Improving Portable Oxygen Concentrator Performance through the development of a New Nasal Interface

by

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A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science

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Abstract

Long term oxygen therapy (LTOT) is used to improve survival for patients with respiratory diseases who experience chronic respiratory failure. During LTOT, supplemental oxygen is supplied to patients from an oxygen source via cannula supply tubing. Portable oxygen concentrators (POCs) are a widely used oxygen source that often employ pulsed delivery modes to conserve oxygen. Pulsed delivery devices send a bolus of oxygen only during the inhalation phase of the user's breath. In contrast, large amounts of oxygen are wasted during exhalation when using stationary, continuous flow sources. However, efficient pulsed delivery requires POCs to be triggered by patient inhalation. Triggering is known to fail during periods of quiet breathing, as occurs during sleep. As a result, the conventional method for delivering oxygen to LTOT patients includes a stationary, continuous flow oxygen source for sleep/rest, and a portable, pulsed flow oxygen source for activity. The need for multiple oxygen sources greatly limits patient autonomy and increases the cost of oxygen therapy. In the present thesis, a new nasal interface was developed to improve triggering of pulsed oxygen delivery from POCs. Ideally, this will eliminate the need for stationary oxygen sources in many cases, increasing patient autonomy and lowering the cost of LTOT.

The pressure drop across the cannula supply tubing, called the "signal pressure" herein, is monitored by the POC to determine when inhalation occurs. The new nasal interface is a tunable device with multiple settings used to control the signal pressure present during patient inhalation. *In vitro* experiments incorporating realistic nasal airway replicas and simulated breathing were conducted to test the performance of the new nasal interface. First, the signal pressure was measured over a range of constant inhalation flow rates with the nasal interface, a standard

cannula, or a flared cannula inserted into the nares of the nasal airway replicas. It was hypothesized that new nasal interface would provide higher signal pressures than the standard and flared nasal cannulas at a given flow rate for each airway replica. Next, POC triggering efficiency and the fraction of inhaled oxygen (FiO_2) were evaluated for the nasal interface and both cannulas when connected to a commercial POC during simulated tidal breathing through the airway replicas. The simulated breathing patterns were representative of chronic obstructive pulmonary disorder (COPD) patients during sleep. It was hypothesized that using the new nasal interface would result in higher POC triggering efficiency and average FiO_2 when compared to the standard and flared nasal cannulas.

At least one new nasal interface setting showed higher signal pressures than either nasal cannula for all flow rates and replicas tested. Also, in every simulated breathing scenario where the standard and/or flared cannula failed to trigger the POC, at least one new nasal interface setting successfully triggered. Average $Fi0_2$ was significantly higher for successful triggering cases than for failed triggering cases.

The new nasal interface is a tunable device designed to control the signal pressure present during patient inhalation. Using the new nasal interface during in vitro testing with realistic airway replicas improved triggering of pulsed oxygen delivery from a POC. This innovation presents a simple solution that could be used with commercially available POCs to reliably supply oxygen during periods of quiet breathing.

Preface

In Chapter 3 of this thesis, work that has been co-authored and has been submitted for publication is contained. Kineshta Pillay, John Z. Chen, Dr. Warren H. Finlay and Dr. Andrew Martin are co-authors on the submitted manuscript. Kineshta Pillay helped design the prototype shown in Chapter 3. The LabVIEW code used for recording experimental data and the Excel spreadsheet used to extract information from the raw data were adapted from those provided by John Z. Chen who established them for work comparing continuous oxygen delivery to pulsed oxygen delivery. I added an algorithm using Excel's Visual Basics for Application to John's existing Excel spreadsheet to make data analysis faster and easier. I was responsible for the prototype design/manufacture, building the experimental set-ups, and the data collection/analysis described in Chapter 3. Dr. Warren H. Finlay provided editorial support for the previously submitted manuscript. The drafting of this manuscript was my responsibility with significant editorial support, direction, and contributions from Dr. Martin, especially for Chapter 3.

Dedication

To my parents,

Reneé and Darren Christianson

whose love and support made it possible for me to pursue higher education and live a happy and healthy life to date.

Acknowledgments

First, I'd like to thank my supervisor Dr. Andrew Martin for his strong leadership during my master's degree. His expertise and passion for inhalation drug delivery continues to play a crucial role in developing our new nasal interface concept. In addition, Dr. Martin has devoted a significant amount of time to help me shape a career path that matches my goals and values. With his guidance, I gained the confidence to move forward in pursuing a research-based career. Thank-you Dr. Martin for being a great role-model.

Next, I'd like to thank Kineshta Pillay, John Chen, and Kelvin Duong for their assistance in my thesis project. Kineshta taught me how to use several pieces of equipment in the lab and played a key role in designing the presented prototype. John Chen made the Excel spreadsheet to which I added a VBA script to complete my data analysis. The work John was able to publish prior to my project was extremely important in validating the need for my project. Kelvin Duong taught me how to program the lung simulator and provided great advice throughout my degree. Thank-you all for your support.

Lastly, I'd like to thank Sameeh Salama, Ahilesh Shankar, and Zeinab Elbarrad from Brass Dome Ventures. Brass Dome Ventures started a pre-accelerator program called imYEG, (Innovation Masterminds Edmonton) which helps researchers bring their innovations to market. As a result of Sameeh, Ahilesh, and Zeinab's efforts, our innovation is much closer to commercialization. Thank-you all for your contributions.

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Chapter 1: Introduction

1.1 Overview

Chronic respiratory diseases are commonly treated with long term oxygen therapy (LTOT). For example, it has been demonstrated that administering LTOT can extend the lives of hypoxemic chronic obstructive pulmonary disease (COPD) patients [1, 2]. Supplemental oxygen is supplied to LTOT patients from one of many different oxygen sources via nasal cannula tubing. In Figure 1-1, the administration of supplemental oxygen from a gas tank via nasal cannula is shown.

Figure 1-1: Patient receiving supplemental oxygen from a gas tank via nasal cannula tubing [3].

In addition to gas tanks, common sources of supplemental oxygen include stationary and portable oxygen concentrators. Oxygen sent from either type of concentrator is delivered to the patient via nasal cannula tubing as well. An example stationary oxygen concentrator and portable oxygen concentrator (POC) are shown in Figure 1-2.

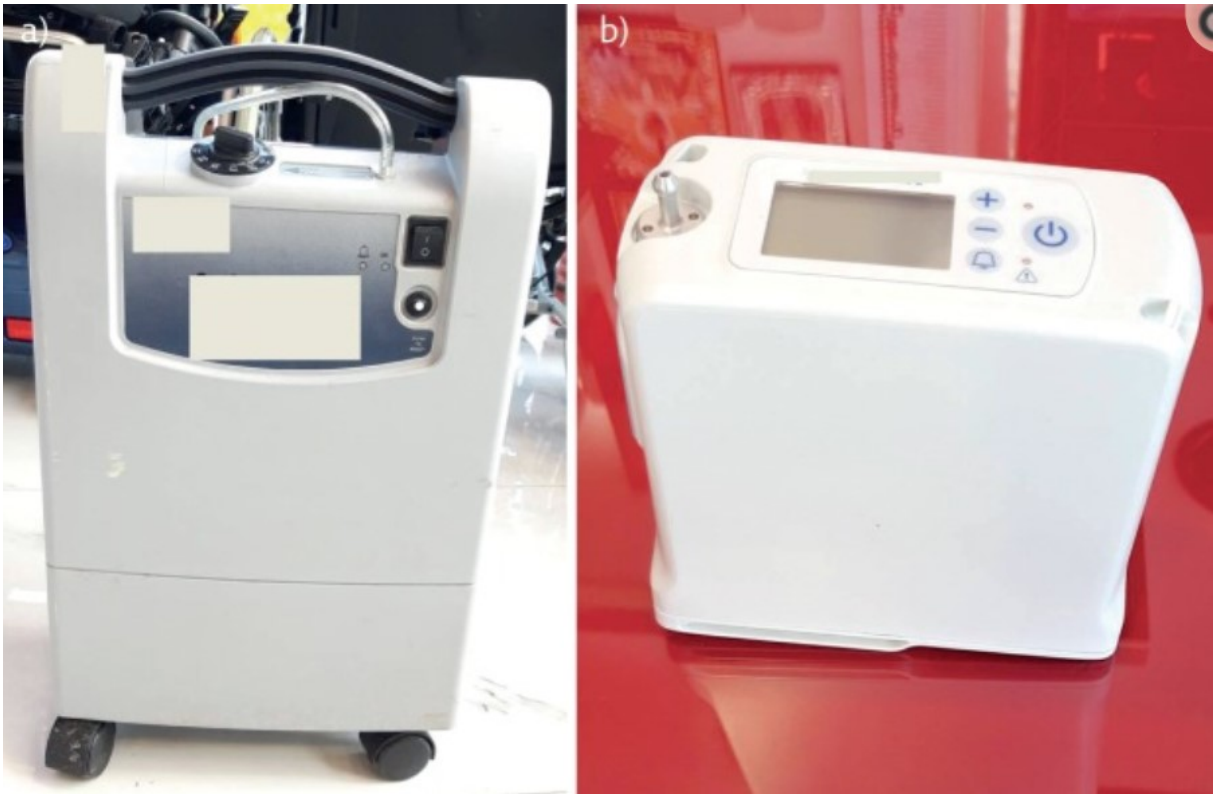

Figure 1-2: a) Stationary oxygen concentrator (b) Portable oxygen concentrator [3].

In the United States, well over 1 million patients receive LTOT in their homes [4]. Oxygen-related Medicare reimbursement costs for COPD patients exceeded $2 billion US in 2011 [5]. In Canada, oxygen therapy accounts for 17% of the entire annual direct costs of COPD care [6].

Despite proven benefits of oxygen therapy to extend patients' lives, LTOT is often prescribed with little thought to the delivery system. Historically, physicians prescribe a level of supplemental oxygen to patients, and the choice of delivery device is left to home healthcare

providers. In a survey including 1,926 adult oxygen users, 51% of respondents indicated oxygen delivery problems. A lack of physically manageable portable systems with high oxygen flow rates was one of the most frequently reported issues [7]. The current state-of-the-art in LTOT, including patients' lack of access to portable delivery devices meeting their needs, has been described as a crisis [8, 9]. Further advancement in oxygen delivery technology is needed to meet the needs and preferences of patients.

1.2 Patient Needs and Preferences

According to a survey that included responses from 836 LTOT patients, POCs are the most common portable oxygen source (61%) and are considered the least burdensome device [10]. While POCs are the preferred device, several LTOT patients must settle for gas tanks due to the cost and oxygen limitations of POCs [10]. Performance and clinical evidence are factors in the home health care provider's decision process, but choosing a delivery device is heavily limited by cost/budget [11].

The reported patient preference is a single source of portable oxygen that can be used in all breathing scenarios [12]. Some POCs have been marketed as single-source, 24-hours-a-day solutions. However, nighttime hypoxemic events are reported frequently during use of POCs, compared with larger, stationary, continuous flow oxygen sources [12]. As a result, it is common for patients to switch from a portable to a stationary system before sleeping.

1.3 Basic Operation of Portable Oxygen Concentrators

POCs offer several advantages over gas tanks by using pressure swing adsorption (PSA) and pulsed flow delivery technology. Utilizing PSA allows POCs to remove nitrogen from entrained ambient air (21% oxygen), creating an oxygen-rich gas stream on demand (~90-95% oxygen). In

contrast, oxygen gas tanks need to be refilled/delivered to patients regularly. Figure 1-3 depicts a basic POC flow schematic.

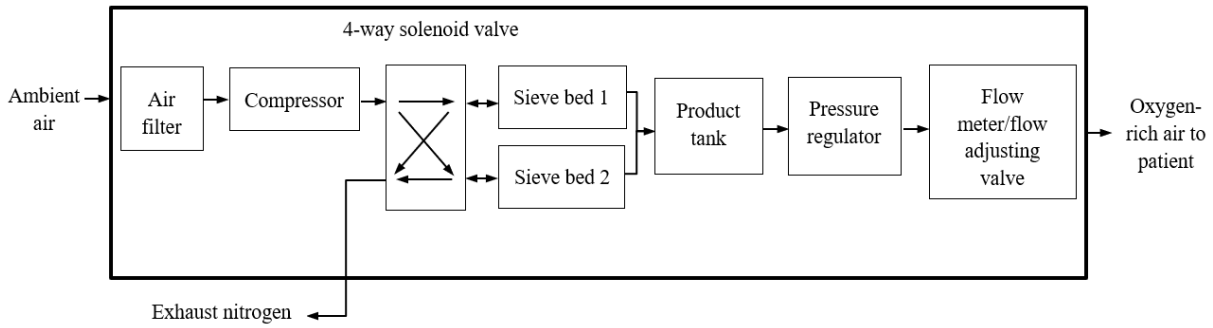

Figure 1-3: Portable Oxygen Concentrator Flow Schematic. Labels outside of the largest black box represent flow components outside of the portable oxygen concentrator.

First, ambient air is drawn into the POC by the compressor. Next, a solenoid valve and molecular sieve beds are used to filter nitrogen out of the entrained air. The molecular sieve beds contain aluminosilicate minerals, known as zeolite, which adsorb nitrogen when ambient air is supplied at a specific pressure [13]. POCs typically contain two sieve beds. After the first bed is full of nitrogen, the solenoid valve changes the ambient air flow path to the second sieve bed. While the second sieve bed fills with nitrogen, the first sieve bed releases nitrogen back into the atmosphere in preparation for more ambient air flow. Oxygen-rich air passes through to the product tanks while nitrogen is filtered out by each sieve bed. Lastly, the pressure regulator, flow meter, and flow adjusting valve ensure oxygen is supplied to the patient at ideal flow conditions.

Moving on, POCs can be made much smaller and lighter than other sources because they incorporate pulsed flow delivery. Pulsed flow delivery technology conserves oxygen by producing an oxygen bolus, or ‘pulse’, only when patient inhalation is detected. In contrast, significant amounts of oxygen are lost during exhalation for continuous flow oxygen delivery.

Unfortunately, POCs may not reliably detect patient inhalation during periods of quiet breathing, such as sleep. To detect inhalation, POCs monitor cannula supply tubing pressure. As the patient begins to inhale, entrainment of room air creates a small drop in pressure across the cannula supply tubing. When the pressure drop exceeds the triggering threshold of the POC, a pulse of oxygen is released. Significant intra- and inter-subject variability in triggering efficiency has been reported when using commercially available nasal cannulas, particularly during periods of breathing characterized by low inhalation flow rates [14].

1.4 Purpose of Research

In attempt to improve the triggering efficiency of POCs, a new nasal interface concept was developed. Using prototypes and an established *in vitro* model of medical gas administration incorporating realistic upper airway replicas and a lung simulator [14, 15, 16, 17], multiple hypotheses were evaluated. It was hypothesized that, at fixed inhalation flow rates, the new nasal interface would create higher pressure drops across the cannula supply tubing when compared to standard or flared nasal cannulas. Next, it was hypothesized that triggering efficiency would improve when using the new nasal interface with a commercial POC instead of a standard or flared nasal cannula. Lastly, it was hypothesized that greater *in vitro* fraction of inspired oxygen (FiO_2) will be achieved when using the new nasal interface, due to improved triggering efficiency.

The goal of this research is to develop a device that eliminates POC triggering issues. If successful, the oxygen capabilities of POCs will increase, and the need for stationary oxygen sources may be eliminated in many cases. The reported patient preference is a single source of

portable oxygen that can be used in all breathing scenarios [12]. By eliminating triggering issues, the new nasal interface being tested will help meet patient preference.

1.5 Thesis Structure

Four chapters are included in this thesis. The current chapter describes the need for such research and technology development. In Chapter 2, previous literature used to design the testing methods shown in Chapter 3 is described. Also, preliminary pressure drop measurements across the cannula supply tubing were conducted using an earlier stage prototype. The preliminary pressure drops are shown in Chapter 2, and were used to design the prototype described in Chapter 3. Chapter 3 focuses on the design and performance testing of the latest nasal interface prototype. To test the performance of the latest nasal interface prototype, more pressure drop measurements across cannula supply tubing were collected, and breathing simulations were conducted to evaluate POC triggering efficiency and *in vitro* tracheal oxygen levels. The technology development process followed is shown in Figure 1-4.

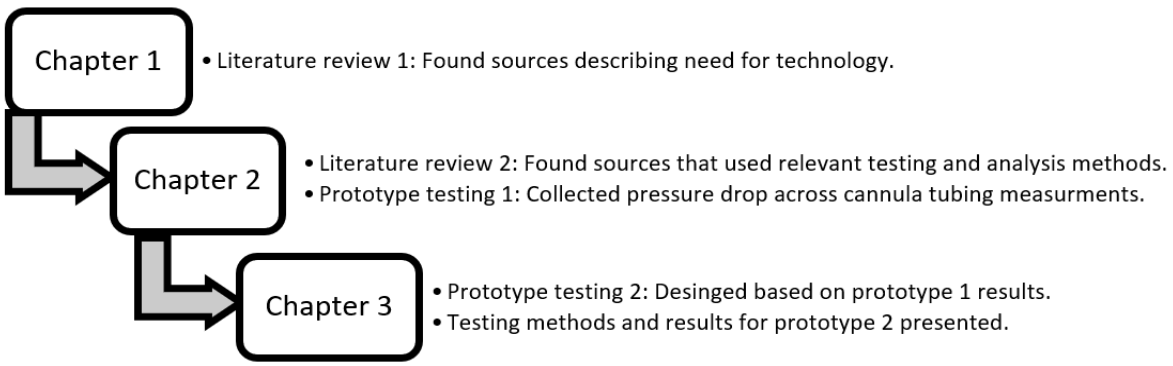

Figure 1-4: Flow chart of technology development process followed and the corresponding thesis chapters.

Lastly, an overall conclusion is provided in Chapter 4.

Chapter 2: Study Design Bases

An established *in vitro* model of medical gas administration was used to test the new nasal interface concept. The upper airway models and data processing logic used for this *in vitro* model are discussed in this chapter. The portable oxygen concentrator (POC) chosen for this study is described as well. Lastly, the first prototype made to test the new nasal interface concept is shown. Data collected using this first prototype was used to create the second edition prototype shown in Chapter 3.

2.1 Realistic Airway Models

For previous studies, fifteen adult nose-throat replicas were built out of acrylic plastic using rapid prototyping. Ten models were based on computed tomography (CT) images, as previously reported [14]. The other 5 models were based on magnetic resonance (MR) images, as previously reported [18]. Each replica includes airway geometries starting from the nares and ending at the trachea entrance. The internal geometries used to create each replica are shown in Figure 2-1.

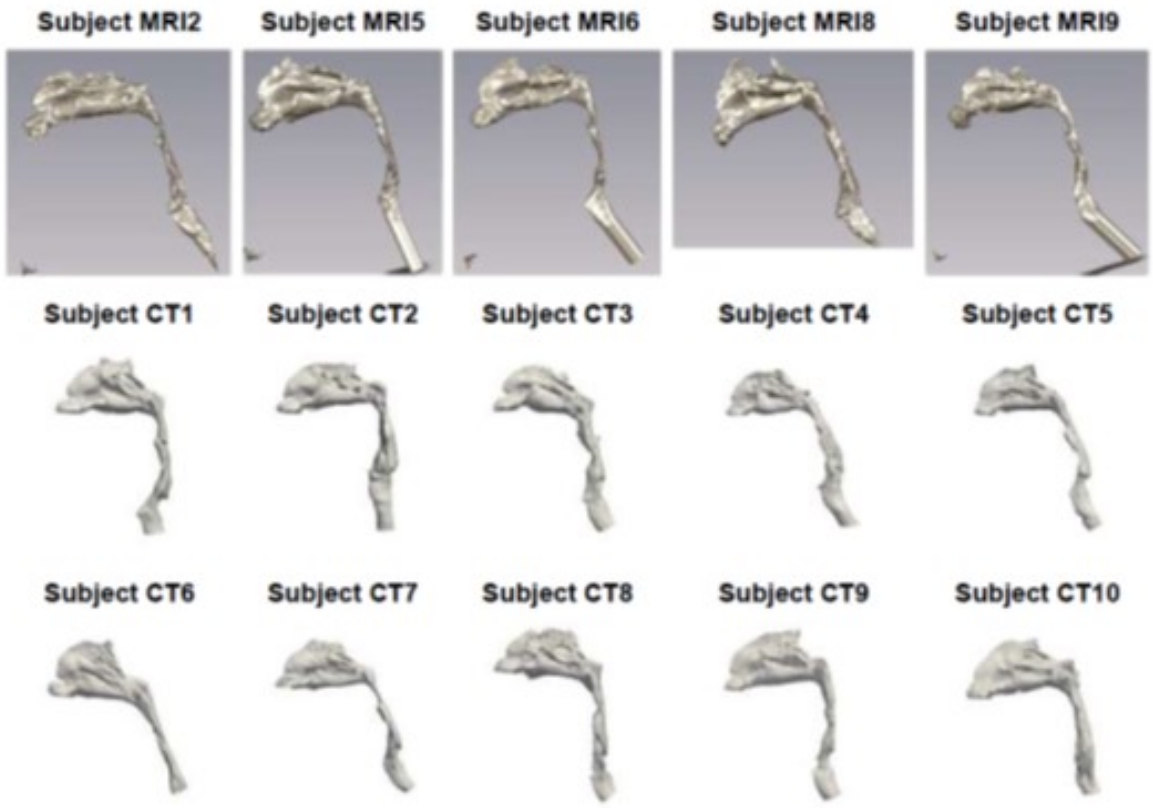

Figure 2-1: Images of internal nose-throat geometries used to create the acrylic airway replicas. Reproduced from Chen et. al, 2017 [14].

As described in Chen et. al, 2017, standard adult nasal cannulas were inserted into the nares of each airway replica. Constant inhalation flow rates were induced through each replica using a vacuum pump. Using a manometer (HHP-103; OMEGA Engineering, Norwalk, CT, USA) and flow meter (TSI Mass Flowmeter 4043; TSI Inc, Shoreview, MN, USA), the pressure drop across the cannula supply tubing was measured at different flow rates, as shown in Figure 2-2.

