Improved 6MWT Distance with a Highly Portable Non-Invasive Ventilator

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Introduction

Patients with chronic lung disease frequently have dramatically reduced capacity for exertion, which limits their ability to complete activities of daily living and eventually results in a loss of functional independence (1). Although exercise tolerance can be improved in the research setting with positive pressure ventilation (e.g. bi-level mask-based ventilation) (2, 3), poor portability and cumbersome patient interfaces have limited the adoption of ambulatory non-invasive ventilatory support in chronic lung disease. A portable ventilatory support system with a comfortable, unobtrusive patient interface could play a valuable role as an adjunct therapy for chronic lung disease by improving exercise tolerance, thus facilitating patient activity.

As an initial step in addressing this important unmet need, we conducted a non-significant risk trial using a small, wearable ventilator with a non-invasive interface (Breathe Technologies, Figure 1). The ventilator weighs less than .5 kg and requires an external pressurized oxygen source. This ventilator and mask system, which are not yet commercially available, have performance characteristics in bench tests that indicate function within a range where traditional mask-based ventilators provide benefit to patients (Figure 2). We hypothesized that this ventilator would be well tolerated by patients in a pulmonary rehabilitation setting and would improve 6MWT distances. Here we present our results from a 30 patient, first-in human, non-significant risk feasibility trial.

Experimental Ventilator with Prototype Interface

Figure 1

7 3/4 inches

Experimental Ventilator Function in Lung Model

Achieving the Goals of Pressure Support

	Standard BiPAP closed system, IPAP=12, EPAP=5	Test Ventilator open system, set at 250 ml
Pressure Support Goals • Improve tidal volume • Reduce work of breathing • Reduce risk of dynamic hyperinflation and rapid shallow breathing	Tidal volume **697 ml** P_{mean} **6.9 cm H_2O** Peak flow **62 lpm**	Tidal volume **869 ml** P_{mean} **2.1 cm H_2O** Peak flow **106 lpm**

Additional Parameters

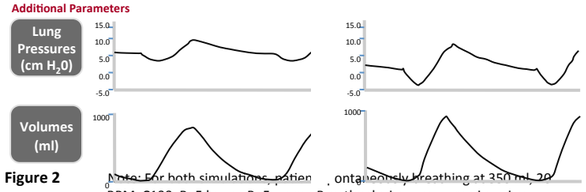

Figure 2 Note: For both simulations, patient is spontaneously breathing at 350 ml, 20 BPM, C100, Rp5 lower, Rp5 upper; Breathe device uses a non-invasive interface.

IngMar Medical ASL 5000 set at constant effort.

Study Description

Non-invasive open ventilation (NOVEL) study:
A non-significant risk (NSR) study to establish feasibility

Purpose

- Evaluate portable, non-invasive ventilator system with respect to patient comfort and device function during rest and exertion over a several hour period at a pulmonary rehabilitation facility

Hypotheses

- Ventilator system will be well-tolerated for 1 hr of use
- Use of ventilator will improve exercise capacity

Study features

- Two community pulmonary rehabilitation centers
- Total of 30 patients with previous enrollment in a pulmonary rehabilitation program
- Prototype, non-optimized open mask-based interface in conjunction with wearable .5 kg ventilator (Breathe Technologies) and oxygen canister

Study Design and Endpoints

- Determine tolerance and device function at rest and with exertion
- Compare exertional tolerance (6MWT or cycle ergometry) with and without ventilator
- Oxygen use to be matched if possible to within 1 lpm between control and experimental exertions

Key Inclusion/Exclusion Criteria

- Chronic lung disease patient with home oxygen prescription at ≥2 lpm
- Diagnosis of obstructive or restrictive lung disease
- Able to participate in some form of physical activity
- No signs of acute illness

