
14/06/2019	Salbutamol	1.45	4.19	35							

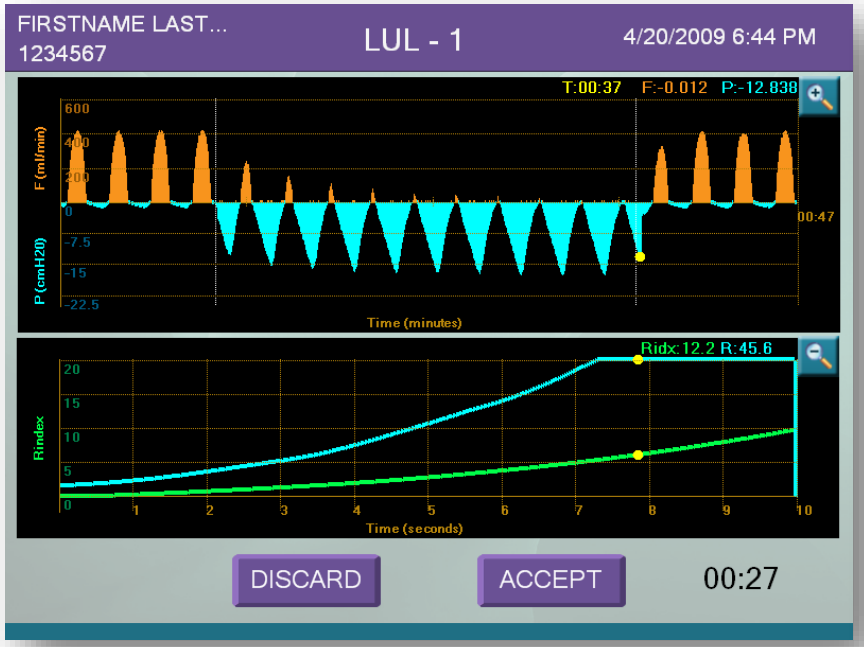
Chartis console and monitor

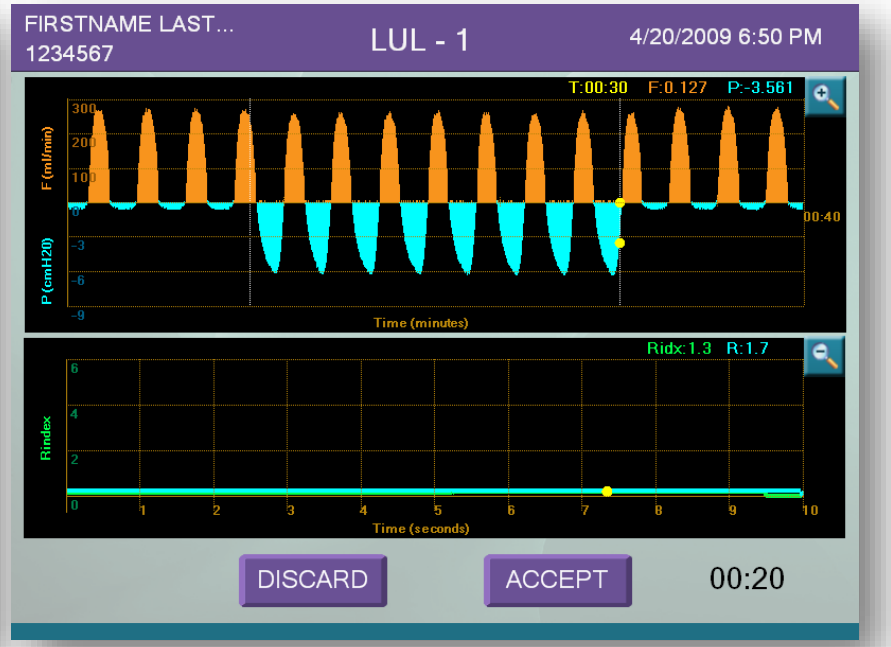




Chartis balloon catheter

CHARTIS


FIRSTNAME LAST...
1234567
LUL - 1
4/20/2009 6:44 PM
T:00:37 F:-0.012 P:-12.838
F (ml/min)
P (cmH20)
Time (minutes)
00:47
Ridx:12.2 R:45.6
Rindex
Time (seconds)
DISCARD
ACCEPT
00:27

