65. Endoscopic lung volume reduction: hype or hope?

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Single session bilateral endoscopic lung volume reduction therapy in advanced upper lobe and homogeneous emphysema using a tissue sealant

Mordechai Kramer[1], Oren Fruchter[1], Moshe-Nimrod Maimon[2], Yael Refaely[3].
[1]Pulmonary and Critical Care Medicine, Bellison Hospital, Rabin Medical Center, Petach Tikva, Israel; [2]Pulmonary Medicine, Soroka Medical Center, Be'er-Sheeva, Israel; [3]Thoracic Surgery, Soroka Medical Center, Be'er-Sheeva, Israel

Objective(s): This open labeled multicenter study was performed to evaluate the safety and efficacy of single-session bilateral 4-site lung volume reduction therapy with the AeriSeal® Emphysematous Lung Sealant System (ELS) in patients with advanced upper lobe heterogeneous (ULP) and homogeneous (Ho) emphysema.
Methods: 20 patients with advanced Ho (n=4) and ULP (n=16) emphysema received 4-site bilateral upper lobe volume reduction with ELS under conscious sedation. Outcome measures include pulmonary function tests (at 6, 12 and 24 wks), exercise capacity, symptoms, and health related quality of life (HRQL, at 12 and 24 wks).
Results: 4-site therapy was well tolerated. Procedure duration was 14±4 minutes. Average hospital length of stay was 0.9±1.5 days. There were 5 SAEs during the first 85±32 days of follow-up (3 treatment related, 1 COPD exacerbation). Interim 6-week results (n=14; ΔFEV_1 = +16.1±27.5%; ΔFVC =+10.7±17.4%) demonstrated clinically significant improvements in spirometry (Δ > +12%) in 8 of 14 patients. 12 week data for the first 4 patients demonstrated additional physiological improvement (ΔFEV_1 = +37.6%; ΔFVC = +14.1%) from their corresponding 6-week responses (ΔFEV_1 = +17.1%; ΔFVC = 8.2%).
Conclusions: Bilateral single session endoscopic lung volume reduction therapy can be achieved safely using ELS in patients with advanced Ho and ULP emphysema under conscious sedation. Initial results indicate that efficacy responses are similar to those reported with surgical volume reduction, and treatment is associated with short hospital length of stay and minimal morbidity.

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Sustained efficacy from 3 to 6 months following bronchoscopic thermal vapor ablation (BTVA) in the treatment of heterogeneous emphysema

Felix Herth[1], Gregory Snell[2], Peter Hopkins[3], Kim Baker[4], Christian Witt[5], Mark H. Gotfried[6], Arshang Valipour[7], Manfred Wagner[8], Franz Stanzel[9], Jim Egan[10], Steven Kesten[11], Armin Ernst[12]. *[1]Pneumology and Critical Care Medicine, Thoraxklinik Heidelberg, Heidelberg, Germany; [2]Allergy Immunology & Respiratory Medicine, The Alfred Hospital, Melbourne, Australia; [3]Lung Transplant Unit, Prince Charles Hospital, Chermside, Australia; [4]Pulmonary and Critical Care Medicine, University of Iowa, Iowa City, United States; [5]Pneumology, Charité Campus-Mitte, Berlin, Germany; [6]Pulmonary Associates, John C. Lincoln Hospital, Phoenix, United States; [7]Ludwig-Boltzmann-Institute for COPD, Otto-Wagner-Hospital, Vienna, Austria; [8]Pneumologie, Klinikum Nürnberg, Nürnberg, Germany; [9]Pneumologie, Zentrum für Pneumologie, Hemer, Germany; [10]Advanced Lung Disease Program, Mater Misericordiae University Hospital, Dublin, Ireland; [11]Clinical Department, Uptake Medical Corp, Tustin, United States; [12]Pulmonary Critical Care and Sleep Medicine, Caritas St. Elizabeth's Medical Center, Boston, United States*

Background: A recent approach to bronchoscopic lung volume reduction (LVR), BTVA, involves the localized application of thermal energy through heated water vapor to targeted areas of emphysematous lung in order to induce LVR.
Objectives: Evaluate efficacy and safety of BTVA in the treatment of heterogeneous emphysema during a clinical trial.
Methods: Open-label, single-arm trial of BTVA in patients with upper lobe predominant emphysema (n=44). Entry criteria: FEV_1 15% - 45% predicted, RV>150%, TLC>100%, 6MWD>140 m, DLCO>20%, previous pulmonary rehabilitation. Primary efficacy endpoint: FEV_1 and SGRQ at 6 months. Other endpoints included FVC, RV, FRC, TLC, mMRC dyspnea, 6MWD.
Results: No procedural complications (mean procedure time=30 min). Lung function changes from baseline (mean (SE)) are summarized in the following table:

Table 1

	FEV1 (ml)	FVC (ml)	RV (ml)	FRC (ml)	TLC (ml)	IC (ml)	DLCO (%)
3 mths	139 (27)	223 (59)	–417 (94)	–313 (94)	–273 (86)	40 (75)	2.4 (1.1)
6 mths	141 (26)	271 (72)	–406 (113)	–369 (97)	–220 (70)	149 (64)	1.7 (1.3)

$p<0.05$ for all values except IC at 3 months and DLCO at 6 months.

