Bronchoscopic lung volume reduction

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CHAPTER

11

The lung volume reduction coil for the treatment of emphysema: a new therapy in development

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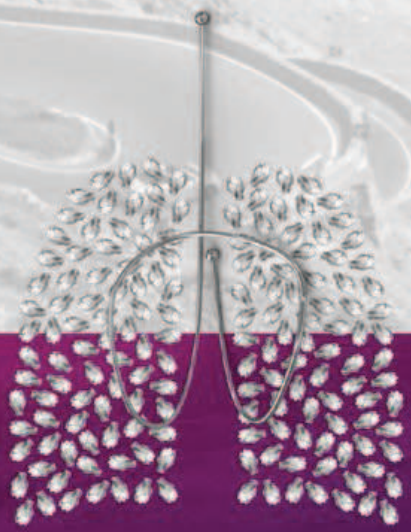

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ABSTRACT

Lung volume reduction coil treatment is a novel therapy for patients with severe emphysema. In this bilateral bronchoscopic treatment, approximately 10 coils per lobe are delivered under fluoroscopic guidance in two sequential procedures.

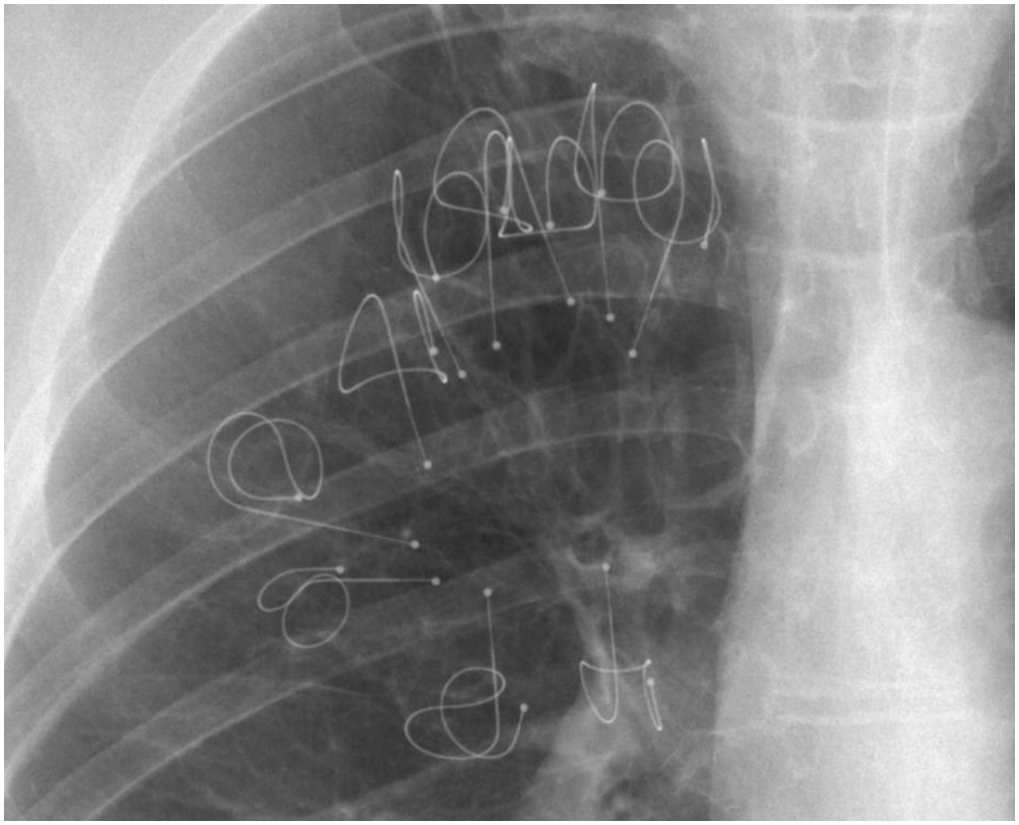
The lung volume reduction coil reduces lung volume by compressing the most destructed areas of the lung parenchyma and restores the lung elastic recoil. Both patients with upper- and lower-lobe predominant emphysema as well as a homogeneous emphysema distribution can be treated.

Lung volume reduction coil treatment results in an improvement of pulmonary function, exercise tolerance and quality of life. The lung volume reduction coil treatment has been evaluated in several European clinical trials since 2008 and received CE mark approval in 2010. Currently, two large multicenter randomized controlled trials are underway in Europe and North America to assess the efficacy and safety of the lung volume reduction coil treatment at 12 months compared with usual care.

In this review, we share our experience with the lung volume reduction coil treatment.