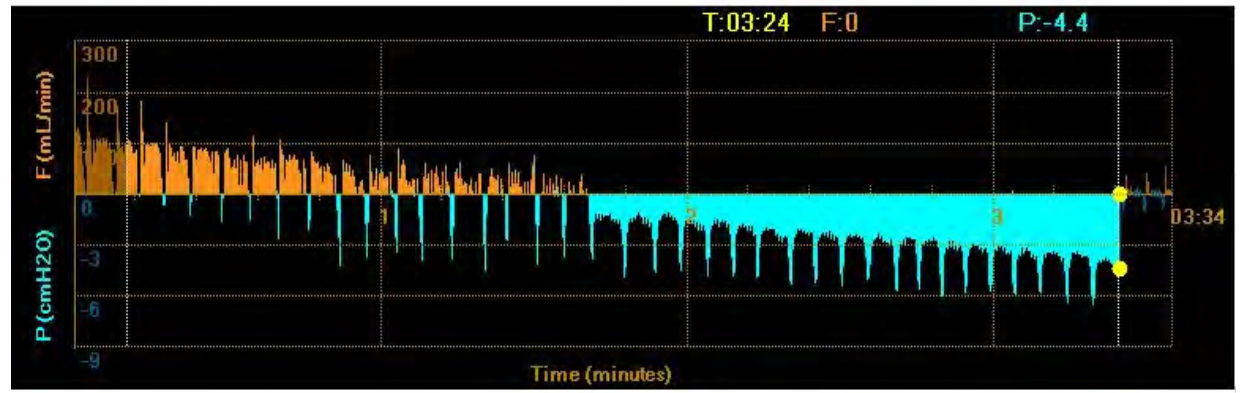

FIRSTNAME LAST...
1234567
LUL - 1
4/20/2009 6:50 PM
T:00:30 F:0.127 P:-3.561
F (ml/min)
P (cmH20)
Time (minutes)
00:40
Ridx:1.3 R:1.7
Rindex
Time (seconds)
DISCARD
ACCEPT
00:20

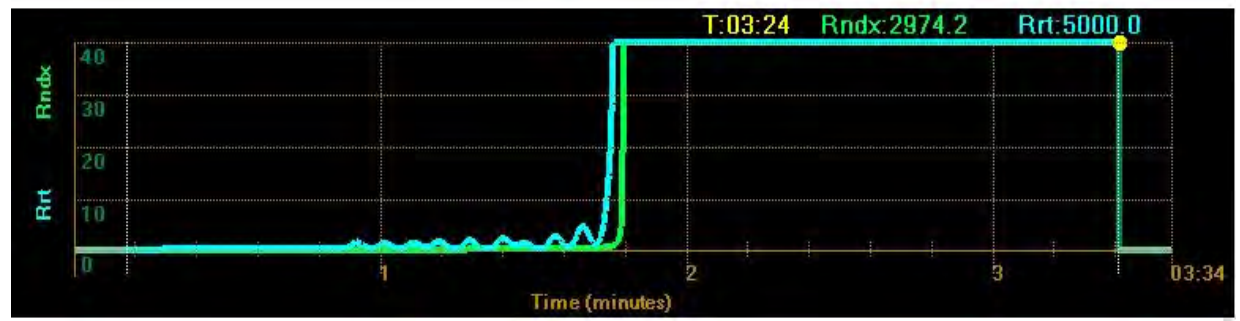
Patient Information

Patient ID:	769216
Date of Assessment:	Thursday, March 03, 2011
Patient Date of Birth:	March 20, 1930

