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Sleep Apnea: BME 300

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Abstract

Sleep Apnea is a common sleeping disorder that affects over 25 million Americans (1). Due to the complex nature of sleep apnea, and the human body, neither an effective nor comfortable treatment option to sleep apnea has been developed. The goal of this project is to design a successful and novel alternative to continuous positive airway pressure (CPAP) therapy that incorporates dead space rebreathing to induce moderately hypercapnic conditions in systematic blood circulation to eliminate apneic events in obstructive, central, and complex sleep apnea patients. A device was designed and fabricated that increases the partial pressure of end-tidal carbon dioxide ($PETCO_2$) through continuous rebreathing. The design is fashioned from a silicon rubber facemask that covers the mouth and nose, a neoprene outer sleeve that secures the mask to the patient's face, and dead space tubing that attaches to the anterior port of the mask. Qualitative and quantitative testing proved the efficacy of the design to be more comfortable than CPAP, and efficient at sufficiently increasing $PETCO_2$ levels to eliminate apneic events due to obstructive, central, and complex sleep apnea.

Contents

Introduction

Background

Sleep apnea is characterized as a disorder where lapses in breathing, ranging from a few seconds to a few minutes, or otherwise shallow breathing is experienced amidst regular breathing patterns during sleep. Each period of irregular breathing is defined as an apneic episode and a person suffering from sleep apnea can experience as many as 30 or more apneas per hour (8). There are three classes of sleep apnea: obstructive sleep apnea (OSA), central sleep apnea (CSA), and complex sleep apnea (CompSA).

Obstructive sleep apnea is conceptually the simplest of the three. OSA results from occlusion of the airway during sleep due to the collapse of soft tissues in the throat. OSA is most prevalent in overweight individuals, especially those with gratuitous amounts of adipose tissue around their pharyngeal or throat region, but can also be seen in individuals with enlarged tonsils/adenoids or a recessed mandible. This demonstrates that not only is lifestyle a deciding factor in OSA patients, but also genetic, anatomical make up of the respiratory tract (9).

Central sleep apnea, the second class of sleep apnea, results when there is a lapse in communication between the central nervous system and respiratory stimuli. In a CSA apneic event, the brain fails to send signals to the muscles of the chest wall, preventing respiration from occurring. The conditions that lead to CSA are most often from afflictions to the central nervous system, such as: arthritis or degenerative changes in the cervical spine, complications of cervical spinal surgery, neurodegenerative diseases (Parkinson's disease), or stroke. The primary concern in patient's suffering from CSA is their inability to effectively control and monitor changes in carbon dioxide concentration levels in the blood stream when breathing ceases.

The final class of sleep apnea, complex sleep apnea, is also the most recently recognized form. CompSA is classified as a subset of central sleep apnea and is identified by the persistence or emergence of central apneas (hyponeas) upon exposure to continuous positive airway pressure therapies. The cause of CompSA is an area of intense study, and still is not well understood; however, it is surmised that patients experience the airway obstructions of OSA, while also demonstrating central breathing control instabilities which lead to chemo-reflex dysfunction (6). In other words, the central nervous system can no longer effectively monitor the levels of carbon dioxide in the blood stream and maintain regular respiratory cycles. In order for CompSA to persist, a high loop gain is required; a loop gain is defined as the ratio of corrective response to a disturbance. If the corrective response is greater than that of the disturbance (the loop gain is greater than one), then small disturbances are maximized and respiratory oscillations develop. In instances of a high loop gain, breathing quickly becomes unstable and out of control (6).

All three forms of sleep apnea force the subconscious mind to "wake up," reverting the individual to regular breathing patterns after each apneic event. This subconscious restart consistently awakes the individual, destroying any rapid eye movement (REM) sleep cycle they may have had, thus, greatly diminishing the quality of sleep. These erratic sleep patterns result in poorly regulated carbon dioxide and

oxygen concentrations levels, and result in severe health complications such as: daytime fatigue, depression, moodiness, hypertension and heart complications (increasing the individual's risk of stroke), and countless others. On top of all these medical complications, the personal annoyance experienced by sleep apnea patients is unparalleled. Patients often wake up with large snort or chocking sounds as their airway reopens; if the airway isn't completely occluded, loud, continual snoring will persist throughout the night (9).

Obstructive sleep apnea specifically is viewed as an exclusive problem stemming from the anatomy of the airway. As a result, continuous positive airway pressure (CPAP) is prescribed as the sole means to prevent occlusions and allow for regular respiratory patterns. Despite this, there is mounting evidence to suggest that obstructive sleep apnea patients demonstrate very high levels of chemosensitivty, something that can be manipulated to control airway stability and respiratory function (5). Current therapies focus on treating the occlusion of the respiratory tract by forcefully introducing highly pressurized air into the airway to force it open; these therapies completely ignore the underlying causes of these obstructions and sleeping irregularities. Current research focuses on the unconscious regulatory mechanisms of the respiratory system, primarily the stimulation of chemoreceptors by sensitivity to carbon dioxide levels at or near the apneic threshold. Hypercapnic conditions stimulate chemosensitivity, thereby stimulating a ventilator overshoot, which in turn stimulates cessation of respiration due to hypocapnic conditions. The more unstable an individual's breathing patterns are, the greater the ventilation overshoot in response to carbon dioxide accumulation and the greater the ventilation undershoot in response to hypocapnia (5).

Research conducted by Ailiang Xie et al. concluded that increasing respiratory motor output using moderate hypercapnia conditions eliminated obstructive sleep apneic events in patients with a wide range of chemosensitivity. This was achieved through the use of dead space rebreathing; a process that increased levels of carbon dioxide concentration during normal breathing by 4.2 ± 1 mmHg in eupneic $PETCO_2$. Throughout Ailiang's research, her and her team's main focus was on the apnea-hypopnea index (AHI), a measure of the number of apneic episodes per hour. As previously mentioned, Ailiang's research focuses on the mechanisms involved in unconscious sleep regulation (rather than just the patient's anatomy); this demonstrated that induced hypercapnic conditions can prevent apneic events in both obstructive and central sleep apnea patients.

Further examination of experimentation done using hypercapnia treatments demonstrated that in twenty-one patient tests, all by four of those who received dead space rebreathing showed a reduction in the sleep apnea-hypopnea index (AHI) in excess of 30% below control. Seventeen of the twenty-one patients displayed extremely successful results, with a reduction of AHI by 94 ± 3% of control (1).

Upon final review it was concluded that the use of continuous, moderate hypercapnia was effective in the treatment of airway obstruction and effectively stabilized central motor output. It was also noted that moderate hypercapnia also recruited dilating musculature of the upper airway, most likely through stimulation of the hypoglossal nerve. In effect, moderate hypercapnia addresses and reduces the symptoms of both obstructive and central sleep apnea.

Motivation

The available therapies for the three classes of sleep apnea present many problems. First and foremost, most therapies don't demonstrate high reliability rates, meaning most therapies are not effective for a high percentage of patients. For example, CPAP, the industrial gold standard for obstructive sleep apnea patients, has a success rate of only 50% (5). It is believed that these low success rates and low levels of patient adherence to CPAP therapy stems from the obtrusive nature and lack of comfort of the treatment. Conversely, EPAP, a less obtrusive therapy, only demonstrated a success rate of 50.7% in a three month study in which patient adherence to therapy was much higher. Research has shown that one out of every two patients seeking therapy will not get proper treatment from current remedies (3). This inefficiency of current therapies and the severity of sleep apnea and its complementary side effects highlight the need for a new design that will demonstrate higher rates of success in patients.

It is important to design a device that can be universally applied to treat all three forms of sleep apnea, eliminating economical inefficiencies, while still adequately preventing apneic events and maximizing patient comfort.