The lung volume reduction coil treatment is a new bronchoscopic therapy for the treatment of patients with severe chronic obstructive pulmonary disease (COPD) (figure 1). Within the COPD phenotypes, the lung volume reduction coil treatment has shown to be effective and has been most extensively tested in the emphysematous, and severely hyperinflated phenotypes. Effective and durable effects have been shown for both upper- and lower-lobe heterogeneous emphysema as well as homogeneous emphysema. Furthermore, the coil works independently of collateral flow.

Figure 1. Part of a X-ray showing 10 coils placed into the right upper lobe.



COPD is one of the major disease entities in the world, affecting millions of people worldwide and an important cause of death.[1] COPD is almost always caused by exogenous factors, like cigarette smoke, air pollution and indoor cooking.[2] Additionally, genetic and endogenous factors contribute to a wide variety in disease susceptibility. COPD constitutes two major disease phenotypes: chronic bronchitis and emphysema. However, these two may show important overlap and include both bronchopathic changes as well as small airways involvement.[3] In patients with COPD, cigarette smoke-induced chronic inflammation results in airway and lung parenchyma damage. This associates with reduced tissue elasticity and decreased elastic recoil leading to increased airway collapse during exhalation. These physiological effects lead to so-called air trapping and progressive increase in lung volume, called hyperinflation.

Hyperinflation reduces the efficiency of the inspiratory muscles, particularly the diaphragm, and leads in emphysema patients to dyspnea, limited exercise capacity and reduced quality of life. When these hyperinflated patients perform exercise, the phenomena of 'dynamic hyperinflation' may occur. Apart from the above-described static hyperinflation, even mild exercise may lead to progressive air trapping and reduced inspiratory capacity, in the end leading to severe feelings of dyspnea.[4]

To date, there is not one single therapy available that will cure COPD. Patients with advanced stages of COPD suffer on a daily basis, and despite a lot of different supportive treatments available, there is a big need for additional treatments for COPD patients. Indeed, modest reductions in symptoms and exacerbation frequency can be achieved by pharmacological interventions. Also smoking cessation and supplemental oxygen therapy may change the prognosis in COPD, whereas pulmonary rehabilitation improves dyspnea, exercise capacity and quality of life.[5] In selected patients, two effective surgical procedures are available for the treatment of severe emphysema: lung volume reduction surgery, and lung transplantation (for all COPD phenotypes). However, both interventions are very invasive and carry a high morbidity and mortality risk.[6] Also the shortage of qualified surgeons to actually perform lung volume reduction surgery and lack of donor lungs available for lung transplantation make these therapies rare. Because of the need for additional therapeutic options, in the last decade, several novel bronchoscopic techniques have been developed or are currently under investigation. These innovative bronchoscopic approaches are minor invasive when compared with lung volume reduction surgery, and are associated with a less overall morbidity and mortality.

Previously investigated bronchoscopic techniques that showed promise, but are not available anymore

The airway bypass procedure

Airway bypass is a bronchoscopic technique designed to release trapped air in patients with severe homogeneous emphysema and abundant collateral flow, by creating extra-anatomic fenestrations. To keep this newly created extra-anatomic tract patent, the bypass is supported with paclitaxel-coated stents.[7] Findings of a large multicenter randomized full-sham controlled trial showed that the airway bypass could be safely created and at day one the airway bypass released trapped air and significantly improved pulmonary function. However, the effect was not sustained at 6 months due to problems with stent patency.[8] Future efforts will have to show if airway bypass patency can be achieved, and revive this proof-of-concept therapy.

Biological lung volume reduction

The AeriSeal® Emphysematous Lung Sealant System was developed to achieve lung volume reduction in patients with upper-lobe predominant heterogeneous emphysema or homogeneous emphysema.[9,10] This bronchoscopic treatment delivers foam of synthetic polymer and a cross-link compound that seals and collapses lung tissue at the sub segmental level in the most diseased areas of the lung. In addition, local inflammation is induced,

followed by fibrosis and sub segmental atelectasis, resulting in the desired volume reduction. This mechanism of action makes this treatment suitable for the treatment of patients independent of collateral ventilation. The device has received CE Mark approval in Europe.[11] In 2012, a large multicenter randomized controlled trial started to demonstrate the safety and efficacy of the AeriSeal treatment in patients with advanced upper-lobe predominant emphysema.[12] Although the efficacy response to the treatment looked promising, the safety issues involved were challenging, especially managing the post-treatment inflammatory response to the sealant. This has led to uncertainty regarding the potential for future product approval, and operations have been aborted in December 2013. Maybe in the future, sequential bilateral or targeted lesion approach still remains valid indication for this therapy.