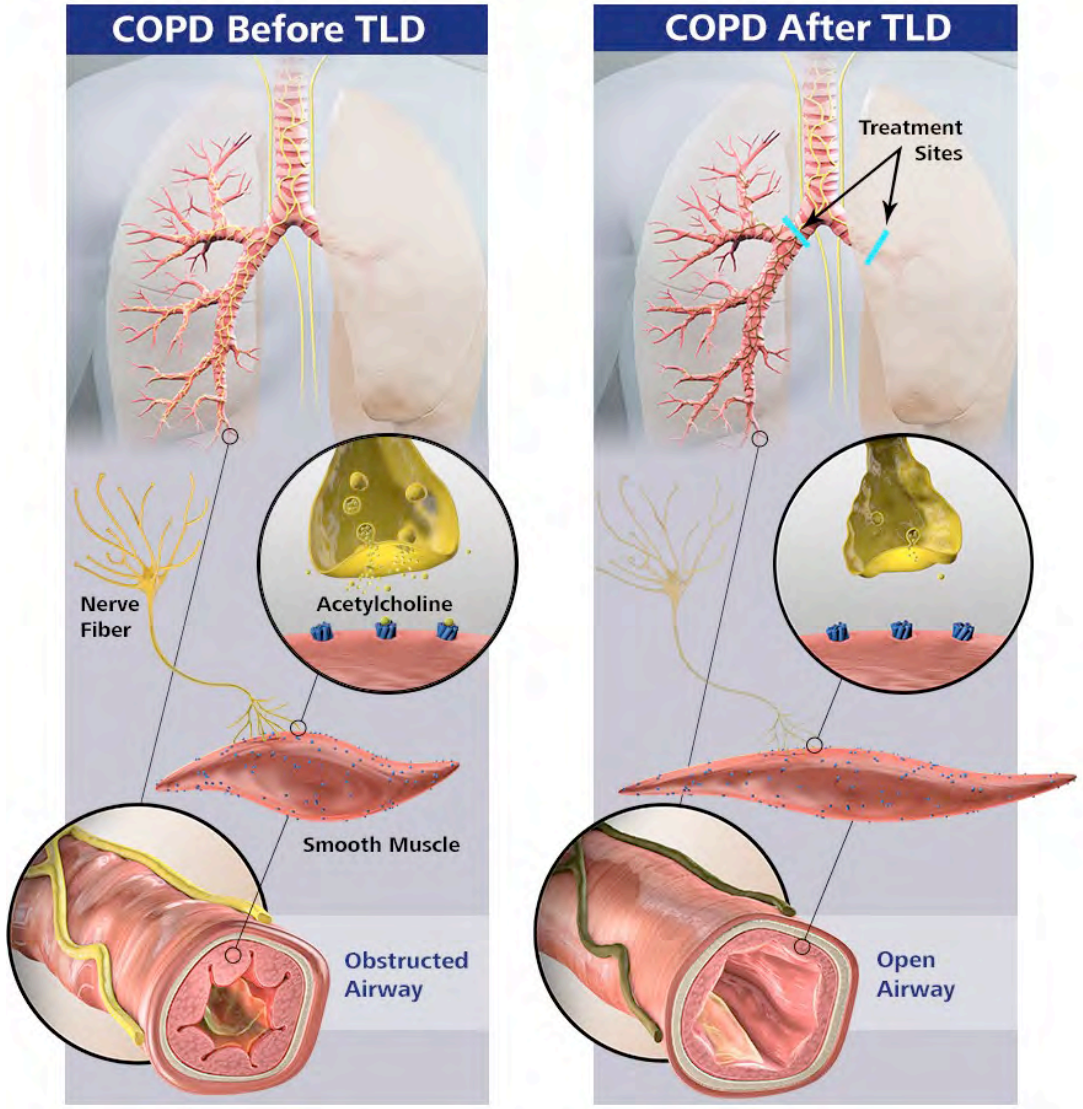
Assessment

Assessed Lobe:	LUL (Assessment #1)
Start Assessment Time:	11:37:43 AM
End Assessment Time:	11:40:58 AM
Assessment Duration:	03:14
Total Exhaled Volume:	79.57 mL
Assessment Result :	Accepted