Problem Statement

Sleep apnea is a common sleeping disorder in which an obstruction of the throat or absence of respiratory response prevents air from entering the lungs. Halted breathing results in increased concentrations of carbon dioxide in the blood stream, resulting in an unconscious, regulatory respiratory response. A device must be designed and fabricated to monitor and maintain carbon dioxide concentration levels during sleep, accordingly adjusting levels to prevent apneas, while also being easy to use, minimally invasive, and universally marketable.

Design Specifications

The proposed design must use carbon dioxide to prevent obstructive, central, and complex forms of sleep apnea by preventing obstruction in the throat and maintaining regular respiratory breathing patterns, while not using positive airway pressure. The design must be comfortable and feasible to the general public, and must be easy to setup and maintain. The device must be adjustable, so as to suit the "shape and size" of all users. The device should be durable, so as to withstand repeated, nightly use and maintain functionality; should the device fail, further breathing difficulty should not arise. The device must remain accurate and effective for the entirety of its life in service. The device should be made of material that is not carbon dioxide permeable and does not react with high concentrations of carbon dioxide; it should be small enough to not be cumbersome or uncomfortable during sleep, and all attachments must be portable. For a full list of design specifications, see Appendix I.

Ethical Considerations

Manufacturing and Testing Considerations

Before providing patients with a device that can effectively treat sleep apnea, the following conditions must be fulfilled. First, the manufacturing process must be consistent. The processes used (procedure, material, testing, etc.) must be constant so as to ensure the safety and security of every device. Second, the testing results must be reproducible (precise) and accurate (by measure against pre-determined standards) to ensure the expected functionality of the device.

Experimental Procedure Considerations

In the United States there are federal laws that protect human subjects in federally funded research; these guidelines are extended to academic institutions to judge the acceptability of human subjects in research. Title 45 part 46 of the Code of Federal Regulations (54 CFR 46) requires that "risks to subjects are reasonable in relation to anticipated benefits" and that "risks to subjects are minimized." In addition, the Declaration of Helsinki (adopted by the World Medical Association in 1964) states, "The benefits, risks, burdens, and effectiveness of a new treatment method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where proven prophylactic, diagnostic or therapeutic method exists….patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option." (4)

Design

Current Therapies

Current therapies for obstructive, central, and complex sleep apnea focus on ameliorating the physiological symptoms of sleep apnea. All current therapies attempt to open the soft tissue of the airway, most often through positive airway pressure, and thereby allow stable breathing without subconscious awakening from rapid eye moment (REM) cycle. There are currently multiple approaches to increase positive airway pressure, including but not limited to continuous positive airway pressure (CPAP), adaptive servo-ventilation (ASV), and expiratory positive airway pressure (EPAP).

Other approaches, while less common, include jaw displacement devices, surgery, and even novel pharmaceuticals. While targeting the direct cause of sleep apnea, closing of the throat and neurological "forgetfulness" to breath, is the primary means to treat apneas, other therapies employ a holistic methodology to treat the associated medical disorders or medication side effects.

Continuous Positive Airway Pressure (CPAP)

Continuous Positive Airway Pressure (CPAP) utilizes a machine that delivers positive air pressure through a facemask during sleep (see Figure 1 below). The air pressure from the mask is greater than the surrounding air, and as a result, the upper airway passages are forced open for the movement of air. Contrary to popular belief, CPAP isn't a ventilator that breathes for the individual; instead it simply keeps the airway open so that the individuals can breath for themselves. Keeping the airway open also prevents snoring, a major complaint of partners of individuals with sleep apnea.

CPAP is the most common and reliable treatment; it is considered the gold standard of sleep apnea therapy. Despite this, many patients find it uncomfortable and cumbersome, reflective of the non-compliance rate of 50% of patients (2). Most often patient dissatisfaction comes from the time and patience required in learning to adjust the CPAP mask, and the noisiness of the built-in humidifier.

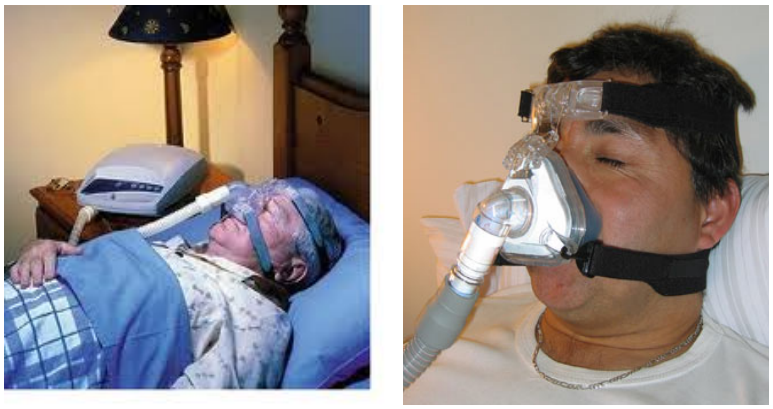


Figure 1: CPAP machine (2).

Adaptive Servo-Ventilation System (ASV)

Adaptive Servo-Ventilation systems use advanced algorithms to monitor, predict, and control respiratory gas levels as well as maintain stable breathing patterns. There are three factors that contribute to these advanced algorithms, including: The patient's most recent, average respiratory rate, the instantaneous rate, direction, and change in patients' airflow, and a backup respiratory rate of 15 breaths per minute (meaning the machine will force air into the lungs if breaths aren't taken.) These features allow for minimal support during stable breathing, however, the moment hypopneas or apneas begin to occur, the machine increases air pressure to stabilize breathing (11).

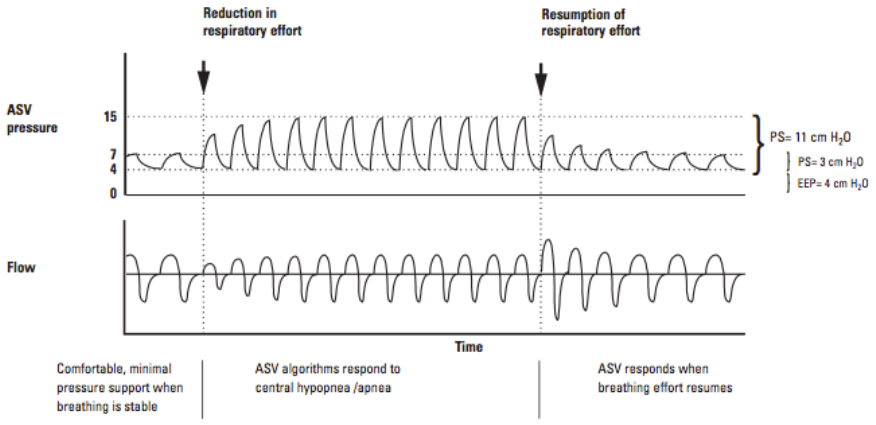


Figure 2: This shows how ASV is constantly monitoring the respiratory cycle in order to compensate for central/complex sleep apnea.

In essence, adaptive servo-ventilation systems ventilate the patient appropriately during periods of hypopneas or apneas, while reducing support during periods of hyperventilation and normal breathing.

Expiratory Positive Airway Pressure (EPAP)

Expiratory Positive Airway Pressure (EPAP) is the most recent therapy to be approved by the FDA. This therapy utilizes small, single use "plugs" that are placed over each nostril before sleeping (see figure 3 below (7)). This device permits air to move in freely, however, it increases air pressure in the dead space upon exhalation, see Figure 4 below (12). The theory is that an increase in dead space airway pressure will keep the throat open, thus, reducing apneic events.

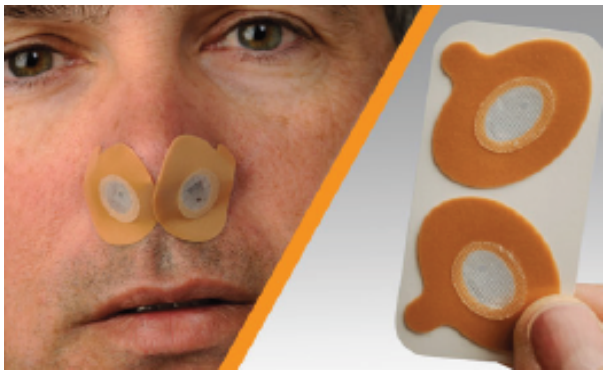


Figure 3: A new therapy for obstructive sleep apnea known as PROVENT.