At 6 months, FEV_1 improvement was ≥12% in 55%. SGRQ improved by 14 (2) units with 73% of patients improving ≥4units, 6MWD increased 47 (11), mMRC improved 0.9 (0.2) units, BODE score improved 1.4 (0.3) units (all $p<0.05$). A total of 29 serious adverse events occurred in 19 patients, with the majority being respiratory. One fatal event was reported 67 days post-BTVA.
Conclusion: Unilateral lobar BTVA treatment of heterogeneous emphysema results in clinically significant improvements in multiple efficacy endpoints that are sustained from 3 to 6 months.

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Lung volume reduction coil treatment for patients with severe heterogeneous emphysema, a multicenter feasibility trial

Dirk-Jan Slebos[1], Karin Klooster[1], Martin Hetzel[2], Franz Stanzel[3], Gaeton Deslee[4], Christian Witt[5], Wolfgang Geseirich[6], Romain Kessler[7], Michael Pfeifer[8], Stefan Blaas[8], Jurgen Hetzel[9], Charles-Hugo Marquette[10], Felix Herth[11]. *[1]Pulmonary Diseases, UMC-Groningen, Groningen, Netherlands; [2]Pulmonary Diseases, Krankenhaus vion Roten Kreutz, Stuttgart, Germany; [3]Lungenklinik, Lungenklinik, Hemer, Hemer, Germany; [4]Pulmonary Diseases, Hopital Maison Blanche CHU Reims, Reims, France; [5]Pulmonary Diseases, Campus Charite Mitte, Berlin, Germany; [6]Pulmonary Diseases, Asklepios, Gauting, Germany; [7]Pulmonary Diseases, CHRU de Strasbourg, Strasbourg, France; [8]Pulmonary Diseases, Klinikum Donaustauf, Donaustauf, Germany; [9]Pulmonary Diseases, University Hospital, Tuebingen, Germany; [10]Pulmonary Diseases, Hopital Pasteur, CHU Nice, Nice, France; [11]Pulmonary Diseases, Thoraxklinik, Heidelberg, Germany*

Introduction: The Lung Volume Reduction Coil (LVRC) is a bronchoscopic device made of self-expandable nitinol wire for the treatment of emphysema. A previous single center pilot study showed safety and efficacy in severe upper-lobe emphysema.
Aim: In this study we investigated the feasibility, safety and efficacy of LVRC treatment in a multicenter cohort trial design in patients with severe upper or lower lobe heterogeneous emphysema.
Methods: 44 patients (23F/21M, 60yrs (±11), FEV1 29.9%pred (±6.9%), RV 249%pred (±52%), TLC 135%pred (±16%)) were bronchoscopically treated under general anesthesia using fluoroscopy with LVRCs (PneumRx, USA) in either one or two lungs (in two sequential procedures) in 10 European centers. Safety was evaluated by recording of all adverse events (AEs). Efficacy as measured by questionnaires, pulmonary function- and exercise testing will be measured at 3, 6 and 12 months post treatment.
Results: 83 LVRC procedures were performed (39 bilateral, 5 unilateral). 33 patients were treated in the upper lobes and 11 in the lower lobes. The mean procedure time was 50 mins (±24), using a median of 10 coils (range 8-14) per lobe. The coil lengths used were 70mm (2x), 85mm (19x), 100mm (352x), 125mm (347x), 150mm (81x) and 175mm (25x). AEs <24hrs after the procedure were: COPD exacerbation (n=2), pneumothorax (n=1), chest pain (n=2), dyspnea (n=3), consolidation (n=1), cough (n=1), and mild hemoptysis (n=5).
Conclusion: The LVRC treatment is technically feasible in both upper and lower lobe emphysema, with a good periprocedural safety profile. At the ERS conference meeting we will also be able to present the follow-up efficacy and safety data for this trial.