Current bronchoscopic treatments under investigation

In the past years, based on the publication of an increasing number of clinical trials, presentations on major symposia and individual exiting case stories, a lot of awareness has been created for these new bronchoscopic lung volume reduction treatments. However, to date no published evidence-based, or 'taskforce' guidelines on bronchoscopic lung volume reduction are available. However, based on the current evidence in the literature[10,11,13,14] and supported by expert opinions[15,16] the absence of collateral ventilation between individual segments in the emphysematous lung is important to assess.

Treatments that aim at complete lobar occlusion in the absence of collateral ventilation, or as surrogate, have a complete interlobar fissure on chest computed tomography, are the key predictors for clinical success in response to the total occlusion of a lobe by using one-way valve treatment. Using the active measurement of collateral flow by the Chartis system® (Pulmonx Corporation, Redwood City, CA, USA) will identify up to 75% of responders to one-way valve treatment. Previous clinical trials using a 'blocking technique' also showed that the number of patients with absence of collateral flow between the adjacent lobes in an unselected heterogeneous emphysema patient group was around 25%. This implies that the majority of emphysema patients has collateral flow between adjacent lobes, and consequently cannot be treated with a blocking device. The majority of patients with severe emphysema thus will have to rely on development of techniques that work independently of collateral flow, or so-called 'non-blocking' devices.

Another important factor that drives response to bronchoscopic lung volume reduction is the level of heterogeneity in emphysema distribution between upper and lower lobes. As well as for blocking- and non-blocking techniques, greater emphysema heterogeneity resulted in a better response to treatment.[7,9,10,13,15] On the other hand, not many bronchoscopic lung volume reduction treatments have been prospectively evaluated in exclusively homogeneous emphysema patients yet, where only for the lung volume reduction coil treatment limited, but successful, prospective data are available.

Presently, there are four bronchoscopic lung volume reduction treatment devices that are still under clinical investigation to proof efficacy. All treatments already received CE Mark approval in Europe and are commercially available in certain countries. In the USA, these devices are only for investigational use limited by federal law (table 1).

Table 1. Bronchoscopic lung volume reduction treatment devices which are still under clinical investigation.

Device	Emphysema type	Current investigation by U.S. federal law
Blocking devices		
Endobronchial valve		
Zephyr® Endobronchial valve Pulmonx Corp. USA CE Mark since 2008	heterogeneous no collateral flow upper and lower lobes	NCT01796392 (LIBERATE study); Estimated primary completion date: DEC/2015 (N=183)
Intrabronchial valve		
IBV™ Valve Spiration Inc. USA CE Mark since 2008	heterogeneous no collateral flow upper and lower lobes	NCT01812447 (EMPROVE study); Estimated primary completion date: SEP/2015 (N=270)
Non-blocking devices		
Thermal vapour ablation		
InterVapor™ System Uptake Medical, USA CE Mark since 2011	heterogeneous upper lobe	NCT01719263 (STEP-UP study); Estimated primary completion date: MAR/2015 (N=69)
Lung volume reduction coil		
RePneu® LVRC System PneumRx Inc. USA CE Mark since 2010	heterogeneus homogeneous upper and lower lobes	NCT01608490 (RENEW study); Estimated primary completion date: SEP/2014 (N =315)

Current investigation by U.S. federal law (Source ClinicalTrials.gov January 2014)

Blocking devices

Endobronchial valves

Endobronchial one-way valve (EBV; Zephyr®, Pulmonx Corporation, Redwood City, CA, USA) treatment reduces the lung volume in patients with heterogeneous emphysema, who do not have significant collateral ventilation.

Post-hoc analysis of a large randomized controlled trial demonstrated that a subgroup of emphysema patients have statistically and clinically significant improvements in quality of life, pulmonary function and exercise tolerance[15] when a technical perfect treatment was performed, and the patients had a heterogeneous disease with complete fissures. In a next trial, the Chartis system, which can actually measure collateral ventilation, showed that responders can be identified up 75%.[16] Since 2011, a European prospective single-center randomized controlled trial (STELVIO trial, NTR2876) is underway to investigate the efficacy of the treatment in patients with high heterogeneity with proven absence of collateral ventilation compared with standard optimal medical care alone.

Endobronchial valve treatment is not approved by the U.S. federal law (FDA) and is considered investigational. Endobronchial valve treatment is commercially available outside the USA on a large scale, with an estimated 5000 patients treated worldwide. In 2013, a large multicenter randomized controlled trial (LIBERATE trial) started to investigate the safety and effectiveness of the endobronchial valve treatment. This trial is FDA supported and will be used for future product approval, with an estimated study completion in December 2015. Endobronchial valve treatment can be effective in a selected group of COPD patients with advanced heterogeneous emphysema.