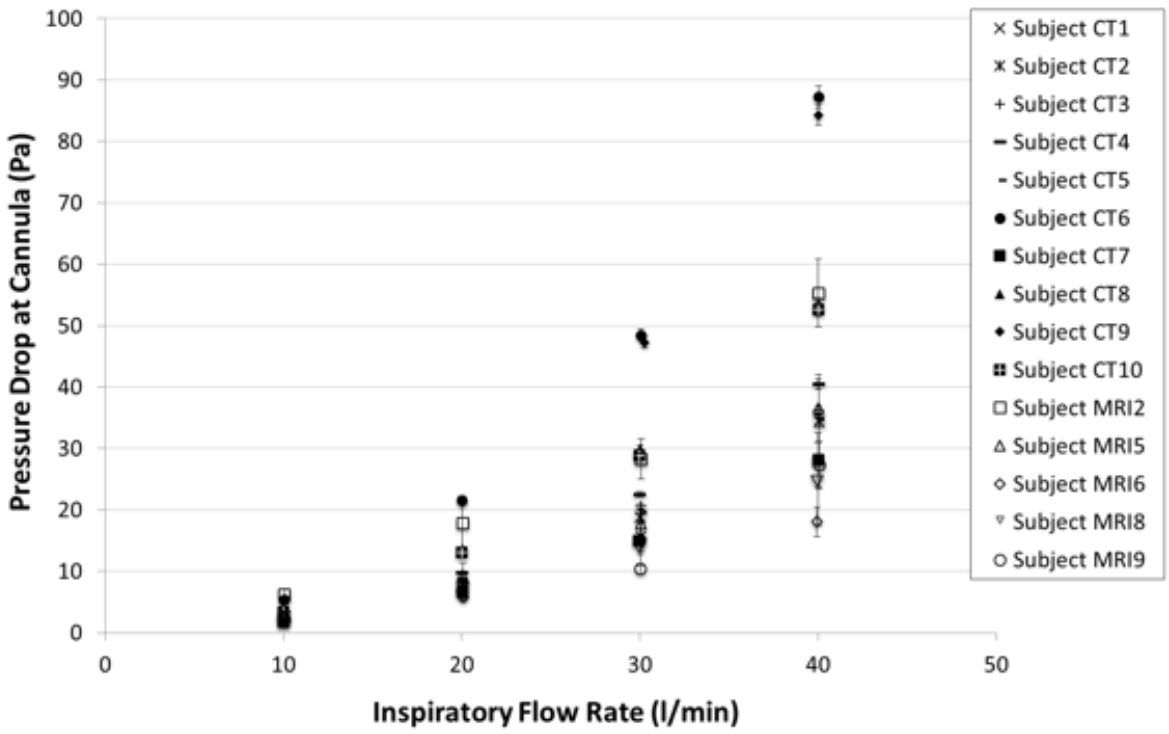

Figure 2-2: Pressure drop across cannula supply tubing at different inspiratory flow rates for 15 nose-throat replicas. Reproduced from Chen et. al, 2017 [14].

During the new nasal interface prototype testing described in Chapter 3, three MRI-based replicas were chosen from this set of fifteen. Only MRI-based replicas were chosen because they include the facial features needed to properly fit the new nasal interface prototypes (lips, cheeks, nose etc.). Figure 2-3 contrasts the two replica types.

Figure 2-3: Example MRI-based replica (left) and CT-based replica (right).

MRI replica 2 was chosen because it showed a relatively high pressure drop across the cannula supply tubing. MRI replicas 6 and 9 were chosen because they showed relatively low pressure drops across the cannula supply tubing. A data set collected using these three replicas covers the wide inter-subject variability shown in Figure 2-2.

2.2 Breathing Simulation Data Processing

During the tests described in Chapter 3, simulated breathing patterns were induced through each chosen airway replica using a lung simulator (ASL 5000 Breathing Simulator; IngMar Medical, Pittsburgh, PA, USA). A plastic tube with an internal diameter of 22 mm and an internal volume of 135 cm^3 was used to connect the lung simulator to each airway replica. These tubing dimensions were chosen because the conducting airway volume from the trachea to the gas-exchange region of the lungs for an average adult with a 3 L function residual capacity is 135 cm^3 [19].

The volume of the test lung chamber (V_i) was recorded at a sampling frequency of 512 Hz using the ASL 5000 software for each breathing simulation. The flow rate at each time point ($\dot{V}_i$) was calculated by using the collected volume data points in the following equation:

$$\dot{V}_i = \frac{(V_{i+1} - V_i)}{\Delta t} \qquad (2.1)$$

Here Δt is the inverse of the lung simulator sampling frequency.

A GA-200 CO2 and O2 Gas Analyzer (iWorx, Dover, NH, USA) was used to measure oxygen concentrations during each simulation at a sampling frequency of 35 Hz. There is an innate measurement delay when using side-stream gas sampling because the gas needs to travel from the sampling site to the gas analyzer through connective tubing. Also, an electronics delay is present. Oxygen concentration measurements were corrected for delay and time constant by approximating the concentration as a first order system and following methods outlined in Langer et al [20]. In this case, the time constant is defined as the time required for the response to reach 63% of its final value as the result of a step increase. The time constant was measured to be 0.227 seconds in previous experiments where the supply to the gas analyzer was rapidly switched using a three-way stopcock between two different gas mixtures of known concentration. The two gas mixtures in this case were air and 100% oxygen [14].

After aligning the flow rate and oxygen concentration measurements, the fraction of inspired oxygen ($\mathrm{FiO_2}$) for individual simulated breaths were calculated. First, the flow rate of oxygen passing through the trachea at a given time ($\dot{V}_{O_{2_x}}$) can be calculated by multiplying inspiration

flow rate with the measured oxygen concentration at the same time point ($\dot{V}_{i_x}$ and $[O_2]_x$), as shown below.

$$\dot{V}_{O_{2_x}} = \dot{V}_{i_x} * [O_2]_x \qquad (2.2)$$

Equation 2.2 was used to calculate the flow rate of oxygen passing through the trachea at every time point corresponding to positive flow rates of a given breath. Inspiratory flow rates are considered positive and expiratory flow rates are considered negative in this case. The start and end times of inspiration were identified as times when flow rates crossed 0.

The flow rates of oxygen during inhalation were then integrated using the trapezoidal rule to calculate the volume of inspired oxygen per breath (V_{O_2}), as shown below.

$$V_{O_2} = \int_{t_i}^{t_n} \dot{V}_{O_2} * dt \cong \sum_{i=1}^{n} \frac{\dot{V}_{O_{2_i}} + \dot{V}_{O_{2_{i+1}}}}{2} * \Delta t_{o_2} \qquad (2.3)$$

Where $t_{i=1}$indicates the time at which inhalation begins, t_n indicates the end of inhalation, and Δt_{o_2} is the inverse of the gas analyzer sampling frequency (35 Hz).

Tidal volume (V_T) was calculated from inspiration flow rates using a similar procedure.

$$V_T = \int_{t_i}^{t_n} \dot{V}_i * dt \cong \sum_{i=1}^{n} \frac{\dot{V}_i + \dot{V}_{i+1}}{2} * \Delta t_{o_2} \qquad (2.4)$$

The volume of inhaled oxygen was then divided by the tidal volume to obtain the fraction of inspired oxygen for an individual breath.

$$\mathrm{FiO_2} = \frac{V_{O_2}}{V_T} \qquad (2.5)$$

The process of aligning the measured flow rate and oxygen concentration data, and using Equations 2.1 - 2.5 to calculate $\mathrm{FiO_2}$ values, was automated via Excel's Visual Basic for Applications (VBA). Using the created VBA code, $\mathrm{FiO_2}$ values for multiple breaths could be calculated simultaneously for a given breathing simulation. The VBA code is described in Appendix A.

2.3 Portable Oxygen Concentrator used in Study

A SimplyGo Mini portable oxygen concentrator (POC) from Phillips Respironics was used in this study. In the SimplyGo Mini User Manual, the inspiratory trigger sensitivity is listed as less than 19.6 Pa (0.2 cm $\mathrm{H_20}$) [21]. To reliably trigger an oxygen pulse from the SimplyGo Mini a pressure drop greater than 19.6 Pa should be present across the cannula supply tubing that connects the POC to the patient's nostrils. If a high enough pressure drop is not present, the SimplyGo Mini defaults to a timed-pulsed back-up mode, where evenly spaced pulses of oxygen are sent 12 times per minute [21].

The SimplyGo mini has 5 operation settings. By changing the POC's operation setting, the volume of oxygen pulse sent during each breath changes. As shown in

Table 2-1, the oxygen pulse volume is also dependent on the breath rate (breaths/minute) detected from the user.

Table 2-1: Oxygen pulse volumes sent from SimplyGo Mini at different device settings and breath rates [21].

	Setting 1	Setting 2	Setting 3	Setting 4	Setting 5
Breath Rate	Pulse Volume (mL)				

15	11.0	22.0	33.0	44.0	55.0
20	11.0	22.0	33.0	44.0	55.0
25	8.8	17.6	26.4	35.2	40.0
30	7.3	14.7	22.0	29.3	33.3
35	6.3	12.6	18.9	25.1	28.6
40	5.5	11.0	16.5	22.0	25.0

2.4 Prototype Design Concept

Conventional nasal cannula prongs fit loosely into patients' nostrils. As a result, the gas inhaled by LTOT patients is a mixture of room air and oxygen-rich air (Figure 2-4).

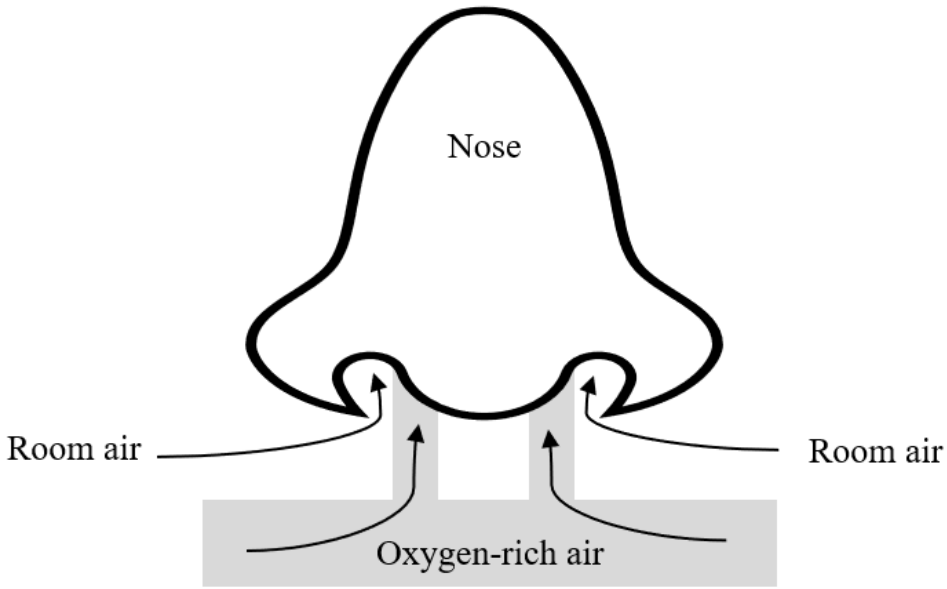

Figure 2-4: Inhaled gas mixture from room air and nasal cannula prongs during oxygen therapy with a conventional nasal cannula.

The 15 airway geometries shown in Figure 2-1 each have unique nostril cross-sectional areas. As the ratio between nostril cross-sectional area and cannula prong cross-sectional area changes, it is

expected that the room air to oxygen-rich air entrainment ratio, and the pressure drop across the cannula tubing, will also change. Figure 2-5 shows that higher nostril to cannula prong cross-sectional area ratios correspond to lower pressure drops across the cannula supply tubing, making successful POC triggering less likely. The pressure drops shown in Figure 2-5 are from Figure 2-2. MeshLab (Visual Computing Laboratory, Istituto di Scienza e Tecnologie dell'Informazione, Italy) and ParaView (Kitware, NY, USA) software was used to find the nostril cross-sectional area for each airway geometry. The large inter-subject variability shown in Figure 2-2 is partially caused by different nostril sizes.

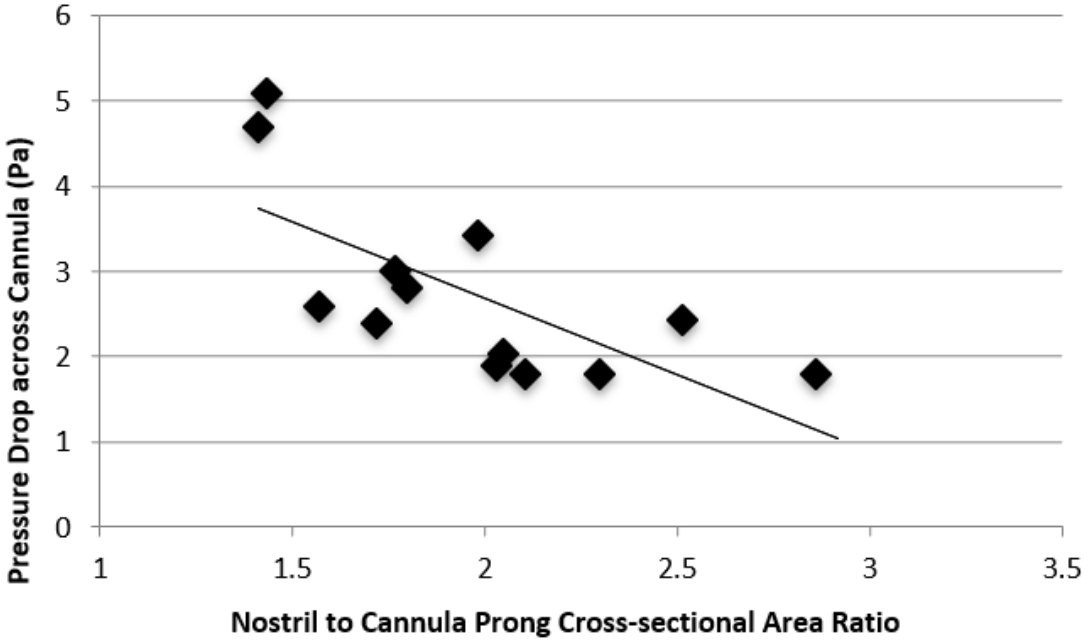

Figure 2-5: Average pressure drop across the cannula supply tubing at 10 L/min vs. the nostril to cannula prong area ratio for each airway replica. Each marker represents a different airway replica. The cannula prong cross-sectional area is 0.62 cm². The nostril cross-sectional area for each airway geometry was found using MeshLab (Visual Computing Laboratory, Istituto di Scienza e Tecnologie dell'Informazione, Italy) and ParaView (Kitware, NY, USA) software.

In contrast, the first prototype created to test the new nasal interface (Figure 2-6) provides a near-complete seal around the replica's nostrils to ensure all the inhaled and exhaled air is directed

through the air entrainment body. The bottom face of the air entrainment body has a sliding mechanism used to change the open area of each slot. The pressure drop across the cannula supply tubing can be controlled by adjusting the open area of the slots.

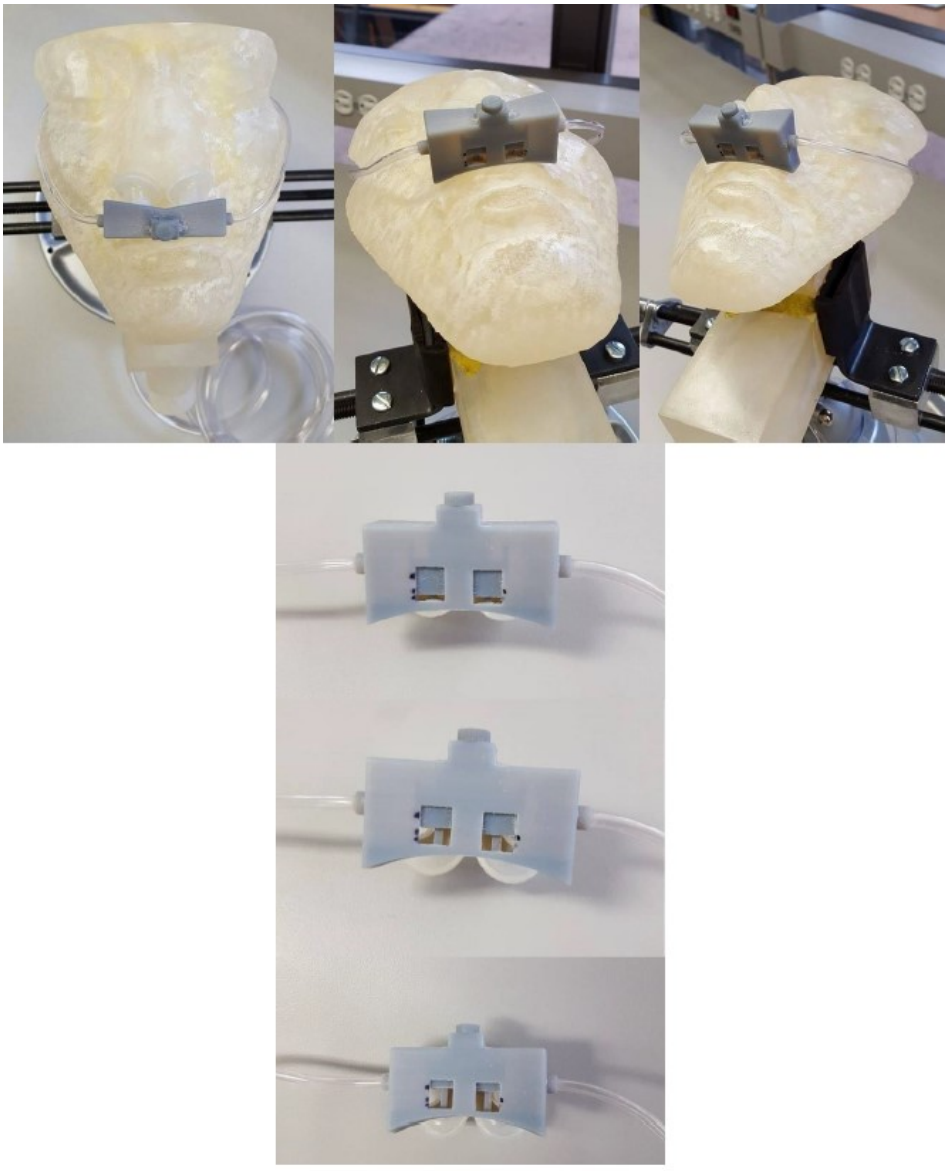

Figure 2-6: First new nasal interface prototype.

The pressure drop across the cannula supply tubing was measured at various flow rates and open slot areas, for multiple MRI-based replicas. An example plot of the collected pressure drop data is shown in Figure 2-7.

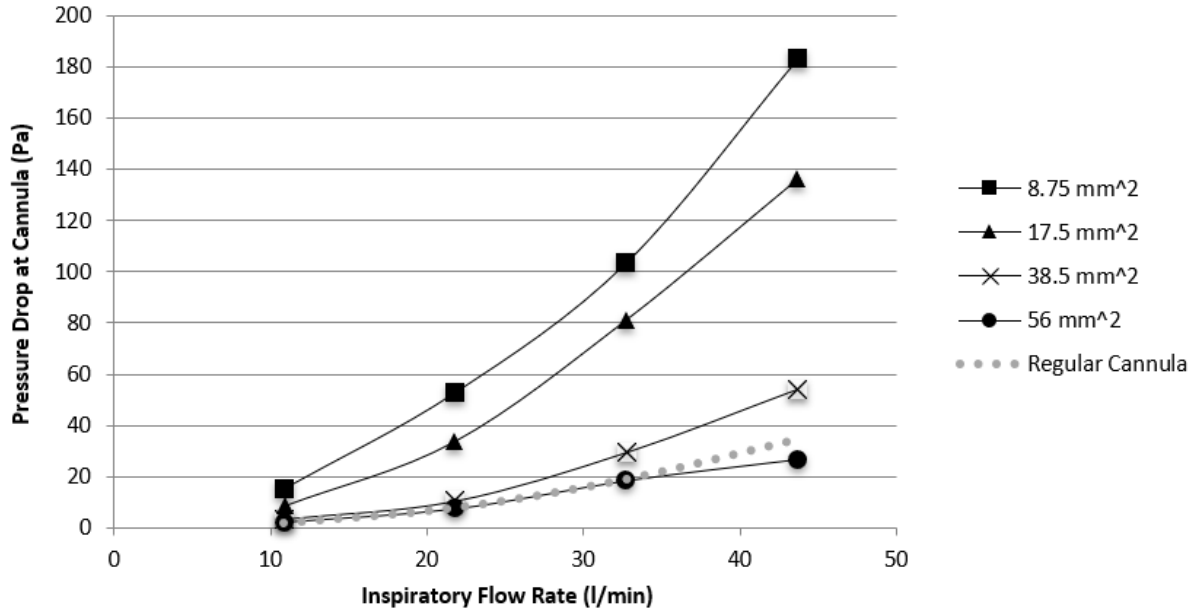

Figure 2-7: Pressure drop across the cannula supply tubing measured while using the first new nasal interface prototype at various flow rates and open slot areas.

The data shown in Figure 2-7 was used to design the second edition prototype shown in Chapter 3. For example, to ensure the pressure drop across the cannula tubing is greater than the SimplyGO Mini inspiratory trigger sensitivity (19.6 Pa) at a flow rate of 30 L/min, the second edition prototype could have a setting with an open slot area of about 38.5 mm².

Chapter 3: Nasal Interface with Air Entrainment Ports Improves Delivery from a Portable Oxygen Concentrator

This chapter has been prepared as a manuscript to be submitted to a scientific journal.

3.1 Introduction

Long-term oxygen therapy (LTOT) is widespread in treatment of chronic respiratory diseases. For patients with hypoxemic chronic obstructive pulmonary disease (COPD), LTOT administered for 15 hours/day or more has been demonstrated to improve survival time [1, 2]. However, the choice of delivery device for administering LTOT is driven by cost as much as by performance or clinical evidence [11]. Technologies used to administer LTOT in the home and in daily life are evolving, with small, portable compressed gas cylinders and liquid dewers increasingly being replaced by portable oxygen concentrators (POCs). POCs range in size and weight; larger devices are typically transported in wheeled carts, whereas smaller (≤ 5 lb) devices may be carried in over-the-shoulder bags. Some POCs have been marketed as single-source, 24-hours-a-day solutions to address patients' oxygen needs both at home and during activity, which meets reported patient preference [12]. However, an elevated frequency of nighttime hypoxemic events has been reported during use of POCs, compared with larger, stationary, continuous flow oxygen sources [12]. Broadly, a majority of LTOT patients report problems with their oxygen delivery systems, most frequently equipment malfunction and lack of physically manageable portable systems [7].

