DEERFIELD®

catalyst

MEDTECH INNOVATION HUB

Next Generation Airway Bypass

VENTANO STENT

The Georgia Medtech Summit

by Clinical Accelerator

Two Approaches To Treating Severe Emphysema

Eliminate or Collapse diseased part of lung to let the healthier parts expand

Lung Volume Reduction Surgery

Invasive and poorly tolerated

One Way Valves, Coils, Steam to collapse a lobe

Successful in select patients

Vent or Drain air out of diseased part of the lung by "bypassing" natural airways

Bronchial Stents to release trapped air

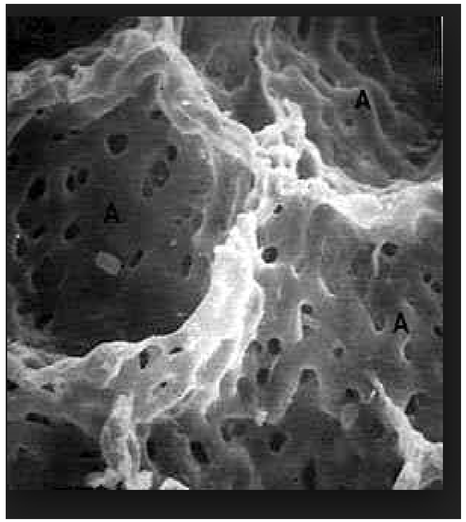
Reducing hyperinflation while preserving "good areas" of gas exchange

Broncus (2011)