Intrabronchial valves

The intrabronchial valve (IBV; IBV™ Valve Spiration Inc., Redmond, WA, USA) treatment is a technique for severe COPD patients with upper-lobe predominant emphysema. The intrabronchial valve is an investigational device designed to redirect air from the less healthy to the more healthy parts of the lung to reduce hyperinflation. In contrast to the treatment with the Zephyr's endobronchial valves, both lungs are treated, and one segment of a target lobe will not be occluded to prevent lobar atelectasis.[17] Recently, a large randomized controlled trial has demonstrated that the modality of bilateral treatment without complete lobar occlusion is not effective in patients with heterogeneous emphysema.[18] However, unilaterally placed intrabronchial valves with complete occlusion of one entire lobe in patients with complete fissures can improve lung function, exercise capacity and quality of life, when compared with the above-described 'classical' intrabronchial valve approach.[19] Currently, intrabronchial valve treatment is commercially available outside the USA and despite lack of supporting clinical trial data, it is almost only used for total lobar occlusion. Not surprisingly, in 2013, the manufacturing company switched its entire treatment approach and started a large multicenter randomized controlled trial to investigate the safety and effectiveness of the intrabronchial valve treatment aiming at lobar atelectasis in patients with complete interlobar fissure. This trial is also supported by the FDA and will be used in future product approval, with the estimated study completion in September 2015.

Non-blocking devices

Thermal vapor ablation

Thermal vapor ablation (InterVapor™ System Uptake Medical®, Tustin, CA, USA) has been studied in COPD patients with upper-lobe predominant emphysema.[14,20,21] Thermal vapor ablation is an investigational device and uses heated water vapor to produce a thermal reaction to the lung tissue. The heated vapor results in a localized inflammatory reaction followed by permanent fibrosis. An open-label single-arm safety and efficacy study showed that the procedure is well tolerated and the expected inflammatory response can be managed with standard medical care. Improvements were seen in lung function, quality of life and exercise capacity.[14] However, follow-up trials showed, similar to the AeriSeal System, safety issues with high energy dosages and bilateral treatments. Just recently, the company reset its strategy by choosing lower energy levels and performing a sequential bilateral treatment. To test this approach, a multicenter randomized controlled trial has been started last year to investigate the safety and effectiveness of this new thermal vapor ablation treatment approach. This trial is also supported by the FDA. The estimated study completion is June 2015.

Introduction of new treatment: the RePneu lung volume reduction coil system

The RePneu lung volume reduction coil system (RePneu lung volume reduction coil system, PneumRx Inc., Mountain View, CA, USA) is a device designed to compress the areas of the most destructed lung parenchyma to reduce lung volume, and restore elastic recoil of these areas. In December 2012, a large multicenter randomized controlled trial was started to compare outcomes after 12 months follow up between the treatment group (lung volume reduction coil system plus optimal medical therapy) and control group (optimal medical therapy alone) in patients with advanced heterogeneous as well as homogeneous emphysema.[22]

The RePneu lung volume reduction coil system & procedure

The RePneu lung volume reduction coil system is a two-part system. The system consists of a delivery system and of nitinol coils that are available in different sizes. All system components are sterile, single use and disposable. The system is designed to be performed using a therapeutic bronchoscope with a 2.8 mm working channel under fluoroscopic guidance. The lung volume reduction coil procedure aims to treat two lungs. A chest computed tomography will be used to identify target lobes in both lungs. Per procedure only one lobe will be treated. The coils will be placed using a standardized (sub-) segmental treatment algorithm independent of specific computed tomography findings, this to aim at an equal anatomical '3D' distribution of the coils. About 10 coils (8–12) are placed in the upper lobes and up to 14 (10–14) can be placed in the lower lobes. The lung volume reduction coil procedure is preferably performed under general anesthesia.

The RePneu lung volume reduction coil system

Delivery system

The delivery system contains a guidewire, a delivery catheter, a biopsy forceps and a loading cartridge.

• *Guidewire*

The specialized metal flexible guidewire, with an a traumatic tip serves as a guide for the delivery catheter, and is used to identify suitable airways for treatment. The guidewire also facilitates the determination of the appropriate coil length.