While POCs offer potential efficiencies for oxygen delivery, their performance is variable [15, 22, 23]. POCs rely on pressure swing adsorption (PSA) technology, where an oxygen-rich gas stream (~90-95% vol O_2) is produced by passing compressed air through zeolite beds used to trap nitrogen. As POCs become smaller, the sizes and capacities of compressors, sieve beds, and

batteries used in the PSA process are reduced. Accordingly, less oxygen can be produced in a given time interval. To compensate, POCs incorporate pulsed flow delivery to conserve oxygen. During pulsed flow delivery, an oxygen bolus, or 'pulse', is delivered through nasal cannula only when patient inhalation is detected. This limits loss of oxygen to the surrounding atmosphere during exhalation. POCs commonly rely on pressure triggering to detect inhalation: as the patient begins to inhale, entrainment of room air creates a small drop in pressure monitored through the cannula supply tubing, referred to herein as the signal pressure. When the signal pressure exceeds the triggering threshold of the POC device, a pulse of oxygen is released. The signal pressure is a function of inhalation flow rate, but is also highly sensitive to the variable fit of conventional nasal prongs within the nostrils of individual patients. This leads to considerable intra- and inter-subject variability in triggering efficiency [14]. In particular, patients may not be able to trigger oxygen delivery during sleep or other periods of quiet breathing characterized by low inhalation flow rates.

In the present work, we report on the design and testing of a new nasal interface intended to improve triggering of pulsed oxygen delivery from POCs. Two hypotheses were evaluated using an established *in vitro* model of medical gas administration incorporating realistic upper airway replicas and a lung simulator [14, 15, 16, 17]. First, it was hypothesized that the new nasal interface would produce higher signal pressures than standard or flared nasal cannulas at fixed inhalation flow rates. Second, when using the new nasal interface with a commercial POC, it was hypothesized that triggering efficiency would improve compared with that observed for standard or flared nasal cannulas, resulting in greater *in vitro* fraction of inspired oxygen (FiO_2) for the new nasal interface.

3.2 Methods

3.2.1 Airway Replicas

Three acrylic plastic adult airway replicas, containing airways starting from the nares through the entrance of the trachea, were used in the present study. Replica geometries were based on magnetic resonance (MR) images previously reported [18]. Geometric parameters for each of the 3 replicas were obtained using MeshLab (Visual Computing Laboratory, Istituto di Scienza e Tecnologie dell'Informazione, Italy) and ParaView (Kitware, NY, USA); these geometric parameters are listed in Table 3-1.

Table 3-1: Airway replica geometric parameters

Subject	Sex	Volume (cm^3)	Wall Surface area (cm^2)	Nostril 1 Inlet Area (cm^2)	Nostril 2 Inlet Area (cm^2)
2	F	44.6	287	0.96	0.79
6	M	50.1	313	1.06	0.89
9	M	45.3	250	1.52	1.33

The three airway replicas were selected based on their propensity to trigger or not trigger pulsed oxygen delivery from a POC, as reported in previous work by Chen *et al.* [14]. The Subject 2 replica was selected as a control, given relatively high signal pressures measured previously, whereas Subject 6 and 9 replicas were selected to evaluate improvement in pulse triggering for the new nasal interface concept, given relatively low signal pressures measured previously in each of these replicas [14].

3.2.2 Patient Interfaces

The prototype shown in Figure 3-1 was created to test the new nasal interface concept. The new nasal interface uses nasal pillows (Mirage Liberty Nasal Pillows, Small, 61333; ResMed Ltd., AUS) to tightly fit the inner walls of the nares. In addition, the new nasal interface includes four

air entrainment ports on its bottom face. The number holes left open was used in the present work to create multiple 'settings':

- Setting 1: 1 large hole open (providing 24 mm^2 open area for air entrainment)
- Setting 2: 2 large holes open (48 mm^2 open area)
- Setting 3: 3 large holes open (71mm^2 open area)
- Setting 4: all 4 holes open (84 mm^2 open area)

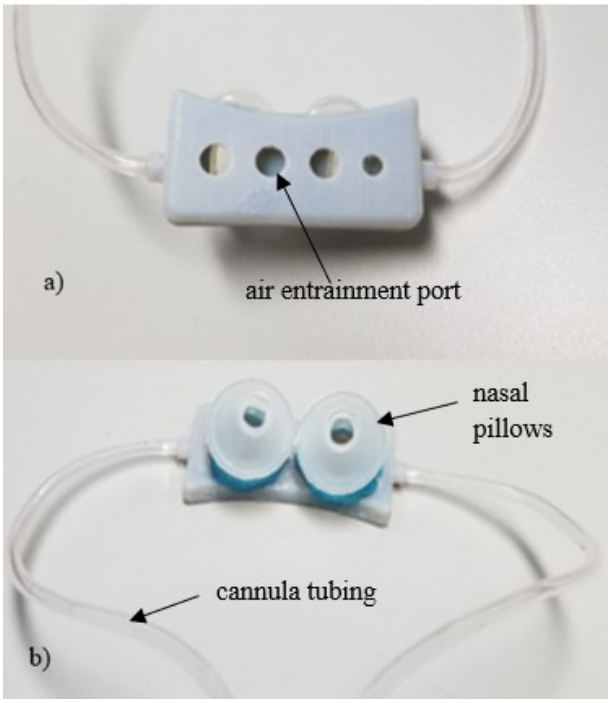

Figure 3-1: Nasal interface apparatus with air entrainment port of adjustable open area. (a) bottom view (b) top view.

A standard (Hudson RCI RUS1103; Teleflex Medical, NC, USA) and a flared nasal cannula (Hudson RCI RUS1104; Teleflex Medical, NC, USA) was used in this study for comparison with the new nasal interface.

3.2.3 Signal Pressure Tests

Signal pressures were measured in a standard nasal cannula, a flared nasal cannula, and for each new nasal interface setting at constant inhalation flow rates of 10, 15, 20, 30 and 40 L/min drawn by vacuum through the airway replicas. Flow rates were measured using a mass flow meter (TSI 4040; E & E Process Instrumentation, ON, CAN). Flow rates are reported as L/min at a standard temperature and pressure of 21.1 C and 101.3 kPa. The cannula or interface was inserted into the nares of each airway replica and a manometer (Digitron 2020P-LIQ; ITM Instruments Inc., QC, CAN) was used to measure signal pressures (Figure 3-2).

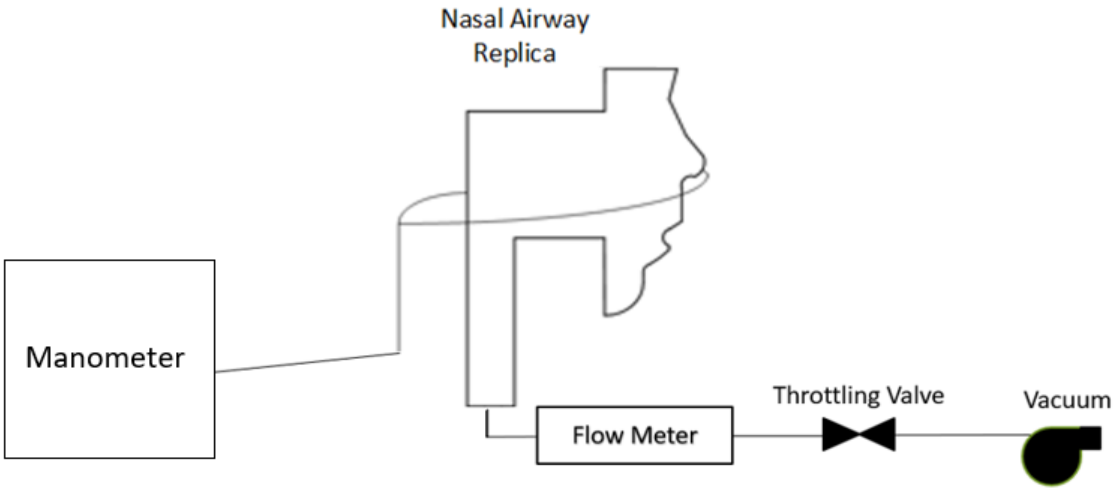

Figure 3-2: Schematic of signal pressure measurement apparatus

3.2.4 Simulated Breathing Tests

Using a set-up similar to that used by Chen *et al.* [14], oxygen concentration and flow rates were measured across a series of simulated breathing tests (Figure 3-3). The resistance imposed by the nasal cannula or interface was also measured during each trial.

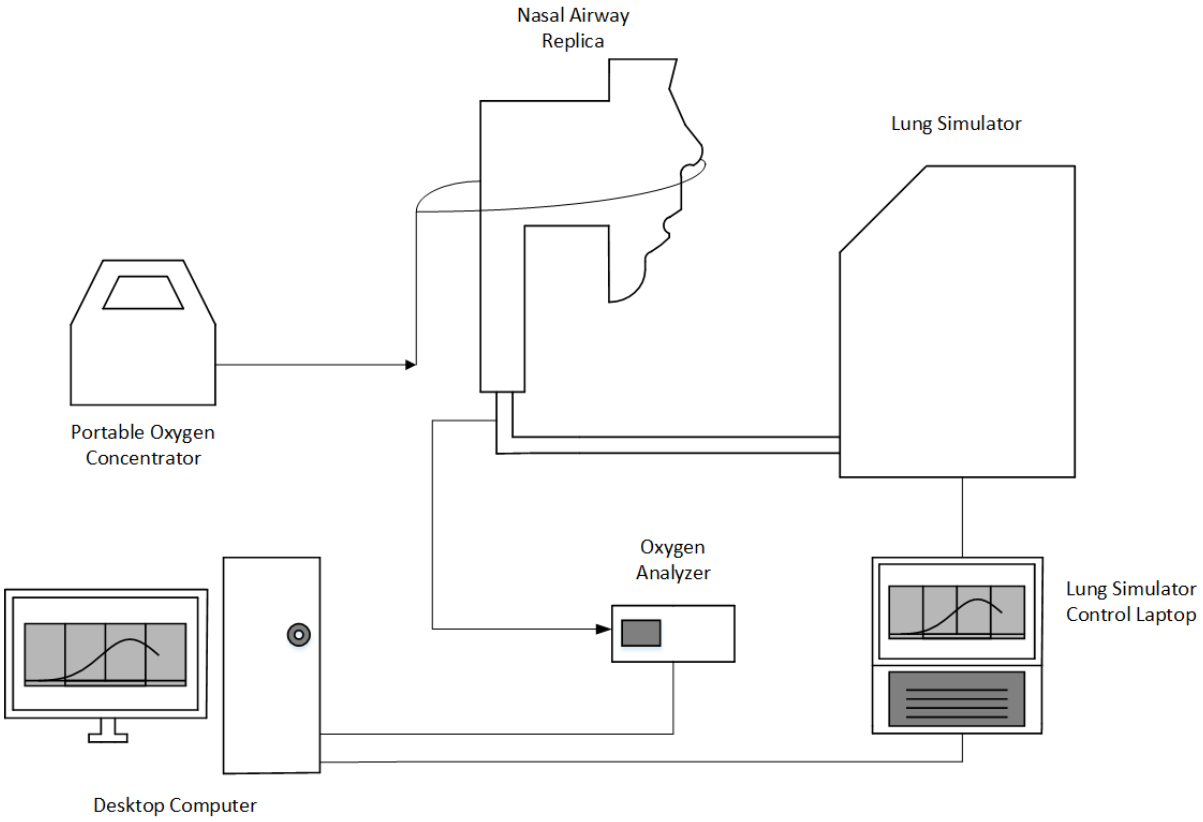

Figure 3-3: Schematic of simulated breathing test apparatus. Reproduced from Chen *et al.* [14].

A lung simulator (ASL 5000 Breathing Simulator; IngMar Medical, PA, USA) was used to induce breathing patterns through the nasal replicas, representative of a COPD patient during sleep (inspiratory time = 1.79 seconds, expiratory time = 2.93, breathing frequency = 13 breaths/min, tidal volume = 520 mL) [14]. This breathing pattern assumed 100% nasal flow; with a peak inspiratory flow rate of 27 L/min. Additionally, a breathing pattern was tested with the same inspiratory time, expiratory time, and breathing frequency, but with substantially reduced nasal ventilation [24]. For these tests only 45% of the sleeping COPD patient tidal volume (234 mL) was used, consistent with the lowest nasal proportion reported in oronasal breath partitioning data [25]. This additional breathing pattern is representative of cases where COPD patients breathe partially through their mouth during sleep. The peak nasal inspiratory flow rate for this pattern was 12.5 L/min.

The volume of the lung simulator chamber and the pressure at the entrance of the lung simulator were recorded a sampling rate of 512 Hz using the ASL 5000 operating software. Oxygen concentrations were recorded using a gas analyzer (GA-200; iWorx, NH, USA), and were corrected for sampling delay and time constant as described previously [14].

A SimplyGo Mini (Philips Respironics, PA, USA) POC was used in this study. The SimplyGo Mini includes multiple nominal pulse delivery settings, each transmitting a different oxygen pulse volume. POC settings 2 and 4 were tested, which are reported by the manufacturer to deliver pulse oxygen volumes of 22 mL and 44 mL, respectively [21].

Experiments were conducted in triplicate for each combination of airway replica, nasal cannula or interface, breathing pattern, and POC setting. To ensure the oxygen concentration profile reached steady-state, each trial lasted approximately 3 minutes (~40 breaths).

3.2.5 Data Analysis

Signal pressure measurements were repeated in triplicate for each replica and nasal cannula/interface combination at 10, 15, 20, 30 and 40 L/min. The average signal pressure and standard deviation across each set of repeated measurements was calculated.

After each breathing simulation, a code created in Excel's Visual Basic for Applications (VBA) was used to manipulate the raw data for chamber volume and oxygen concentration. The VBA code imports and sorts the appropriate raw data, creates oxygen concentration and flow rate profiles, and calculates FiO_2 values for a selected series of breaths. The VBA code was programmed to follow the same procedure as Chen *et al* when creating oxygen concentration and flow rate waveforms, and when calculating FiO_2 values for each simulated breath [14]. First, the

flow rate of oxygen passing the trachea was determined by multiplying inhalation flow rate by oxygen concentration on each time point. Next, the oxygen flow rate was numerically integrated between start and end of inhalation using the trapezoidal rule to calculate the volume of oxygen inhaled. The volume of inhaled oxygen was then divided by the tidal volume to calculate FiO_2. For more information on the VBA code used to perform these calculations, see Appendix A.

FiO_2 values for either 15 or 18 breaths were included in the average FiO_2 calculation for each POC setting, breathing pattern, airway replica, and nasal cannula/interface combination. In scenarios where the POC successfully triggered on all breaths for all three repeated trials, 5 breaths from each trial were used in calculating the average FiO_2, for a total of 15 breaths per scenario. Conversely, when the POC did not trigger, it defaulted to a timed pulse setting. The SimplyGo Mini timed pulse setting operates with a 12 breath/min frequency [21], whereas the simulated breathing frequency was 13 breaths/min for all tests. As a result, the timed pulses cycled between being completely in-phase with inhalation and being completely in-phase with exhalation; to capture this entire cycle in the average FiO_2 calculation, 18 breaths were required.

After splitting the data in groups based on subject number, a one-way ANOVA for each POC setting/breathing pattern combination was executed with FiO_2 and nasal cannula/interface setting being the dependent and independent variables, respectively. Tukey-Kramer tests further evaluating FiO_2 differences were conducted after each one-way ANOVA. A significance level of 5% was used in all cases. More details on the statistical analyzes are provided in Appendix B.

The pressure drop (below ambient) measured at peak inspiratory flow was used to evaluate imposed inspiratory resistance for each nasal cannula/interface setting. To calculate the imposed inspiratory resistance, a baseline pressure drop for each airway replica, with no cannula nor

interface in place, was measured at peak inspiratory flow rate in triplicate. After averaging the three measurements, the appropriate baseline pressure drop was subtracted to calculate the imposed pressure drop at peak inspiratory flow due to the nasal cannula or interface. Then, each imposed pressure drop at peak inspiratory flow was divided by the flow rate to obtain the imposed resistance at peak inspiratory flow, measured in units of [cm H2O*s/L].

3.3 Results

Signal pressure test results are summarized in Figure 3-4. Subjects 6 and 9 recorded lower signal pressures using the standard and flared cannula than when using any new nasal interface setting at any flow rate. However, Subject 2 recorded signal pressures using a flared cannula that were higher than that of interface setting 4 at all flow rates, and higher than that of interface setting 3 at all flow rates except for 40 L/min. At least one new nasal interface setting resulted in higher signal pressures than that of the standard and flared nasal cannulas at all flow rates, for all subjects.

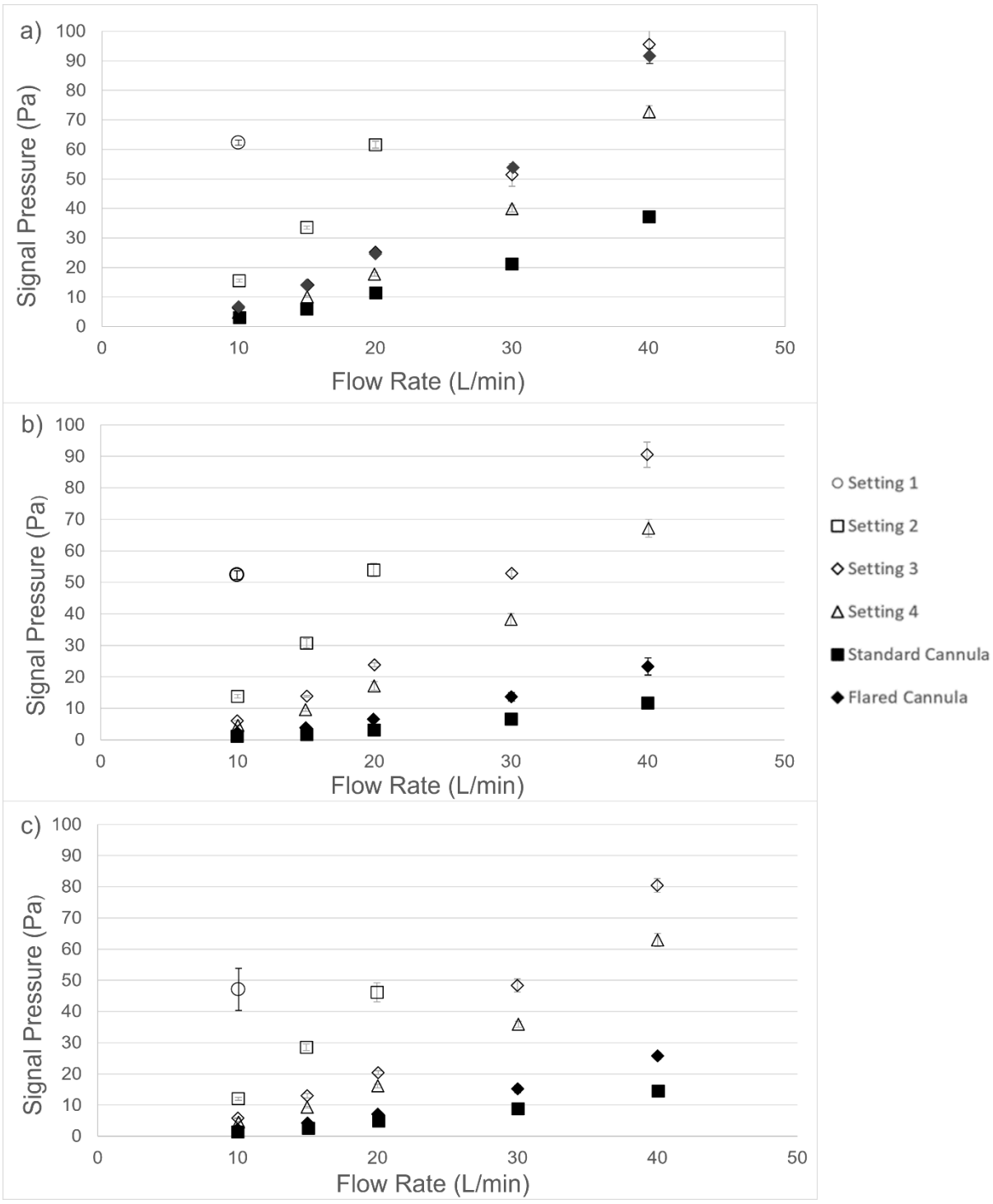

Figure 3-4: Signal pressure data for (a) Subject 2 (b) Subject 6 and (c) Subject 9 using nasal interface settings 1 through 4, a standard cannula, and a flared cannula. Error bars indicate the standard deviation around average values for 3 repeated measurements. Where error bars are not visible, they are smaller than the marker size. For the nasal interface at setting 2, the signal pressure was above 100 Pa for flow rates of 30 L/min and above. For the nasal interface at setting 1, the signal pressure was above 100 Pa for flow rates of 15 L/min and above.

Three main results were recorded during every simulated breathing trial: triggering type, FiO_2, and imposed inspiratory resistance. Example oxygen concentration and flow rate profiles for successful triggering, inconsistent triggering and failed triggering types are shown in Figure 3-5. In Figure 3-6 and Figure 3-7, the average FiO_2 for each scenario is provided.

There were three cases of inconsistent triggering. First, while using the flared cannula Subject 6 successfully triggered the POC during 2 of 3 100% nasal flow POC setting 4 trials. On the third trial however, Subject 6 triggered the POC for only half of the breaths. As a result, the overall triggering success rate for this scenario was approximately 83%, so 15 out of 18 FiO_2 values included in the scenario average FiO_2 calculation were taken from breaths where successful triggering occurred. For the 45% nasal flow POC setting 2 trials, both Subjects 6 and 9 inconsistently triggered during all trials while using nasal interface setting 3. The overall triggering success rate was approximately 50% for Subject 6, and approximately 55% for Subject 9. Overall triggering success rates were reflected in the average FiO_2 calculations for these scenarios as well.