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One year follow-up in the European multicenter study for the treatment of advanced emphysema with bronchial valves

Vincent Ninane[1], Michela Bezzi[2], Christian Geltner[3], Xavier Gonzalez[4]. *[1]Respiratory Medicine, St. Pierre Hospital, Brussels, Belgium; [2]Respiratory Medicine, Hospedale Civili di Brescia, Brescia, Italy; [3]Respiratory Medicine, LKH Natters, Innsbruck, Austria; [4]Clinical Research, Spiration Inc., Redmond, WA, United States*

We have reported positive results of a blinded and randomized sham bronchoscopy controlled study that evaluated the IBV® Valve System (Spiration Inc.) in subjects with advanced upper lobe predominant emphysema. After a 3-month evaluation, subjects in the treatment and sham control groups were un-blinded. Then, the control group was allowed to receive valve treatment. In 3 of the 7 centers participating in the study, Ethics approval was obtained for an additional evaluation at approximately 1 year of treatment.
Methods: After approximately one year of receiving valves, the evaluations included physical examination, imaging (CT scan to evaluate regional volumetric changes), pulmonary function, questionnaires, exercise and blood gases.
Results: All subjects were in stable condition, and satisfied with the outcome. Complete data for paired analysis was available in 25 of 29 subjects that returned for the evaluation. The average time for the evaluations was 13.5±1.3 months. Results are summarized in a table format.

Variables	Baseline	1 year+	P-value
UL volume (liters)	3.13±0.9	2.95±0.75	0.018
Non-UL Volume (liters)	3.48±0.8	3.79±0.78	0.001
TLC plethy (liters)	7.4±1.3	7.7±1.5	0.175
FEV1 (liters)	0.9±0.3	0.9±0.3	0.35
SGRQ (scale 0 to 100)	59.9±9.3	50.7±20.6	0.018
MMRC (scale 0 to 4)	2.9±0.8	2.0±1.0	0.0003
6MWT (meters)	367±97	374±137.4	0.89
PO2 (mmHg)	65±8.6	67.6±9.7	0.19
BODE (scale)	5.5±1.6	4.7±2.3	0.05

Conclusions: Improvements with IBV Valve treatment are sustained after 1 year. Subjects with advanced emphysema have a fast slope of decline however, palliative treatments with bronchial valves could affect the natural course of this disease.

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Study of the use of Chartis® pulmonary assessment system to optimize subject selection for endobronchial lung volume reduction (ELVR) – Results and subgroup analysis

Daniela Gompelmann[1], Dirk-Jan Slebos[2], Joachim Ficker[3], Frank Reichenberger[4], Bernd Schmidt[5], Lars Ek[6], Ralf Eberhardt[1]. *[1]Pneumology, Thoraxklinik at University Hospital, Heidelberg, Germany; [2]Pneumology, University Medical Center, Groningen, Netherlands; [3]Pneumology, Klinikum Nürnberg, Nürnberg, Germany; [4]Pneumology, University Hospital, Giessen, Germany; [5]Pneumology, University Hospital, Halle, Germany; [6]Pneumology, University Hospital, Lund, Sweden*

Introduction: Collateral ventilation (CV) has been shown to prevent lung volume reduction (LVR) after Endobronchial Valve (EBV) treatment. Direct measurement of CV may predict patients who will achieve significant LVR. The Chartis® Pulmonary Assessment System quantifies the average collateral resistance. When the resistance value >10, the patient is "CV Negative;" when the resistance value ≤10, the patient is "CV Negative;".

Abstract 373 – Table 1

	Average mL Volume Reduction (primary endpoint)	Average Target Lobe Volume Reduction	Average Heterogeneity Score	Percentage of Upper Lobe Treatments	FEV1	6-MWD	SQRG
CV+ (n=10)	–90,5	–6,1%	24,1%	80%	–3,1%	9,7%	0.7 (n=8)
CV– (n=14)	–1264.8	–79.0%	13.2%	50%	12.5%	9.0%	–8.1(n=7)
Δ	1174.3	72.9%	10,9%		16.0%	0,1%	7,4%

Objective: To evaluate the effectiveness of the Chartis® system in predicting subjects with heterogeneous emphysema who will achieve significant (≥350mL) LVR from EBV therapy.
Methods: Patients with heterogenous emphysema were enrolled. Following Chartis assessment of the targeted lobe, that was determined by using HRCT, all patients were treated with Zephyr® EBV. Primary endpoint was HRCT-measured LVR in the treated lobe at 30-days. FEV_1, SGRQ and 6MWT were evaluated as secondary endpoints.
Results: To date, primary endpoint is collected for 24 patients. Primary and Secondary Endpoints for 75-80 patients are anticipated. Subgroup analyses will focus on patient selection criteria.
Conclusion: Chartis System predicts significant LVR after EBV treatment. Results suggest that expanded patient selection criteria will enable successful treatment for a broader population of emphysema patients.