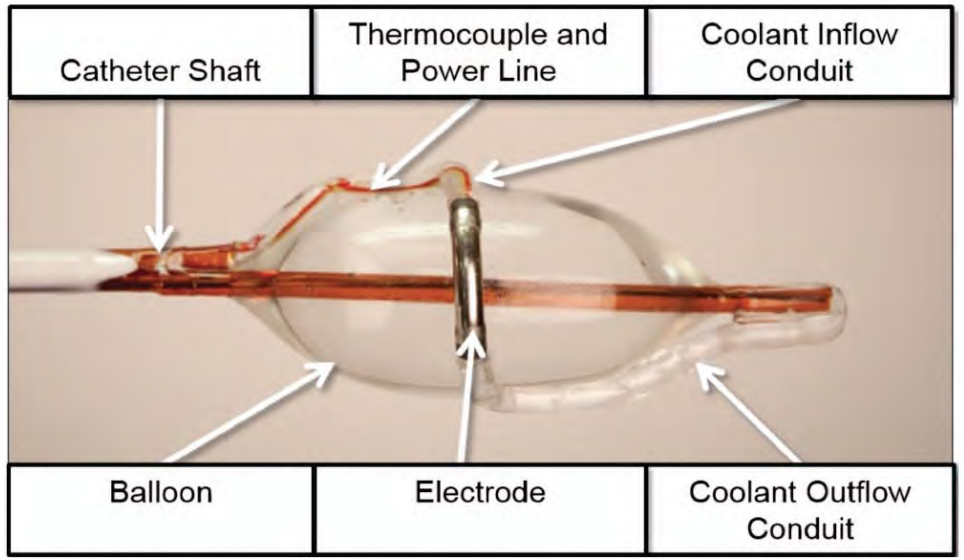




Targeted Lung Denervation - Holaira




HOLAIRA
dNerva

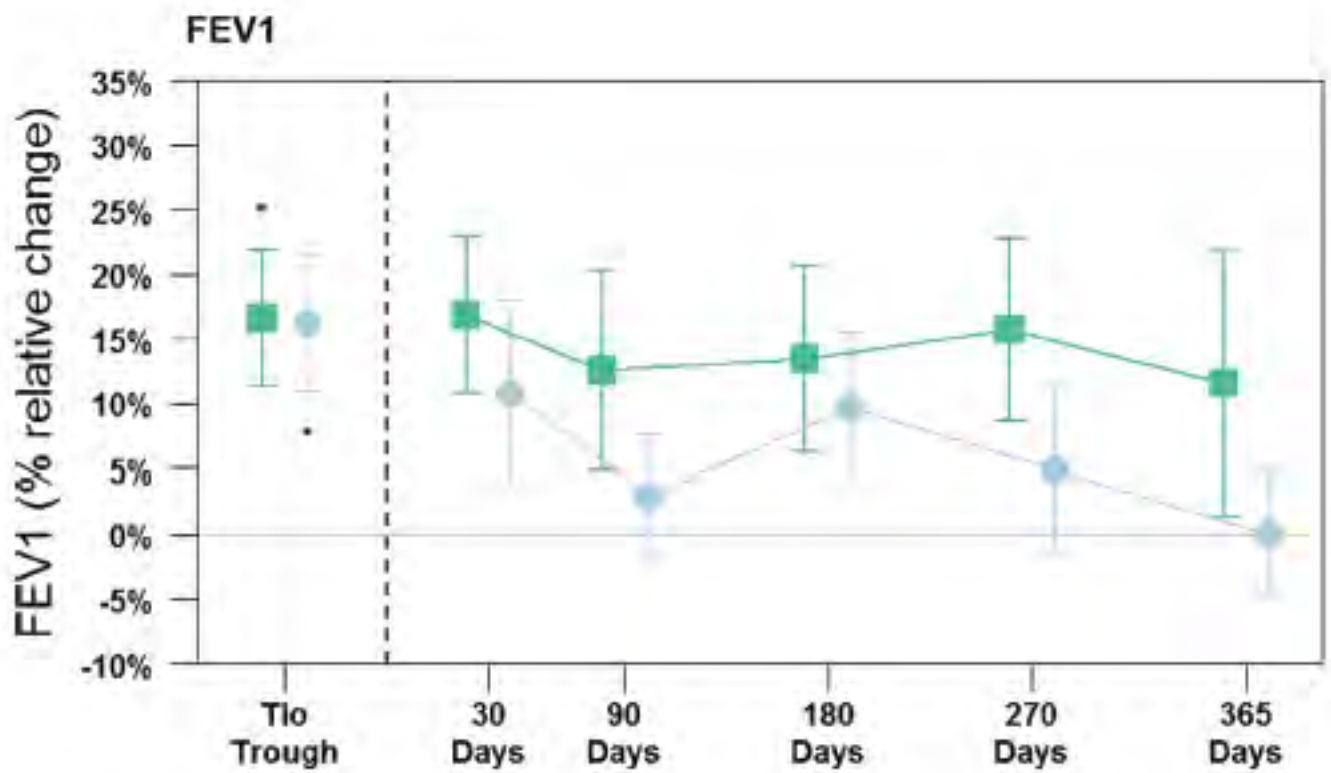

Catheter Shaft
Thermocouple and Power Line
Coolant Inflow Conduit
Balloon
Electrode
Coolant Outflow Conduit