Flowchart of Study Procedure

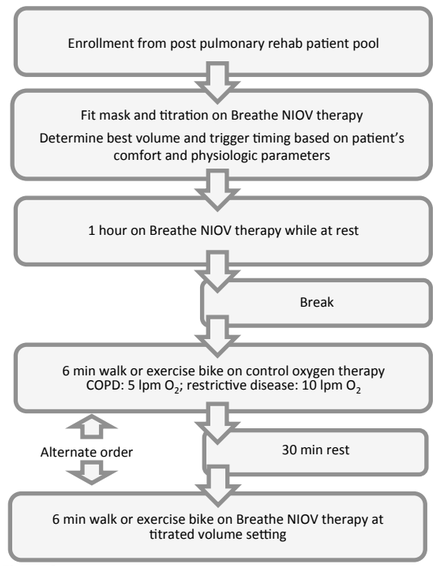

Figure 3

Results 1: Test ventilator and mask system was well tolerated

All Patients

	Change in SpO_2 During Exercise		Change in Borg Dyspnea Scale (BDS) During Exercise	
	Control	Test	Control	Test
Mean change	-5.3	-6.7	3.1	3.2
Standard deviation	0.04	0.05	1.57	1.77
Minimum change	1.0	0.0	0.0	0.0
Maximum change	-14.0	-19.0	6.0	7.0
N (all patients)	30 patients		30 patients	

Table 1

Results 2: Change in walk distance for all patients

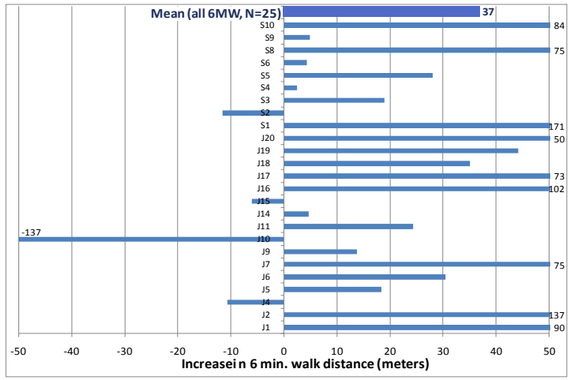

Figure 4 Legend: J=John Muir patient, S=Seton Medical Center patient
5 patients (not graphed) performed seated exercise or did not complete the 6MW.

Results 3: Substantial 6MWT improvement in COPD patient subset

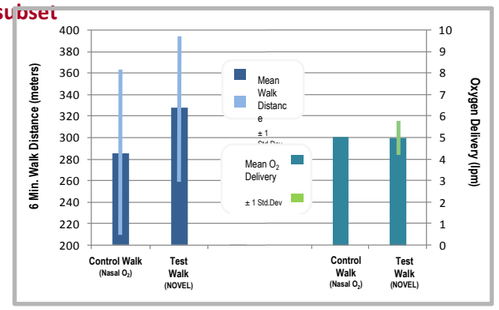

Figure 5 COPD Subset Criteria:

- Diagnosis of obstructive lung disease based on PFTs
- Performed 6MW
- Ventilator/mask performed adequately (Patient-Vent synchrony ≥ 80%)
- Excludes J10, an outlier who required 15 lpm O_2

Patient Characteristics – COPD Subset (N=18)

	Age	FEV1%	O_2 Rx w/ exercise	Vent Triggering *
Mean	70.0	33.3	4.0	90%
Standard deviation	9.2	13.1	0.8	6.8%
Minimum	48.2	16.0	3.0	80%
Maximum	83.4	56.0	5.0	99%

* Accuracy of patient-ventilator synchrony during test 6MW

Table 2

Conclusions

The successful completion of this 30 patient trial supports a number of conclusions.

- **The system is well tolerated.** Every patient tested was able to comfortably use the therapy for one hour at rest without complaints. Each patient was also able to comfortably participate in physical exertion while using the device (Table 1).
- **Use of the device improves exercise tolerance in a 6MWT.** 21/25 patients that completed walks with both control therapy and test therapy (vent.) walked further while using the ventilator ($p < .01$). The mean improvement was 37 meters (Figure 4).
- **A subset of patients with COPD had a clinically significant improvement in 6MWT distance.** Improvements in 6MWT are used to justify interventions in a variety of illnesses (4). Expert opinion indicates that a minimum improvement of 35-54 meters in 6MWT distance associated with a therapeutic intervention is clinically significant in lung disease (5, 6). The average improvement in 6MWT in a subset of COPD patients in this study was 43 meters (Figure 5).
- **Additional research is needed to determine the utility of the ventilator in improving patient mobility, QOL, and health-care resource utilization with longer term use.**

Collaborators, Contact Information and Funding

R. Escobar, and T. Hazlehurst (Seton Medical Center, Daly City, CA/US) collaborated on this work. For further information on this ventilator system, please contact Tony Wondka at tonyw@breathetechnologies.com or carlam@breathetechnologies.com.

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