ORIGINAL ARTICLE

Airway Scaffolds for Emphysema-related Hyperinflation
Six-Month Results from the BREATHE Trial

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Abstract

Rationale: Despite advancements in emphysema treatment, high morbidity and mortality rates highlight the need for innovative therapies. A novel self-expanding nitinol airway scaffold was designed to alleviate lung hyperinflation by connecting emphysematous parenchyma with central bronchi, releasing trapped air.

Objectives: To assess the feasibility, safety, and initial outcomes of airway scaffolds in treating emphysema-related hyperinflation.

Methods: We conducted a pooled analysis of two first-in-human studies (NCT05949645, NCT05854550) involving patients with heterogeneous or homogeneous emphysema treated bronchoscopically with up to three permanent airway scaffolds per lung.

Measurements and Main Results: The primary outcome was safety, measured by procedure- and/or device-related serious adverse events over 6 months. Secondary outcomes were technical feasibility, pulmonary function, quality of life, symptoms, exercise capacity at 3 and 6 months, and airway patency assessment by high-resolution computed tomography. Sixty severe emphysema patients (33 female, 27 male; mean age, 66 ± 8 yr; mean residual volume percent predicted, 255 ± 47%) were included. Ninety-eight procedures were performed, and 328 airway scaffolds were successfully placed. A proportion of 21.7% of patients experienced at least one related serious adverse event within 6 months, including pneumonia (10.0%) and chronic obstructive pulmonary disease exacerbation (5.0%), but no pneumothoraxes occurred. Residual volume improved (decreased) from baseline by a mean [95% confidence interval] of 866 [626, 1,106] ml at 3 months and 753 [512, 994] ml at 6 months. Clinically meaningful improvements were further observed in spirometry, quality of life, symptoms, and exercise capacity.

Conclusions: This study provides the first clinical evidence of the feasibility, safety, and initial outcomes after treatment with airway scaffolds in patients with emphysema-related hyperinflation.

Keywords: emphysema; bronchoscopy; hyperinflation; airway bypass; chronic obstructive pulmonary disease

For patients with severe emphysema, most approaches for the management of chronic obstructive pulmonary disease (COPD) are largely ineffective. These patients and their physicians have been in desperate need of a treatment that is safe, effective, and durable and have considered many types of invasive treatment, such as endobronchial coils (1, 2) and airway bypass (3–5). However, only a few besides lung volume reduction surgery (6, 7) are commercially available, including bronchoscopic thermal vapor ablation (8, 9) and bronchoscopic lung volume reduction with endobronchial valves (10–15). Although the use of endobronchial valves has been included in treatment guidelines, this treatment is dependent on the emphysema distribution and degree of collateral

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*A complete list of BREATHE Study Group members may be found before the beginning of the References.

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At a Glance Commentary

Scientific Knowledge on the Subject: Emphysematous lung destruction can lead to airway collapse during exhalation that in turn leads to air trapping and lung hyperinflation. Creation of direct connections between regions of emphysematous lung and the external environment or central airways that effectively "bypass" expiratory airway collapse can effectively allow release of trapped air and decrease in hyperinflation. Tissue reaction and lung healing in these approaches have limited durability of the effect.

What This Study Adds to the Field: This is the first demonstration of a novel self-expanding nitinol airway scaffold that is designed to be placed bronchoscopically in native airways and connect emphysematous, hyperinflated lung parenchyma with central bronchi, is capable of releasing trapped air, and can safely and effectively alleviate lung hyperinflation in patients with severe emphysema.

ventilation; thus, only a small proportion of patients are able to benefit.

Hyperinflation is particularly significant for patients with emphysema because it is the main contributor to dyspnea and much of the associated morbidity (16). Hyperinflation is associated with poor exercise capacity, impaired pulmonary function, and diminished quality of life and can contribute to appetite loss, depression, cardiac issues, and increased mortality (17–18). Many COPD treatments fail because they do not address the root cause of hyperinflation: air trapping due to expiratory airway collapse.

The EASE (Exhale Airway Stents for Emphysema) trial (5), which addressed hyperinflation by the creation of transbronchial passages supported with paclitaxel-eluting stents directly connecting emphysematous lung tissue with central airways, evaluated whether airway bypass could improve pulmonary function and symptoms in patients with homogeneous emphysema and severe hyperinflation. Although this trial did demonstrate proof of principle in that air trapping was reduced and pulmonary function was improved in patients immediately after treatment, it failed to show sustained long-term benefits. The loss of the initial benefits was believed to be caused by the loss of airway bypass patency (obstruction due to mucus and granulation tissue) and stent dislodgment (13% at stents were lost by 6 mo).

To address this, a novel, helix-shaped, self-expanding nitinol airway scaffold was developed. Designed to be bronchoscopically placed with one end positioned in emphysematous lung tissue and the other in more central bronchi, the scaffolds reinforce and expand the collapsible native bronchial tree, allowing trapped air to escape during exhalation. These airway scaffolds are also designed to prevent occlusion and migration, offering a durable, effective solution for releasing trapped air and improving patient symptoms.

The main goal of this study was to evaluate the safety of the airway scaffolds in patients with hyperinflation caused by emphysema by combining the results from two prospective first-in-human studies. Secondary objectives were the assessment of technical feasibility and preliminary efficacy. Some of the results of these studies were previously reported in the form of an abstract (19).