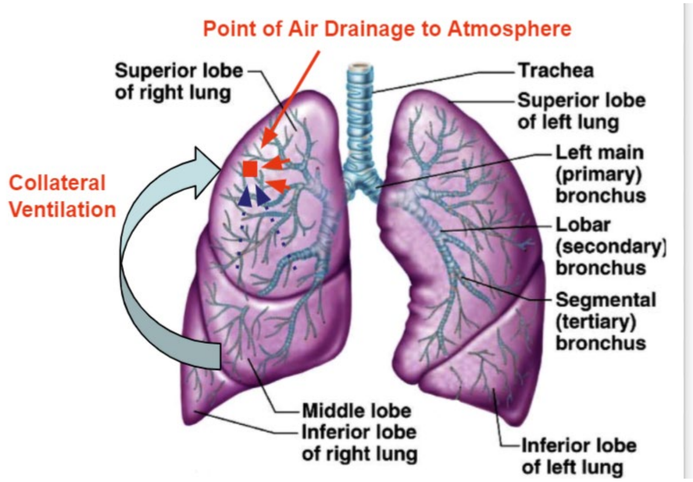
Acute success, but lacked durability

Endobronchial Valves (EBV) Have Significant Limitations

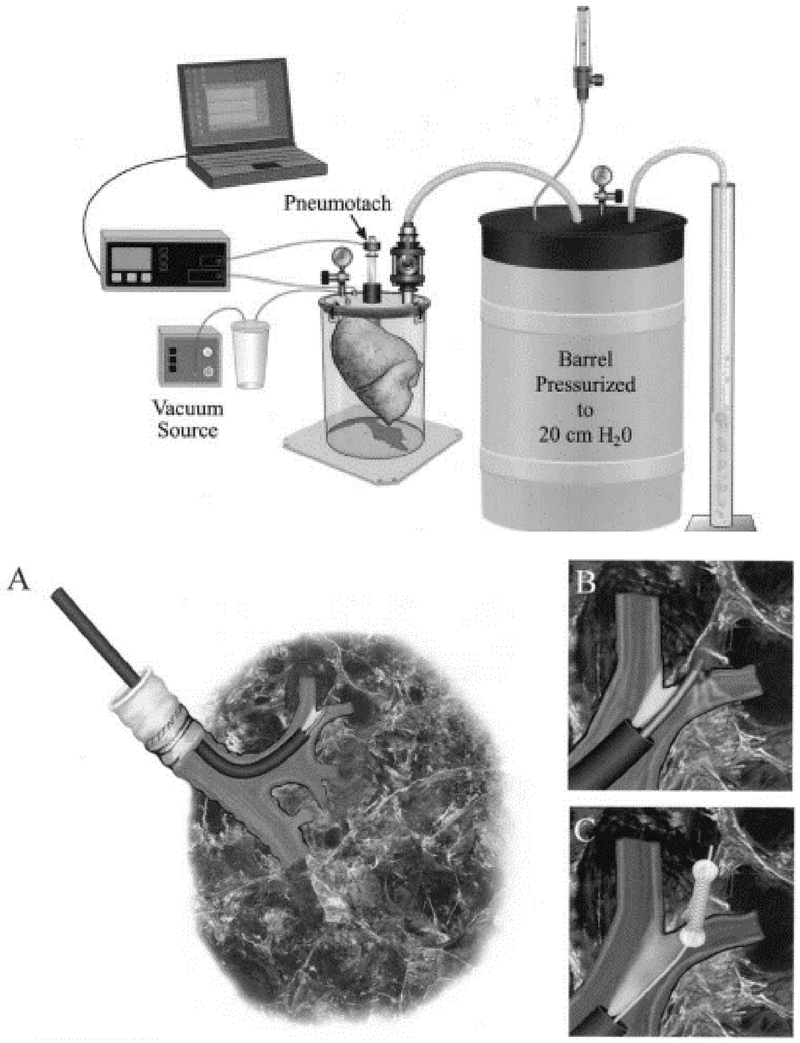
- **Interlobar fissures allow air to move from non-treated lobes into the treated lobe, preventing its collapse**
- **In addition, pneumothorax is a serious complication occurring in 23% of patients**
  - Necessitates 3-day inpatient observation period



There is an significant unmet clinical need for a treatment option for > 80% of emphysema patients who are ineligible for EBV



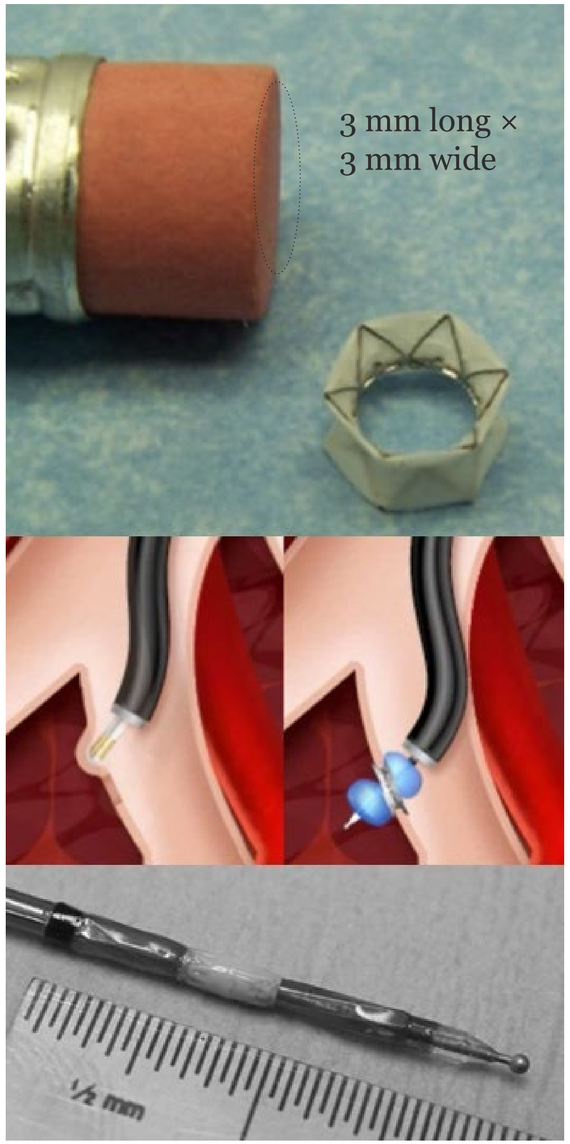
Airway Bypass: Potentially Superior Approach