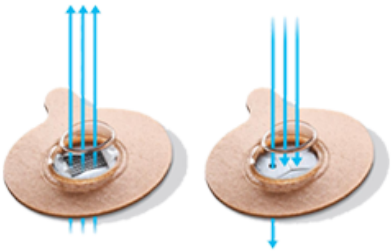


Figure 4: This is the theory behind the PROVENT device, where air can easily entire the device but it can't easily exit, thereby increasing air pressure in the dead space of the respiratory system.

According to a recent study by Kryger et al. over a twelve-month period the number of events per hour was decreased from 15.7 to 4, meaning a decrease of nearly 71.3% (7). Furthermore, snoring was reduced by 74.4% and there was a compliance rate of 89.3% compared to a reported 46 to 83% of patients being *noncompliant* to the traditional CPAP therapy (7, 15).

Surgery

Surgery is a therapy option available to sleep apnea patients that offers limited effectiveness. Surgery is only effective in patients suffering from obstructive sleep apnea, as it only treats the physical occlusion of the airway. The most common type of surgery performed is Uvulopalatopharyngoplasty (UPPP), which involves removing excess tissue of the throat in an attempt to widen the airway (13); such tissues can include the uvula, part of the roof of the mouth or the soft palate, the tonsils, adenoids, and tonsils. (See Figures 5, 6 and 7 below (14).

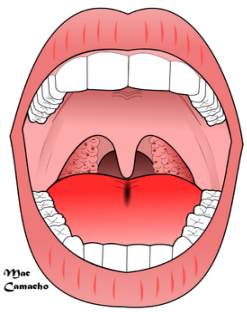


Figure 5: Oral cavity before UPP

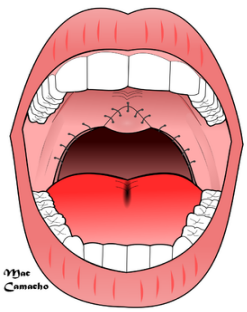


Figure 6: Oral cavity post UPP

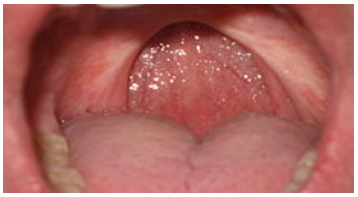


Figure 7: Actual patient post UPP

Maxillomandibular advancement, or MMA, is a more invasive procedure that has proven effective 90% of the time for individuals with recessed chins, small jaws, or airways narrowed by facial structures. This procedure slices the jaw in half and moves it forward in order to open up the airway (see Figures 8 and 9 below (10).

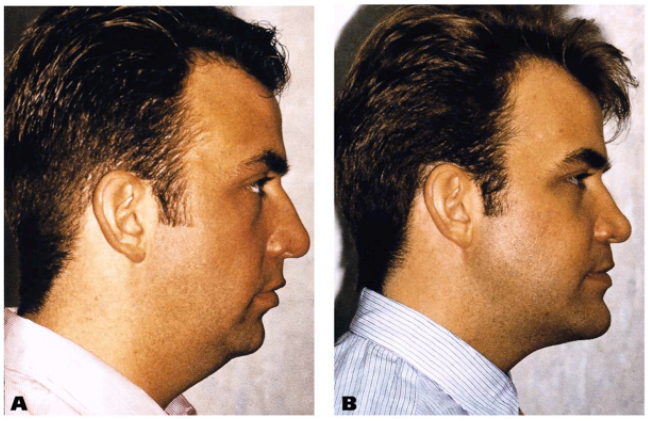


Figure 8: Man before and after MMA (10).

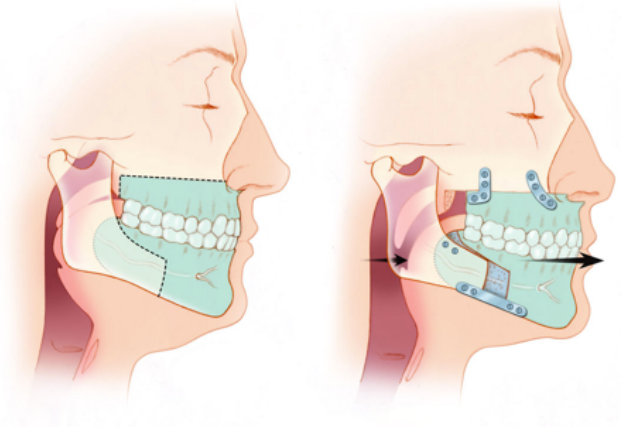


Figure 9: An outline of the MMA procedure showing the upper (maxilla) and lower (mandible) jaws being moved forward, enlarging the airway (10).

Design Alternatives

"Snorkel Mask"

A recent study conducted at University of Wisconsin-Madison's Veteran's Association hospital showed that continuous dead space rebreathing (an increase in anywhere from 2-5 mmHg of carbon dioxide) led to the stabilization of the central respiratory output and prevented airway obstruction in a significant percentage of patients with mild to severe obstructive sleep apnea. This increase in carbon dioxide effectively stopped apneas from occurring during sleep. This design alternative would utilize a "modified snorkel" to increase dead space rebreathing, therefore, increasing carbon dioxide levels and stimulating similar responses to those observed in the University of Wisconsin-Madison's study. The general principle behind this design is not only to prevent apneas by utilizing rebreathable dead space, but also to improve upon the comfort and effectiveness of current CPAP masks.

The concept behind the "snorkel" design is based on two concepts. First, the snorkel increases dead space while minimizing the effort needed to breath. Second, it allows for more comfort during overnight wear (eliminating the mask apparatus used in many CPAP therapies).

This design would utilize the existing nasal mask (or plugs) used in some forms of CPAP therapy, attached to a snorkel mouthpiece. This design allows for breathing to occur through either the mouth or

Figure10: The "Snorkel Mask" design

nose, subject to an increased volume of rebreathable dead space, and an increased level of comfort. The length and diameter of the snorkel tube can be calculated so as to accurately increase levels of carbon dioxide by 2-5 mmHg.

Furthermore, this design would be extremely feasible and very user friendly. This design, unlike current CPAP therapies, does not require any external energy input, and therefore, is extremely versatile and does not involve extensive preparation time before each use. Also, due to the simplicity of this design, it is very user friendly and conveniently portable. The economics involved in production of this design are also an added benefit; because objects very similar to the components of this design already exist, it is understood that molds and methods for making these products already exist, thus, reducing the cost to the customer.

Despite the abundant positive aspects of this design, there are some problems that could potentially arise. One potential problem includes the user opening their mouth excessively wide during sleep. This would result in the user breathing in "outside" air, rather than air from the snorkel. This would effectively eliminate the presence of the extra dead space and potentially result in apneic breathing patterns. Another problem relates to the stability and safety of this design. The design utilizes stability straps, which are intended to hold the device (specifically the mouthpiece) in the same location in the user's mouth the entire night. The problem arises when the user repositions the mouthpiece within their mouth; because of the stability straps, the mouthpiece cannot be removed from the mouth, and thus, the mouthpiece presents a choking hazard. If the user's mouth is open too wide or too much movement of the mouthpiece occurs, this design presents a choking hazard to the user. Despite the potential problems with this design, overall the ability to utilize rebreathable dead space to prevent apneic events in a user friendly, comfortable, feasible manner is a major success.