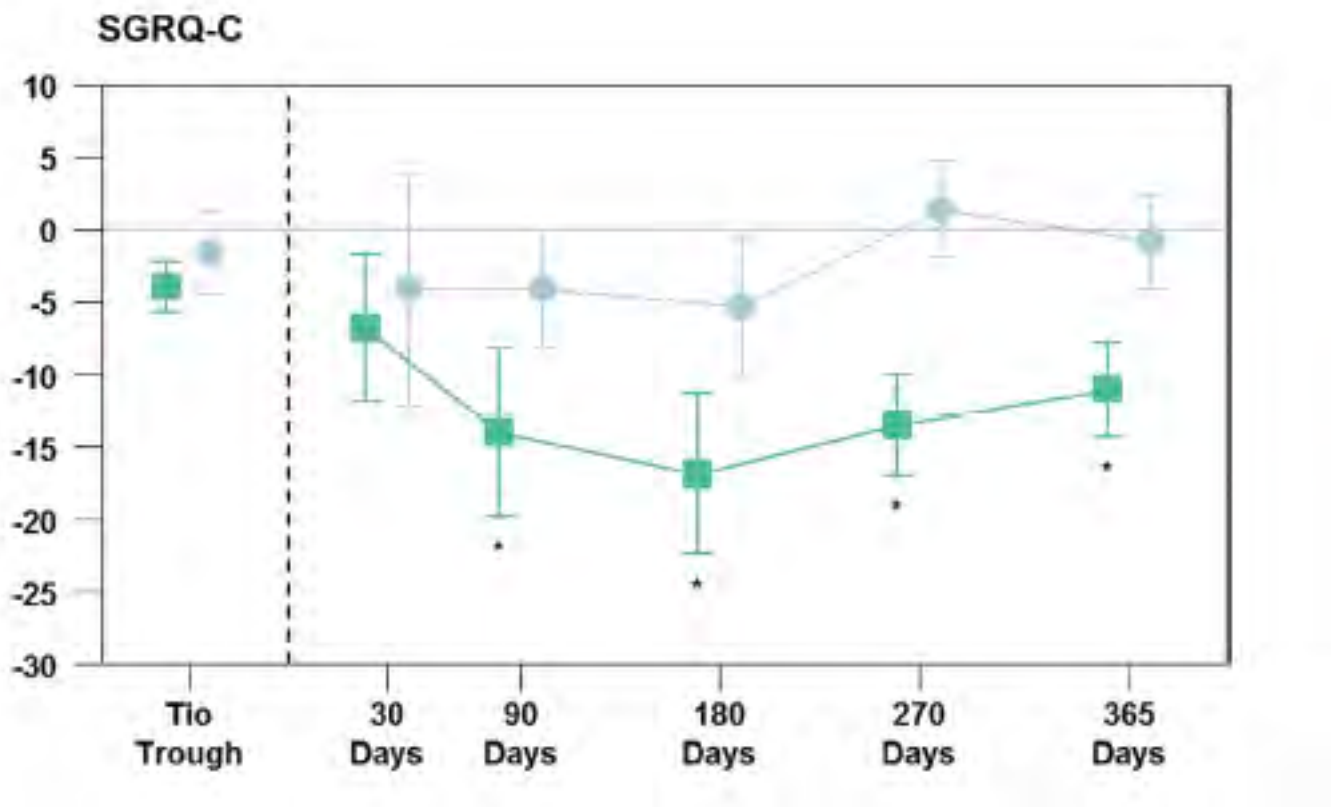
ORIGINAL ARTICLE

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

Dirk-Jan Slebos,[1] Karin Klooster,[1] Coenraad F N Koegelenberg,[2] Johan Theron,[3] Dorothy Styen,[2] Arschang Valipour,[4] Martin Mayse,[5] Chris T Bolliger[2,3]

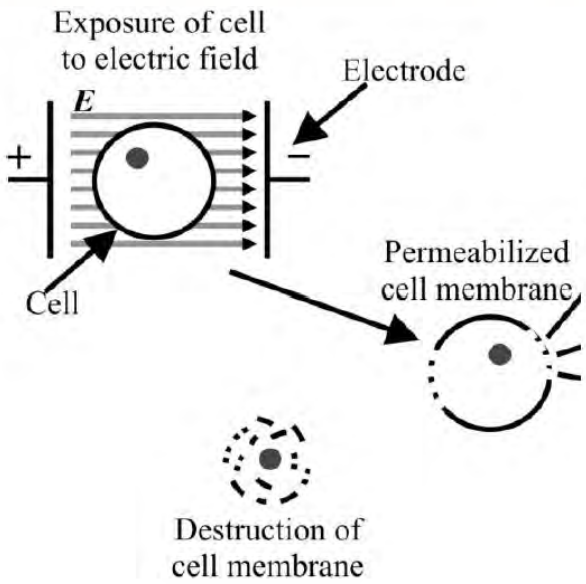
Slebos D-J, *et al*. *Thorax* 2015;**0**:1–9. doi:10.1136/thoraxjnl-2014-206146


FEV1
FEV1 (% relative change)
35%
30%
25%
20%
15%
10%
5%
0%
-5%
-10%
Tio Trough
30 Days
90 Days
180 Days
270 Days
365 Days


SGRQ-C
10
5
0
-5
-10
-15
-20
-25
-30
Tio Trough
30 Days
90 Days
180 Days
270 Days
365 Days