Methods

Study Design and Oversight

The BREATHE study (Study to Assess Safety, Feasibility, and Preliminary Efficacy of the Apreo Implant for Severe Emphysema) comprised two prospective, multicenter, single-arm clinical trials: BREATHE-1 (NCT05854550) in Australia and BREATHE-2 (NCT05949645) in Europe. Both studies followed very similar protocols with minor differences in study procedures and eligibility criteria. Procedures differed with BREATHE-1 patients undergoing one fewer computed tomographic (CT) scan and BREATHE-2 patients undergoing one fewer bronchoscopy during the follow-up interval. Eligibility differed with respect to inclusion criteria (baseline FEV_1, 20–50% predicted for patients enrolled in BREATHE-1 vs. 15–50% predicted for those enrolled in BREATHE-2) and exclusion criteria (three or more acute exacerbations of COPD in the prior year, history of excessive dynamic collapse of the trachea or main bronchi, and coronary artery disease with angina were exclusionary for BREATHE-1 patients). BREATHE-1 also complied with Australian regulations, whereas BREATHE-2 followed European Union Medical Device Reporting and U.K. Medical Device Reporting requirements. Written informed consent was obtained from all participants, approved by local ethics committees.

Patients

Eligible patients were aged 35–80 years, had post-bronchodilator FEV_1 between 15% and 50% of predicted volume, residual volume (RV) $\geq$180% of predicted volume, an RV to TLC ratio $\geq$0.55, with a score on the modified Medical Research Council (mMRC) dyspnea scale of 2 or more at the time of screening. The study required CT scan evidence of emphysema with >35% destruction based on −950 Hounsfield units in at least one lobe. Patients with heterogeneous or homogeneous emphysema and with or without complete lobar fissures were allowed.

Exclusion criteria included a D_{LCO} <20%, recent COPD exacerbation or infection, prior lung volume reduction surgery, giant bullae, and symptomatic bronchiectasis. A detailed list of all inclusion

All requests for raw and analyzed data and materials will be reviewed by the corresponding author to verify whether the request is subject to confidentiality obligations.

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This article has a related editorial.

A data supplement for this article is available via the Supplements tab at the top of the online article.

Artificial Intelligence Disclaimer: No artificial intelligence tools were used in writing this manuscript.

and exclusion criteria is provided in the data supplement.

Airway Scaffold Description

The airway scaffold (Apreo Health) consisted of a permanent implant that was precrimped down to a 2.1-mm delivery profile and mounted on the distal end of a single-use delivery system. This profile allowed the user to insert the delivery system into an adult therapeutic bronchoscope with a 2.8-mm working channel. The airway scaffold had a maximum unconstrained diameter of 10 mm with a nonoverlapping, reciprocating, helical coil design constructed from a single nitinol wire that self-expands upon deployment (Figure 1). The airway scaffold was available in four lengths: 55, 70, 85, and 100 mm.

Trial Procedures

Baseline inspiratory and expiratory CT scans of the chest were performed, and quantitative CT measurements of emphysema destruction score, air volume, and air trapping index at the lobar and segmental level were also performed. Up to three target segments per lung were selected on the basis of the combination of significant emphysematous destruction, relatively high inspiratory volume, and evidence of air trapping. Patients with bilateral disease received up to six airway scaffolds (three per lung) either in a single procedure or over two procedures separated by 30 days. Patients with unilateral disease received a total of three airway scaffolds in the diseased lung.

The implant procedures were performed with the patient under general anesthesia, and the airway scaffolds were deployed under direct bronchoscopic and fluoroscopic visualization. Airway scaffolds were deployed with the distal tip of the delivery system 10–20 mm from the outer surface of the lung with the intent to land the proximal end of the airway scaffold in a third-generation airway. Prophylactic antibiotics and corticosteroids were administered periprocedurally and for at least 2 days after the procedure.

Follow-up visits were scheduled at 1 month (BREATHE-2 patients who underwent a single procedure only), 3 months, and 6 months after the first procedure and included adverse event (AE) assessment, spirometry, body plethysmography, St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C), COPD Assessment Test (CAT), mMRC dyspnea scale, 6-minute-walk test (6MWT), and bronchoscopic assessment of implanted airways. Spirometry, body plethysmography, and the 6-minute-walk test were conducted in accordance with American Thoracic Society/European Respiratory Society guidelines (20–22). Spirometry was performed 30 minutes after administration of a bronchodilator, and the test was conducted with the patient in a seated position at the same time of day throughout the study. Global Lung Function Initiative reference equations were applied to determine percent predicted values for pulmonary function parameters. Inspiratory and expiratory chest CT was performed either at 1 month or 3 months for BREATHE-2 study patients, depending on whether they underwent a single procedure or two procedures; all patients had CT performed at 6 months.