"Carbon Dioxide Room"

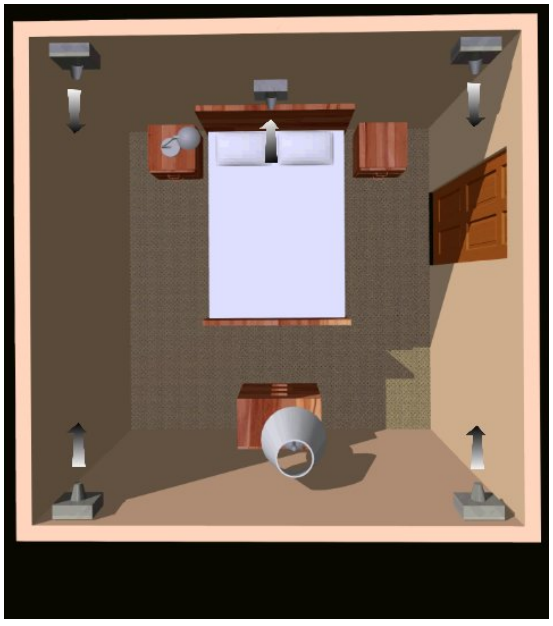


Figure 11: Carbon dioxide room layout

Another possible design alternative would be to consider a design system that eliminates any form of air administration through a facial apparatus or device. This type of design would minimize patient discomfort resulting from the use of an invasive mask, and eliminate any adjusted sleeping patterns due to nightly therapy (5). Also, this type of design would reduce several sanitation concerns such as: cleaning of a facial apparatus on the macroscopic and microscopic level, skin irritation, and other respiratory illnesses.

The concept behind a noninvasive, "non-facial mask" design system is that it incorporates a carbon dioxide enriched "shell" or "surrounding" made from semi-permeable or non-permeable plastic that encompasses the individual. The surrounding acts as a sealed compartment that allows for the administration of carbon dioxide in precise and controllable amounts, so as to

prevent hyper and hypo capnic events (5). A small device within the surrounding would be used to monitor (and maintain) carbon dioxide concentration levels. Reservoirs of compressed carbon dioxide are located near the head of the surrounding, which function to accurately release carbon dioxide when the monitoring device indicates levels are too low. A fan is also located near the head of the surrounding, which functions to release air from inside when the monitoring device indicates carbon dioxide levels are too high. In addition, the surrounding would be attached to a heated humidifier so as to treat any discomfort caused by dry air inhalation during the pressurized sleep apnea treatment, producing a more soothing environment. Due to the complexity and expenses associated with a "surrounding" like this, it is much easier to envision this design system as a room with carbon dioxide reservoirs and fans located throughout.

This noninvasive design system aims to fulfill the demands of unsatisfied CPAP users by eliminating the intrusive characteristics of facial apparatuses. This design maximizes patient comfort through the use of carbon dioxide monitors and pumps in variable locations, and the reduction of sanitation concerns.

Despite the desire for patient comfort, there are several concerns that surround this design. The first is that this design system must ensure that carbon dioxide and oxygen levels inside the system remain at non-life-threatening levels, and can be monitored and adjusted accordingly. Another concern involves the esthetics of this design. It would be impractical for a married couple to sleep together in a single subject's treatment facility. It would also be inconvenient for a patient to have to go through a lengthy procedure in order to enter and exit the treatment environment in the middle of the night. Along with concerns surrounding esthetics, economically this design would be extremely expensive to install and maintain. Despite these concerns, the idea that some people prefer esthetics to functionality supports the principle that a noninvasive treatment using carbon dioxide monitoring devices could be marketable.

"Modified Face Mask"

One final possible design alternative is a design that utilizes an existing CPAP facemask, modifying it slightly to maximize patient comfort. Similar to the snorkel design, this "modified facemask" would use an adjustable dead space attachment at the point where the CPAP facemask previously connected to the external airway tube. The dead space attachment would allow for tubes of adjustable sizes and length, thus, allowing for varying patient conditions. The dead space tubing itself would demonstrate accordion-style functionality, allowing for the tube to fold into the mask for easy storage and portability.

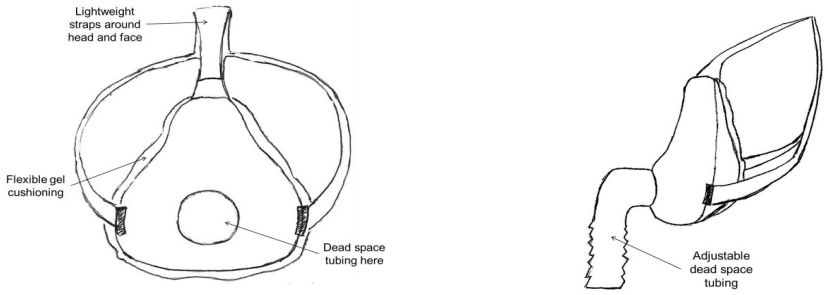


Figure 12: A front view of the modified face mask showing attachment for dead space tubing, gel cushioned perimeter, and the lightweight straps. B. Side view, showing the adjustable dead space tubing.

This design is extremely user friendly in that it would eliminate the annoyance of any bulky and noisy machinery characteristic to CPAP and related therapies. It is also appealing to the user in that this design allows for maximal comfort and flexibility. Modifications have been made to the existing facemask so as to allow for adjustable, lighter, and less invasive cloth straps; the utilization of dead space also eliminates the need for an "airtight" seal between the patient and the facemask, so as to maximize comfort. Another alteration is the option to apply a gel-like coating around the perimeter of the mask so as to minimize facial annoyances. These modifications allow for optimal adjustability, and maximize functionality and comfort.

Not only does this design favor the customer through comfort and functionality, it also favors the customer economically. This design would be easy and inexpensive to manufacture seeing that similar designs (and design components) already exist. Likewise, because similar, extremely functional, facemask designs already exist, the customer should be reasonably confident that a similar facemask design will be analogously functional.

Despite the numerous advantages to this design, there are some disadvantages as well. Because the patient will be repeatedly using the same facemask night after night, there is the potential for the mask itself to become unsanitary. The build up of moisture and bacteria on the inside of the mask can lead to illness or disease if proper sanitary precautions are not taken. One other disadvantage of this design is that it is somewhat obtrusive- it still contains the obtrusive characteristics of a facemask. Although the mask will be more comfortable than others, it still covers the majority of the face, affording the user a hindrance that could potentially be removed unconsciously during sleep.

Design Matrix

The main way in which the three designs were evaluated was through a design matrix (see Figure 13 below). The following categories-listed from most important to least important-were considered: effectiveness, comfort, safety, reliability, cost, ease of use, feasibility, portability. Effectiveness was chosen as the most important category because the final design must not only consistently provide an effective treatment to sleep apnea, but also achieve or exceeds the standards established by current therapies. The carbon dioxide room won the effectiveness category because its noninvasive design eliminates the probability that the user will compromise therapy procedures during sleep. The other two designs were a close second and third, but because of their more obtrusive designs the effectiveness is dependent on the comfort of the user.

Comfort, safety and reliability were listed as the next in order of importance. In order to achieve the goal of creating a more desirable sleep apnea therapy, comfort must be maximized. Current therapies are obtrusive and less effective due to compromised therapeutic methods analogous with patient discomfort. The carbon dioxide room won this category as well for similar reasons as those mentioned in effectiveness; a noninvasive design eliminates device contact with the patient and minimizes discomfort. Behind the carbon dioxide room was the scuba mask; this design utilizes a mouthpiece and light, comfortable straps, again minimizing contact with the user's face. The modified mask falls short because of the face blocking design. The next area of emphasis was safety; safety is of great concern with all the design alternatives. Choking and suffocation hazards are important areas of emphasis in designs that orient near the mouth or nose regions. Because current sleep apnea therapies utilize an FDA regulated

facemask, the similar, modified facemask design won the safety category. The scuba mask ranked second because of the potential choking hazards that accompany any mouth guard or mouth oriented device. The carbon dioxide room received the lowest safety ranking because monitoring and controlling carbon dioxide concentrations within a room setting can be very complex and sometimes imprecise. If conditions are not maintained properly, life-threatening dangers could arise. Equally relevant was the next category of emphasis, reliability. Sleep apnea therapies must be applied repeatedly, night after night, with consistent, successful results. The facemask won this category because of its proven effectiveness with CPAP users. The carbon dioxide room ranked second because (with proper maintenance and calibration) successful conditions can be assumed throughout the duration of therapeutic use. The scuba mask received the lowest rank due to the possibility of the mouth guard relocating or falling out of the patient's mouth during sleep.