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6-month follow-up in patients with advanced homogeneous emphysema treated with endobronchial lung sealant therapy

Arschang Valipour[1], Felix Herth[2], Ralf Eberhardt[2], Franz Stanzel[3], Reiner Bonnet[4], Juergen Behr[5], Charles Marquette[6], Mordechai Kramer[7].
[1]Respiratory and Critical Care Medicine, Otto Wagner Hospital, Vienna, Austria; [2]Pneumology and Critical Care, Thoraxklinik University of Heidelberg, Heidelberg, Germany; [3]Pneumology II and Endoscopy Service, Lungenklinik Hemer, Hemer, Germany; [4]Pneumology, Zentralklinik Bad Berka GmbH, Bad Berka, Germany; [5]Medizinischer Klinik III, University Bergmannsheil, Bochum, Germany; [6]Service of Pneumology, Hospital Pasteur University of Nice, Nice, France; [7]Pulmonary and Critical Care Medicine, Rabin Medical Center, Bellinson Hospital, Petach Tikva, Israel

Objective(s): Bronchoscopic lung volume reduction therapy using endobronchial valves (Scuirba F et al., NEJM, 2010;363) and coils (Herth FJ et al. Therap Adv Resp Dis, 2010;4) has shown limited efficacy in patients with advanced homogenous emphysema (AHoE). This study summarizes responses to AeriSeal® Emphysematous Lung Sealant (ELS) therapy in patients with AHoE out to 6 months.
Methods: Patients with AHoE and scintigraphy scans showing reduced perfusion to the upper lung zones (n=12) were included in this study, which was performed at 8 investigational centers in Europe and Israel. All patients received initial 2-site upper lobe bronchoscopic ELS therapy; approximately 2/3 received a second treatment at 2 additional sites in the contralateral lung. Follow-up was performed at 3 and 6 months post treatment.
Results: Upper lobe ELS therapy in this cohort of AHoE patients (8 male, age 64±7 yrs) was well tolerated, and was associated with improvements in pulmonary function, functional capacity, and quality of life. Three (3) and 6 month changes in FEV_1 (+12.6±13.1%; 9.5±13.9%), FVC (8.1±12.1%; 8.6±13.1%), RV/TLC ratio (-3.6±8.7%; -5.1±8.3%), MRCD (-0.2±0.83U; -0.4±0.90U), 6MWT (+15.4±45.8m; +16.6±47.7m), and SGRQ (-7.9±17.6U; -13.3±23.0U) were observed. MCID improvements in spirometry (>12% improvement in FEV_1 and/or FVC) were observed in ≥ 50% of patients at both time points.
Conclusions: ELS therapy produces durable improvements in pulmonary function and quality of life in patients with AHoE, and represents a new therapeutic option for patients with homogeneous emphysema who remain symptomatic despite maximal medical therapy.

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Efficiency of the endo-bronchial volum reduction treatment for severe heterogeneous emphysema

Turhan Ece[1], Aysen Erer[1], Zuleyha Bingol[2], Tugce Hürkal[2], Alper Toker[3], Ferah Ece[2]. *[1]Pulmonary Department, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey; [2]Pulmonary Department, Istanbul Bilim University, Istanbul, Turkey; [3]Thoracic Surgery Department, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey*

Background: Patients with advanced chronic obstructive pulmonary disease (COPD) have limited treatment options. Exercise capacity and health related quality of life (HRQL) of the patients are affected by the progress of respiratory failure. Volum reduction surgery is reported to be effective for selected patients with severe COPD. But there is a high risk for the surgery of these patients with hypoxemia hypercapnia. Endo-bronchial volum reduction treatment (EBVRT) by a valve application which is a minimally invasive method has been come up for these patients.
Method: To study the safety and effectiveness of the EBVRT for heterogeneous emphysema.
Result: EBVRT were applied to 21 patients. Most of the patients were male (66.6%). Valves were placed into upper lobe (n=15), lower lobes (n=5) and middle lobe (n=1). There were no procedure-related deaths. Only one patient with ischemic heart disease was died at the 3rd month. Device related complication was occurred in two patients; one patient was intubated and the other patient's valve was occluded and worked inversely. Functional capacity was improved in 71% (n=15) of the patients but only 66% (n=10) of these patients were feeling and doing better. In these patients mean 10mmHG increase of PaO2 and mean 4.5mmHG decrease of PaCO2 were observed at 3rd month. HRQL were improved in 48% (n=10) of the patients. However, pulmonary functions, 6 minute walking distance were not significantly changed.
Conclusion: Although FEV 1, 6 minute walking distance were not changed, PaO2, functional status and HRQL improvement were observed with EBVRT of advanced emphysema patients. EBVRT is a new method with acceptable safety for the patients with severe COPD.