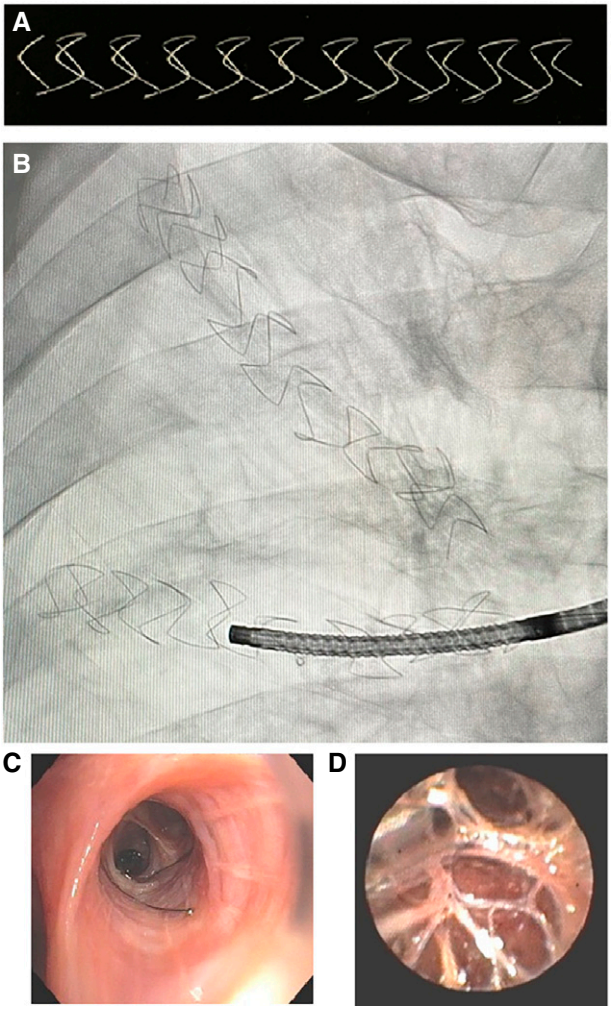

Figure 1. The airway scaffold. (*A*) A single airway scaffold. The airway scaffold is available in four lengths varying from 55 to 100 mm. (*B*) Fluoroscopic image of two airway scaffolds *in situ*. A bronchoscope is visible in the lumen in one implanted airway. (*C*) Bronchoscopic image of the proximal end of a deployed airway scaffold. (*D*) Bronchoscopic image obtained at the distal end of an airway scaffold where emphysematous parenchyma is visible.

Outcomes

The primary outcome was safety, measured by serious adverse events (SAEs) related to device or procedure over 6 months (refer to the data supplement). Secondary outcomes included technical feasibility and preliminary efficacy. Technical feasibility was assessed by the ability to successfully deploy the airway scaffold in the targeted airway, as determined by the operator. Appropriate placement of the proximal region of the deployed airway scaffold with respect to airway generation (e.g., segmental vs. subsegmental) was

determined bronchoscopically immediately postdeployment and at 3 and 6 months during follow-up bronchoscopies, as well as by review of inspiratory CT images obtained at 3 and 6 months. Appropriate placement of the distal end of the implant (targeted to be approximately 10–20 mm from the pleural surface) was assessed from CT images obtained at 3 and 6 months by measuring the distance between the distal end of the airway scaffold to the pleura obtained along the longitudinal axis of the airway scaffold.

Preliminary efficacy was assessed as improvements in RV, RV/TLC, FEV_1, FVC, SGRQ-C total score, CAT score, mMRC dyspnea scale, and 6-minute-walk distance (6MWD) at 3 and 6 months. The minimal clinically important differences used to evaluate improved clinical response were a 0.31-L decrease in RV, a 4% decrease in RV/TLC, a 100-ml increase in FEV_1, a 4-point reduction in SGRQ-C total score, a 2-point decrease in CAT score, a 1-point decrease in mMRC dyspnea scale score, and a 25-meter increase in 6MWD (23–27).

Airway diameters were measured at approximately the middle, 10 mm proximal to the distal end of the airway (distal region), and 10 mm distal to the proximal end of the scaffold (proximal region) by quantitative analysis of the expiratory CT images (VIDA Diagnostics) obtained at 6-month follow-up. Airway diameters at 6 months were compared with measurements obtained from the baseline (preimplant) expiratory CT images at approximately the same level along the airway. Airway scaffold patency and mucus were also assessed bronchoscopically in the proximal, middle, and distal thirds post-procedure at 3- and 6-month visits using a semiquantitative scale (refer to the data supplement).

Baseline quantitative CT measurements from inspiratory scans were used to categorize treated patients *post hoc* with respect to emphysematous disease distribution and the presence or absence of complete lobar fissures. A patient was categorized as having homogeneous emphysema if both lungs had an absolute difference of less than 15% in the emphysema destruction score (percentage of voxels less than −910 HU) between the upper and lower lobes. Otherwise, the patient was categorized as having heterogeneous emphysema. A patient was categorized as having complete fissures if fissure integrity scores bilaterally were ⩾85% complete. Otherwise, the patient was categorized as having incomplete fissures.