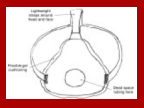
Design / **Criteria (Weight)**	**Scuba Mask** 		**CO_2 Room** 		**Face Mask**  	
Effectiveness (20)	3	12	5	**20**	4	16
Comfort (15)	3	9	5	**15**	2	6
Safety (15)	4	12	1	3	5	**15**
Reliability (15)	2	6	3	9	4	**12**
Cost (10)	2	4	1	2	3	**6**
Ease of Use (10)	4	8	5	**10**	4	8
Feasibility (10)	4	8	1	2	5	**10**
Portability (5)	5	**5**	1	1	5	**5**
Total		64		62		**78**

Figure 13: Design matrix

The next three categories, all carrying equal importance, were cost, ease of use, and feasibility. Cost is an extremely important consideration during the design process for two reasons: the economic significance to the client and the economic significance to the consumer. Overall, utilizing components of current therapies or easily accessible equipment can minimize cost; for example: old CPAP facemasks, old tubing, reusable carbon dioxide sensing equipment, etc. The facemask and scuba mask scored similarly in this category because the materials used in both designs are relatively inexpensive and easily attainable from current therapies. The carbon dioxide room scored the lowest because of the expensive equipment necessary to maintain precise carbon dioxide concentrations (carbon dioxide reserves, sensors, electronics and programing, fans, intake/outtake valves, etc.) The next category, ease of use, is another important consideration of all designs. The device needs to be easy for the patient to use, meaning it is easy to put on, take off, control, adjust, and maintain. The carbon dioxide room scored highest in this category

because once completely installed and programmed, the user only needs to push a button to administer treatment. The facemask and scuba masks scored equally because both designs require similar set up, adjustments, and maintenance. The final area of emphasis, feasibility, stresses the ease of manufacturing the device and the time/resources necessary to complete that within the course of a semester. The facemask received the highest rank in this category because all of the components of this design already exist in current therapies and are easily accessible. The scuba mask received the second highest rank because this design requires the purchasing of new materials and some elementary fabrication. The carbon dioxide room scored very poorly in this category because much research and work would need to be done in order to fabricate, control, and maintain such a system.

The final category was portability. Because the new design should be universally marketable and more desirable than current therapies, it should easily adapt and function in various settings. Both the facemask and the scuba mask ranked equally successful in this category because of their similarity in size, set up, therapeutic administration. The carbon dioxide room scored lower because of its restraint to one location (and the inconvenience associated with relocating).

After analyzing each design using the areas of emphasis outlined in the design matrix, it was calculated that the modified facemask design won with a "score" of 78/100 points. The scuba mask and carbon dioxide room followed close behind, with the scuba mask obtaining a 64/100 and the carbon dioxide room obtaining a 62/100. The facemask proved to be the most safe, reliable, cost effective, feasible, and portable. The scuba mask, while most portable, proved to be unreliable; this was ultimately this design's downfall. The carbon dioxide room was in theory a great design; however, because of feasibility, time constraints, and budget, this design did not seem reasonable to fabricate in the allotted time.

Initial Testing & Evaluation

Initial Testing

Initial testing involved the use of an analogous facemask that covered the mouth and nasal region and allowed for the attachment of adjustable, rebreathable dead space volumes. A test subject was chosen who was predisposed to experiencing sleep apnea; additional measures were taken to further induce apneic events by asking the subject to sleep in the supine position, depriving the subject of sleep the night prior, and providing the subject with an alcoholic beverage. The subject was then attached to an electroencephalogram (EEG) to measure brain activity, a pulse oximeter to measure oxygen saturation, and a stretch band accelerometer to measure diaphragm movement; the subject was then fitted to the dead space facemask. The mask was further fitted with a carbon dioxide sensor to measure carbon dioxide concentration and a spirometer to measure flow rate. Once prepared, the subject was asked to fall asleep. Apneic events were measured under three distinct dead space conditions: a control (no added dead space), 450 mL added dead space, and 570 mL added dead space.

Evaluation

The initial testing and experimental analysis was used to prove the efficacy of increased $PETCO_2$ (mmHg) on decreasing apneic episodes. Under "control" conditions, periodic breathing with recurrent stagnation and no airflow (obstructive apneas), as well as, frequent and dramatic dips in saturated oxygen

concentration are observed. Also, airway obstruction was confirmed through the paradoxical movements of the chest versus abdomen. When the chest expanded, the abdomen contracted, and as a result, no airflow between the upper airway and the lungs was seen and obstructive apneas occurred.

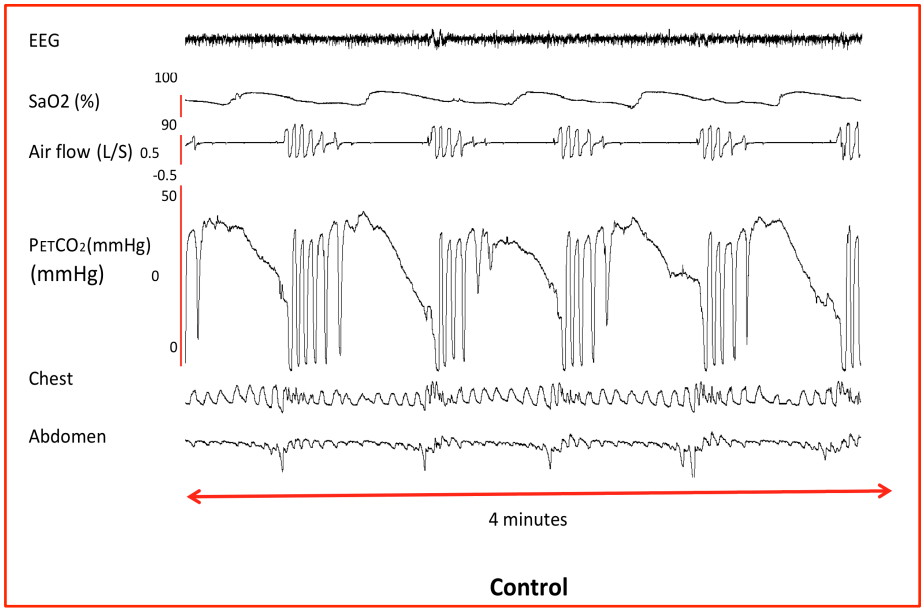


Figure 14: Observed experimental data under "control" conditions

Under "low" dead space conditions (450 mL added dead space), respiration still demonstrated paradoxical chest versus abdomen movements, few apneic episodes, and several short hypopneas (decreases in saturated oxygen levels). It is also important to note that under "low" dead space conditions the post-hypopnea airflow increased significantly due to extra chemical stimulation.