Nasal interface setting 1 was not tested during any trial where 100% nasal flow was assumed. Since interface settings 2, 3 and 4 successfully triggered for all 100% nasal flow trials, imposing higher breathing resistance to increase signal pressure further was not necessary.

While using nasal interface setting 3, all subjects either failed to trigger or inconsistently triggered the POC under the 45% nasal flow pattern. Nasal interface setting 4 was not tested during any 45% nasal flow pattern because doing so would lead to lower signal pressures and failed triggering cases.

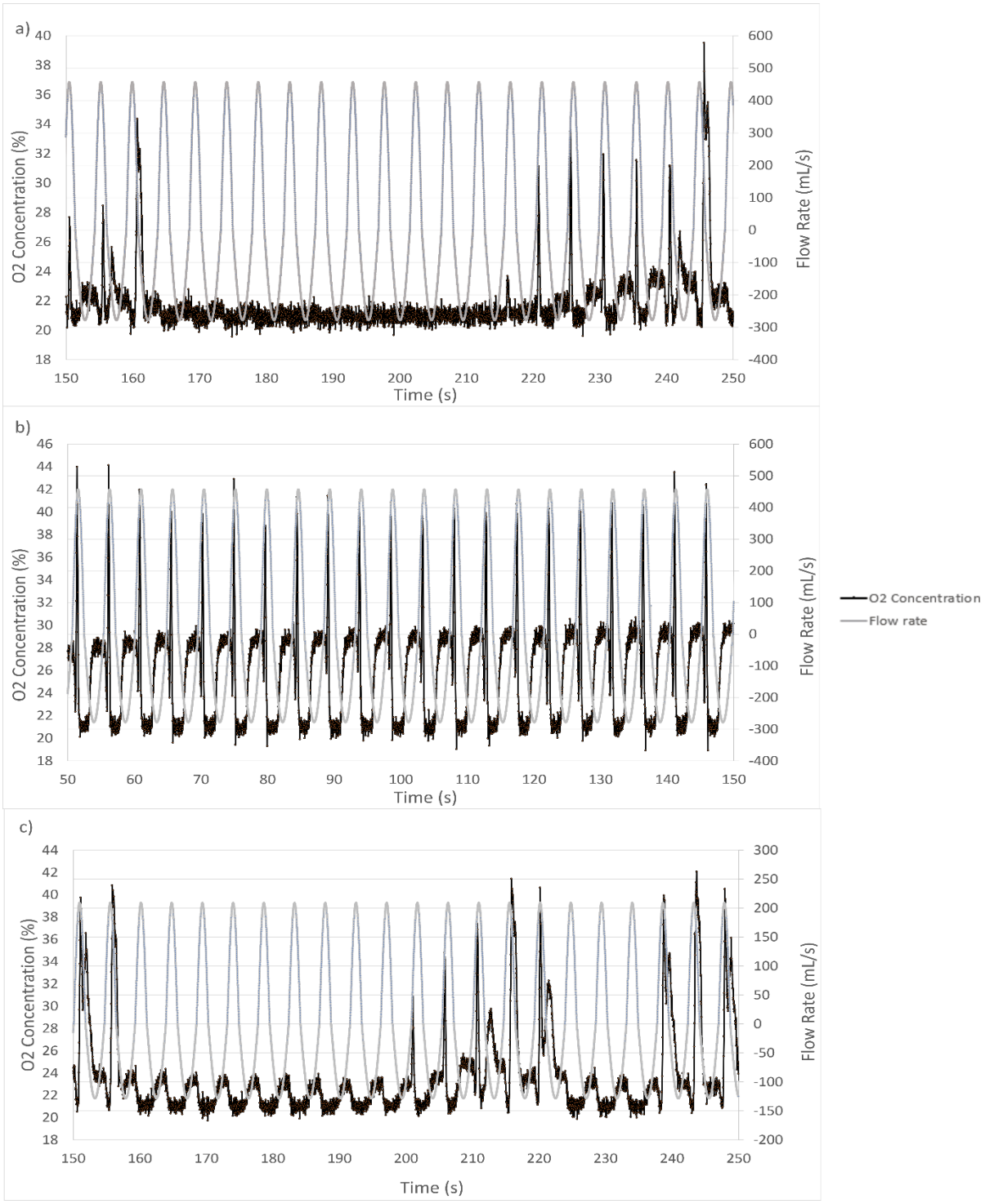

Figure 3-5: Example oxygen concentration profile for a) unsuccessful triggering: subject 9, standard cannula, portable oxygen concentrator setting 2, 100% nasal flow; b) successful triggering: subject 6, nasal interface setting 4, portable oxygen concentrator setting 4, 100% nasal flow; c) inconsistent triggering: subject 6, nasal interface setting 3, portable oxygen concentrator setting 2, 45% nasal flow. Flow rates generated by the lung simulator are also shown, where positive values indicated inspiratory flows and negative values indicate expiratory flows.

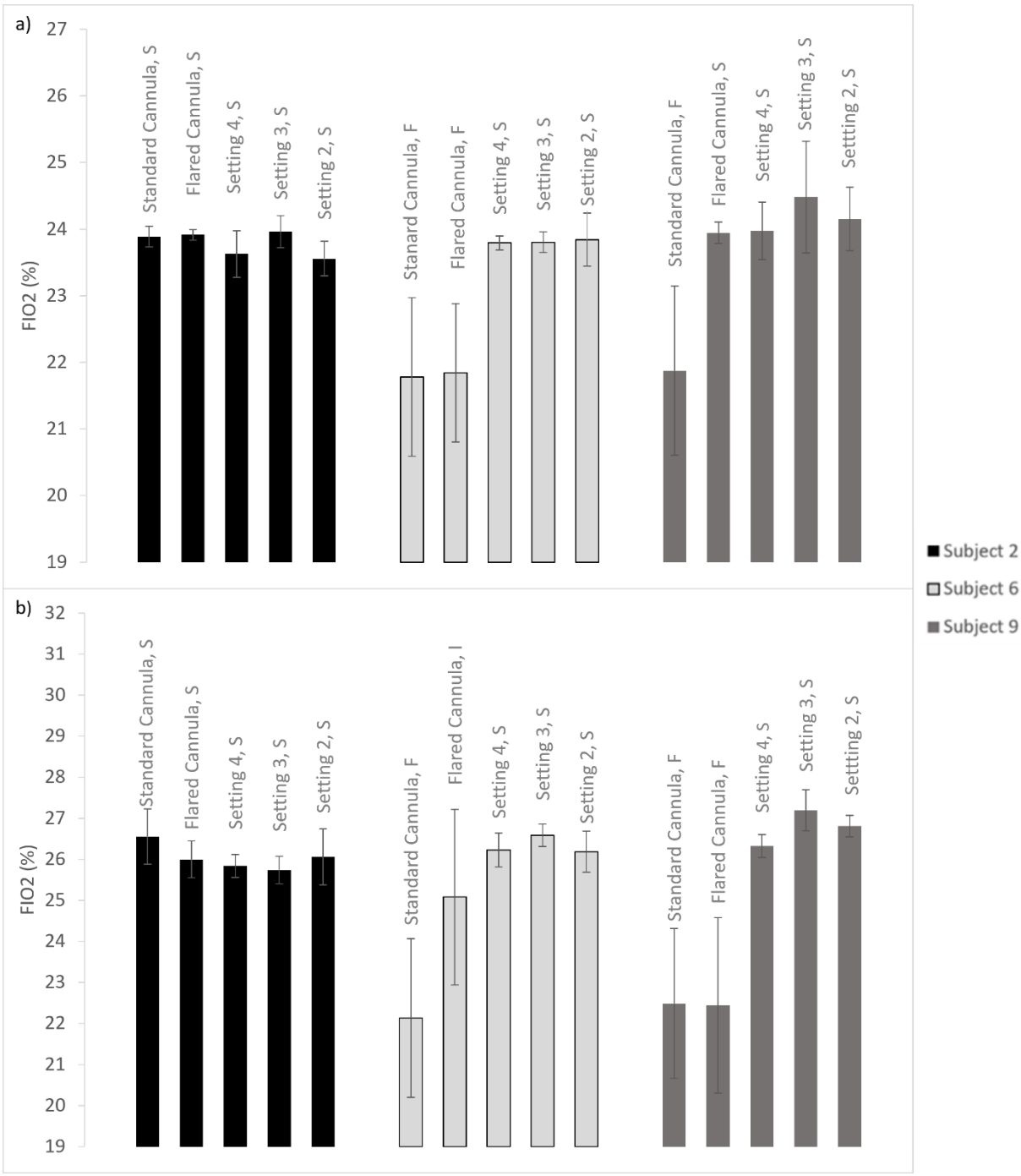

Figure 3-6: Fraction of inspired oxygen using 100% nasal flow, measured for a) portable oxygen concentrator setting 2, and b) portable oxygen concentrator setting 4. Error bars indicate the standard deviation around average values for 15 repeated measurements where triggering was successful, and around 18 repeated measurements where triggering was inconsistent or unsuccessful. Bars labelled with "S" correspond to scenarios where successful triggering occurred in all trials. Bars labelled with "I" correspond to scenarios where inconsistent triggering occurred in at least 1 of 3 trials. Bars labelled with "F" correspond to scenarios where the POC failed to trigger in all trials.

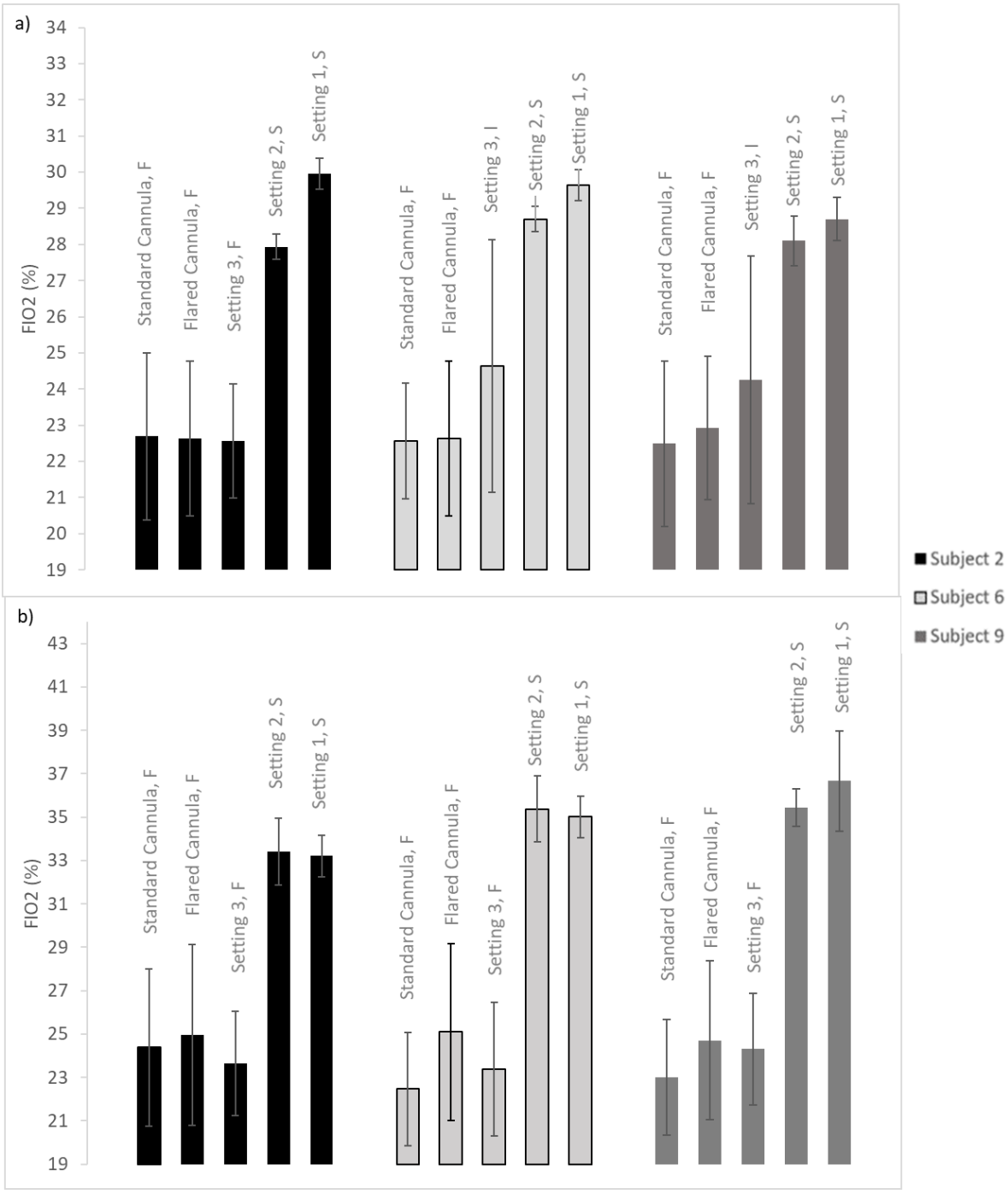

Figure 3-7: Fraction of inspired oxygen using 45% nasal flow, measured for a) portable oxygen concentrator setting 2, and b) portable oxygen concentrator setting 4. Error bars indicate the standard deviation around average values for 15 repeated measurements where triggering was successful, and around 18 repeated measurements where triggering was inconsistent or unsuccessful. Bars labelled with "S" correspond to scenarios where successful triggering occurred in all trials. Bars labelled with "I" correspond to scenarios where inconsistent triggering occurred in at least 1 of 3 trials. Bars labelled with "F" correspond to scenarios where the POC failed to trigger in all trials.

Tukey-Kramer posthoc tests indicated that, for a fixed breathing pattern and POC setting, average FiO2 values from successful triggering cases were significantly higher than failed triggering cases, regardless of subject group or nasal cannula/interface face group. The inconsistent triggering cases with success rates of 50% and 55% lead to mean FiO_2 values significantly lower than all successful triggering cases within the same breathing pattern and POC setting scenario as well. However, during the 100% nasal flow POC setting 4 trials, the successful triggering cases observed while Subject 6 used nasal interface settings 2 and 4 lead to mean FiO_2 values that are not significantly different than the mean FiO_2 value corresponding to the inconsistent triggering case observed while Subject 6 used the flared cannula (with 83% success rate). The inconsistent triggering scenario with an 83% success rate was the only case where an inconsistent or failed triggering scenario was not significantly lower than all successful triggering cases within the same POC setting and breathing pattern group.

The imposed resistances at peak inspiratory flow for each combination of nasal cannula/interface setting, breathing pattern, and airway replica are depicted in Figure 3-8. Error bars in Figure 3-8 represent the propagated error from baseline pressure drop measurements and the pressure drop measurements at peak inspiratory flow for each trial.

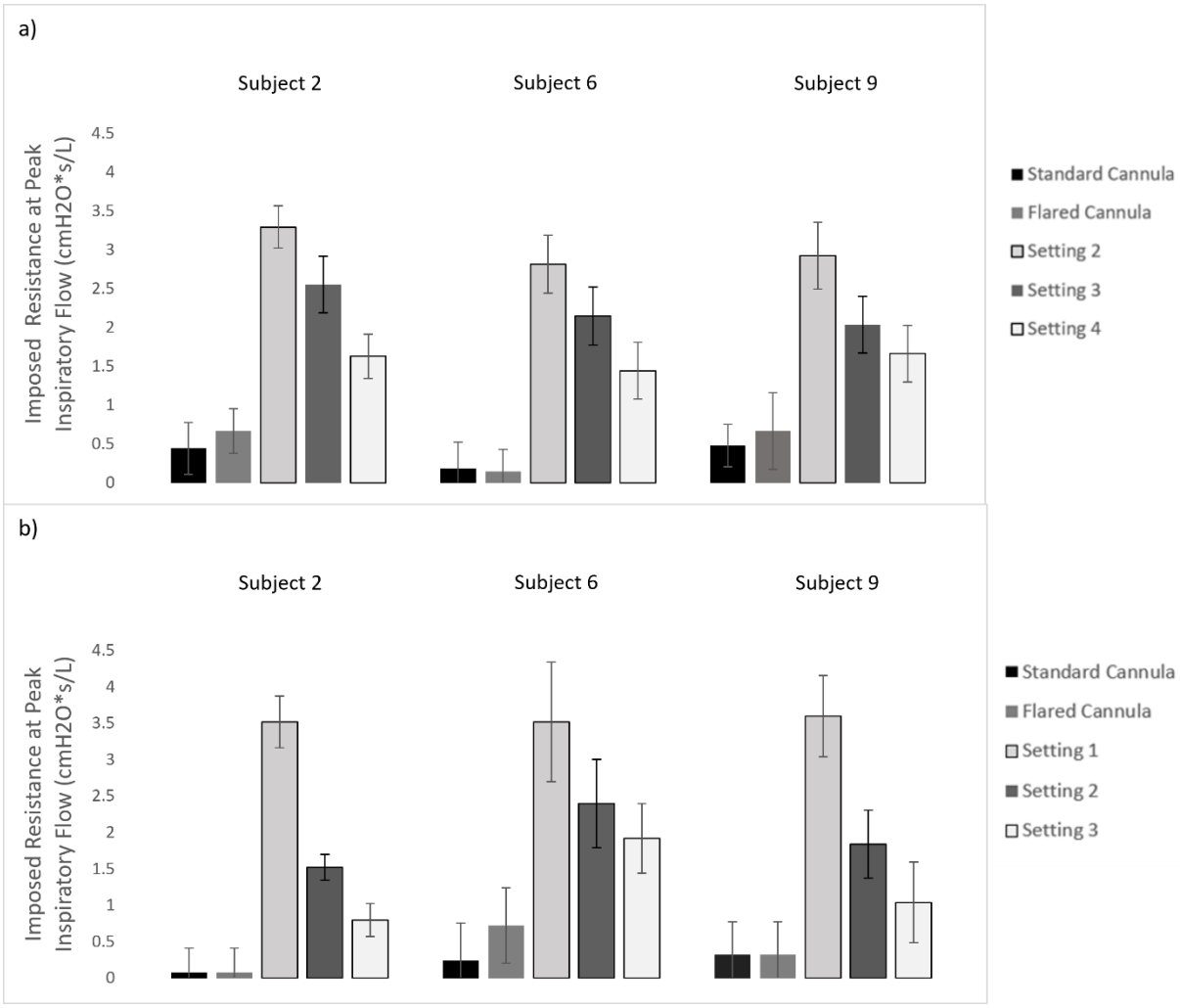

Figure 3-8: Imposed resistance at maximum inspiratory flow rate for each type of nasal cannula and nasal interface setting for a) 100% nasal flow and b) 45% nasal flow. Error bars represent the propagated error from baseline pressure drop measurements and the pressure drop measurements at peak inspiratory flow for each trial. The maximum inspiratory flow rate was 27 L/min for 100% nasal flow, and 12.5 L/min for 45% nasal flow.

3.4 Discussion

The present article describes a new nasal interface designed to improve triggering of pulsed oxygen delivery from POCs. The nasal interface incorporates pillows-type nasal prongs to snugly fit the nostrils, and draws ambient air through a series of entrainment ports. By adjusting the area of air entrainment ports (the 'setting') on the nasal interface, higher signal pressures were achieved than for standard and flared nasal cannulas at all flow rates, and for all three nasal

airway replicas, studied. As a result, the nasal interface was able to trigger a POC in cases where flared and standard nasal cannulas failed to trigger. For a fixed breathing pattern and POC setting, average FiO_2 values for successful triggering cases were significantly higher than values for failed triggering cases, regardless of subject group or nasal cannula/interface group.

While only three nasal airway replicas were tested in this study, these replicas were carefully selected from a larger set of fifteen replicas studied in our previous work [14]. As reported by Chen *et al.* [14], relatively high signal pressures were measured for the Subject 2 replica, whereas relatively low signal pressures were measured for Subjects 6 and 9 [14]. Therefore, these three replicas were included in the present work to evaluate the new nasal interface concept against conventional nasal cannulas in cases where triggering both was, and was not, expected.

Although the nasal interface clearly improved POC triggering in this *in vitro* study, the acceptability of such an interface to patients is unproven. Given that nasal pillows contact the nostrils, the nasal interface may be less comfortable than conventional nasal cannula when worn for extended periods of time. Additionally, aesthetic concerns may make some patients hesitant to wear the nasal interface outside the home. However, as triggering issues are known to often occur during sleep, some patients might use a pillows-style nasal interface during sleep only. In the sleep setting, there is a strong precedent for the use of nasal pillows interfaces in the delivery of continuous positive airway pressure for treatment of obstructive sleep apnea.

A further consideration is the resistance imposed by the nasal interface. As shown in Figure 3-8, the imposed resistance at maximum inspiratory flow rate caused by the nasal interface is higher than that caused by the standard or flared cannula. In selecting an appropriate setting for the nasal interface, a trade-off exists between increasing signal pressure and increasing imposed

resistance. For the 100% and 45% nasal flow breathing patterns, successful triggering was respectively observed at settings 4 and below, and at settings 2 and below (Figure 3-6 and Figure 3-7). At these settings, the imposed resistance at maximum inspiratory flow was on average ~1.5 and ~2 cm H_2O*s/L, for 100% and 45% nasal flow breathing patterns, respectively (Figure 3-8). By way of comparison, these values are similar to the resistances of bacterial/viral breathing circuit filters [26], similar to resistances permitted in certification testing of N95 respirators used as personal protective equipment [27], and are below the resistances of gas masks that have been shown to have only slight impact on the respiratory effort of stable COPD patients [28]. Whether or not these imposed resistances are acceptable to patients requiring LTOT remains to be evaluated.

3.5 Conclusion

One of the most frequently reported problems from LTOT patients is the lack of physically manageable portable systems [7]. Based on reported patient preference, the ideal oxygen supply is a single source unit that can be used during sleep, rest, and activity [12]. Pairing POCs with the nasal interface presented herein would provide control over, and increase the attainable range of, the signal pressures sent to POCs, and could minimize events where triggering fails. The interface therefore presents a simple solution that could be used with commercially-available POCs to provide patients with a physically manageable oxygen source that can reliably supply oxygen in all common daily use circumstances.