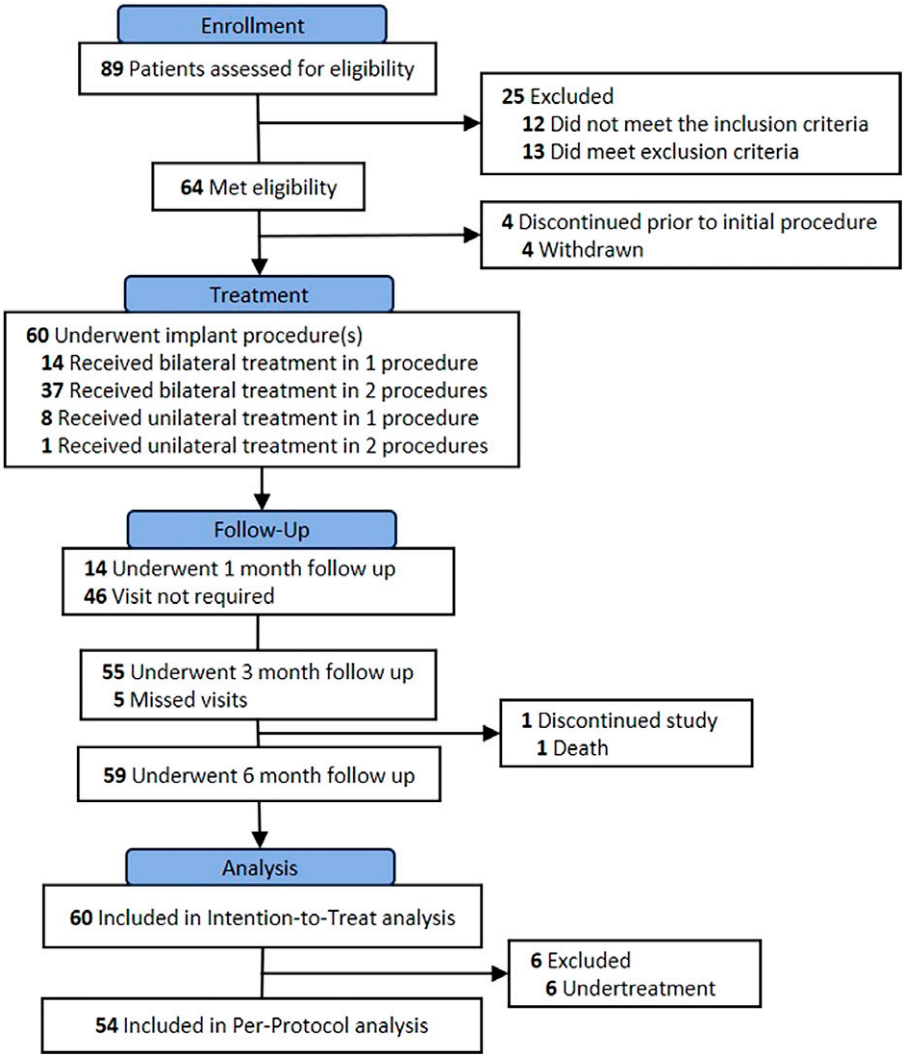

Figure 2. Flow diagram of patient inclusion and exclusion.

Statistical Analysis

Because this was a first-in-human study, no primary statistical hypothesis was proposed. The study sample size was not based on formal statistical power calculations. The cohort of 60 patients was determined by clinical judgment, accounting for potential attrition. The results presented represent a retrospective pooled analysis of two prospective studies (BREATHE-1 and BREATHE-2). The pooled analysis was not prespecified. Continuous and ordinal variables were presented as means, SDs, and 95% confidence intervals, whereas categorical data were reported as frequencies. All analyses were based on available data, and no imputation of missing data was performed. AEs were tabulated as the number and percentage of subjects reporting an event as well as the total number of each event type. A subject with more than one event was counted only once toward the event rate, based on the total number of subjects with AEs. One-sample *t* tests or Wilcoxon signed-rank tests were performed on changes between baseline and 3- and 6-month time points for efficacy parameters. *P* values are presented as summary statistics and are not used to make binary statistical significance determinations.

Analysis populations defined from the pooled dataset were the intention-to-treat (ITT) population, the safety population, and the per-protocol evaluable (PPE) population. The safety population, which included all

patients enrolled in the study for whom treatment was attempted, was identical to the ITT population; therefore, only the ITT population is referenced. The PPE population included all patients who had bilateral disease and received bilateral treatment and patients who had unilateral disease and received unilateral treatment; patients with bilateral disease who received only unilateral treatment were excluded. Patients enrolled with protocol waivers for eligibility criteria were not excluded from the PPE population.

Results

Study Patients

The study was conducted between May 2023 and October 2024. The study screened 89 patients, with 60 ultimately undergoing treatment (Figure 2). Baseline demographics (Table 1) show that participants had moderate to severe emphysema with significant hyperinflation.

Device Implantation

A total of 98 procedures were performed, and 328 airway scaffolds were placed. The median number of airway scaffolds per patient was 6 (range, 3 to 6). Three patients with unilateral disease received treatment in either a single procedure ($n = 2$) or over two procedures ($n = 1$). Among 57 patients with bilateral disease, 37 underwent staged bilateral treatment provided in two procedures, 14 received bilateral treatment in a single procedure, and 6 had a single unilateral procedure. The reasons for unilateral treatment in these six patients with bilateral disease were limited patency of airway scaffolds placed during initial procedure ($n = 2$), anatomical constraints ($n = 2$), and ongoing SAEs ($n = 1$ pneumonia, $n = 1$ COVID-19 infection). For a detailed description of the procedure, see the data supplement.