• *Delivery catheter*

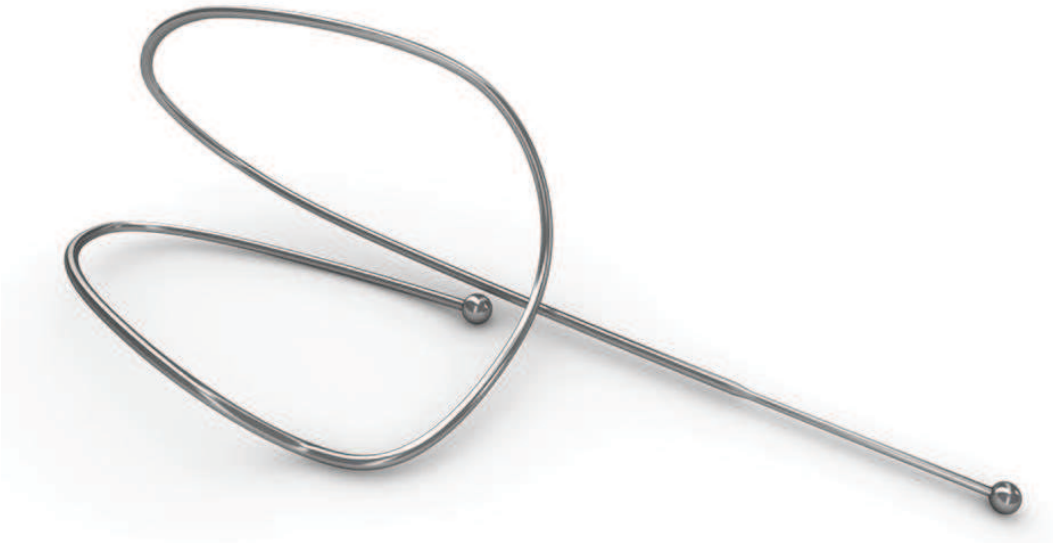
The catheter, used for the delivery of the coil, is passed over the guidewire and will be aligned with the distal tip of the guidewire under fluoroscopy. The braided construction of the catheter provides column strength, reduces risk of kinking and supports the coil implant during delivery. The tip is soft and radiopaque for visibility under fluoroscopy within the airway.

• *Biopsy forceps*

The forceps is used to grasp and fixate the proximal end of the coil, which is then pulled into the loading cartridge. Once loaded, the forceps delivers the coil through the delivery catheter into the targeted airway, and can also be used to reposition or retrieve the coil, if necessary. The forceps has a one-hand locking mechanism to lock the jaws. A marker band indicates when the coil is exiting the catheter.

• *Loading cartridge*
The loading cartridge is slid over the forceps and then the coil will be straightened during the manual uploading into the cartridge. After loading, the cartridge is coupled with the catheter. The luer-lock secures the cartridge to the catheter.

The coil
The coil is composed of nitinol (a nickel–titanium alloy), a biocompatible super-elastic material that has been used extensively in implantable medical devices.[21,23,24] Nitinol is also compatible with the use of magnetic resonance imaging due to its non-ferromagnetic nature. Nickel ion release after implantation of coils is below the allowable limit. The coil derives its elastic properties from the nitinol wire, and is shaped in a special pre-determined double-loop. The distal and proximal ends of the coil are terminated with a smooth a traumatic ball. To reduce rigidity and lessen pressure of the coil on the airway wall, the diameter of the most proximal end of the coil is smaller than the rest of the coil. The coil is available in various lengths to accommodate different-sized airways. The most common used lengths are 100, 125 and 150 mm. The coil is self-actuating and is delivered straight into an airway and recovers to a non-straight, pre-determined shape upon deployment. Multiple coils need to be placed in different airways to achieve adequate treatment effect.



The step-by-step lung volume reduction coil procedure

1. Navigate the bronchoscope to the target airway and position at the ostium of a sub segmental airway.

2. Insert both the catheter and guidewire into the working channel of the bronchoscope.

3. Advance and navigate the guidewire into the distal targeted airway (figure 2A) under fluoroscopy guidance; stay minimal 3 cm away from the pleura.

4. Hold the guidewire position fixed relative to the bronchoscope and advance the catheter (figure 2B) distally up to but not past the point where the tip of the catheter is aligned with the tip of the guidewire.