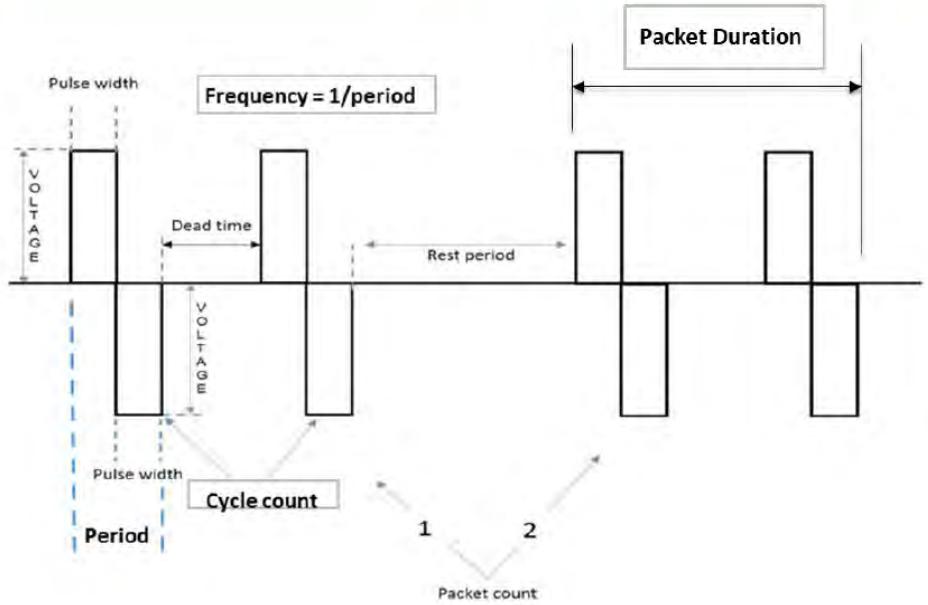
Gala Developed A Non-Thermal Treatment

Irreversible Electroporation (IRE) Mechanism



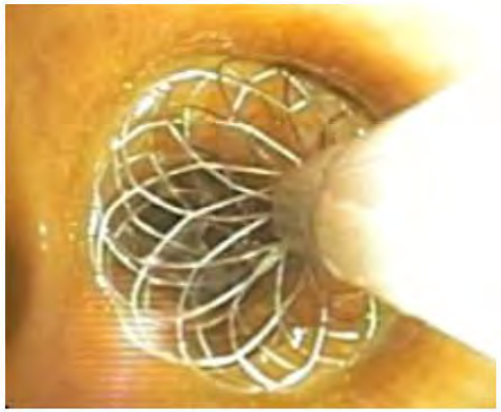
- A high voltage electric field is applied in order to create pores in the cell membrane
- The pores cannot close, allowing ions and eventually organelles to leak
- Cells die via necrosis and apoptosis