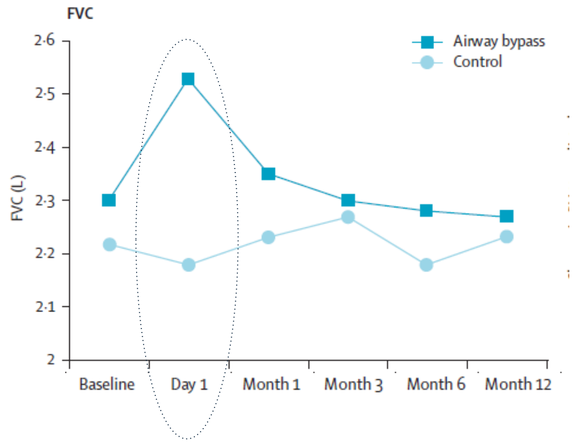
- In 2003 Joel Cooper demonstrated in explanted lungs that endobronchial fenestration of airways led to acute benefits exceeding lung volume reduction surgery
- Three fenestrations were made and coronary stents were placed and expanded in the emphysematous lungs.
- Forced expiratory volume in 1 second (FEV1) increased from 245 mL to 666 mL ($p < 0.001$).
- **Dr. Cooper's initial experiments showed that airway bypass offers advantages vs. endobronchial valves: no lung sacrifice and no eligibility limitations**

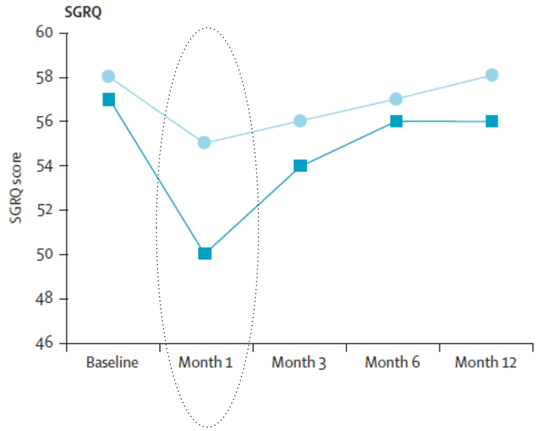
Lausberg HF, Chino K, Patterson GA, Meyers BF, Toeniskoetter PD, Cooper JD. Bronchial fenestration improves expiratory flow in emphysematous human lungs. Ann Thorac Surg. 2003;75(2):393-398.

Airway Bypass: Bronchus



- Broncus Technology developed implantable endobronchial stents to vent trapped air by “bypassing” collapsible native airways
- EASE pivotal trial in 315 patients with severe emphysema (randomized 2:1) had promising acute improvement in lung function (FVC) and QoL (SGRQ)
- **However, benefits seen at 1 day and 1 month were not sustained through the 6M due to technical issues**





Shah PL, Slebos DJ, Cardoso PF, et al. Bronchoscopic lung-volume reduction with Exhale airway stents for emphysema (EASE trial): randomised, sham-controlled, multicentre trial. Lancet. 2011;378(9795):997-1005.

Bronchus Postmortem: Good Early, But Not Durable

Reduction in RV in lobes in which stents were graded as completely clear at 6 months was similar in improvement to day 1

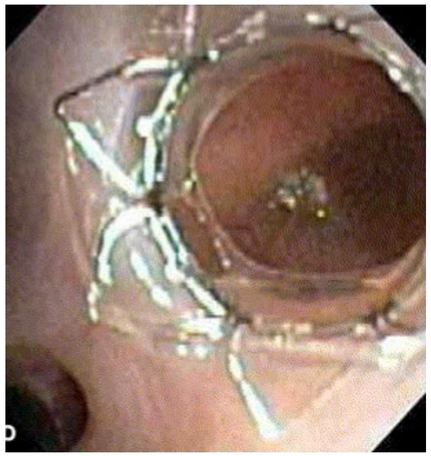
However, two technical issues were identified as responsible for the poor long-term outcomes:

- **Stent occlusion**: patients with clear stents decreased from 66% (n=421) to 21% (n=124) in 6 months