5. Use the radiopaque markers on the guidewire to measure the airway length.

6. Remove the guidewire from the catheter while maintaining the catheter position.

7. The desired size coil can be loaded into the cartridge.

8. Connect the cartridge to the luer-lock hub of the catheter, and lock into place.

9. Deliver the coil into the catheter by advancing the forceps and coil.

10. Align the distal end of the coil with the distal end of the catheter.

11. Position the coil using fluoroscopy (figure 3).

12. Have an assistant hold the bronchoscope fixed relative to the patient.

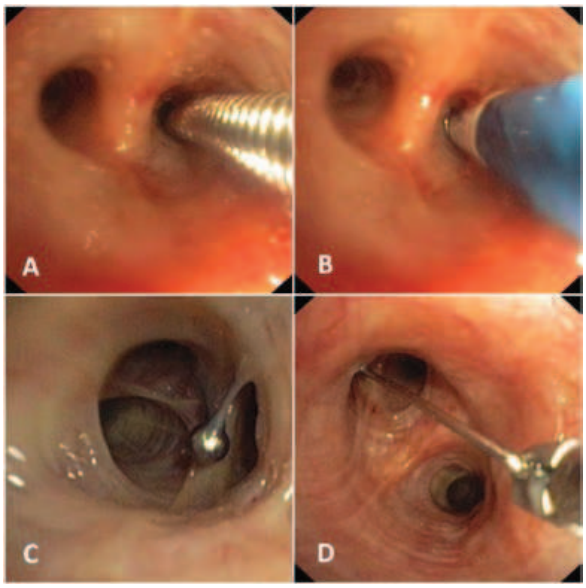
13. Deploy the coil using fluoroscopy by withdrawing the catheter with one hand, while holding the coil position fixed with the forceps using the other hand.

14. Verify the position of the coil under fluoroscopy and release the coil by unlocking the forceps.

15. Remove the forceps from the catheter (figure 2C & figure 2D).

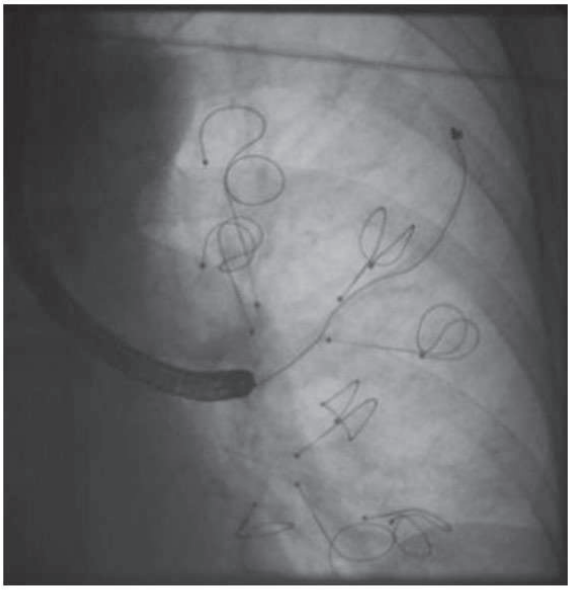
16. The catheter may continue to be used to repeat steps 3–15 to deploy additional coils. The coil can be removed or repositioned by reversing this implantation process.

Figure 2. Illustrative airway aspect during the lung volume reduction coil procedure.



(A) Bronchoscopic view of the guidewire enters into a segmental airway; (B) The delivery catheter positioned over the guidewire at the entrance of the same airway; (C) Bronchoscopic aspect of the proximal end of a coil sticking out of a subsegmental airway and (D) The biopsy forceps grasping the coils' proximal end to recover it before removing the coil.

Figure 3. Fluoroscopic image during the treatment, showing the distal end of the coil being aligned with the distal end of the catheter position.



Mechanism of action

The lung volume reduction coil is designed to improve the elastic recoil of lung tissue and reduce the airway resistance and hyperinflation in emphysema patients. Furthermore, reduction of the residual volume of the hyperinflated lung improves diaphragmatic function and inspiratory muscle function. The treatment effects are independent of collateral ventilation. The improvement of the lung elastic recoil is still a hypothetical mechanism of action, as no data are currently available to clinically support this. However, based on the nitinol properties of the coil, the lung recoil strength is thought to be significantly improved. Reduction in static hyperinflation is supported by clinical trial observations showing a significant reduction in both residual volume and residual volume/total lung capacity.[24,25] Recently, we also showed that airway resistance significantly improves after lung volume reduction coil treatment.[3,26] It is known from lung volume reduction surgery literature that improvement in static lung volumes also improves diaphragm function. Summarizing the mechanisms of action of the coil might also imply a beneficial effect on diaphragm function. However, to date, there are no supporting data besides incidental chest X-rays showing changes in diaphragm position after treatment.[27] Further research is necessary to learn more about the mechanism of action of the coil.