Chapter 4: Conclusion

4.1 Summary

The purpose of this thesis is to present a new nasal interface designed to improve oxygen delivery from portable oxygen concentrators (POCs). POCs are one type of device used to administer supplemental oxygen to people with chronic respiratory disorders. POCs use pulse-flow technology, where a bolus of oxygen is sent only during the inhalation phase of the user's breath. While POCs are the patient-preferred device, they are not reliable in breathing scenarios characterized by low inspiratory flow rates, such as sleep, because the device cannot detect user inhalation [10, 14]. Most oxygen users will use a continuous-flow device during sleep to avoid pulse triggering failures.

The new nasal interface is designed to eliminate POC triggering failures by controlling the pressure drop across the cannula supply tubing that connects the POC to the user. Nasal pillows are used to provide a snug fit on the user's nostrils, ensuring that the inhaled and exhaled air is directed through the air entrainment body. The air entrainment body has a series of holes on the bottom face which are plugged in different combinations to create "settings." Each device setting has a different open area for air entrainment, resulting in different pressure drops across the cannula tubing during inhalation. The pressure drop across the cannula tubing during inhalation is called the signal pressure in the presented work.

It was hypothesized that the new nasal interface would produce higher signal pressures than standard or flared nasal cannulas at fixed inhalation flow rates. The signal pressure test results, presented in section 3.2.3, show that at least one new nasal interface setting increased the signal pressure at every flow rate, for all airway replicas tested. Next, it was also hypothesized that

when using the new nasal interface with a commercial POC, the triggering efficiency would improve compared with that observed for standard or flared nasal cannulas. As shown in section 3.2.4, at least one new nasal interface setting successfully triggered the POC in all cases where either the standard or flared nasal cannula failed. Lastly, it was hypothesized that greater *in vitro* fraction of inspired oxygen (FiO_2) will be achieved when using the new nasal interface, due to improved triggering efficiency. Based on the Tukey-Kramer test results discussed in section 3.3, average FiO2 values from successful triggering cases were significantly higher than failed triggering cases for a fixed breathing pattern and POC setting, regardless of subject group or nasal cannula/interface face group. The new nasal interface successfully improved the performance of the SimplyGO mini POC during breathing simulations. Using this new nasal interface concept could improve the performance of several pulse-flow medical oxygen administration devices.

4.2 Future Work

In the presented work only one portable oxygen concentrator (POC) was tested with the new nasal interface. Future trials should include more POCs, because different POC models may have different features that alter the performance of the new nasal interface. There are many POCs available on the market, and POC technology is continually advancing. A better understanding of how the new nasal interface works with different POC models is important for future development of the device.

Lastly, a trade-off exists between increasing signal pressure and increasing imposed resistance when choosing the appropriate nasal interface setting. High imposed breathing resistance will cause discomfort for the user. Ideally, the signal pressure is increased just enough to trigger a

POC consistently while avoiding unnecessarily high imposed resistance. While the imposed resistances observed in this study were comparable to levels presented in earlier works, it is still unclear if the imposed resistance necessary to improve triggering efficiency will be acceptable to users. Additionally, the presented prototypes were designed for in-lab proof-of-concept purposes only. Usability trials should be conducted once more ergonomic and aesthetically pleasing prototypes are available to evaluate user acceptability.

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Appendices

Appendix A: Detailed Description of VBA Code

180 breathing simulations were conducted, creating over 100,000 oxygen concentration and chamber volume data points each. John Chen created an Excel spreadsheet that plots oxygen concentration and flow rate vs. time. Also, the data processing spreadsheet has cells dedicated to calculating FiO_2 values for individual breaths within each simulation. The methods described in Chen et. al 2017 are used in the spreadsheet to make the plots and calcualte FiO_2 values [14]. To use the data processing spreadsheet, the user has to manually import the raw data and, through trial and error, set the transport delay to align the oxygen concentration and flow rate plots. The user then has to choose which oxygen concentration and flow rate data points to include in the FiO_2 calculation of each chosen breath. Once selected, the user has to manually copy and paste the data points to differnet cells in the data processing spreadsheet to calculate FiO_2. The VBA code described herein introduces four command buttons that make this process faster and more consistent.

The first step when using the VBA code is to import the appropriate raw data into the data processing spreadsheet. The command button labelled as “Import Data,” shown in Figure A-1, is dedicated to this task. After clicking this button, the user is prompted to provide a file extension describing where the data processing spreadsheet and raw data files are located. Next, the user is prompted to provide the names of the data processing spreadsheet and the raw data files. Once the location and names of the files have been declared, the VBA code imports the chamber volume and oxygen concentration raw data to columns D and G, respectively (Figure A-1). The time values from the oxygen concentration raw data file are copied to column F. Once the raw data has been imported, columns C, E, H, and I are automatically updated based on the in-cell

equations written previously by John Chen. Lastly, the time delay shown in cell A2 is calculated using values from the raw data files as well. See subsection A.1 for the full VBA script corresponding to the "Import Data" button. New users will likely need to update the VBA script to match their file folder organization scheme.

	A	B	C	D	E	F	G	H	I
1	**Time Delay (ASL and O2 analyzer) (s)**	**Transport Delay (s)**	**Time (s)**	**Volume (mL)**	**Flow rate (mL/s)**	**Time (s)**	**O2 Concentration**	**Corrected Time (s)**	**Corrected O2 Concentration**
2	36.08	33.97563112	**2.10873**	0	**1.220623624**	0	2091	**-1.89**	**0.207534591**
3			**2.11068**	0.002384	**1.220623624**	0.029002	2089	**-1.860998**	**0.209682732**
4			**2.11264**	0.004768	**1.221135631**	0.058003	2090	**-1.831997**	**0.204303772**
5			**2.11459**	0.007153	**1.220623624**	0.087005	2084	**-1.802995**	**0.210021371**
6			**2.11654**	0.009537	**4.272182684**	0.115006	2086	**-1.774994**	**0.217992456**
7			**2.11849**	0.017881	**4.27269469**	0.144008	2098	**-1.745992**	**0.205746718**
8	**Raw data files extracted**		**2.12045**	0.026226	**4.27269469**	0.17201	2093	**-1.71799**	**0.203821068**
9	E:\COPD breathing -45nasal\Setting 2\2.2\Test 2.2.1 O2 concentration.csv		**2.1224**	0.034571	**4.272182684**	0.201012	2086	**-1.688988**	**0.212513658**
10	E:\COPD breathing -45nasal\Setting 2\2.2\Test 2.2.1 Volume.csv		**2.12435**	0.042915	**7.019097844**	0.230013	2091	**-1.659987**	**0.208289344**
11	Oxygen data processing 1.xlsm		**2.12631**	0.056624	**7.019097844**	0.258015	2090	**-1.631985**	**0.207434537**
12			**2.12826**	0.070333	**7.019609851**	0.287016	2088	**-1.602984**	**0.210365409**
13			**2.13021**	0.084043	**7.019097844**	0.316018	2090	**-1.573982**	**0.209782705**
14	Import Data	Align Plot	**2.13217**	0.097752	**10.0706569**	0.34502	2091	**-1.54498**	**0.2091**
15			**2.13412**	0.117421	**10.07116891**	0.373021	2091	**-1.516979**	**0.209882705**
16			**2.13607**	0.137091	**10.0706569**	0.402023	2092	**-1.487977**	**0.2092**
17			**2.13803**	0.15676	**10.07116891**	0.431025	2092	**-1.458975**	**0.209982732**
18	Find FIO2	Find FE02	**2.13998**	0.17643	**12.97015002**	0.460026	2093	**-1.429974**	**0.206868031**
19			**2.14193**	0.201762	**12.97015002**	0.488028	2090	**-1.401972**	**0.212913523**
20			**2.14388**	0.227094	**12.97015002**	0.51703	2095	**-1.37297**	**0.204020879**
21			**2.14584**	0.252426	**12.97015002**	0.546031	2088	**-1.343969**	**0.210421313**

Figure A-1: Command button layout for fraction of inspired oxygen calculation spreadsheet.

After importing the raw data, a plot showing oxygen concentration and flow rate vs. time is automatically updated, as shown in Figure A-2. At this stage it is apparent that the oxygen concentration and flow rate curves are not aligned because the initial spike of oxygen does not occur at the same time of an inhalation.

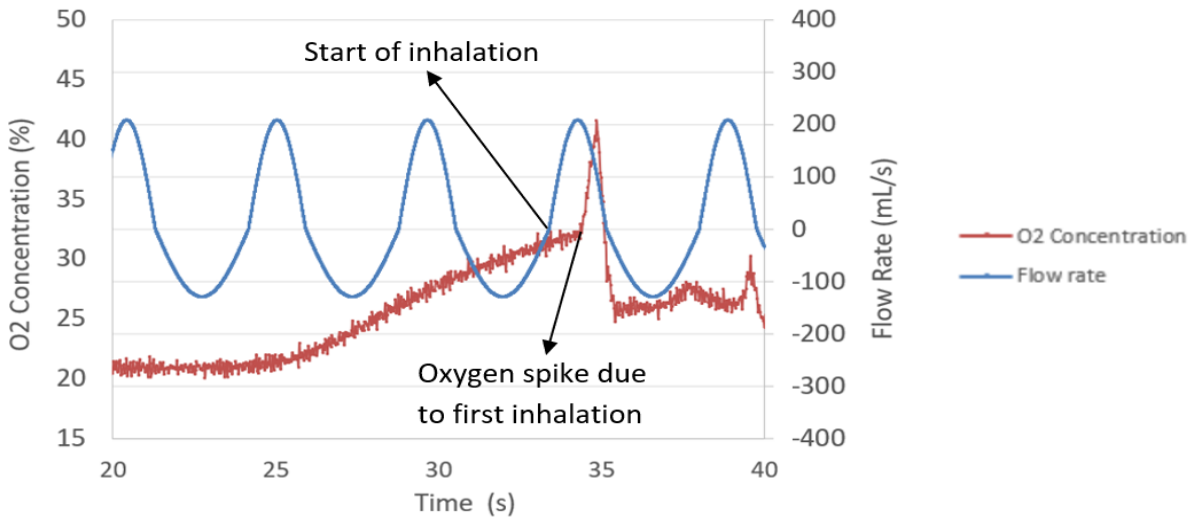

Figure A-2: Example oxygen concentration and flow rate plot before using the "Align Plot" command button in the created VBA code.

At the start of each simulation, a continuous flow of oxygen is sent to the connected airway replica. Before a simulated breath occurs, the O2 concentration steadily increases due to the continuous flow from the POC. Upon the first simulated inhalation, a spike of oxygen passes the oxygen concentration measurement point (trachea) within the replica. The "Align Plot" button ensures that the initial spike of oxygen takes place at the same time as an inhalation by iteratively manipulating the transport delay shown in cell B2 of Figure A-1. An updated plot created after using the "Align Plot" button is shown in Figure A-3.

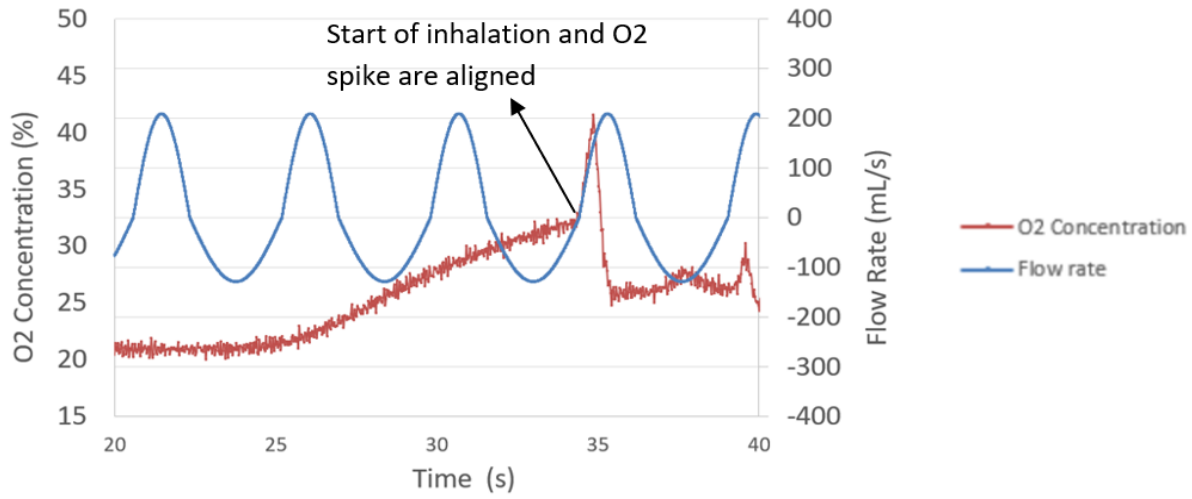

Figure A-3: Example oxygen concentration and flow rate plot after using the "Align Plot" command button in the created VBA code.

To use the "Align Plot" button, the user first needs to enter an initial guess for the transport delay. A good first guess is just below the time delay shown in cell A2 (Figure A-1). See subsection A.2 for the full VBA script corresponding to the "Align Plot" command button.

Now that the plots are aligned, the user needs to decide which breaths FiO_2 values should be calculated for. After clicking the "Find FiO_2" button, the user will be prompted to enter a time value that takes place just before the first inhalation of interest. The user also needs to enter how many consecutive breaths FiO_2 values should be calculated for, and the period of a single breath for the breathing pattern used during the simulation. For example, assume the user wants to find the FiO_2 values for the 5 inhalations boxed in green in Figure A-4. The user could enter 112 for the time value, because the first inhalation of interest starts at approximately 113 s. The user should then enter 5 for the number of consecutive breaths, and the period is 4.7 s for the simulated breathing pattern used in this case. FiO_2 values will be printed in the "FiO_2" sheet of the data processing spreadsheet after entering the appropriate values in the user prompts (Figure A-5). See subsection A.3 for the full VBA script corresponding to the "Find FiO_2" button.

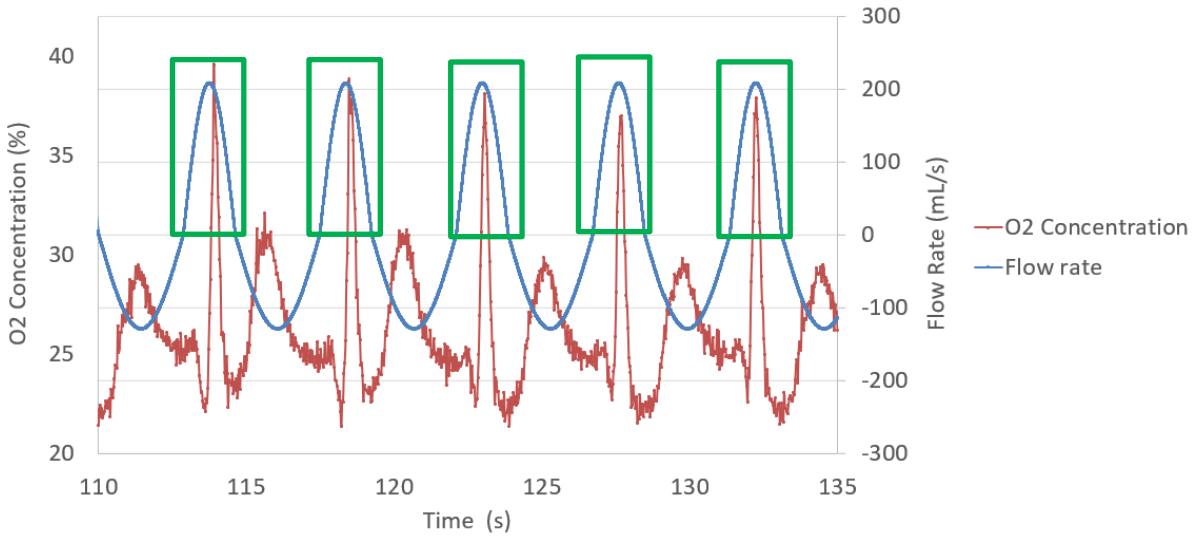

Figure A-4: Example plot that highlights the start and end of inhalation used for fraction of inspired calculations.

	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
1	Breath1				Breath2				Breath3				Breath4				Breath5		
2	time	O2	**FIO2**				**FIO2**				**FIO2**				**FIO2**				**FIO2**
3	112.8716	0.252389	**0.275771**		117.4898	0.242925	**0.275358**		122.0881	0.242404	**0.274963**		126.7054	0.245186	**0.27558**		131.3506	0.249435	**0.277429**
4	112.8996	0.251535			117.5178	0.252596			122.1171	0.248065			126.7344	0.244686			131.3796	0.248368	
5	112.9286	0.246638			117.5468	0.246152			122.1461	0.242004			126.7634	0.248911			131.4076	0.248152	
6	112.9576	0.259144			117.5758	0.247417			122.1751	0.242969			126.7914	0.254462			131.4366	0.249389	
7	112.9866	0.249757			117.6048	0.243236			122.2041	0.2457			126.8204	0.243521			131.4646	0.253231	
8	113.0146	0.256514			117.6328	0.246717			122.2321	0.2457			126.8494	0.242625			131.4936	0.246586	
9	113.0436	0.251479			117.6618	0.255507			122.2611	0.244135			126.8774	0.256992			131.5226	0.25	
10	113.0716	0.256031			117.6898	0.246052			122.2901	0.2455			126.9064	0.249583			131.5506	0.257044	
11	113.1006	0.257996			117.7188	0.245752			122.3181	0.248631			126.9354	0.249711			131.5796	0.253248	

Figure A-5: Example of fraction of inspired oxygen results presented in the Excel spreadsheet using the created VBA code.

To ensure the calculated FiO_2 values are reasonable, users can compare their FiO_2 values to the fraction of expired oxygen (FeO_2) directly following each inhalation. To do this, users should click the "Find FeO_2" button. The user will be prompted to enter a time value that takes place just before the first exhalation of interest. The user also needs to enter how many consecutive breaths FeO_2 values should be calculated for, and the period of a single breath for the breathing pattern used during the simulation. For example, assume the user wants to validate the FiO_2 values previously calculated for the inhalations boxed in green (Figure A-4). The user could enter 114 for the time value because the first exhalation of interest starts at approximately 115 s.

The user should then enter 5 for the number of consecutive breaths, and the period is 4.7 s for the simulated breathing pattern used in this case. FeO_2 values will be printed in the "FeO_2" sheet of the data processing spreadsheet after entering the appropriate values in the user prompts (Figure A-6). For this example, the largest discrepancy between adjacent FiO_2 and FeO_2 occurs during breath 5. However, there is only a 3.1% difference in this case, indicating that the calculated FiO_2 and FeO_2 values are consistent. See subsection A.4 for the full VBA script corresponding to the "Find FeO_2" button.

	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
1	Breath1				Breath2				Breath3				Breath4				Breath5		
2	time	O2	FEO2				FEO2				FEO2				FEO2				FEO2
3	114.6197	0.236225	**0.276356**		119.2499	0.226463	**0.274684**		123.8642	0.226886	**0.268717**		128.4845	0.224421	**0.269408**		133.1047	0.225369	**0.268973**
4	114.6487	0.231794			119.2789	0.231882			123.8932	0.213863			128.5135	0.225957			133.1337	0.21675	
5	114.6777	0.237725			119.3069	0.238135			123.9222	0.221715			128.5415	0.220973			133.1617	0.215742	
6	114.7057	0.227829			119.3359	0.232455			123.9502	0.228183			128.5705	0.223104			133.1907	0.230779	
7	114.7347	0.239235			119.3649	0.232925			123.9792	0.220456			128.5995	0.225579			133.2197	0.222757	
8	114.7637	0.242221			119.3929	0.2379			124.0082	0.225035			128.6275	0.228565			133.2477	0.222469	
9	114.7917	0.23219			119.4219	0.2379			124.0372	0.230656			128.6565	0.218283			133.2767	0.221147	
10	114.8207	0.245179			119.4499	0.234769			124.0692	0.224652			128.6845	0.227665			133.3047	0.220004	
11	114.8497	0.241211			119.4789	0.242196			124.0982	0.228321			128.7135	0.2263			133.3337	0.2241	

Figure A-6 Example of fraction of exspired oxygen results presented in the Excel spreadsheet using the created VBA code.