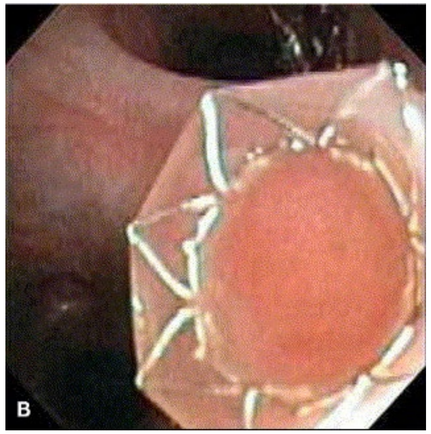
  Openings were thought to be occluded initially with mucus and exudate as well as granulation

- **Stent expectoration**: 11.5 % of patients coughed out at least 1 stent

Patent Stent



Occluded Stent



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Strategy to Achieve Sustained Benefits of Airway Bypass

Developed by Deerfield Catalyst, a medical device incubator based in NY, with intent to preserve physiological success of airway bypass, but address issues with expectoration and patency

DEERFIELD® catalyst
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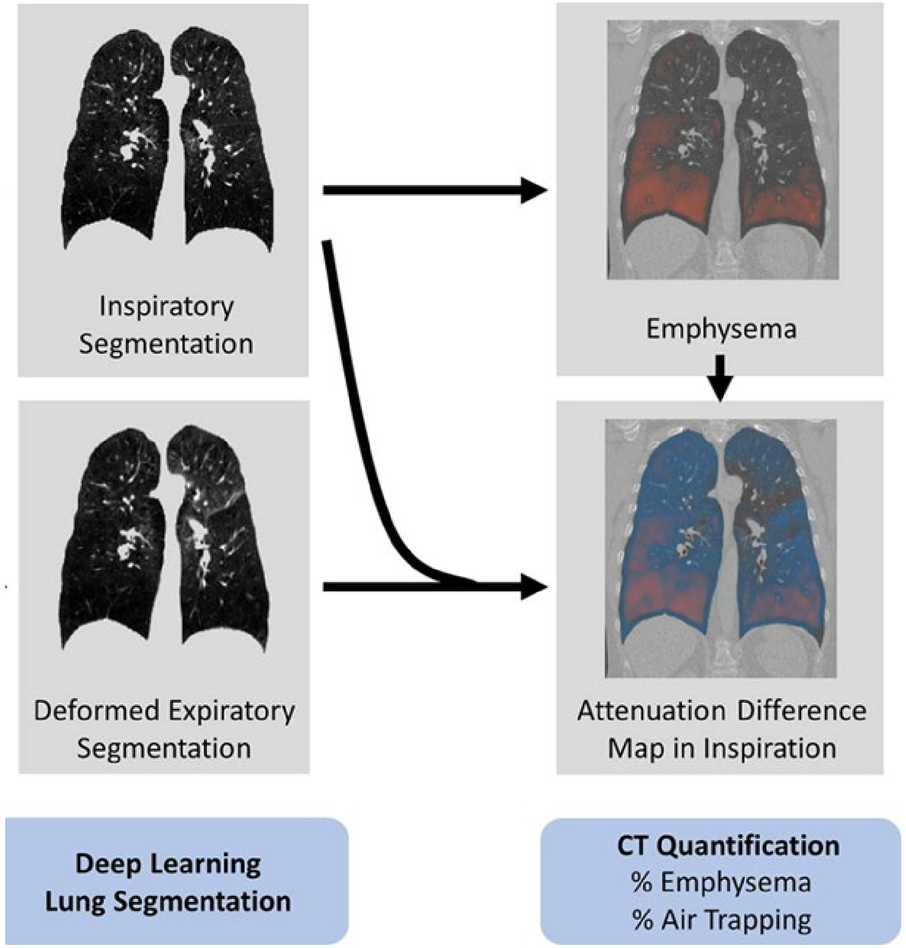
1. **Ventano Stent**
   - Larger diameter to facilitate more flow and shear to help maintain patency
   - Stent shape designed to prevent expectoration
2. **Target site selection** - More emphysematous areas (lower tissue density) to help maintain patency and stabilization
3. **Patient selection** – Previous clinical data suggests higher degree of hyperinflation helped maintain patency and efficacy