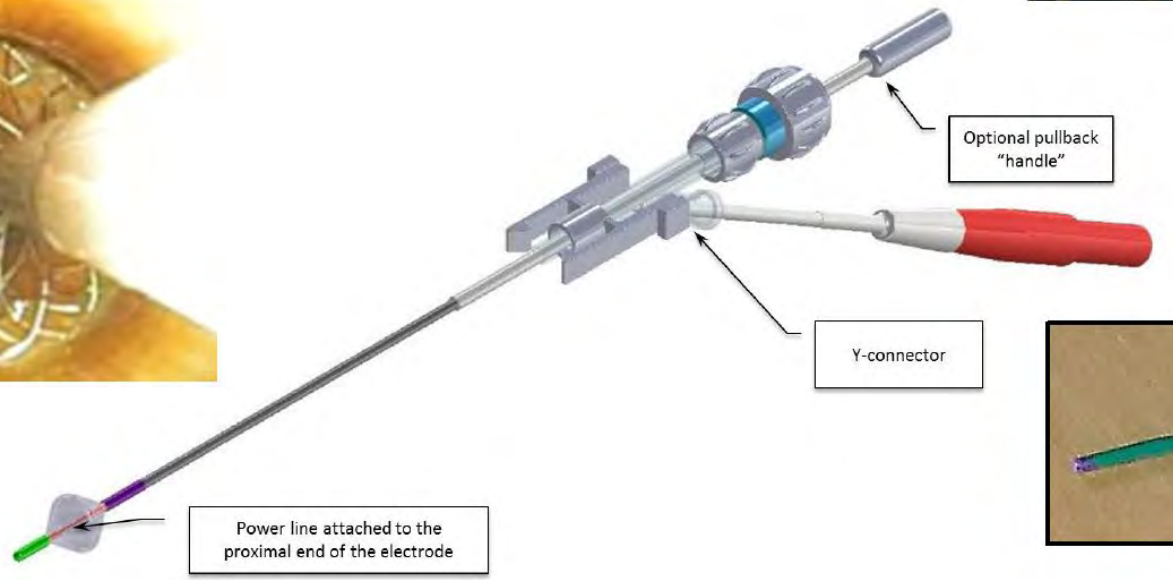
Waveform

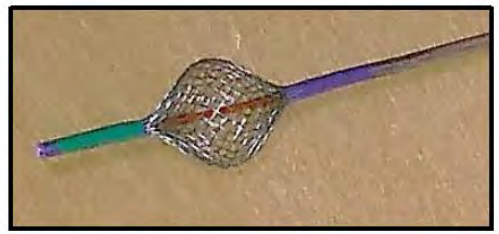


- Voltage
- Frequency
- Wave Shape
- Packet duration/timing

Gala Catheter and Generator

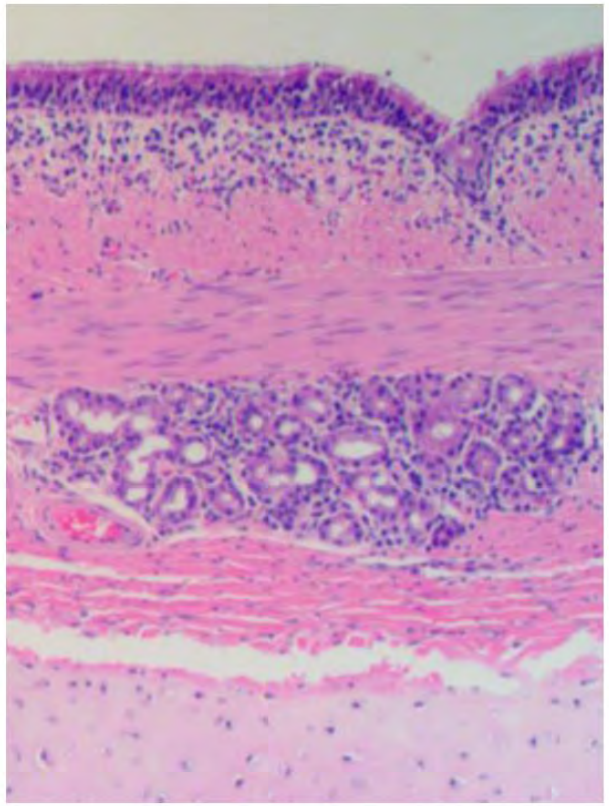




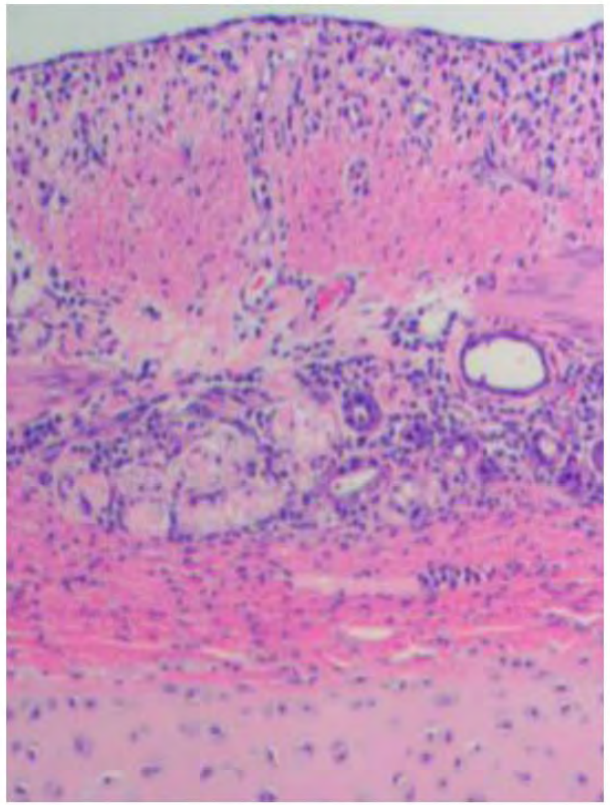


Pre-Clinical Program — Histologic Progression

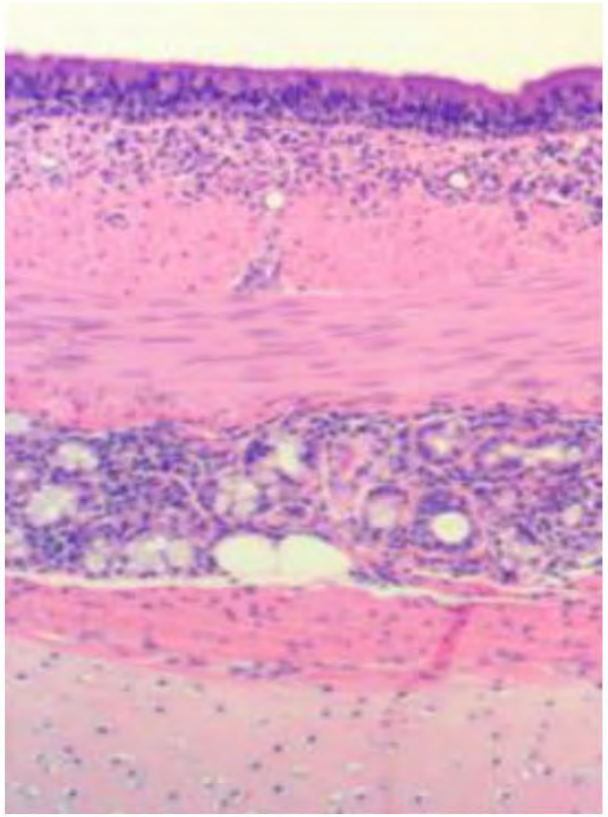
1 Baseline

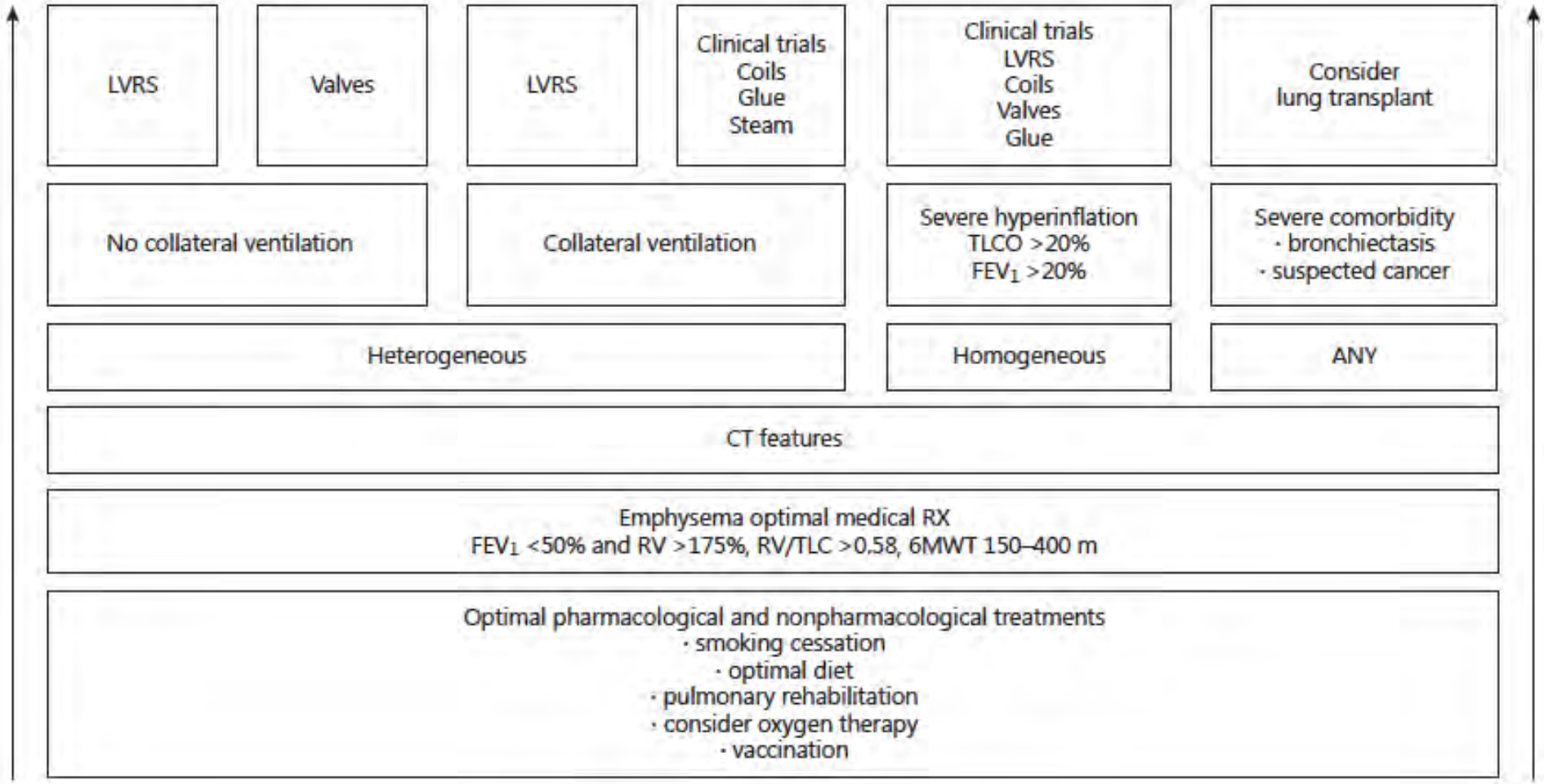


2 24 Hours post treatment



3 7 Days post treatment




LVRS
Valves
LVRS
Clinical trials
Coils
Glue
Steam
Clinical trials
LVRS
Coils
Valves
Glue
Consider
lung transplant
No collateral ventilation
Collateral ventilation
Severe hyperinflation
TLCO >20%
FEV1 >20%
Severe comorbidity
· bronchiectasis
· suspected cancer
Heterogeneous
Homogeneous
ANY
CT features
Emphysema optimal medical RX
FEV1 <50% and RV >175%, RV/TLC >0.58, 6MWT 150–400 m
Optimal pharmacological and nonpharmacological treatments
· smoking cessation
· optimal diet
· pulmonary rehabilitation
· consider oxygen therapy
· vaccination