Table 1. Baseline Characteristics of Intention-to-Treat Population

Characteristics	BREATHE-1 and BREATHE-2 (*N = 60*)
Female sex, *n* (%)	33 (55)
Age, yr	66 ± 8
Body mass index, kg/m^2	23.3 ± 4.5
Smoking history	
Ever smoked, *n* (%)	60 (100)
Pack-years, mean (SD)	40.5 ± 19.8
Lung function	
FEV_1	
Liters	0.70 ± 0.22
Percent predicted value	26 ± 8
FVC	
Liters	2.6 ± 0.9
% of predicted value	75 ± 21
RV	
Liters	5.3 ± 1.2
% of predicted value	255 ± 47
TLC	
Liters	8.1 ± 1.6
% of predicted value	140 ± 15
Ratio of RV to TLC, %	66 ± 8
D_{LCO}	
Milliliters of carbon monoxide/min/mm Hg	7.9 ± 2.2
% of predicted value	35 ± 7
Arterial blood gas, mm Hg	
Partial pressure of oxygen	71 ± 9
Partial pressure of carbon dioxide	40 ± 6
Distance on 6-min-walk test, m	299 ± 91
Quality-of-life scores, no. of points	
St. George's Respiratory Questionnaire for COPD	64.8 ± 14.7
Modified Medical Research Council dyspnea scale	3.0 ± 0.8
COPD Assessment Test	21.0 ± 5.6
HRCT findings	
Emphysema destruction*, %	37.5 ± 10.0
Emphysema distribution†, *n* (%)	
Homogeneous	31 (52)
Heterogeneous	29 (48)
Fissure integrity‡, *n* (%)	
Incomplete	49 (82)
Complete	11 (18)

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; HRCT = high-resolution computed tomography; RV = residual volume.
Plus-minus values are mean ± SD.
*Emphysema destruction score was the percentage of voxels below −950 Hounsfield units.
†Emphysema distribution was assessed as the difference in destruction (percentage of voxels less than −910 Hounsfield units) between upper and lower lobes, with a difference of less than 15% defined as homogeneous and a difference of 15% or more defined as heterogeneous. A patient with bilateral homogeneity was categorized as having homogeneous disease.
‡A patient was categorized as having complete fissures if fissure integrity scores were ⩾85% for both lungs.

Primary Study Outcomes

Thirteen patients (21.7% of the ITT population) experienced at least one device- and/or procedure-related SAE within the 6 months after the initial procedure, with a total of 21 SAEs reported (Table 2). The most frequently reported SAEs were pneumonia (10.0% of patients) and COPD exacerbation (5.0% patients). When comparing patients who underwent staged bilateral procedures ($n = 37$) with those who underwent a single bilateral procedure ($n = 14$), the rate of device- and/or procedure-related SAEs was higher (29.7% vs. 7.1%). One patient with pneumonia required airway scaffold removal on Day 37 after the implant procedure. No pneumothorax was reported within 6 months, and one death caused by respiratory failure occurred 103 days after the initial procedure, which was not considered related to the device.

Secondary Study Outcomes

The technical success rate (successful deployment in the targeted airway as assessed by the investigator) was 92.4% (328 of 355 attempted deployments). The ease of airway scaffold deployment was rated as "no difficulty" for 94.6% of attempted deployments assessed (335 of 354 deployments assessed), "some difficulty" for 3.1% (11 of 354), "moderate difficulty" for 1.4% (5 of 354), and "very difficult" for 0.8% (3 of 354).

Table 2. Serious Adverse Events Related to Procedure and/or Device during 6 Months of Follow-Up (Intention-to-Treat Population)

Event	BREATHE-1 and BREATHE-2 (*N* = *60*) *N* (%) of Patients [*N* Events]
Related serious events	13 (21.7) [21]
Pneumonia	6 (10.0) [6]
COPD exacerbation	3 (5.0) [4]
Respiratory tract infection	2 (3.3) [1]
Respiratory failure	1 (1.7) [1]
Lower respiratory tract infection	1 (1.7) [1]
Pulmonary hemorrhage	1 (1.7) [1]
Bronchitis	1 (1.7) [1]
Bronchospasm	1 (1.7) [1]
Hemoptysis	1 (1.7) [1]
Hypoxia	1 (1.7) [1]
Sputum retention	1 (1.7) [1]
Rib fracture	1 (1.7) [1]
Angina pectoris	1 (1.7) [1]
Pneumothorax	0 (0.0) [0]

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.
Serious adverse events were adverse events that were fatal, required prolonged hospitalization, caused substantial risk of death at the time of the event, resulted in permanent impairment of a body function, or required medical or surgical intervention to prevent permanent impairment of a body function.

The predominant reason for lack of technical success in the 7.6% (27 of 355 attempted deployments) was airway placement either farther proximal or distal than intended. In all cases where the initial deployment was not considered successful, the airway scaffold was removed and a new airway scaffold was successfully deployed in the same target airway. The ease of airway scaffold removal, as assessed by the investigator, was rated as "no difficulty" for 88.9% (24 of 27) of the scaffolds removed, "some difficulty" for 3.7% (1 of 27) of removals, and "moderate difficulty" for 7.4% (2 of 27) of removals. No significant injury was caused by airway scaffold removal.

Of the implants assessed at the 6-month follow-up bronchoscopy, all implants remained present in the implanted airway and the proximal location had not changed (relative to immediately postdeployment) for 73.2% of the airway scaffolds, as assessed by the investigator. Quantitative measurements from CT scans demonstrated that the average change in the distance between the distal end of the scaffold and the pleura between 3 and 6 months was −0.2 mm (range, −13.5 mm to 16.1 mm), with 59.0% of implants assessed being within 2.5 mm of the distance measured at 3 months and 97.8% of implants being within 10.0 mm.