Deerfield Catalyst
Ventano Stent

Strategy to Achieve Sustained Benefits: Targeting

- Broncus did not specify target locations for individual stents
- *QCT can identify areas of both lower tissue density and gas trapping that may benefit patency*



Strategy to Achieve Sustained Benefits: Hyperinflation

- The duration of benefit appeared to correlate with the degree of pretreatment hyperinflation.[1]
- In subjects with baseline RV/TLC above the median, RV is reduced by 1040 mL (16.2%; P.001) at 1 month and 870 mL (14%; P.022) at 6 months. For subjects with RV/TLC at and below the median, RV (400 mL; P.048), FVC (11.1%; P.026) and 6MW (28.6; P.021) had a statistically significant improvement at 1 month, but none of the benefits were maintained at 6 months, with most parameters returning to near or below baseline.[2]
- Based on findings from the clinicaltrials.gov (NCT00391612), the RV/TLC criteria was originally >0.69, but it was ultimately lowered to 0.65

TABLE 2. Results for patients with baseline RV/TLC above the median of 0.67

Parameter	Baseline (n = 18)	1 Month (n = 16)	Change (*P* value)*	6 Months	Change (*P* value)*
RV (L)	5.92 ± 1.21	5.09 ± 1.10	−1.04 L, −16.2% (.001)	5.20 ± 1.56	−0.87 L, −14.1% (.022)
TLC (L)	7.80 ± 1.38	7.41 ± 1.23	−0.61 L, −7.1% (.016)	7.45 ± 1.62	−0.46 L, −5.6% (.120)
FVC (L)	1.78 ± 0.46	2.08 ± 0.50	22.6% (.006)	2.01 ± 0.56	17.8% (.065)
FEV_1 (L)	0.64 ± 0.16	0.70 ± 0.24	7.9% (.113)	0.67 ± 0.25	4.1% (.396)
mMRC (points)	2.7 ± 0.8	2.0 ± 1.0	−0.7 (.007)	2.2 ± 1.2	−0.5 (.035)
6MW (m)	307.4 ± 106.8	349.7 ± 129.9	44.7 (.002)	306.4 ± 121.8	−1.0 (.948)
SGRQ (points)	57.1 ± 15.3	49.9 ± 19.4	−7.1 (.007)	52.4 ± 18.7	−4.7 (.100)

Data are mean ± standard deviation. *L*, liters; *m*, meters; *RV*, residual volume; *TLC*, total lung capacity; *FVC*, forced vital capacity; FEV_1, forced expiratory volume in one second; *mMRC*, modified Medical Research Council; *6MW*, 6-minute walk; *SGRQ*, St George's Respiratory Questionnaire. *Absolute and percent change from baseline reported for RV, percent change from baseline for TLC, FVC, and FEV_1, and absolute change for mMRC, 6MW, and SGRQ. *P* values are derived from a 2-tailed paired *t* test for differences from baseline. Average changes only include patients with data for 1 or 6 months.

TABLE 3. Results for patients with baseline RV/TLC at and below the median of 0.67

Parameter	Baseline (n = 18)	1 Month	Change (*P* value)*	6 Months	Change (*P* value)*
RV (L)	4.77 ± 0.88	4.55 ± 0.71	−0.40 L, −7.7% (.048)	4.78 ± 0.86	0.03 L, −0.4% (.723)
TLC (L)	7.80 ± 1.18	8.03 ± 1.05	−0.09 L, −0.9% (.569)	7.72 ± 1.38	−0.05 L, −0.6% (.718)
FVC (L)	2.81 ± 0.75	2.99 ± 0.73	11.1% (.026)	2.67 ± 0.79	−2.9% (.285)
FEV_1 (L)	0.85 ± 0.17	0.90 ± 0.28	6.7% (.191)	0.81 ± 0.198	−3.6% (.301)
mMRC (points)	2.6 ± 0.7	2.1 ± 0.9	−0.5 (.120)	2.1 ± 1.1	−0.5 (.216)
6MW (m)	374.3 ± 90.1	410.4 ± 86.7	28.6 (.021)	349.5 ± 122.6	−24.4 (.170)
SGRQ (points)	58.6 ± 15.0	56.5 ± 13.5	−2.1 (.374)	61.6 ± 14.3	1.7 (.468)