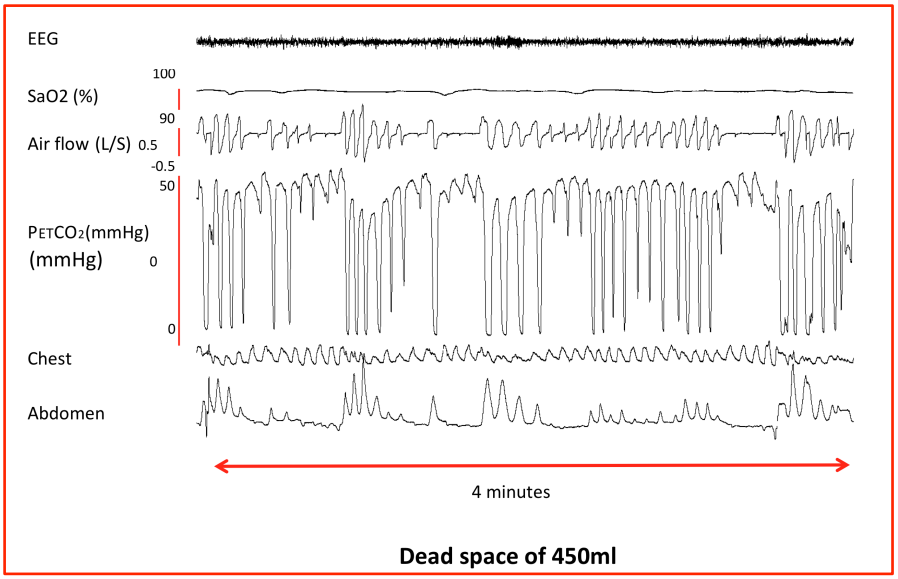


Figure 15: Observed experimental data under "low" dead space conditions (450 mL)

Under “high” dead space conditions (570 mL added dead space) no apneas or hypopneas were observed; also, no fluctuations in saturated oxygen concentration indicate stable, steady breathing patterns. It is also important to note that airflow remained relatively unchanged (compared to the previous two conditions), due to the lack of hypopneas and related chemical-mechanical stimulations

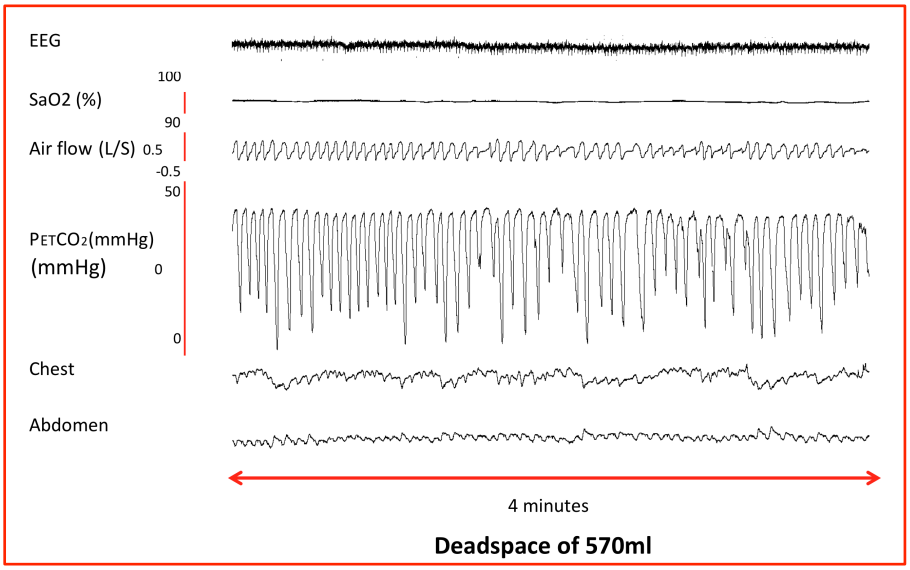


Figure 16: Observed experimental data under “high” dead space concentrations (570mL)

Testing Over a 4 Minute Sampling Period

	Apneic Episodes	Hypopnic Episodes	SaO2 (%) range	Max PETCO2 (mmHg)	Max PETCO2 (%)
Control	5	0	98-91	35	4.86
+450 mL dead space	2	4	98-95	53	7.36
+570 mL dead space	0	0	97	42	5.83

Table 1. Demonstrates the effectiveness of increased $P_{ET}CO_2$ and decreased apneic events.

The breathing regularity evident in Figure 14 - Figure 16 (and Table 1) demonstrates the effectiveness of induced hypercapnic conditions to decrease apneic episodes.

Final design

Modified Facemask Design

The final design prototype is a combination of various, unique design elements. The mask itself is a prefabricated Elevation Training Mask 2.0 (purchased online for $80). The mask originally restricted airflow, however, it was repurposed to accommodate a dead space attachment at the front, central port. The mask is comprised of a silicon shell that covers both the nasal and oral airways, and is secured to the face with a Velcro neoprene sleeve. The neoprene attachment system provides a secure fit via attachment around and behind the ears, as well as, exhibits breathable, comfortable characteristics. These breathable and secure qualities eliminate risk of the mask falling off or being removed subconsciously due to discomfort during sleep. Each lateral port permits sensor attachment during testing; each sensor is attached to the cap's small opening, and further secured with adhesive putty. These attachments allow for the relaying of vital information such as carbon dioxide and oxygen saturation, humidity, and flow rate.

Figure 17: Modified Elevation Training Mask 2.0. Contains a silicon nasal/mouth shell, outer neoprene sleeve, dead space attachment at central port, and sensor attachment at lateral ports.

The mask itself, without any tubing, is able to increase the patient's dead space volume by 150 mL. The mask has also been designed to allow for dead space attachments to be actively modified (added or taken away) during the patient's sleep without disturbance. Four adapters make incremental variations of dead space possible, and these adapters are essential to making an accurate diagnosis that is tailored to each individual. Each adapter was designed using SolidWorks, employs a quick twist release mechanism, and was fabricated using ABS thermoplastic. The four adapters form two coupling sets. One set secures the initial dead space tubing to the silicon mask; one adapter is imbedded within the silicon membrane of the mask and the other adapter is attached to the dead space tubing. The second set secures sequential segments of dead space to the initially attached tuning; both adapters are attached to the dead space tubing. The adapters were printed using a fused deposition printer located in the Engineering Centers Building (purchased for a total of $101)

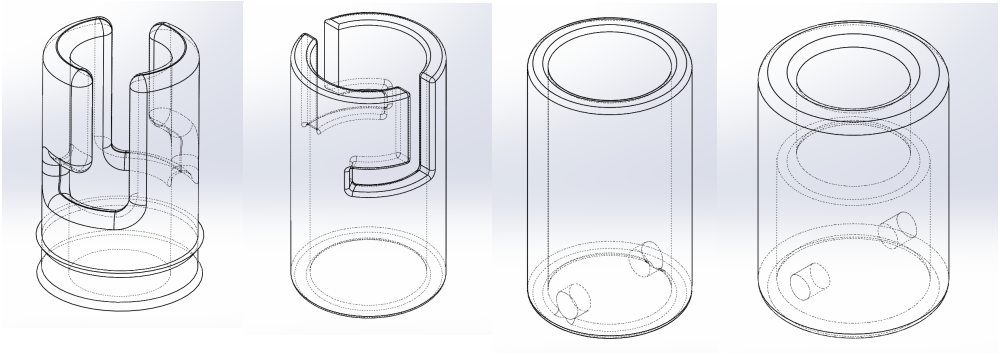


Figure 18: SolidWorks schematics of four adapters.

The tubing used in the incremental additions of dead space is capable of providing 230 mL segments of dead space (at a cost of $2) per additional segment. The final prototype utilized 230 mL segments; however, the tubing can be cut into smaller, variable sized pieces at a very low cost. Use of this tubing provides an inexpensive way to vary dead space volumes, without placing burdens or restrictions on the medical advising staff. This ease of use, in combination with the ease of attachment, is essential to forming a tailored diagnosis for each individual.

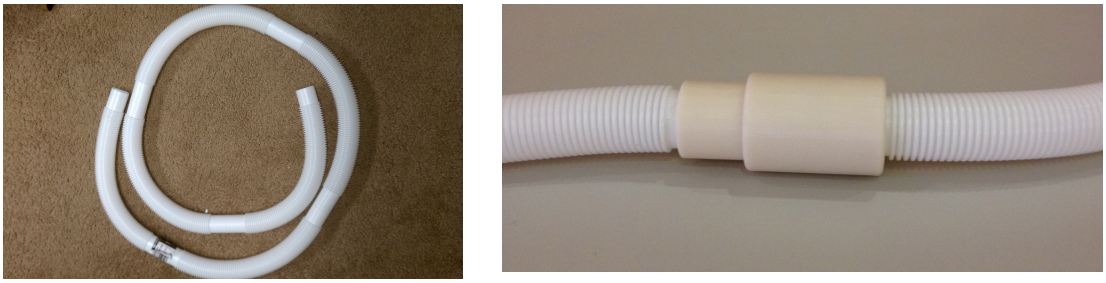


Figure 19: Image of the hosing used in incremental dead space attachments (left). Attachment showing the adaptor connection between incremental dead space tubing

Overall, the final design prototype incorporates a secure and breathable mask that is capable of incremental additions of dead space to diagnosis and treat sleep apnea patients (for under $200).