A.1 Import Data Command Button Script

```
Private Sub CommandButton1_Click()

'Get file location and name from user to import appropriate raw data

'Declare variable types

Dim folderfilename As String

Dim Workbook As String

Dim Workbook2 As String

Dim Workbook3 As String

'the following user input variables are used to choose the correct raw data
files from the user's folders. In this case, the raw data file's location
followed the following format:

'"USBext":\COPD breathing -45nasal\Setting "pocsetting"\"subject"."cannula"
```

```
'or for example, E:\COPD breathing -45nasal\Setting 2\2.2 which denotes that
POC setting 2, subject number 2, and cannula setting 2 were used in this
example simulation using 45% nasal flow.For the oxygen concentration raw data
file names, the following format was followed:

'Test "subject"."cannula"."trial" O2 concentration

'or for example, "Test 2.2.1 O2 concentration.csv" which denotes that this
data correspondss to subject 2,using cannula setting 2, in trial number 1 of
3. Similarly, the volume raw data for this case would be named: "Test 2.2.1
Volume.csv". It is important to note the following legend for the "cannula"
numbering scheme:

'cannula = 1 - standard cannula

'cannula = 5 - flared cannula

'cannula = 2, 3 or 4 - for new nasal interface settings 2,3 and 4,
respectively, during 100% nasal flow trials

'for 45% nasal flow trials, new nasal interface setting 1 corresponds to
cannula = 4.

folderfilename = InputBox("What is the file extension for the Oxygen
Concentration raw data?")

Workbook = InputBox("What is the file name of the .xlsm where the raw data
should be copied? don't include .xlsm at the end")

Workbook2 = InputBox("What is the file name for the Oxygen Concentration raw
data .csv? don't include .csv at the end")

Workbook3 = InputBox("What is the file name for the Volume raw data .csv?
don't include .csv at the end")

'Open selected workbooks

Workbooks.Open folderfilename & "\" & Workbook2 & ".csv"

Workbooks.Open folderfilename & "\" & Workbook3 & ".csv"

'As a check, the code prints the declared raw data file location and name in
cells A9 and A10 of the activated workbook

'The activated workbook name where data will be pasted is printed in cell A11.

Range("A9").Value = folderfilename & "\" & Workbook2 & ".csv"
```

```
Range("A10").Value = folderfilename & "\" & Workbook3 & ".csv"

Range("A11").Value = Workbook & ".xlsm"

'Copy and paste O2 concentration raw data to desired location

Workbooks(Workbook2 & ".csv").Worksheets(Workbook2).Range("A2:B450000").Copy _

Workbooks(Workbook & ".xlsm").Worksheets("Test Code").Range("F2")

'Copy and paste volume raw data to desired location

Workbooks(Workbook3 & ".csv").Worksheets(Workbook3).Range("B1:B450000").Copy _

Workbooks(Workbook & ".xlsm").Worksheets("Test Code").Range("D2")

'The time delay between the ASL breating simulator and Gas analyzer is
calculated as follows

Workbooks(Workbook & ".xlsm").Worksheets("Test Code").Range("A2") =
Workbooks(Workbook3 & ".csv").Worksheets(Workbook3).Range("C1") -
Workbooks(Workbook2 & ".csv").Worksheets(Workbook2).Range("A1")

'The raw data files are then closed

Workbooks(Workbook2 & ".csv").Close

Workbooks(Workbook3 & ".csv").Close

End Sub
```

A.2 Align Plot Command Button Script

```
Private Sub CommandButton2_Click()

'At the start of each simulation, a POC set in continuous flow mode was
connected to the replica. Before a simulated breath occurs, the O2
concentration steadily increases due to the continuous flow from the POC. Upon
the first simulated breath, a spike of oxygen passes the O2 measurement point
(trachea). The command button described here finds the time at which the
initial O2 spike occurs, and then iteratively manipulates the transport delay
until an early inhalation flow rate is plotted at the same time of the O2
spike.

'To avoid making any changes to the spread sheet John Chen created, O2 raw
data is copied to a new sheet with the appropriate headings.
```

```
Worksheets("Code Calcs").Range("A1") = "Time"

Worksheets("Code Calcs").Range("B1") = "Raw O2 data"

Worksheets("Code Calcs").Range("A2:B12000").Value = Worksheets("Test
Code").Range("H2:I12000").Value

'The plot for the raw O2 data vs. time is very jagged. The random, rapid
changes in slope make finding the initial O2 spike difficult. This portion of
the code finds the 3rd period average of the raw O2 data to smooth the plot.
Once smooth, the code finds the point where the slope of the n3 plot is above
a certain value for 5 continuous data points. The first point of 5 where the
slope is above a given value is considered the start of the O2 concentration
spike, which is when the first simulated breath takes place. By trial and
error, it was found that searching for 5 consecutive points with slopes
greater than 0.1 consistently resulted in finding the O2 pulse.

Dim j As Integer

Dim i As Integer

'create column with 3rd period averages of O2 data in "Code Calcs" sheet.

Worksheets("Code Calcs").Range("C1") = "O2 n3"

Worksheets("Code Calcs").Range("C2") =
Application.WorksheetFunction.Average(Worksheets("Code Calcs").Range("B" & 2))

Worksheets("Code Calcs").Range("C3") =
Application.WorksheetFunction.Average(Worksheets("Code Calcs").Range("B" & 2 &
":B" & 3))

j = 3

Do Until Worksheets("Code Calcs").Range("B" & j + 1).Text = "#DIV/0!" Or j =
8000 'maximum j-value set through trial and error.

    Worksheets("Code Calcs").Range("C" & j) =
Application.WorksheetFunction.Average(Worksheets("Code Calcs").Range("B" & j -
1 & ":B" & j + 1))

    j = j + 1

Loop

'create row with slopes of 3rd period average plot, need to do first 5
separately because of the next Do loop conditions applied.
```

```
Worksheets("Code Calcs").Range("D1") = "Slope n3"

i = 0

a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)

Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

Slope0 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

i = 1

a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)

Slope1 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

i = 2

a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)
```

```
Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

Slope2 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

i = 3

a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)

Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

Slope3 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

i = 4

a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)

Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

Slope4 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

i = 5

'find slopes of 3rd period average plot until O2 pulse is found. By trial and
error, finding a minimum slope of 0.1 for 5 consecutive points consistently
found the O2 pulse.

Do Until Slope0 > 0.1 And Slope1 > 0.1 And Slope2 > 0.1 And Slope3 > 0.1 And
Slope4 > 0.1
```

```
a = Worksheets("Code Calcs").Range("A2").OffSet(Rowoffset:=i, ColumnOffset:=0)

B = Worksheets("Code Calcs").Range("A3").OffSet(Rowoffset:=i, ColumnOffset:=0)

C = Worksheets("Code Calcs").Range("C2").OffSet(Rowoffset:=i, ColumnOffset:=0)

D = Worksheets("Code Calcs").Range("C3").OffSet(Rowoffset:=i, ColumnOffset:=0)

Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i, ColumnOffset:=0) =
(D - C) / (B - a)

Slope4 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i,
ColumnOffset:=0)

Slope3 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i - 1,
ColumnOffset:=0)

Slope2 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i - 2,
ColumnOffset:=0)

Slope1 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i - 3,
ColumnOffset:=0)

Slope0 = Worksheets("Code Calcs").Range("D2").OffSet(Rowoffset:=i - 4,
ColumnOffset:=0)

Worksheets("Code Calcs").Range("E1") = "O2 on point"

Worksheets("Code Calcs").Range("E2") = i - 2

i = i + 1

'The final i-value from the Do loop, minus 2, represents the row in the excel
spreadsheet at which the O2 pulse occurs. Save this value and use it to find
time at which O2 pulse occurs.

Loop

'After finding the row in the Excel spreadsheet that corresponds to the O2
pulse start point, the time at which the O2 pulse is found by using the
previously found i-value (called OffSet here).

Dim OffSet As Integer

OffSet = Worksheets("Code Calcs").Range("E2").Value 'renames i-value from
previous loop as Offset
```

```
Worksheets("Code Calcs").Range("F2") = Worksheets("Code Calcs").Range("A" &
OffSet)

Worksheets("Code Calcs").Range("F1") = "Start time for O2 Pulse"

'Next, since the volume raw data was collected at a time interval different
than the O2 concentration raw data, the closest time point from the volume raw
data when compared to the O2 Pulse start time needs to be found.

Dim k As Single

k = 2

'This Do loop compares the O2 Pulse start time to the volume raw data times
collected. The loop continues until a time value within 0.001s of the O2 pulse
time is found in the volume raw data time row. 0.001s was determined to be the
condition requirement through trial and error. The k-value is saved here to
indicate the row at which the closest volume raw data time point is. It is
important to note that the volume raw points are used to calculate the flow
rates vs. time directly in the Excel file John Chen created. By simply pasting
the volume raw data properly, the flow rate column will be updated.

Do

    If Abs(Worksheets("Code Calcs").Range("F2") - Worksheets("Test
Code").Range("C" & k)) < 0.001 Then

    Worksheets("Code Calcs").Range("G2") = Worksheets("Test Code").Range("C" &
k)

    Worksheets("Code Calcs").Range("G1") = "Start time for volume"

    Worksheets("Code Calcs").Range("H1") = "row number for volume start time"

    Worksheets("Code Calcs").Range("H2") = k

    Exit Do

    Else

    k = k + 1

    End If

Loop
```

```
'To line up the flow rate and O2 concentration plots, the transport delay
needs to be manipulated such that the flow rate value in row k is as small as
possible, and the flow rate curve is on an upward slope (this is where the
onset of inhalation would take place). By changing the transport delay, the
flow rate data is essentially shifted down the time axis. The flow rate data
is shifted down the time axis until the appropriate O2 concentration and flow
rate data points align. To start, the user has to guess an initial time
constant. A good first guess is typically just below the time delay (see cell
A2 on "Test Code" sheet). After declaring a first guess, the flow rate value
in row k is checked. If the flow rate in row k is below 8 ml/s, and the flow
rate curve is on the upward curve, the Do loop stops. Otherwise, the transport
delay is changed to further shift the flow rate data down the time axis. 8
ml/s was chosen through trial and error, and in the "fine tune" section, the
flow rate in row k is brought is even closer to 0 ml/s.

i = InputBox("guess transport delay h-cell value")

Do

    If Abs(Worksheets("Test Code").Range("E" & k)) < 8 And Worksheets("Test
Code").Range("E" & k + 20) > 0 Then

    Exit Do

    Else

        Worksheets("Test Code").Range("B2").Formula = Worksheets("Test
Code").Range("A2") - (Worksheets("Test Code").Range("H" & i) +
Worksheets("Test Code").Range("H" & i + 1)) / 2

        i = i + 1

        k = 2

        Do

            If Abs(Worksheets("Code Calcs").Range("F2") - Worksheets("Test
Code").Range("C" & k)) < 0.001 Then

            Worksheets("Code Calcs").Range("G2") = Worksheets("Test
Code").Range("C" & k)

            Worksheets("Code Calcs").Range("H2") = k

            Exit Do

            Else
```

```
            k = k + 1

            End If

        Loop

    End If

Loop

'After the Do loop is broken, the flow rate in row k, as well as the
orientation of the flow rate curve is checked and printed in the cells I1:J2
of the "Code Calcs" sheet.

Worksheets("Code Calcs").Range("I2") = Worksheets("Test Code").Range("E" & k)

Worksheets("Code Calcs").Range("I1") = "Starting flow rate"

Worksheets("Code Calcs").Range("J2") = Worksheets("Test Code").Range("E" & k +
20)

Worksheets("Code Calcs").Range("J1") = "Correct orientation check, positive?"

'After getting the flow rate and O2 concentration data in pretty good
alignment, the "Fine tune" section ensures that the flow rate in row k has an
absolute value of less than 1 ml/s. The Do loop here is used to calculate how
many rows away the current flow rate in row k is from  a flow rate with an
absolute value less than 1 ml/s (saved here as j). Depending on the sign of
the current flow rate value in row k, the flow rate column is shifted up or
down by a value of j.

j = 0

Worksheets("Fine Tune").Range("C1") = "Time"

Worksheets("Fine Tune").Range("D1") = "Flow"

Do

    If Abs(Worksheets("Test Code").Range("E" & k)) > 1 And Worksheets("Test
Code").Range("E" & k) < 0 Then

    j = j + 1

    k = Worksheets("Code Calcs").Range("H2").Value + j
```

```
    ElseIf Abs(Worksheets("Test Code").Range("E" & k)) > 1 And
Worksheets("Test Code").Range("E" & k) > 0 Then

    j = j - 1

    k = Worksheets("Code Calcs").Range("H2").Value + j

    ElseIf j > 0 Then

    Worksheets("Code Calcs").Range("k2") = k

    Worksheets("Code Calcs").Range("k1") = "fine tuned row"

    Worksheets("Code Calcs").Range("l2") = j

    Worksheets("Code Calcs").Range("l1") = "fine tune offset"

    Worksheets("Fine Tune").Range("C2") = Worksheets("Test
Code").Range("C2").Value

    aj = Abs(j)

            Worksheets("Test Code").Range(Range("D" & 2 + aj), Range("D" & 2 +
aj).End(xlDown)).Copy _

        Worksheets("Fine Tune").Range("D2")

    Exit Do

    Else

    Worksheets("Code Calcs").Range("k2") = k

    Worksheets("Code Calcs").Range("k1") = "fine tuned row"

    Worksheets("Code Calcs").Range("l2") = j

    Worksheets("Code Calcs").Range("l1") = "fine tune offset"

    Worksheets("Fine Tune").Range("C2") = Worksheets("Test
Code").Range("C2").Value

    aj = Abs(j)
```

```
            Worksheets("Test Code").Range(Range("D2"),
Range("D2").End(xlDown)).Copy _

         Worksheets("Fine Tune").Range("D" & 2 + aj)

    Exit Do

    End If

Loop

End Sub
```

A.3 Find FiO_2 Command Button Script

```
Private Sub CommandButton3_Click()

'This command button is used to calculate the FIO2 values for a certain amount
of breaths, starting from a time point chosen by the user.

Dim Steady As Single

Dim k As Double

Dim Breath As Integer

Dim Row As Integer

Dim Column As Integer

'clear data from previous use of command button

Worksheets("FIO2").Range("A1:DA800").ClearContents

'First the user has to declare at which time point their 1st breath of
interest approximately is. The user should pick a time point that is during
the exhalation phase of the breath immediately prior to the first breath of
interest. The user also needs to declare how many consecutive breaths FIO2
values should be calculated for, and the period of a single breath in seconds.

Steady = InputBox("At what time should FIO2 calculation start? Enter an
integer value", "Intial guess should be during exhalation")

BreathCount = InputBox("How many breaths should be analyzed?")
```

```
Period = InputBox("What is the period of a single breath in seconds?") '4.69 s for sleeping COPD patient

'Breathe, Row and Column, are used as counter variables here to ensure the right amount of FIO2s values are calculated, and to control where the results are printed.

Breath = 1

Row = 2

Column = 0

Do Until Breath > BreathCount

'First, the time point from the volume raw data that most closely matches the users input time needs to be found. The row value k corresponding to this time is saved.

k = 2

Do

    If Abs(Steady - Worksheets("Fine Tune").Range("C" & k)) < 0.01 Then

    Exit Do

    Else

    k = k + 1

    End If

Loop

'Next, the closest positive flow rate from the user's initial guess is found to determine when the start of inhalation occurs.

Dim j As Integer

j = 2

Worksheets("FIO2").Range("A1") = "Inhalation start row"

Worksheets("FIO2").Range("B1") = "Inhalation start time, flow"
```

```
Worksheets("FIO2").Range("C1") = "Starting flow rate"

Worksheets("FIO2").Range("F1") = "O2 at inhale"

Worksheets("FIO2").Range("E1") = "time at inhale, O2"

Worksheets("FIO2").Range("D1") = "O2 start row"

Worksheets("FIO2").Range("H2") = "time"

Worksheets("FIO2").Range("I2") = "O2"

Worksheets("FIO2").Range("H1").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
"Breath" & Breath

Do

    If Worksheets("Fine Tune").Range("E" & k).Value <= 0 Then

    k = k + 1

    Else

    Worksheets("FIO2").Range("A" & Row) = k

    Worksheets("FIO2").Range("B" & Row) = Worksheets("Fine Tune").Range("c" &
k)

    Worksheets("FIO2").Range("C" & Row) = Worksheets("Fine Tune").Range("E" &
k)

'The oxygen concentration raw data was collected at different time intervals
than the volume raw data, so this embedded Do loop is necessary to match the
volume raw data time in row k to the closest oxygen concentration raw data
time in column h of the "Test Code" sheet. The oxygen concentration at row "j"
is the concentration at the start of inhalation.

    Do

        If Abs(Worksheets("Fine Tune").Range("C" & k) - Worksheets("Test
Code").Range("H" & j)) > 0.02 Then

        j = j + 1

        Else
```

```
        Worksheets("FIO2").Range("F" & Row) = Worksheets("Test
Code").Range("I" & j)

        Worksheets("FIO2").Range("E" & Row) = Worksheets("Test
Code").Range("H" & j)

        Worksheets("FIO2").Range("D" & Row) = j

        Exit Do

        End If

    Loop

    Exit Do

    End If

Loop

'The next Do loop is used to copy and paste the oxygen concentration vs time,
starting the row "j", to the "FIO2" sheet. The Do loop continues to copy the
oxygen concentration vs. time data until a negative flow rate is reached,
indicating the end of inhalation.

Dim i As Integer

i = 3

Do

    If Worksheets("Fine Tune").Range("E" & k) > 0 Then

    Worksheets("FIO2").Range("I" & i).OffSet(Rowoffset:=0,
ColumnOffset:=Column) = Worksheets("Test Code").Range("I" & j)

    Worksheets("FIO2").Range("H" & i).OffSet(Rowoffset:=0,
ColumnOffset:=Column) = Worksheets("Test Code").Range("H" & j)

    j = j + 1

    i = i + 1

'Once again, an embedded Do loop is required to match flow rates and oxygen
concentration data at a set time because the time interval used to collect
each type of data varied.
```

```
    Do

        If Abs(Worksheets("Fine Tune").Range("C" & k) - Worksheets("Test
Code").Range("H" & j)) > 0.001 Then

        k = k + 1

        Else

        Exit Do

        End If

    Loop

    Else

    Exit Do

    End If

Loop

'Once the oxygen concentration vs. time data for an entire inhalation has been
copied to the "FIO2" sheet, the data is then copied to column L of the "Test
Code" sheet. By updating the values in this column, a FIO2 value is given in
cell T67 because, that how John Chen design the Excel spreadsheet. The FIO2
value given in cell T67 is then printed on the "FIO2" sheet.

Worksheets("FIO2").Range("H3:I101").OffSet(Rowoffset:=0,
ColumnOffset:=Column).Copy _

    Worksheets("Test Code").Range("L2")

Worksheets("FIO2").Range("J3").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
Worksheets("Test Code").Range("T67")

Worksheets("FIO2").Range("J2").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
"FIO2"

'The Do loop continues to calculate FIO2 values for consecutive breaths until
BreathCount is reached.

Breath = Breath + 1

Steady = Steady + Period
```

```
Row = Row + 5

Column = Column + 4

Loop

End Sub
```

A.4 Find FeO_2 Command Button Script

```
Private Sub CommandButton4_Click()

'This command button is used to calculate the FEO2 values for a certain amount
of breaths, starting from a time point chosen by the user.

Dim Steady As Single

Dim k As Double

Dim Breath As Integer

Dim Row As Integer

Dim Column As Integer

'clear data from previous use of command button

Worksheets("FEO2").Range("A1:DA800").ClearContents

'First the user has to declare at which time point their 1st breath of
interest approximately is. The user should pick a time point that is during
the inhalation phase of the breath immediately prior to the first breath of
interest. The user also needs to declare how many consecutive breaths FEO2
values should be calculated for, and the period of a single breath in seconds.

Steady = InputBox("At what time should FEO2 calc start? Enter an integer
value", "Intial guess should be during Inhalation")

BreathCount = InputBox("How many breaths should be analyzed?")

Period = InputBox("What is the period of a single breath in seconds?") '4.69 s
for sleeping COPD patent

'Breathe, Row and Column, are used as counter variables here to ensure the
right amount of FEO2s values are calculated, and to control where the results
are printed.
```

```
Breath = 1

Row = 2

Column = 0

Do Until Breath > BreathCount

'First, the time point from the volume raw data that most closely matches the
users input time needs to be found. The row value k corresponding to this time
is saved.

k = 2

Do

    If Abs(Steady - Worksheets("Fine Tune").Range("C" & k)) < 0.01 Then

    Exit Do

    Else

    k = k + 1

    End If

Loop

'Next, the closest negative flow rate from the user's initial guess is found
to determine when the start of exhalation occurs.

Dim j As Integer

j = 2

Worksheets("FEO2").Range("A1") = "Exhalation start row"

Worksheets("FEO2").Range("B1") = "Exhalation start time, flow"

Worksheets("FEO2").Range("C1") = "Starting flow rate"

Worksheets("FEO2").Range("F1") = "O2 at exhale"

Worksheets("FEO2").Range("E1") = "time at exhale, O2"
```

```
Worksheets("FEO2").Range("D1") = "O2 start row"

Worksheets("FEO2").Range("H2") = "time"

Worksheets("FEO2").Range("I2") = "O2"

Worksheets("FEO2").Range("H1").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
"Breath" & Breath

Do

    If Worksheets("Fine Tune").Range("E" & k).Value >= 0 Then

    k = k + 1

    Else

    Worksheets("FEO2").Range("A" & Row) = k

    Worksheets("FEO2").Range("B" & Row) = Worksheets("Fine Tune").Range("c" &
k)

    Worksheets("FEO2").Range("C" & Row) = Worksheets("Fine Tune").Range("E" &
k)

'The oxygen concentration raw data was collected at different time intervals
than the volume raw data, so this embedded Do loop is necessary to match the
volume raw data time in row k to the closest oxygen concentration raw data
time in column h of the "Test Code" sheet. The oxygen concentration at row "j"
is the concentration at the start of exhalation.

    Do

        If Abs(Worksheets("Fine Tune").Range("C" & k) - Worksheets("Test
Code").Range("H" & j)) > 0.02 Then

        j = j + 1

        Else

        Worksheets("FEO2").Range("F" & Row) = Worksheets("Test
Code").Range("I" & j)

        Worksheets("FEO2").Range("E" & Row) = Worksheets("Test
Code").Range("H" & j)
```

```
        Worksheets("FEO2").Range("D" & Row) = j

        Exit Do

        End If

    Loop

    Exit Do

    End If

Loop

'The next Do loop is used to copy and paste the oxygen concentration vs time,
starting the row "j", to the "FEO2" sheet. The Do loop continues to copy the
oxygen concentration vs. time data until a positive flow rate is reached,
indicating the end of exhalation.

Dim i As Integer

i = 3

Do

    If Worksheets("Fine Tune").Range("E" & k) < 0 Then

    Worksheets("FEO2").Range("I" & i).OffSet(Rowoffset:=0,
ColumnOffset:=Column) = Worksheets("Test Code").Range("I" & j)

    Worksheets("FEO2").Range("H" & i).OffSet(Rowoffset:=0,
ColumnOffset:=Column) = Worksheets("Test Code").Range("H" & j)

    j = j + 1

    i = i + 1

'Once again, an embedded Do loop is required to match flow rates and oxygen
concentration data at a set time because the time interval used to collect
each type of data varied.

    Do

        If Abs(Worksheets("Fine Tune").Range("C" & k) - Worksheets("Test
Code").Range("H" & j)) > 0.001 Then
```

```
        k = k + 1
        Else
        Exit Do
        End If
    Loop
    Else
    Exit Do
    End If
'Once the oxygen concentration vs. time data for an entire exhalation has been
copied to the "FEO2" sheet, the data is then copied to column Y of the "Test
Code" sheet. By updating the values in this column, a FEO2 value is given in
cell AH103. AH103 is then printed on the "FEO2" sheet.
Loop
Worksheets("FEO2").Range("H3:I101").OffSet(Rowoffset:=0,
ColumnOffset:=Column).Copy _
    Worksheets("Test Code").Range("Y2")
Worksheets("FEO2").Range("J3").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
Worksheets("Test Code").Range("AH103")
Worksheets("FEO2").Range("J2").OffSet(Rowoffset:=0, ColumnOffset:=Column) =
"FEO2"
'The Do loop continues to calculate FIO2 values for consecutive breaths until
BreathCount is reached.
Breath = Breath + 1
Steady = Steady + Period
Row = Row + 5
Column = Column + 4
Loop
```

```
End Sub
```

Appendix B: FiO_2 Data Summary and Statistical Analyses

Four breathing scenarios were simulated during the collection of FiO_2 values: 100% nasal flow while using POC setting 2, 100% nasal flow while using POC setting 4, 45% nasal flow while using POC setting 2 and, 45% nasal flow while using POC setting 4. The FiO_2 values calculated, and the statistical analyses conducted, for each simulated breathing scenario are summarized in the following subsections.