Clinical profile

The lung volume reduction coil treatment has been evaluated in a few European clinical trials. The RePneu lung volume reduction coil system has consistently demonstrated in animal studies.[28] and clinical studies, the ability to perform safely within the clinical use environment.[24,25] The procedure is safe to perform under general anesthesia. No procedural events occurred. All events that occurred in these studies could be treated with the standard medical treatment. During the procedure, the coil can be removed or repositioned by reversing the implantation process. In clinical practice, it is hardly necessary for any medical reason to remove a coil after the initial treatment. However, when a medical reason occurs (e.g., pleural pain), an individual coil can be removed on condition that the proximal end (ball) of the coil can be recovered with the biopsy forceps. Animal studies confirmed that it is feasible to remove coils within 2 months after implantation.[28]

In 2008, in Germany, a clinical pilot study was performed to primarily evaluate the safety of the first-generation lung volume reduction coil system. Eleven patients with severe heterogeneous (N=3) as well as homogeneous emphysema (N=8) were included according to the inclusion and exclusion criteria of the National Emphysema Treatment Trial. Ten patients underwent two-times and one patient once the lung volume reduction coil treatment. During each procedure, three to six coils were implanted with a procedure time between 20 and 75 minutes. All procedures were performed under general anesthesia, were feasible and well tolerated by the patients. In the follow-up period of at least 7 and up to 11 months, a total of 33 mild-to-moderate adverse events were reported. All events could be treated with the standard medical treatment. Nineteen adverse events (N=10 dyspnea, N=5 coughing, N=3 COPD exacerbations and N=1 chest pain) were reported as possibly related to the device or bronchoscopic procedure. Although this study was not powered to evaluate the statistical significance between patients with heterogeneous and homogeneous emphysema, in this

study, patients with heterogeneous emphysema seem to have better outcomes in lung function parameters, quality of life and exercise. This first study using coils in these severely diseased patients has showed us that the procedure is safe and feasible.[13]

In 2009, in the Netherlands, the second lung volume reduction coil study was performed to evaluate the safety and efficacy of the lung volume reduction coil treatment in patients with a heterogeneous emphysema distribution. Sixteen patients with heterogeneous emphysema were included. In this uncontrolled, open-label trial, the lung volume reduction coil treatment was optimized by increasing the number of coils per lobe from 6 to 10, and using the implantation of a new second-generation coil. Twelve patients underwent bilaterally treatment in two sequential procedures and four patients received the lung volume reduction coil treatment in one lung. During each procedure, a median of 10 (range 5–12) coils were placed with a procedure time of 36.5 (range 20–60) minutes. All procedures were performed under general anesthesia and the lung volume reduction coil procedure was well tolerated by the patients. No adverse events were observed during the lung volume reduction coil procedure. In 28 procedures, one pneumothorax occurred 1 hour after the bronchoscopy. This patient responded within a day to chest tube drainage. During the recovery period, defined as <1 month after each coil procedure, slight hemoptysis (<5 ml in 21 procedures) and transient chest pain (in four procedures) were reported as adverse events, and all these events resolved within a few days after the procedure without medical intervention. In the follow-up period defined as more than 1 month up to 6 months, a total of 14 COPD exacerbations were reported as possibly related to the procedure. All adverse events in this study could be managed with standard medical treatment. At 6 months follow-up after the final treatment, more than 50% of the patients responded better than the minimal clinical important difference for forced expiratory volume in 1 second, distance on 6 minute walk test and the St. George Questionnaire.[29-32] This second study showed us that the lung volume reduction coil treatment has an acceptable safety profile and results in significant improvements in quality of life, lung function and exercise capacity in patients with upper-lobe predominant emphysema.[24]

In 2010, a third lung volume reduction coil study was conducted in the UK. Forty-seven patients with both heterogeneous as well as homogeneous emphysema were included in this prospective, randomized controlled multicenter trial. In the treatment group, 21 patients underwent bilateral lung volume reduction coil treatment and 2 patients a unilateral treatment. The 24 patients who were randomized to the control (usual care) group did not receive the lung volume reduction coil treatment but underwent the same assessments, except the bronchoscopy, as the patients in the treatment group. Both groups were compared after 3 months follow-up after the final treatment. In the bilateral treated patients, a mean number of 18.5 coils (17.1–20.0) were placed with a mean procedure time of 44.9 minutes (range 20–88) per procedure. Six procedures were performed under general anesthesia and 38 procedures were done under deep conscious sedation. In the 44 procedures performed, two pneumothoraces occurred 2 hours after the bronchoscopy. Both patients responded within a day to chest tube drainage. During the recovery period, defined as <1 month after each lung volume reduction procedure, there were two COPD exacerbations and two lower respiratory tract infections in the treatment group and one COPD exacerbation in the usual