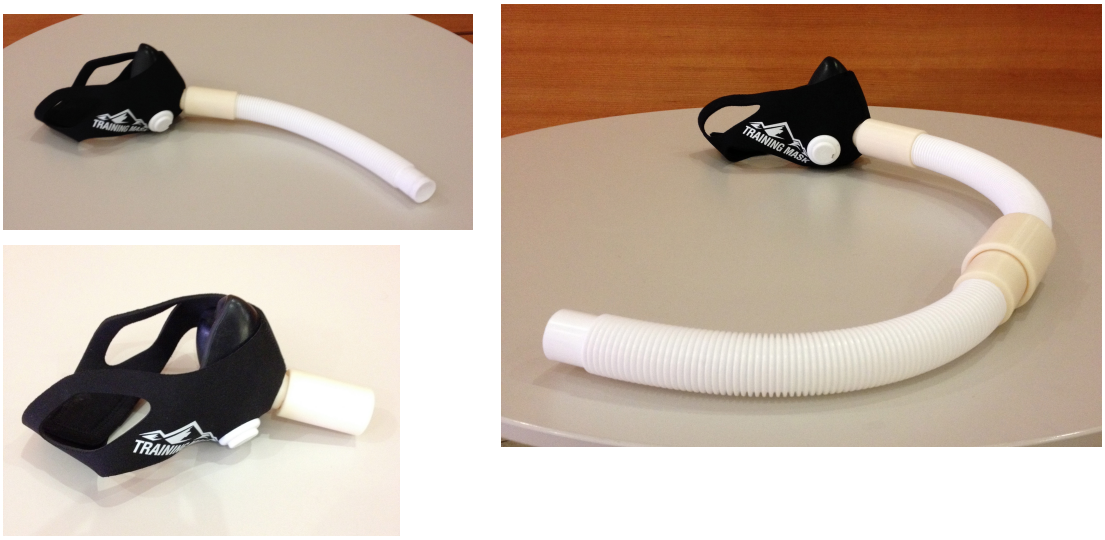


Figure 20: Images of final design prototype. Includes a secure breathable mask, incremental dead space attachments, quick twist adapters, and ports for sensor input.

Item	Price
Elevation Training Mask 2.0	$80
ABS Adapters	$101
230 mL Tubing	$4
Total Cost	$185

Figure 21: Cost breakdown of final design

Testing & Results

Testing Procedure

In order to ensure the design prototype was an effective treatment to sleep apnea, two tests were performed. The first, preliminary test involved the use of an analogous facemask that covered the mouth and nasal region and allowed for the attachment of adjustable, rebreathable dead space volumes. (See Initial Testing Section.) The second used the final design prototype itself and focused on the changes in carbon dioxide levels, oxygen saturation, and flow rate with varying dead space volumes. A test subject was chosen from amongst the team members, someone who had no disposition to sleep apnea. Additional measures were taken to further induce apneic events by asking the subject to sleep in the supine position and depriving the subject of sleep the night prior. The subject was then attached to an electroencephalogram (EEG) to measure brain activity, a pulse oximeter to measure oxygen saturation, and a stretch band accelerometer to measure diaphragm movement; the subject was then fitted to the dead space facemask. The mask was further fitted with a carbon dioxide sensor to measure carbon dioxide concentration and a spirometer to measure flow rate. Once prepared, the subject was asked to fall asleep. Despite numerous attempts, the subject was unable to fall asleep and remained awake for the entirety of the testing procedure. Never the less, carbon dioxide levels, oxygen saturation, and flow rates were recorded for three conditions: a control (no added dead space – 150 mL), 450 mL added dead space, and 750 mL added dead space

Quantitative Testing Results

The experimental testing procedure and experimental analysis focused on the changes in carbon dioxide concentration, oxygen saturation, and flow rate at varying dead space volumes to determine the effectiveness of the final design. Under “control” conditions, the baseline $PETCO_2$ was established. These $PETCO_2$ provide a reference for future tests using different dead space volumes.

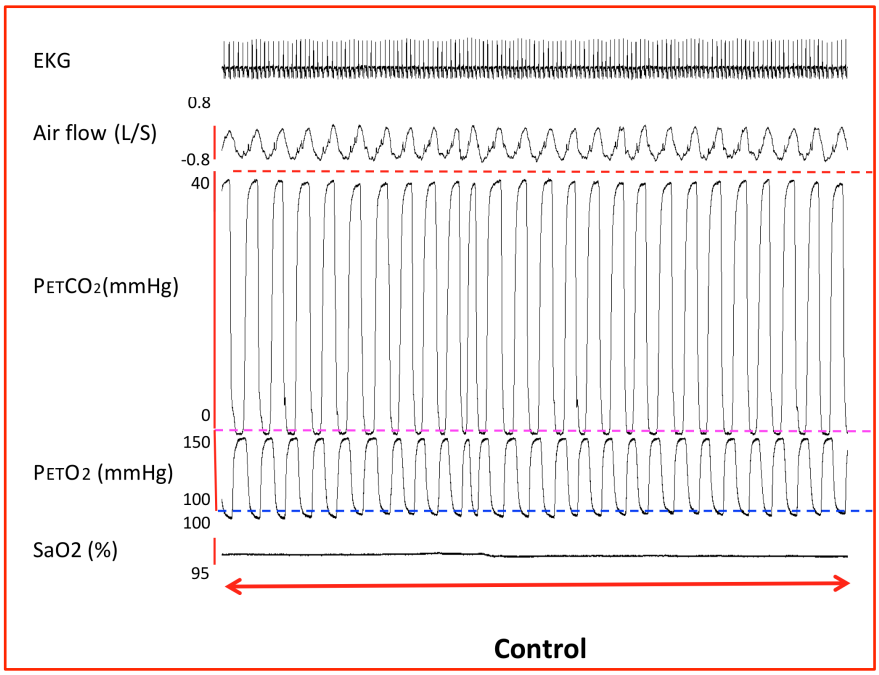


Figure 22: Experimental data for "control" (150 ml of dead space)

Under "low" dead space conditions (450 mL added dead space) it can be observed that $PETCO_2$ increases upon inspiration, compared to control conditions. It can also be observed that $PETO_2$ decreases in comparison to the control.