B.1 100% Nasal Flow and POC Setting 2

The FiO_2 values collected for individual breaths during each 100% nasal flow POC setting 2 breathing simulation are summarized in Table B-1 through

Table B-3. The mean values in each of these tables are reflected in Figure 3-6.

Table B-1: Subject 2 FiO_2 Values from 100% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	23.53	23.83	23.35	23.68	23.56
2	23.79	23.86	23.18	23.71	23.57
3	23.75	23.97	23.61	23.64	23.61
4	23.88	23.97	23.43	23.77	23.73
5	23.74	24.13	23.91	23.87	23.83
6	23.86	23.80	24.02	23.80	23.18
7	23.91	23.93	24.10	23.83	23.25
8	23.76	23.93	24.01	23.90	23.13
9	23.94	23.90	24.00	24.01	23.32
10	23.98	23.96	24.08	23.92	23.28
11	23.92	23.89	23.28	24.29	23.69
12	24.03	23.90	23.37	24.25	23.80
13	24.03	23.86	23.29	24.19	23.84
14	24.02	23.90	23.32	24.33	23.86
15	24.15	23.90	23.43	24.25	23.71
Mean	23.89	23.91	23.63	23.96	23.56

Table B-2: Subject 6 FiO_2 Values from 100% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	21.14	22.28	23.84	23.68	23.55
2	21.08	23.43	23.81	23.61	23.38
3	21.07	23.56	23.86	23.72	23.54
4	21.00	23.72	23.93	23.77	23.33
5	21.00	24.28	23.87	23.79	23.47
6	21.00	23.08	23.68	24.03	24.14
7	20.94	21.22	23.60	24.16	24.38
8	20.96	21.07	23.68	23.86	24.55
9	21.01	21.10	23.69	23.78	24.28
10	21.16	21.07	23.67	23.81	24.24
11	21.76	21.00	23.93	23.95	24.05
12	22.31	20.95	23.84	23.67	23.73
13	22.90	20.97	23.84	23.89	23.58
14	23.29	20.98	23.82	23.70	23.79
15	23.55	20.90	23.84	23.61	23.64
16	23.96	20.97	-	-	-
17	22.66	21.11	-	-	-
18	21.26	21.44	-	-	-
Mean	21.78	21.84	23.79	23.80	23.84

Table B-3: Subject 9 FiO_2 Values from 100% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	21.32	23.99	25.02	24.63	23.51
2	22.66	23.92	24.35	24.32	23.49
3	23.55	23.84	24.32	24.11	23.54
4	23.86	24.00	24.20	23.78	23.54
5	23.71	24.00	24.46	23.81	23.54
6	23.97	23.45	23.55	23.85	24.62
7	23.69	23.83	23.60	23.71	24.55
8	20.73	24.04	23.53	23.72	24.51
9	21.17	24.15	23.42	23.81	24.52
10	21.13	24.10	23.71	23.78	24.27
11	21.07	23.99	23.98	24.89	24.71
12	21.02	23.94	23.94	25.55	24.44
13	21.00	23.99	23.89	25.57	24.33
14	21.00	24.01	23.90	25.76	24.28
15	20.99	23.90	23.73	25.91	24.43

16	20.90	-	-	-	-
17	20.89	-	-	-	-
18	21.06	-	-	-	-
Mean	21.87	23.94	23.97	24.48	24.15

After splitting the data shown in Table B-1 through

Table B-3 based on subject number, one-way ANOVAs were conducted where cannula/interface setting was the independent variable and FiO_2 was the dependent variable. The one-way ANOVA results are shown in Table B-4 through Table B-6.

Table B-4: Subject 2 One-way ANOVA Results for 100% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	15	358.299	23.887	0.024	0.337	0.061	23.766	24.008
Flared Cannula	15	358.707	23.914	0.006	0.087	0.061	23.793	24.035
Setting 4	15	354.393	23.626	0.122	1.706	0.061	23.505	23.747
Setting 3	15	359.437	23.962	0.058	0.814	0.061	23.841	24.084
Setting 2	15	353.358	23.557	0.066	0.928	0.061	23.436	23.678
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	2.032	4	0.508	9.184	5.05E-06	2.503	0.782	0.304
Within Groups	3.871	70	0.055					
Total	5.903	74	0.080					

Table B-5: Subject 6 One-way ANOVA Results for 100% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	392.041	21.780	1.078	18.322	0.182	21.418	22.142
Flared Cannula	18	393.149	21.842	1.422	24.169	0.182	21.480	22.204
Setting 4	15	356.888	23.793	0.011	0.148	0.199	23.396	24.189
Setting 3	15	357.023	23.802	0.024	0.338	0.199	23.405	24.198
Setting 2	15	357.635	23.842	0.157	2.201	0.199	23.446	24.239
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	80.158	4	20.040	33.711	3.66E-16	2.492	1.422	0.618

Within Groups	45.178	76	0.594
Total	125.337	80	1.567

Table B-6: Subject 9 One-way ANOVA Results for 100% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	393.738	21.874	1.611	27.382	0.182	21.512	22.236
Flared Cannula	15	359.167	23.944	0.026	0.363	0.199	23.548	24.341
Setting 4	15	359.591	23.973	0.187	2.619	0.199	23.576	24.369
Setting 3	15	367.202	24.480	0.701	9.815	0.199	24.084	24.877
Setting 2	15	362.278	24.152	0.226	3.162	0.199	23.755	24.548
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	73.635	4	18.409	31.006	4.38E-15	2.497	1.342	0.606
Within Groups	43.341	73	0.594					
Total	116.977	77	1.519					

The results from the one-way ANOVAs show that significant differences in FiO_2 due to cannula setting are present for all subjects. Tukey-Kramer tests were conducted to further investigate the differences between cannula setting groups within each subject number category. Tukey-Kramer test results are summarized in Table B-7 through Table B-9. Comparisons showing significant differences are bolded.

Table B-7: Subject 2 Tukey-Kramer Results for 100% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	23.887	15	0.337		
Flared	23.914	15	0.087		
Setting 4	23.626	15	1.706		
Setting 3	23.962	15	0.814		
Setting 2	23.557	15	0.928		
		75	3.87	70	3.959

Q TEST									
group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**0.329**	**0.061**	**5.425**	**0.089**	**0.570**	**0.002**	**0.240**	**1.401**
Standard	Setting 3	0.076	0.061	1.249	-0.165	0.316	0.902	0.240	0.323

Standard	**Setting 4**	**0.260**	**0.061**	**4.289**	**0.020**	**0.501**	**0.027**	**0.240**	**1.108**
Standard	Flared	0.027	0.061	0.448	-0.213	0.268	0.998	0.240	0.116
Setting 2	**Setting 3**	**0.405**	**0.061**	**6.675**	**0.165**	**0.646**	**0.000**	**0.240**	**1.723**
Setting 2	Setting 4	0.069	0.061	1.136	-0.171	0.309	0.929	0.240	0.293
Setting 2	**Flared**	**0.357**	**0.061**	**5.873**	**0.116**	**0.597**	**0.001**	**0.240**	**1.516**
Setting 3	**Setting 4**	**0.336**	**0.061**	**5.539**	**0.096**	**0.577**	**0.002**	**0.240**	**1.430**
Setting 3	Flared	0.049	0.061	0.802	-0.192	0.289	0.979	0.240	0.207
Setting 4	**Flared**	**0.288**	**0.061**	**4.737**	**0.047**	**0.528**	**0.011**	**0.240**	**1.223**

Table B-8: Subject 6 Tukey-Kramer Results for 100% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	21.780	18	18.322		
Flared	21.842	18	24.169		
Setting 4	23.793	15	0.148		
Setting 3	23.802	15	0.338		
Setting 2	23.842	15	2.201		
		81	45.178	76	3.952

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**2.062**	**0.191**	**10.820**	**1.309**	**2.815**	**0.000**	**0.753**	**2.675**
Standard	**Setting 3**	**2.021**	**0.191**	**10.606**	**1.268**	**2.775**	**0.000**	**0.753**	**2.622**
Standard	**Setting 4**	**2.012**	**0.191**	**10.559**	**1.259**	**2.766**	**0.000**	**0.753**	**2.610**
Standard	Flared	0.062	0.182	0.339	-0.657	0.780	0.999	0.718	0.080
Setting 2	Setting 3	0.041	0.199	0.205	-0.746	0.827	1.000	0.787	0.053
Setting 2	Setting 4	0.050	0.199	0.250	-0.737	0.836	1.000	0.787	0.065
Setting 2	**Flared**	**2.001**	**0.191**	**10.497**	**1.248**	**2.754**	**0.000**	**0.753**	**2.595**
Setting 3	Setting 4	0.009	0.199	0.045	-0.778	0.796	1.000	0.787	0.012
Setting 3	**Flared**	**1.960**	**0.191**	**10.283**	**1.207**	**2.713**	**0.000**	**0.753**	**2.542**
Setting 4	**Flared**	**1.951**	**0.191**	**10.236**	**1.198**	**2.704**	**0.000**	**0.753**	**2.530**

Table B-9: Subject 9 Tukey-Kramer Results for 100% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	*21.874*	*18*	*27.382*		
Flared	23.944	15	0.363		
Setting 4	23.973	15	2.619		
Setting 3	24.480	15	9.815		
Setting 2	24.152	15	3.162		
		78	43.341	73	3.956

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**2.277**	**0.190**	**11.957**	**1.524**	**3.031**	**0.000**	**0.753**	**2.956**
Standard	**Setting 3**	**2.606**	**0.190**	**13.680**	**1.852**	**3.359**	**0.000**	**0.753**	**3.382**
Standard	**Setting 4**	**2.098**	**0.190**	**11.016**	**1.345**	**2.852**	**0.000**	**0.753**	**2.723**
Standard	**Flared**	**2.070**	**0.190**	**10.868**	**1.317**	**2.824**	**0.000**	**0.753**	**2.687**
Setting 2	Setting 3	0.328	0.199	1.650	-0.459	1.115	0.770	0.787	0.426
Setting 2	Setting 4	0.179	0.199	0.900	-0.608	0.966	0.969	0.787	0.232
Setting 2	Flared	0.207	0.199	1.042	-0.580	0.994	0.947	0.787	0.269
Setting 3	Setting 4	0.507	0.199	2.550	-0.280	1.294	0.380	0.787	0.659
Setting 3	Flared	0.536	0.199	2.692	-0.251	1.323	0.325	0.787	0.695
Setting 4	Flared	0.028	0.199	0.142	-0.759	0.815	1.000	0.787	0.037

B.2 100% Nasal Flow and POC Setting 4

The FiO_2 values collected for individual breaths during each 100% nasal flow POC setting 4 breathing simulation are summarized in Table B-10 through Table B-12. The mean values in each of these tables are reflected in Figure 3-6.

Table B-10: Subject 2 FiO_2 Values from 100% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	26.09	25.84	25.58	25.58	26.35
2	26.19	25.88	25.46	25.46	26.70
3	26.51	26.04	25.75	25.75	26.39
4	24.42	25.86	25.69	25.69	26.64
5	26.36	26.16	25.67	25.67	26.61
6	26.65	26.40	25.71	25.76	26.42
7	26.70	26.54	26.00	26.85	26.30
8	26.49	26.48	25.82	25.79	26.34
9	27.00	26.64	25.68	25.93	26.43
10	27.19	26.62	25.94	25.56	26.45
11	26.94	25.50	26.52	25.47	26.27
12	26.83	25.59	26.22	25.49	25.05
13	27.00	25.40	26.09	25.66	25.04
14	27.00	25.42	25.55	25.70	24.72
15	26.97	25.61	25.87	25.74	25.15
Mean	26.55	26.00	25.84	25.74	26.06

Table B-11: Subject 6 FiO_2 Values from 100% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	20.92	26.01	26.07	26.73	25.55
2	20.82	26.18	26.25	26.42	25.85
3	20.89	26.49	26.40	26.81	25.97
4	20.91	27.05	26.27	27.19	25.95
5	20.82	26.30	26.45	27.04	26.33
6	20.95	25.28	26.58	26.32	26.81
7	20.88	26.50	26.75	26.33	26.43
8	21.17	24.68	26.75	26.36	26.93
9	21.39	25.46	26.47	26.71	26.71
10	22.36	26.13	26.68	26.70	26.94
11	24.36	26.35	25.43	26.29	25.53
12	25.28	26.29	25.59	26.34	25.58
13	25.97	26.94	25.79	26.42	25.81
14	21.03	26.82	25.94	26.57	26.25
15	26.46	21.64	26.03	26.54	26.15
16	21.52	21.23	-	-	-
17	21.42	21.08	-	-	-
18	21.27	21.04	-	-	-
Mean	22.13	25.08	26.23	26.58	26.19

Table B-12: Subject 9 FiO_2 Values from 100% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 4	Setting 3	Setting 2
1	21.86	21.20	26.07	26.95	26.78
2	23.34	22.98	26.19	26.76	26.42
3	24.29	25.41	25.62	26.75	26.68
4	25.49	26.33	26.01	26.67	26.76
5	27.06	26.60	26.29	26.97	26.68
6	25.31	26.53	26.81	27.74	27.50
7	22.10	21.89	26.54	28.49	27.07
8	21.84	21.40	26.53	27.48	26.99
9	21.64	21.24	26.44	27.66	26.67
10	21.46	21.20	26.41	27.34	26.73
11	21.40	21.13	26.31	27.28	26.63
12	21.24	21.10	26.33	27.06	26.79
13	21.18	21.21	26.40	26.69	26.55

14	21.15	21.07	26.51	27.22	26.93
15	21.07	21.03	26.40	26.85	26.95
16	21.09	21.05	-	-	-
17	21.16	21.12	-	-	-
18	22.09	21.46	-	-	-
Mean	22.49	22.44	26.32	27.19	26.81

After splitting the data shown in Table B-10 through Table B-12 based on subject number, one-way ANOVAs were conducted where cannula/interface setting was the independent variable and FiO_2 was the dependent variable. The one-way ANOVA results are shown in Table B-13 through Table B-15.

Table B-13: Subject 2 One-way ANOVA Results for 100% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	15	398.345	26.556	0.454	6.361	0.132	26.293	26.820
Flared Cannula	15	*389.975*	*25.998*	*0.202*	*2.829*	*0.132*	*25.735*	*26.262*
Setting 4	15	387.554	25.837	0.079	1.100	0.132	25.573	26.101
Setting 3	15	386.097	25.740	0.111	1.559	0.132	25.476	26.004
Setting 2	15	390.857	26.057	0.466	6.522	0.132	25.793	26.321
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	6.000	4	1.500	5.716	4.87E-04	2.503	0.617	0.201
Within Groups	18.371	70	0.262					
Total	24.371	74	0.329					

Table B-14: Subject 6 One-way ANOVA Results for 100% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	398.427	22.135	3.742	63.621	0.333	21.471	22.799
Flared Cannula	18	451.467	25.081	4.789	81.413	0.333	24.418	25.745
Setting 4	15	393.459	26.231	0.171	2.394	0.365	25.503	26.958
Setting 3	15	*398.762*	*26.584*	*0.076*	1.064	0.365	25.857	27.311
Setting 2	15	392.791	26.186	0.246	3.439	0.365	25.459	26.913
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*

Between Groups	228.134	4	57.033	28.530	1.76E-14	2.492	1.292	0.576
Within Groups	151.929	76	1.999					
Total	380.063	80	4.751					

Table B-15: Subject 9 One-way ANOVA Results for 100% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	*404.763*	*22.487*	*3.334*	*56.680*	*0.320*	*21.850*	*23.124*
Flared Cannula	18	403.964	22.442	4.574	77.750	0.320	21.805	23.079
Setting 4	15	394.852	26.323	0.077	1.081	0.350	25.626	27.021
Setting 3	15	407.918	27.195	0.249	3.481	0.350	26.497	27.892
Setting 2	15	402.138	26.809	0.067	0.933	0.350	26.111	27.507
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	*377.451*	*4*	*94.363*	*51.253*	*7.55E-21*	*2.492*	*1.755*	*0.713*
Within Groups	139.926	76	1.841					
Total	517.377	80	6.467					

The results from the one-way ANOVAs show that significant differences in FiO_2 due to cannula setting are present for all subjects. Tukey-Kramer tests were conducted to further investigate the differences between cannula setting groups within each subject number category. Tukey-Kramer test results are summarized in Table B-16 through Table B-18. Comparisons showing significant differences are bolded.

Table B-16: Subject 2 Tukey-Kramer Results for 100% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	26.556	15	6.361		
Flared	25.998	15	2.829		
Setting 4	25.837	15	1.100		
Setting 3	25.740	15	1.559		
Setting 2	26.057	15	6.522		
		75	*18.371*	*70*	*3.960*

Q TEST									
group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	Setting 2	0.499	0.132	*3.774*	*-0.025*	*1.023*	*0.069*	*0.524*	*0.975*

Standard	**Setting 3**	**0.817**	**0.132**	***6.173***	***0.293***	***1.340***	***0.000***	***0.524***	***1.594***
Standard	**Setting 4**	**0.719**	**0.132**	***5.439***	***0.196***	***1.243***	***0.002***	***0.524***	***1.404***
Standard	**Flared**	**0.558**	**0.132**	***4.219***	***0.034***	***1.082***	***0.031***	***0.524***	***1.089***
Setting 2	Setting 3	0.317	0.132	*2.399*	*-0.206*	*0.841*	*0.443*	*0.524*	*0.619*
Setting 2	Setting 4	0.220	0.132	*1.665*	*-0.304*	*0.744*	*0.764*	*0.524*	*0.430*
Setting 2	Flared	0.059	0.132	*0.444*	*-0.465*	*0.583*	*0.998*	*0.524*	*0.115*
Setting 3	Setting 4	0.097	0.132	*0.735*	*-0.427*	*0.621*	*0.985*	*0.524*	*0.190*
Setting 3	Flared	0.259	0.132	*1.955*	*-0.265*	*0.782*	*0.641*	*0.524*	*0.505*
Setting 4	Flared	0.161	0.132	*1.220*	*-0.362*	*0.685*	*0.909*	*0.524*	*0.315*

Table B-17: Subject 6 Tukey-Kramer Results for 100% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	22.135	18	63.621		
Flared	25.081	18	81.413		
Setting 4	26.231	15	2.394		
Setting 3	26.584	15	1.064		
Setting 2	26.186	15	3.439		
		81	151.93	76	3.952

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**4.051**	**0.350**	**11.591**	**2.670**	**5.432**	**0.000**	**1.381**	**2.865**
Standard	**Setting 3**	**4.449**	**0.350**	**12.730**	**3.068**	**5.831**	**0.000**	**1.381**	**3.147**
Standard	**Setting 4**	**4.096**	**0.350**	**11.718**	**2.715**	**5.477**	**0.000**	**1.381**	**2.897**
Standard	**Flared**	***2.947***	***0.333***	**8.842**	**1.630**	**4.264**	**0.000**	**1.317**	**2.084**
Setting 2	Setting 3	0.398	0.365	1.091	-1.045	1.841	0.938	1.443	0.282
Setting 2	Setting 4	0.045	0.365	0.122	-1.398	1.487	1.000	1.443	0.031
Setting 2	Flared	1.105	0.350	3.160	-0.277	2.486	0.178	1.381	0.781
Setting 3	Setting 4	0.354	0.365	0.969	-1.089	1.796	0.959	1.443	0.250
Setting 3	**Flared**	**1.503**	**0.350**	**4.299**	**0.121**	**2.884**	**0.026**	**1.381**	**1.063**
Setting 4	Flared	1.149	0.350	3.288	-0.232	2.530	0.148	1.381	0.813

Table B-18: Subject 9 Tukey-Kramer Results for 100% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	*22.487*	*18*	*56.680*		
Flared	22.442	18	77.750		
Setting 4	26.323	15	1.081		
Setting 3	27.195	15	3.481		

Setting 2	26.809	15	0.933		
		81	139.93	76	3.952

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	***4.322***	***0.335***	***12.886***	***2.997***	***5.648***	***0.000***	***1.326***	***3.186***
Standard	**Setting 3**	**4.708**	**0.335**	***14.035***	***3.382***	***6.033***	***0.000***	***1.326***	***3.470***
Standard	**Setting 4**	**3.837**	**0.335**	***11.438***	***2.511***	***5.162***	***0.000***	***1.326***	***2.828***
Standard	Flared	0.044	0.320	*0.139*	*-1.219*	*1.308*	*1.000*	*1.264*	*0.033*
Setting 2	Setting 3	0.385	0.350	*1.100*	*-0.999*	*1.770*	*0.936*	*1.384*	*0.284*
Setting 2	Setting 4	0.486	0.350	*1.386*	*-0.899*	*1.870*	*0.863*	*1.384*	*0.358*
Setting 2	**Flared**	**4.367**	**0.335**	***13.018***	***3.041***	***5.692***	***0.000***	***1.326***	***3.218***
Setting 3	Setting 4	0.871	0.350	*2.486*	*-0.513*	*2.256*	*0.405*	*1.384*	*0.642*
Setting 3	**Flared**	**4.752**	**0.335**	***14.167***	***3.427***	***6.078***	***0.000***	***1.326***	***3.502***
Setting 4	**Flared**	**3.881**	**0.335**	***11.570***	***2.556***	***5.207***	***0.000***	***1.326***	***2.860***

B.3 45% Nasal Flow and POC Setting 2

The FiO_2 values collected for individual breaths during each 45% nasal flow POC setting 2 breathing simulation are summarized in Table B-19 through Table B-21. The mean values in each of these tables are reflected in Figure 3-7.