Data are mean ± standard deviation. *L*, liters; *m*, meters; *RV*, residual volume; *TLC*, total lung capacity; *FVC*, forced vital capacity; FEV_1, forced expiratory volume in 1 second; *mMRC*, modified Medical Research Council; *6MW*, 6-minute walk; *SGRQ*, St George's Respiratory Questionnaire. *Absolute and percent change from baseline reported for RV, percent change from baseline for TLC, FVC, and FEV_1, and absolute change for mMRC, 6MW, and SGRQ. *P* values are derived from a 2-tailed paired *t* test for differences from baseline. Average changes only include patients with data for 1 or 6 months.

[1] Choong CK, Cardoso PF, Sybrecht GW, Cooper JD. Airway bypass treatment of severe homogeneous emphysema: taking advantage of collateral ventilation. Thorac Surg Clin. 2009 May;19(2):239-45.

[2]Cardoso PF, Snell GI, Hopkins P, Sybrecht GW, Stamatis G, Ng AW, Eng P. Clinical application of airway bypass with paclitaxel-eluting stents: early results. J Thorac Cardiovasc Surg. 2007 Oct;134(4):974-81.

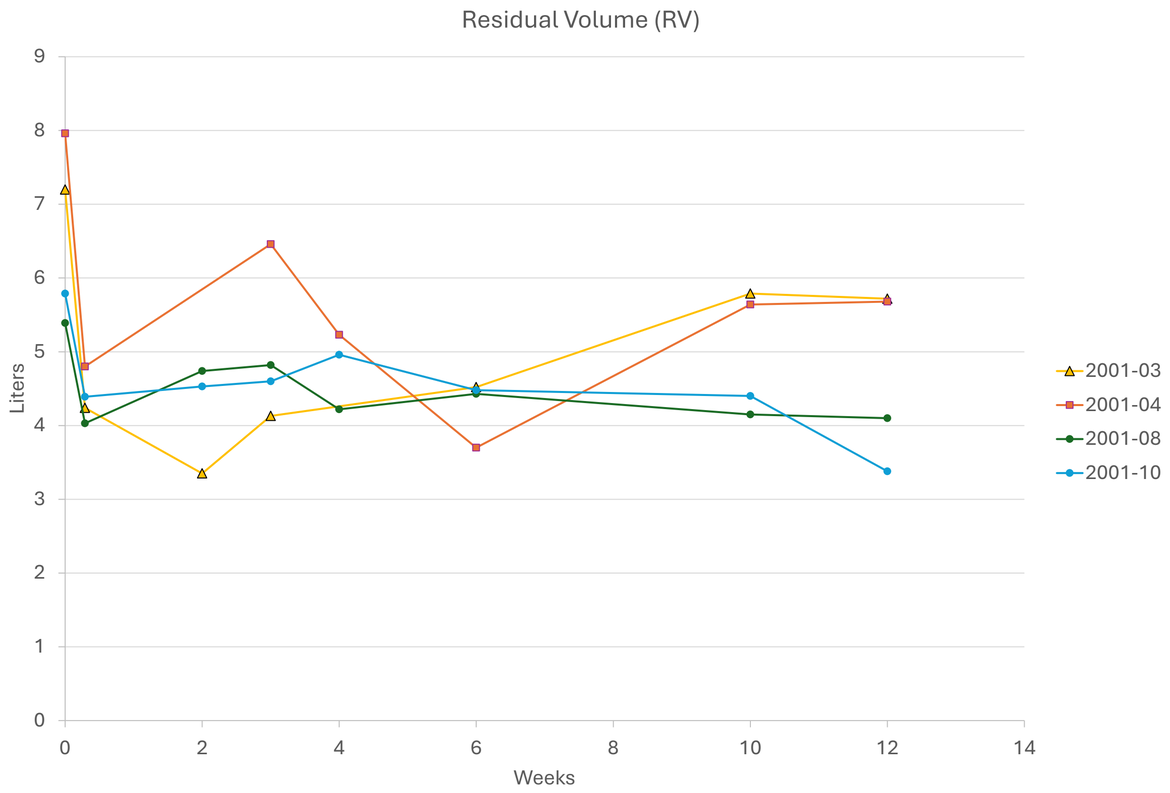
Airway Bypass - Safety and Feasibility Study (AIRWAY)