care group reported as serious adverse events. All events resolved within 7 days after the procedure. In the follow-up period defined as more than 1 month up to 3 months after final treatment, a total of three COPD exacerbations were reported in the treatment group and two COPD exacerbations and one lower respiratory tract infection were reported as serious adverse events. All adverse events in this study could be managed with standard medical treatment. At 3 months follow-up after the final treatment, a significant number of patients in the treatment group responded to above the minimal clinical important difference: 74% for the distance on 6 minute walk test, 57% for the forced expiratory volume in 1 second and 65% of the patients for the St. George's Respiratory Questionnaire. This third lung volume reduction coil study showed improvement of lung function, exercise capacity and quality of life in the lung volume reduction coil treatment group compared with the usual care group.[25]

In 2011, a fourth lung volume reduction coil study was conducted. Ten patients with homogeneous emphysema were included in this single-arm, open-label study in the Netherlands. All patients received, under general anesthesia, maximally 12 coils in each upper lobe, in two sequential procedures. Tests were performed at baseline and at 6 months. Two COPD exacerbations and one small pneumothorax (which spontaneously resolved without a chest tube) were recorded as serious adverse event. At 6 months, follow-up compared with baseline bilateral coil treatment resulted in a significant improvement in exercise performance, pulmonary function and quality of life. This fourth study showed us that the coil treatment is not limited to patients with heterogeneous emphysema, as patients with homogeneous emphysema can benefit as well.[26]

These four European clinical trials showed that the lung volume reduction coil treatment is safe, feasible and effective in patients with both heterogeneous as well as homogeneous emphysema. Efficacy results of these studies are listed in table 2. Recently data has been published from a European multicenter Feasibility Study of PneumRx's Lung Volume Reduction Coil trial.[33]

Table 2. Efficacy results of the lung volume reduction coil treatment from 4 European clinical trials. Follow up is post 2nd treatment.

	1st study[12] 3 month FU	2nd study[23] 6 month FU	3rd study[24] 3 month FU	4th study[29] 4 month FU
	N=11	N=14	N=23	N=10
FVC	-1.5±6%	+13.4±12.9%	-	+10,0% (-8 to +57)
FEV_1	-5.0±2.9%	+14.9±17%	+14.2% (7 to 22)	+16.6% (-16 to +55)
RV	+3.3±4.6%	-11.4±9.0%	-0.51 Liter (-0.7 to -0.3)	-0.79 Liter (-1.20 to +0.04)
6MWD, %	+5.6±8.5	+32.9±36.5	-	-
6MWD, meter	-	+84±73	+51 (28 to75)	+42 (+15 to +141)
SGRQ	-6.1±4.4	-14.9±12.1	-8.1 (-14 to -2)	-11 (-25 to +6)

Future prospective randomized controlled trial data will have to confirm the efficacy of the lung volume reductioncoil treatment in both heterogeneous and homogeneous populations when compared with usual care. Currently, two larger randomized controlled trials using lung volume reduction coils are underway: RENEW study[22] (N=315) and REVOLENS study[34,35] (N=100).

Current status in the medical field

Lung volume reduction coil treatment is commercially available outside the USA on a large scale. Lung volume reduction coil treatment is not approved by the FDA and is considered investigational in the USA.

Expert commentary & five-year view

Lung volume reduction coil treatment is a novel therapy, independent of collateral flow, for patients with both heterogeneous as well as homogeneous emphysema. The procedure is feasible, and the treatment has an acceptable safety profile. The efficacy results have shown promising improvements in pulmonary function, exercise capacity and quality of life. Randomized controlled trials are underway to confirm these results.

The first 12 months follow-up results of the current multicenter randomized controlled trials are available within 2 years. Depending on the safety and efficacy results from these trials, the lung volume reduction coil treatment can be approved by the FDA, and other health authorities outside the USA will consider approval and reimbursement for this treatment.

Key messages

The lung volume reduction coil treatment is a straightforward and safe procedure to perform.

The lung volume reduction coil treatment has an acceptable safety profile.

The lung volume reduction coil treatment reduces lung volume by compressing the most destructed areas of the lung parenchyma and restores the lung elastic recoil.

The lung volume reduction coil treatment results in an improvement of lung function, exercise performance and quality of life.

The lung volume reduction coil treatment is effective in both upper- and lower-lobe predominant emphysema.

Patients with homogeneous emphysema can benefit from the lung volume reduction coil treatment.

The efficacy of the lung volume reduction coil treatment is independent of collateral flow.

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