Table B-19: Subject 2 FiO_2 Values from 45% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1
1	21.61	21.80	21.85	27.50	31.09
2	21.49	21.77	21.89	27.56	29.89
3	21.63	21.51	21.81	27.74	29.68
4	21.40	21.46	21.79	27.55	29.66
5	21.37	21.42	21.88	27.71	29.41
6	25.23	21.44	23.07	27.65	29.44
7	20.84	21.35	24.38	27.84	29.62
8	21.51	21.65	26.15	27.78	29.61
9	21.44	23.43	26.71	27.98	30.21
10	21.42	25.91	21.53	27.91	29.96
11	21.27	27.72	22.02	28.38	30.21
12	21.21	27.71	21.91	28.30	30.19
13	21.44	21.65	21.73	28.13	30.16
14	21.80	21.80	21.63	28.50	30.20
15	23.70	21.57	21.68	28.53	29.99

16	25.42	21.58	21.53	-	-
17	27.16	22.12	21.66	-	-
18	28.51	21.61	22.81	-	-
Mean	22.69	22.64	22.56	27.94	29.95

Table B-20: Subject 6 FiO_2 Values from 45% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1
1	21.49	21.56	21.84	28.47	30.47
2	21.54	21.54	22.83	28.69	29.98
3	21.44	21.48	25.03	28.44	30.78
4	21.70	21.48	28.44	29.05	29.44
5	22.26	21.56	27.19	28.93	28.98
6	23.20	22.48	28.97	29.20	29.76
7	24.52	25.04	28.40	28.97	29.28
8	26.18	27.04	28.50	28.85	29.53
9	26.45	28.50	28.66	29.06	29.16
10	21.89	24.04	27.53	28.96	29.62
11	21.65	22.05	21.22	28.27	29.82
12	21.59	21.82	21.14	28.23	30.10
13	21.54	21.61	21.08	28.47	29.84
14	21.61	21.65	21.08	28.52	29.77
15	21.50	21.55	20.73	28.44	28.09
16	21.83	21.51	21.17	-	-
17	22.51	21.56	21.15	-	-
18	23.21	20.86	28.47	-	-
Mean	22.56	22.63	24.64	28.70	29.64

Table B-21: Subject 9 FiO_2 Values from 45% Nasal Flow POC Setting 2 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1
1	21.57	21.84	21.17	27.00	28.22
2	21.61	21.79	21.21	27.46	28.68
3	21.41	21.65	21.22	27.41	27.85
4	21.43	21.57	21.84	27.30	27.86
5	21.43	21.66	22.83	27.85	27.62
6	21.81	21.71	25.03	27.58	28.46
7	22.50	21.78	28.44	28.01	29.31
8	23.71	21.84	27.19	27.74	28.76
9	24.42	21.65	28.97	28.31	28.98

10	24.47	21.47	28.40	28.62	28.75
11	21.15	23.48	28.50	28.59	29.67
12	21.15	24.80	28.66	28.97	28.93
13	21.30	25.75	27.53	29.17	29.45
14	30.12	27.01	21.22	28.69	28.99
15	22.85	27.10	21.14	28.79	28.92
16	22.59	24.25	21.08	-	-
17	20.97	22.13	21.08	-	-
18	20.28	21.03	21.09	-	-
Mean	22.49	22.92	24.26	28.10	28.70

After splitting the data shown in Table B-19 through Table B-21 based on subject number, one-way ANOVAs were conducted where cannula/interface setting was the independent variable and FiO_2 was the dependent variable. The one-way ANOVA results are shown in Table B-22 through Table B-24.

Table B-22: Subject 2 One-way ANOVA Results for 45% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	408.425	22.690	5.322	90.467	0.389	21.917	23.464
Flared Cannula	18	407.489	22.638	4.577	77.811	0.389	21.865	23.412
Setting 3	18	406.040	22.558	2.486	42.265	0.389	21.784	23.331
Setting 2	15	419.047	27.936	0.123	1.724	0.426	27.089	28.784
Setting 1	15	449.319	29.955	0.182	2.553	0.426	29.107	30.802
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	800.23	4	200.058	73.571	7.38E-26	2.487	2.142	0.776
Within Groups	214.82	79	2.719					
Total	1015.1	83	12.230					

Table B-23: Subject 6 One-way ANOVA Results for 45% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	406.106	22.561	2.532	43.042	0.486	21.594	23.528
Flared Cannula	18	407.336	22.630	4.567	77.631	0.486	21.663	23.597
Setting 3	18	443.434	24.635	12.230	207.911	0.486	23.668	25.602

Setting 2	15	430.557	28.704	0.100	1.401	0.532	27.644	29.763
Setting 1	15	444.612	29.641	0.404	5.657	0.532	28.581	30.700

ANOVA Results

Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	727.16	4	181.790	42.788	4.73E-19	2.487	1.626	0.666
Within Groups	335.64	79	4.249					
Total	1062.8	83	12.805					

Table B-24: Subject 9 One-way ANOVA Results for 45% Nasal Flow POC Setting 2 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	404.769	22.487	5.013	85.215	0.505	21.481	23.493
Flared Cannula	18	412.519	22.918	3.949	67.129	0.505	21.912	23.924
Setting 3	18	436.592	24.255	11.723	199.289	0.505	23.249	25.261
Setting 2	15	421.485	28.099	0.463	6.479	0.554	26.997	29.201
Setting 1	15	430.454	28.697	0.359	5.030	0.554	27.595	29.799

ANOVA Results

Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	550.355	4	137.59	29.932	3.71E-15	2.487	1.361	0.579
Within Groups	363.142	79	4.597					
Total	913.497	83	11.006					

The results from the one-way ANOVAs show that significant differences in FiO_2 due to cannula setting are present for all subjects. Tukey-Kramer tests were conducted to further investigate the differences between cannula setting groups within each subject number category. Tukey-Kramer test results are summarized in Table B-25 through Table B-27. Comparisons showing significant differences are bolded.

Table B-25: Subject 2 Tukey-Kramer Results for 45% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	22.690	18	90.467		
Flared	22.638	18	77.811		
Setting 3	22.558	18	42.265		
Setting 2	27.936	15	1.724		

Setting 1	29.955	15	2.553		
		84	*214.82*	*79*	*3.948*

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**5.246**	**0.408**	**12.87**	**3.637**	**6.856**	**0.000**	**1.609**	**3.181**
Standard	Setting 3	0.133	0.389	0.341	-1.402	1.667	0.999	1.535	0.080
Standard	**Setting 1**	**7.264**	**0.408**	**17.82**	**5.655**	**8.874**	**0.000**	**1.609**	**4.405**
Standard	Flared	0.052	0.389	0.134	-1.483	1.587	1.000	1.535	0.032
Setting 2	**Setting 3**	**5.379**	**0.408**	**13.19**	**3.769**	**6.988**	**0.000**	**1.609**	**3.262**
Setting 2	**Setting 1**	***2.018***	***0.426***	**4.740**	**0.337**	**3.699**	**0.011**	**1.681**	**1.224**
Setting 2	**Flared**	**5.298**	**0.408**	**12.98**	**3.689**	**6.908**	**0.000**	**1.609**	**3.213**
Setting 3	**Setting 1**	**7.397**	**0.408**	**18.15**	**5.787**	**9.006**	**0.000**	**1.609**	**4.486**
Setting 3	Flared	0.081	0.389	0.207	-1.454	1.615	1.000	1.535	0.049
Setting 1	**Flared**	**7.316**	**0.408**	**17.95**	**5.707**	**8.926**	**0.000**	**1.609**	**4.437**

Table B-26: Subject 6 Tukey-Kramer Results for 45% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	22.561	18	43.042		
Flared	22.630	18	77.631		
Setting 3	24.635	18	207.91		
Setting 2	28.704	15	1.401		
Setting 1	29.641	15	5.657		
		84	342.74	79	3.948

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**6.142**	**0.510**	**12.055**	**4.131**	**8.154**	**0.000**	**2.012**	**2.980**
Standard	**Setting 3**	**2.074**	**0.486**	**4.269**	**0.156**	**3.992**	**0.027**	**1.918**	**1.006**
Standard	**Setting 1**	**7.079**	**0.510**	**13.893**	**5.068**	**9.091**	**0.000**	**2.012**	**3.435**
Standard	Flared	0.068	0.486	0.141	-1.850	1.986	1.000	1.918	0.033
Setting 2	**Setting 3**	**4.069**	**0.510**	**7.985**	**2.057**	**6.080**	**0.000**	**2.012**	**1.974**
Setting 2	Setting 1	0.937	0.532	1.761	-1.164	3.038	0.725	2.101	0.455
Setting 2	**Flared**	**6.074**	**0.510**	**11.920**	**4.062**	**8.086**	**0.000**	**2.012**	**2.947**
Setting 3	**Setting 1**	**5.006**	**0.510**	**9.824**	**2.994**	**7.017**	**0.000**	**2.012**	**2.428**
Setting 3	**Flared**	**2.005**	**0.486**	**4.128**	**0.087**	**3.924**	**0.036**	**1.918**	**0.973**
Setting 1	**Flared**	**7.011**	**0.510**	**13.759**	**4.999**	**9.023**	**0.000**	**2.012**	**3.401**

Table B-27: Subject 9 Tukey-Kramer Results for 45% Nasal Flow POC Setting 2 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	22.487	18	85.215		
Flared	22.918	18	67.129		
Setting 3	24.255	18	199.29		
Setting 2	28.099	15	6.479		
Setting 1	28.697	15	5.030		
		84	363.14	79	3.948

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**5.612**	**0.530**	**10.588**	**3.519**	**7.704**	**0.000**	**2.093**	**2.617**
Standard	**Setting 3**	1.768	0.505	3.498	-0.227	3.763	0.107	1.995	0.825
Standard	**Setting 1**	**6.210**	**0.530**	**11.716**	**4.117**	**8.302**	**0.000**	**2.093**	**2.896**
Standard	Flared	0.431	0.505	0.852	-1.565	2.426	0.974	1.995	0.201
Setting 2	**Setting 3**	**3.844**	**0.530**	**7.252**	**1.751**	**5.936**	**0.000**	**2.093**	**1.793**
Setting 2	Setting 1	0.598	0.554	1.080	-1.588	2.784	0.940	2.186	0.279
Setting 2	**Flared**	**5.181**	**0.530**	**9.776**	**3.089**	**7.274**	**0.000**	**2.093**	**2.417**
Setting 3	**Setting 1**	**4.442**	**0.530**	**8.381**	**2.349**	**6.534**	**0.000**	**2.093**	**2.072**
Setting 3	Flared	1.337	0.505	2.647	-0.658	3.333	0.341	1.995	0.624
Setting 1	**Flared**	**5.779**	**0.530**	**10.904**	**3.687**	**7.872**	**0.000**	**2.093**	**2.696**

B.4 45% Nasal Flow and POC Setting 4

The FiO_2 values collected for individual breaths during each 45% nasal flow POC setting 4 breathing simulation are summarized in Table B-28 through Table B-30. The mean values in each of these tables are reflected in Figure 3-7.

Table B-28: Subject 2 FiO_2 Values from 45% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1
1	22.69	23.02	22.60	30.76	31.80
2	22.58	23.32	22.63	31.51	32.28
3	22.61	23.19	22.48	32.26	32.66
4	22.59	22.95	22.61	32.39	33.10
5	23.23	22.86	23.67	32.30	33.99
6	25.64	26.87	25.66	35.46	33.14
7	28.89	32.29	28.84	34.67	33.22

8	33.65	35.76	30.36	34.93	34.14
9	32.69	32.93	23.03	35.39	34.85
10	23.05	23.45	22.64	35.53	35.12
11	22.61	22.96	22.46	32.33	32.03
12	22.36	22.81	22.32	32.86	32.84
13	22.22	22.69	22.16	33.19	32.68
14	22.18	22.77	22.10	33.49	33.26
15	22.29	22.34	22.12	34.21	33.16
16	22.19	22.53	22.03	-	-
17	22.21	22.62	23.00	-	-
18	25.16	24.10	24.93	-	-
Mean	24.38	24.97	23.65	33.42	33.21

Table B-29: Subject 6 FiO_2 Values from 45% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1
1	20.96	23.75	21.98	34.70	34.72
2	20.94	23.46	21.98	34.77	35.24
3	20.89	20.09	21.87	34.29	36.40
4	20.91	23.49	21.92	34.26	36.55
5	20.99	24.88	23.32	34.90	36.54
6	21.14	28.18	30.46	35.54	33.63
7	21.75	34.07	32.14	35.46	34.56
8	22.73	35.87	23.27	35.60	34.61
9	24.38	28.34	22.36	35.23	35.28
10	27.14	23.93	22.00	35.52	35.31
11	28.89	23.24	21.80	35.78	34.22
12	27.17	23.17	21.70	35.93	34.17
13	21.67	22.89	21.69	36.24	34.38
14	21.22	22.79	21.77	36.24	34.60
15	21.30	22.93	21.73	36.18	35.11
16	21.26	22.86	21.79	-	-
17	20.98	23.11	23.24	-	-
18	20.13	24.62	25.88	-	-
Mean	22.50	25.09	23.38	35.38	35.02

Table B-30: Subject 9 FiO_2 Values from 45% Nasal Flow POC Setting 4 Trials

Breath #	Standard	Flared	Setting 3	Setting 2	Setting 1

1	22.01	23.18	24.01	36.09	37.08
2	21.94	23.12	23.43	36.37	36.64
3	21.86	23.08	23.35	36.23	37.76
4	21.93	22.94	23.12	36.11	37.17
5	21.95	22.79	22.95	35.88	37.74
6	21.87	24.70	23.09	34.33	34.75
7	22.10	28.57	23.77	33.94	33.75
8	22.23	33.29	25.42	34.00	33.93
9	24.51	33.06	26.99	34.43	33.12
10	28.47	28.00	29.74	34.93	33.12
11	31.16	23.64	30.99	35.59	38.69
12	24.09	24.58	23.09	35.88	38.74
13	22.31	23.26	23.06	36.00	38.73
14	22.01	23.15	25.74	35.58	39.10
15	21.92	23.15	22.14	36.07	39.61
16	21.95	22.77	22.30	-	-
17	21.79	21.78	22.03	-	-
18	20.28	19.67	22.25	-	-
Mean	23.02	24.71	24.31	35.43	36.66

After splitting the data shown in Table B-28 through Table B-30 based on subject number, one-way ANOVAs were conducted where cannula/interface setting was the independent variable and FiO_2 was the dependent variable. The one-way ANOVA results are shown in Table B-31 through Table B-33.

Table B-31: Subject 2 One-way ANOVA Results for 45% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	438.846	24.380	13.154	223.611	0.682	23.023	25.738
Flared Cannula	18	449.438	24.969	17.374	295.363	0.682	23.611	26.327
Setting 3	18	425.650	23.647	5.704	96.976	0.682	22.289	25.005
Setting 2	15	501.261	33.417	2.352	32.922	0.747	31.930	34.905
Setting 1	15	498.269	33.218	0.914	12.799	0.747	31.731	34.705
ANOVA Results								
Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	1573.21	4	393.303	46.958	3.80E-20	2.487	1.708	0.686

Within Groups	661.67	79	8.376
Total	2234.88	83	26.926

Table B-32: Subject 6 One-way ANOVA Results for 45% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	404.452	22.470	6.799	115.584	0.625	21.226	23.713
Flared Cannula	18	451.670	25.093	16.552	281.380	0.636	23.827	26.358
Setting 3	18	420.914	23.384	9.437	160.422	0.625	22.141	24.627
Setting 2	15	530.648	35.377	0.444	6.209	0.684	34.015	36.738
Setting 1	15	525.297	35.020	0.796	11.139	0.684	33.658	36.382

ANOVA Results

Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	2637.25	4	659.31	90.626	1.01E-28	2.487	2.372	0.810
Within Groups	574.73	79	7.275					
Total	3211.98	83	38.699					

Table B-33: Subject 9 One-way ANOVA Results for 45% Nasal Flow POC Setting 4 Trials

group	*count*	*sum*	*mean*	*variance*	*ss*	*std err*	*lower*	*upper*
Standard Cannula	18	414.411	23.023	7.107	120.814	0.621	21.788	24.258
Flared Cannula	18	444.724	24.707	13.483	229.216	0.621	23.472	25.942
Setting 3	18	437.495	24.305	6.625	112.627	0.621	23.070	25.541
Setting 2	15	531.437	35.429	0.736	10.301	0.680	34.076	36.782
Setting 1	15	549.937	36.662	5.339	74.748	0.680	35.309	38.016

ANOVA Results

Sources	*ss*	*df*	*MS*	*F*	***p-value***	*F crit*	*RMSSE*	*omega sq*
Between Groups	2832.22	4	708.06	102.129	2.06E-30	2.487	2.520	0.828
Within Groups	547.71	79	6.933					
Total	3379.93	83	40.722					

The results from the one-way ANOVAs show that significant differences in FiO_2 due to cannula setting are present for all subjects. Tukey-Kramer tests were conducted to further investigate the differences between cannula setting groups within each subject number category. Tukey-Kramer test results are summarized in Table B-34 through Table B-36. Comparisons showing significant differences are bolded.

Table B-34: Subject 2 Tukey-Kramer Results for 45% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	24.380	18	223.611		
Flared	24.969	18	295.363		
Setting 3	23.647	18	96.976		
Setting 2	33.417	15	32.922		
Setting 1	33.218	15	12.799		
		84	661.672	79	3.948

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**9.037**	**0.715**	**12.632**	**6.212**	**11.862**	**0.000**	**2.825**	**3.123**
Standard	Setting 3	0.733	0.682	1.075	-1.960	3.426	0.941	2.693	0.253
Standard	**Setting 1**	**8.838**	**0.715**	**12.353**	**6.013**	**11.662**	**0.000**	**2.825**	**3.054**
Standard	Flared	0.588	0.682	0.863	-2.105	3.282	0.973	2.693	0.203
Setting 2	**Setting 3**	**9.770**	**0.715**	**13.656**	**6.946**	**12.595**	**0.000**	**2.825**	**3.376**
Setting 2	Setting 1	0.199	0.747	0.267	-2.751	3.150	1.000	2.950	0.069
Setting 2	**Flared**	**8.449**	**0.715**	**11.809**	**5.624**	**11.273**	**0.000**	**2.825**	**2.919**
Setting 3	**Setting 1**	**9.571**	**0.715**	**13.378**	**6.746**	**12.395**	**0.000**	**2.825**	**3.307**
Setting 3	Flared	1.322	0.682	1.937	-1.372	4.015	0.649	2.693	0.457
Setting 1	**Flared**	**8.249**	**0.715**	**11.530**	**5.425**	**11.074**	**0.000**	**2.825**	**2.850**

Table B-35: Subject 6 Tukey-Kramer Results for 45% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	22.470	18	115.584		
Flared	25.093	18	281.380		
Setting 3	23.384	18	160.422		
Setting 2	35.377	15	6.209		
Setting 1	35.020	15	11.139		
		84	574.734	79	3.948

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**12.90**	**0.667**	**19.357**	**10.274**	**15.539**	**0.000**	**2.633**	**4.785**
Standard	Setting 3	0.915	0.636	1.439	-1.595	3.425	0.847	2.510	0.339
Standard	**Setting 1**	**12.55**	**0.667**	**18.822**	**9.918**	**15.183**	**0.000**	**2.633**	**4.653**
Standard	**Flared**	**2.623**	**0.636**	**4.126**	**0.113**	**5.133**	**0.036**	**2.510**	**0.973**
Setting 2	**Setting 3**	**11.99**	**0.667**	**17.986**	**9.360**	**14.625**	**0.000**	**2.633**	**4.446**
Setting 2	Setting 1	0.357	0.696	0.512	-2.393	3.106	0.996	2.750	0.132

Setting 2	**Flared**	**10.28**	**0.667**	**15.423**	**7.651**	**12.916**	**0.000**	**2.633**	**3.813**
Setting 3	**Setting 1**	**11.64**	**0.667**	**17.451**	**9.003**	**14.268**	**0.000**	**2.633**	**4.314**
Setting 3	Flared	1.709	0.636	2.688	-0.801	4.219	0.326	2.510	0.633
Setting 1	**Flared**	**9.927**	**0.667**	**14.888**	**7.295**	**12.560**	**0.000**	**2.633**	**3.680**

Table B-36: Subject 9 Tukey-Kramer Results for 45% Nasal Flow POC Setting 4 Trials

group	*mean*	*n*	*ss*	*df*	*q-crit*
Standard	23.023	18	120.814		
Flared	24.707	18	229.216		
Setting 3	24.305	18	112.627		
Setting 2	35.429	15	10.301		
Setting 1	36.662	15	74.748		
		84	547.705	79	3.948

Q TEST

group 1	*group 2*	*mean*	*std err*	*q-stat*	*lower*	*upper*	*p-value*	*mean-crit*	*cohen d*
Standard	**Setting 2**	**12.41**	**0.651**	**19.060**	**9.836**	**14.976**	**0.000**	**2.570**	**4.712**
Standard	Setting 3	1.282	0.621	2.066	-1.168	3.733	0.590	2.450	0.487
Standard	**Setting 1**	**13.64**	**0.651**	**20.955**	**11.070**	**16.209**	**0.000**	**2.570**	**5.180**
Standard	Flared	1.684	0.621	2.713	-0.766	4.134	0.316	2.450	0.640
Setting 2	**Setting 3**	**11.12**	**0.651**	**17.090**	**8.554**	**13.694**	**0.000**	**2.570**	**4.225**
Setting 2	Setting 1	1.233	0.680	1.814	-1.451	3.917	0.702	2.684	0.468
Setting 2	**Flared**	**10.72**	**0.651**	**16.473**	**8.152**	**13.292**	**0.000**	**2.570**	**4.072**
Setting 3	**Setting 1**	**12.36**	**0.651**	**18.984**	**9.787**	**14.927**	**0.000**	**2.570**	**4.693**
Setting 3	Flared	0.402	0.621	0.647	-2.049	2.852	0.991	2.450	0.153
Setting 1	**Flared**	**11.96**	**0.651**	**18.368**	**9.386**	**14.525**	**0.000**	**2.570**	**4.541**