Improvements in efficacy outcomes were seen in RV, RV/TLC, FEV_1, FVC, SGRQ-C, CAT, mMRC, and 6MWD at both the 3- and 6-month follow-up visits, with the mean magnitude of these changes exceeding the minimal clinically important difference (refer to Figure E2 in data supplement). RV improved (decreased) from baseline by a mean [95% CI] of 866 [626, 1,106] ml at 3 months and 753 [512, 994] ml at 6 months ($P < 0.0001$). Individual-subject changes from baseline to 6 months for efficacy outcomes are provided in waterfall plots (Figure 3). Subgroup analyses of efficacy outcomes stratified by fissure integrity and homogeneous/heterogeneous emphysema distribution are provided in Tables E7 and E8.

Preserved airway patency through 6 months was observed in the majority of evaluable airways (Figure 4). Airway diameters measured from CT images obtained at 6 months at the levels of the proximal, middle, and distal airway scaffold were increased relative to baseline, suggesting persistent expansion of airways postimplant (Figure 5).

Given the limitations of peripheral bronchoscopy, bronchoscopic assessments of airway scaffold narrowing and mucus were not possible in all airway scaffolds at all follow-up time points. However, available data supported stability of airway patency between 3 months and 6 months (Figure E4).

Device Removals

Expectoration of an airway scaffold was not reported during the follow-up duration, and review of CT images obtained at 6 months confirmed the presence of the airway scaffolds in the originally placed locations in the lung. Two findings of possible airway scaffold migration were reported during follow-up bronchoscopies; otherwise, no evidence of significant airway scaffold migration was observed. Removal of six airway scaffolds in four patients (6.7%) was attempted via bronchoscopy, occurring 51 ± 13 days (range, 37–65 d) after implantation. Reasons for removal were airway kinking with accompanying dyspnea, lack of patency, and pneumonia as an SAE. Removal of five of six airway scaffolds was successful and not associated with tissue injury or other complications. One removal attempt was unsuccessful because the distal end of the device could not be freed with traction via forceps. Because the situs of the proximal portion of the airway scaffold was altered in the removal attempt, the investigator elected to sever this proximal portion, resulting in the removal of an approximately one-fourth length of the airway scaffold; the remaining portion of the airway scaffold was positioned well within the airway. The patient did experience an SAE (respiratory tract infection) associated with the partial removal of the airway scaffold, which resolved without sequelae 18 days after scaffold removal. No clinically significant findings were noted upon bronchoscopic evaluation approximately 3 months after the airway scaffold removal (6-month follow-up visit), and the remainder of the airway scaffold was still positioned in the airway.

Discussion

This pooled first-in-human, multicenter, single-arm study suggests that treatment with self-expanding airway scaffolds to tent open the culprit airways of patients with emphysema-related hyperinflation is technically feasible. The safety profile demonstrated a low risk of COPD exacerbation and a pneumonia rate consistent with endobronchial valve therapy (14, 29). In contrast to valve therapy for emphysema, pneumothorax was not reported during the follow-up period. A high deployment success rate was demonstrated, and the devices were retained within the