- Single center, prospective, single arm study to evaluate the safety and feasibility of the Airway Bypass System
- Up to N=10 patients
- Primary Endpoint: Safety through 6- and 12-month follow-ups
- Secondary Endpoints: Procedural success, QoL, Lung Function, Exercise Tolerance
- Key Inclusion Criteria: moderate-to-severe COPD with evidence of hyperinflation
  - Post- bronchodilator FEV1 less than or equal to 50% of predicted
  - Total Lung Capacity > 100% of predicted
  - Residual volume ≥ 225 % of predicted
  - RV/TLC > 0.69
- Major Exclusion Criteria
  - Change in FEV1 >20% post-bronchodilator
  - Inability to walk at least 140 meters in 6 minutes or ability to walk greater than 450 meters in 6 minutes
  - Clinically significant bronchiectasis

AIRWAY: Summary

- **Location:** Israeli-Georgian Medical Research Clinic Healthycore Tbilisi, Georgia
- **Number of procedures:** 5 patients were treated
- **Investigators:**
  - Felix Herth (Heidelberg, Germany)
  - David Tchkonia (Tbilisi, Georgia)
  - Kakha Vacharadze (Tbilisi, Georgia)
- **Safety**
  - 1 SAE deemed by the site investigators and independent safety reviewer as unrelated to the device (septic shock over a week post implantation from pseudomonas pneumonia)
- **Efficacy**
  - Benefits sustained through at least 12-weeks in all surviving patients:
  - Significant reduction in residual volume
  - Improvement in quality-of-life measures
  - Improvement in functional capacity

AIRWAY: Summary



- Baseline RV: 6.6 L [5.4 to 7.9]
- Sustained reduction of RV from the time of discharge
  - Discharge (N=4):

    -2.2 L [range: -1.4 to -3.2]

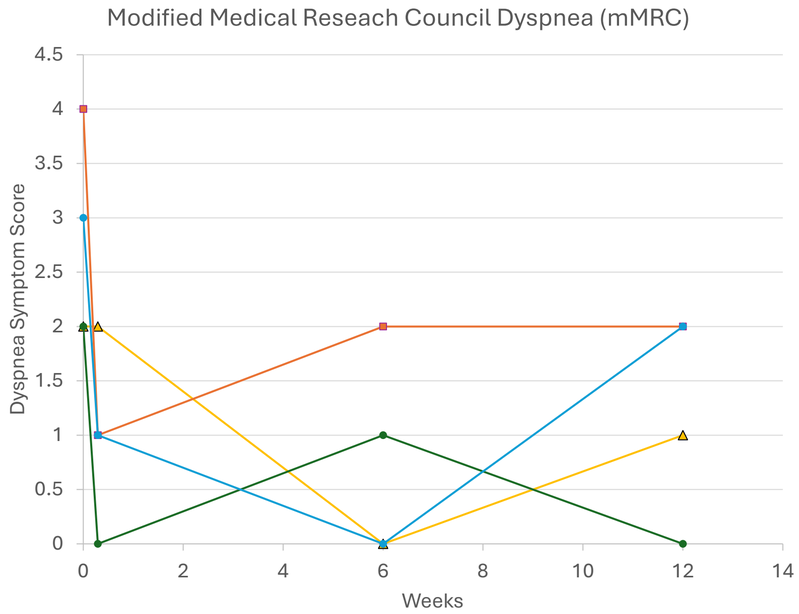
  - 12 Weeks (N=4):