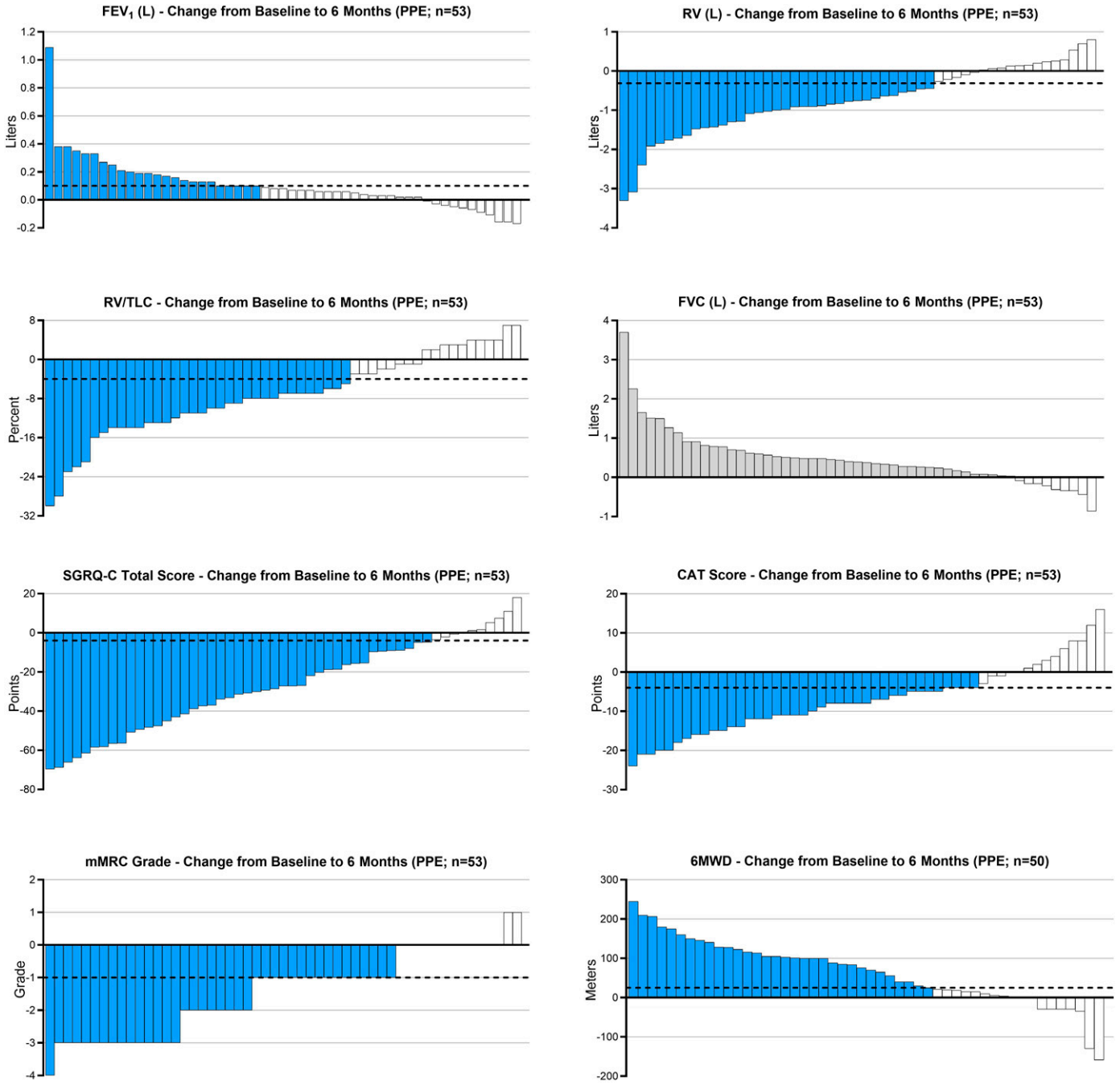

Figure 3. Efficacy outcomes. Shown are waterfall plots at 6 months for the 54-patient per-protocol evaluable population. Each bar represents the change from baseline for an individual subject. Blue bars represent subjects who met or exceeded the minimal clinically important difference (MCID). Dotted lines represent the MCIDs: FEV_1 (0.1 L), residual volume (RV) (−0.31 L), RV/TLC (−4%), St. George's Respiratory Questionnaire for Chronic Obstructive Pulmonary Disease (COPD) Patients (SGRQ-C) total score (−4 points), COPD Assessment Test (CAT) score (−2 points), modified Medical Research Council (mMRC) dyspnea scale score (−1 point), 6-minute-walk distance (+25 m). No MCID was defined for FVC. Scores on the SGRQ-C range from 0 to 100, with higher scores indicating worse quality of life. The mMRC dyspnea scale ranges from 0 to 4, with higher scores indicating more severe dyspnea. Horizontal lines represent the MCID for the following outcomes: RV, a decrease of 310 ml; RV/TLC ratio, a decrease of 4%; FEV_1, an increase of 100 ml; SGRQ-C, a reduction of 4 points; CAT score, a decrease of 2 points; mMRC, a reduction of 1 point; 6-minute-walk distance, an increase of 25 meters.

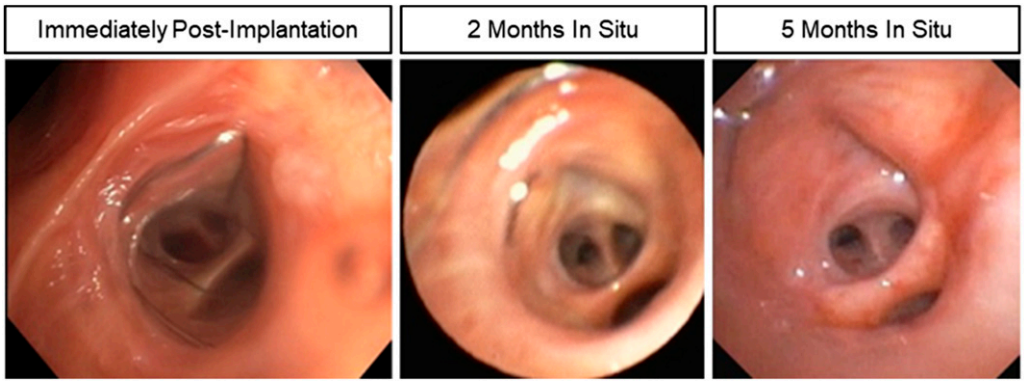

Figure 4. Post-treatment bronchoscopic images from a study patient. The same airway is shown immediately after implantation and at 2 and 5 months postimplantation. The airway is patent with no evidence of narrowing or obstruction.

targeted airway for the 6-month duration with little evidence to suggest that the airway scaffolds are prone to displacement. Overall, the foreign body response to the airway scaffolds was modest, although a small number were removed because a physician assessed lack of patency.

This study included a wide range of patients with severe emphysema. Participants had significant airflow obstruction (Global Initiative for Chronic Obstructive Lung Disease grade 3 or 4) and hyperinflation (RV ⩾180% predicted), with both homogeneous and heterogeneous disease, and a mix of fissure integrity status. Although the broad inclusion criteria limited the ability to study specific subgroups, preliminary evidence suggests the airway scaffolds may benefit patients, regardless of disease pattern or fissure integrity.

The primary goal of the airway scaffolds is to release trapped air from the lungs, and this was demonstrated by reductions in RV at both 3- and 6-month follow-up visits. This reduction in air trapping led to clinically meaningful improvements from baseline for all other major physiological and clinical outcomes measured. The favorable stability and lack of a notable foreign body response to the airway scaffolds likely underlies the preservation of airway scaffold patency and persistent treatment responses observed over the 6-month follow-up period.