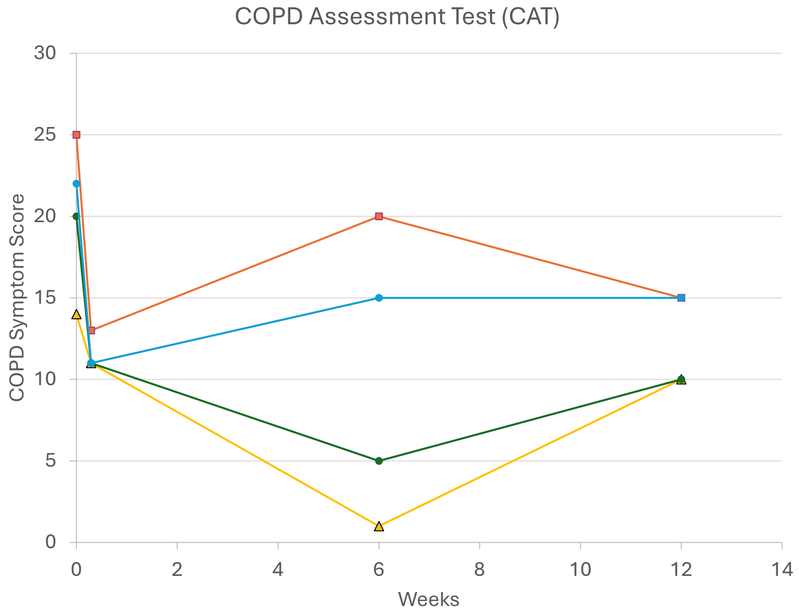
    -1.9 L [range: -1.3 to -2.4]

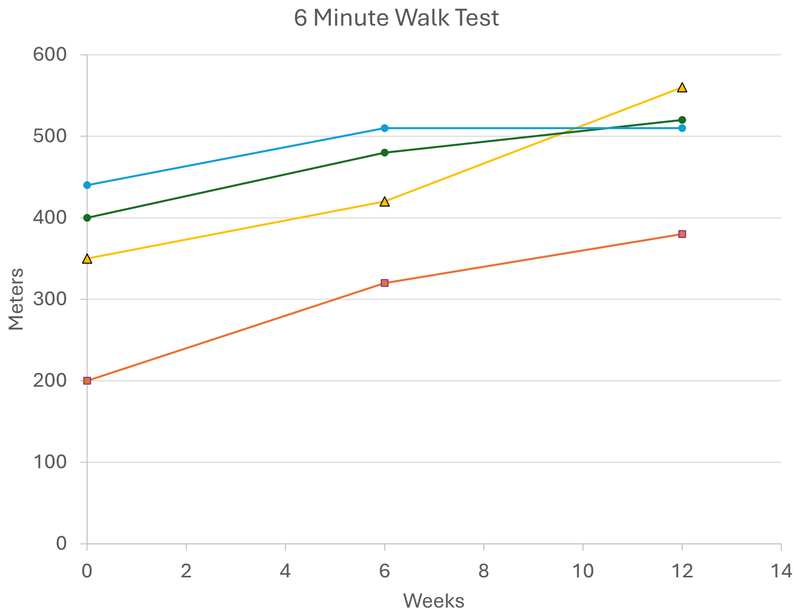
MCID = 0.3L

EBV = 0.5 L

AIRWAY: Summary







-1.5 at 12 weeks (N=4)

MCID: -1

-7.8 at 12 weeks (N=4)

MCID: -2

+145 m at 12 weeks (N=4)

MCID: +30 m

Conclusions

- Venting trapped air is a proven strategy to treat moderate to severe COPD patients with hyperinflation
- Attempts to take advantage of this physiology with an airway bypass (connecting trapped air with a proximal airway via a stent placed across the airway wall) have so far failed due to limited durability of the effects
- Deerfield Catalyst approach with the **Ventano Stent** therapy so far demonstrates durability through at least 3 months in some patients
- Additional follow up data and larger randomized control trials are needed to fully understand the safety, efficacy and durability of effect for this therapy