This result is in sharp contrast to the EASE trial stents, which had a high rate of occlusion and dislodgment (5). This difference

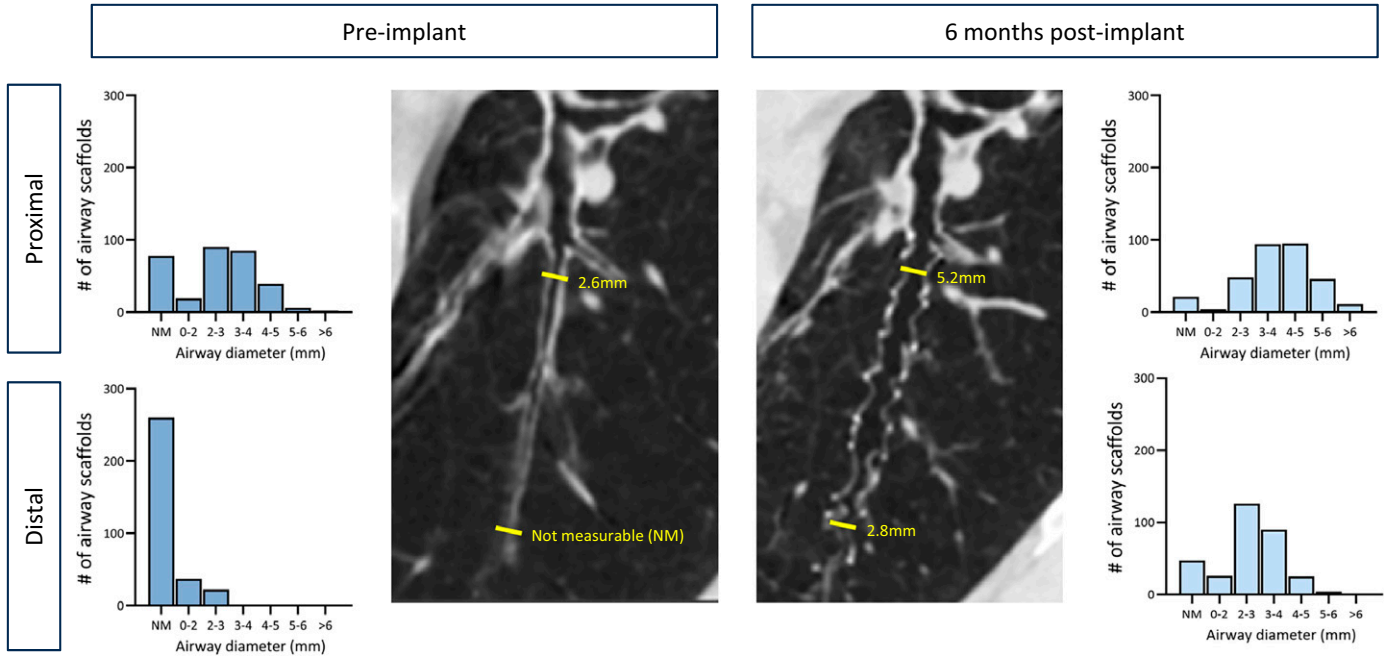

Figure 5. Topographic multiplanar rendered (tMPR, VIDA Diagnostics) computed tomographic images of target airway demonstrating tenting of the airway with an increase in diameter at 6 months postimplant relative to preimplant. Topographic multiplanar rendering displays the airways and associated parenchyma on the same plane (28). Distribution of treated airway diameters preimplant and at 6-month follow-up visit measured in the proximal and distal regions of the airway scaffold by quantitative computed tomographic analysis. Preimplant airway diameters, particularly at the distal regions of the implant, were frequently NM, likely because of collapse. At 6 months after initial implant procedure, most airway diameters could be measured, and diameters were larger than preimplant. NM = not measurable.

may be related to key design and use differences between the airway scaffolds of the present study and the EASE trial stents. First, the airway scaffolds are made from a single wire and constructed in a way that enables them to elongate, shorten, and flex during breathing/coughing, minimizing local tissue stress when implanted, unlike the EASE trial stents, which, when transbronchially implanted, would impose high tissue stress on the airway wall and likely induce tissue injury and foreign body response. Second, the airway scaffolds are designed to have minimal tissue contact density (defined as surface area of scaffold–tissue contact relative to the total area of the supported airway) such that any tissue reaction to the scaffold is likely limited only to the region of direct scaffold–tissue contact as opposed to the EASE trial stents, which had a relatively high tissue contact density and tissue reaction along its entire length. Third, the airway scaffolds have a relatively long length such that they engage with the native airways over multiple generations to help ensure scaffold stability, unlike the EASE trial stents, which were short and deployed across the airway wall, which made them prone to dislodgment.

Although the findings from this study are promising, the results of this first-in-human experience could have been affected by patient selection, identification of target airways and device placement. Refinements in these areas may further improve results. Another potential limitation of this study is that the study sample size was not based on formal statistical power calculations. In addition, without a control group, direct comparisons with other treatments are not possible. The most frequently reported SAEs, pneumonia and COPD exacerbation, may have been related to frequent bronchoscopic follow-up procedures, but this cannot be concluded because of the lack of a control group.

In conclusion, the study demonstrated the technical feasibility of a novel airway scaffold placement to tent open airways to reduce hyperinflation in patients with emphysema. The initial safety and clinical outcomes of this approach are promising and warrant further investigation. ■

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