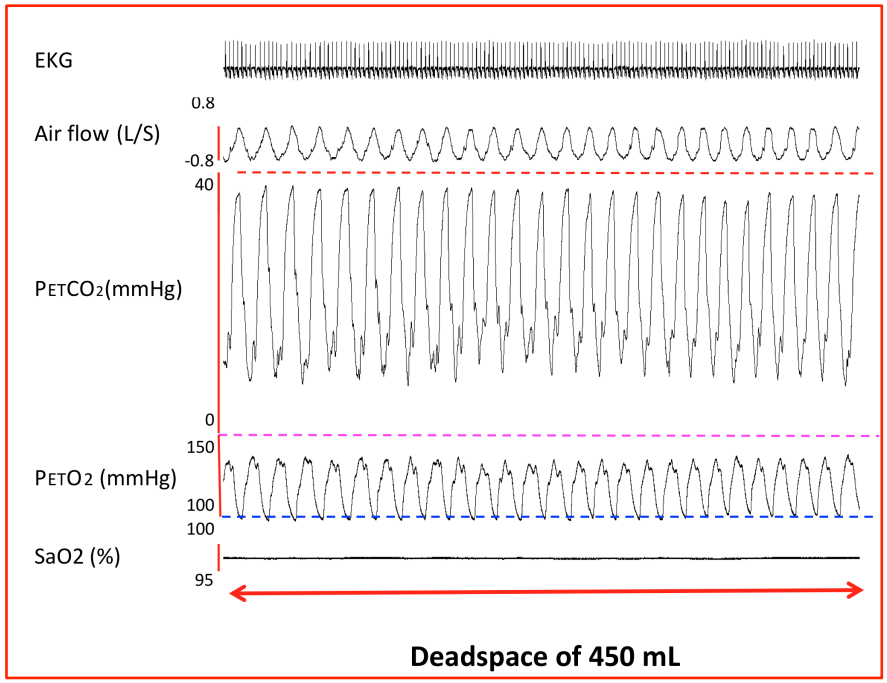


Figure 23: Experimental data for "low" conditions (450 ml of dead space)

Under "high" dead space conditions (750 mL added dead space) it can be observed that $PETCO_2$ greatly increases upon inspiration, compared to both 450 mL added dead space and control conditions. It can also be observed that $PETO_2$ became irregular throughout the duration of the testing period. One important thing to notice is that under "high" dead space conditions there was a large increase in airflow due to large inhalation compensate for the increased dead space volume.

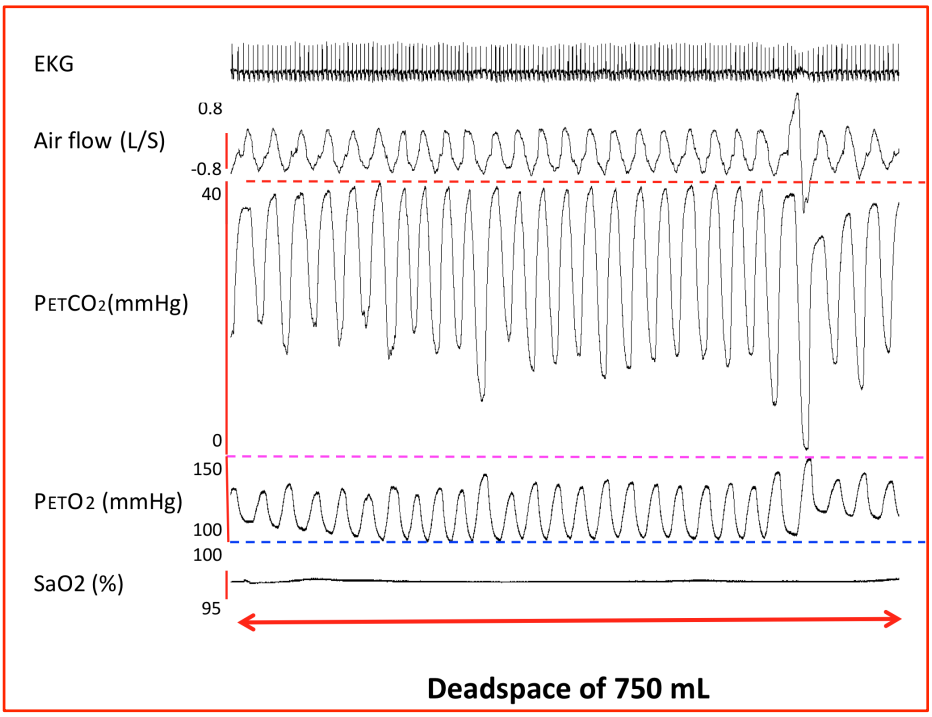


Figure 24: Experimental data for "high" conditions (750 ml of dead space)

Although sleep apnea was not induced in the subject due to lack of adipose tissue in the airway, valuable CO_2 and O_2 saturation and partial pressure values were recorded. These experimental values greatly paralleled breathing regularity and variable respiratory tidal volume. CO_2, O_2, tidal volume, and breathing frequency values obtained for the 750 ml and 450 ml of dead space were compared to that of the control conditions (150 mL added dead space).

A very drastic physiological response was illustrated using 750 mL added dead space. $PETO_2$ levels upon inhalation dropped a mere 15 ml of mercury on average compared to control; however, these values were highly irregular and $PETCO_2$ varies from the same value as control to 20 mmHg above control. Surprisingly, the O_2 saturation was increased even compared to the 450 ml dead space test. The only explanation for this must be due to increased breathing frequency and tidal volume. When comparing 750 ml of added dead space to the control, the most obvious difference is a drastic change in breathing pattern. While the frequency compared the control remained the same, the 750 ml of dead space is accompanied by a large increase in tidal volume. It is also important to note that during testing the test subject's eyes became red, his skin became flushed, and he looked as though he was straining from the effort of breathing through the excess dead space.

Changes In Quantitative Measurements for Control, 450 ml dead space, 750 ml dead space			
Quantitative Measurement	**Control (150 ml total dead space)**	**450 ml of total dead space**	**750 ml of total dead space**
Change in $PETCO_2$ (mmHg) upon exhalation (relative to control)	-	+10	+20
Change in $PETO_2$ (mmHg) upon exhalation (relative to control)	-	+10	+15
Respiratory Rate (sec/breath)	9.23	9.23	9.23
SaO_2 (%) (relative to control)	-	+1%	+3%
Inhaled Tidal Volume (relative to control)	-	Very similar if not identical	Much larger volume
Breathing Regularity (relative to control)	-	Very regular	Extremely irregular

Table 2: Summary of experimental testing results

The prototype system was highly effective at increasing $PETCO_2$, thereby increasing blood CO_2 concentration and effectively stimulating the chemical receptors in the airway. This in stimulates the phrenic and hypoglossal nerves to enervate the muscles of the pharynx and diaphragm. Comparing these results to those obtained from the initial testing, it can be estimated that ≈ 600 ml of added dead space should be used to increase $PETCO_2$ levels to an effective amount. This "effective amount" would provide an adequate increase in inhaled CO_2 concentration but not excessive amounts so as the individual must strain to breath.

Qualitative Testing Results

Qualitative experimentation is a poor measurement of efficacy due to personal opinion and bias. Through use of a survey, it was found that when comparing the final prototype to the currently accepted CPAP therapy the mask generally considered more comfortable.

In most cases it was concluded that preference was based upon the idea that the final prototype doesn't required the positive airway pressure, a vital component to CPAP's functionality. Since air isn't being forced into the lungs an airtight seal isn't necessary. This means that the final prototype is free to utilize lightweight and comfortable materials that are inappropriate for CPAP therapy. Furthermore, the positive airway pressure of CPAP requires a loud electric motor for functionality. The annoyance of a motor isn't seen in the design prototype because of the use of dead space rebreathing.

Conclusion

Sources of Error

Within this project there were many potential sources of error. One of these sources arose because the testing preparation was extremely time-consuming and required an entire night for testing/evaluation. As a result, the experimental sample size was limited to one person. Throughout the course of the semester, evaluating the final prototype on multiple test subjects was difficult, and more formal procedures would have been required had testing been conducted on outside subjects. With the small sample size it is impossible to evaluate the significance of experimental results, therefore, no statistical conclusions could be drawn. Another limitation was the availability of potential test subjects. Ideally a formal sleep apnea test would use human test subjects who have been diagnosed with sleep apnea; however, attaining the qualifications and approvals necessary to conduct such a study was not feasible in the allotted time. Due to these restrictions, a team member was chosen to undergo testing; unfortunately, no apneas could be induced. In all, the inability to induce apneic conditions upon one of our own team members limited our ability to test the effectiveness of our final design.

Another source of error arose from the 3D printed adapters. One of the adapters (the male facemask adapter) was imbedded in the silicon membrane of the mask, and as a result, was unable to form an airtight seal between the adapter and the mask. Consequently, when the male adapter was inserted into the female adapter, a tiny gap was present between the two adapters. This small gap allowed for trace amounts of carbon dioxide rich air to escape the dead space tubing. This gap was ultimately corrected through the used of adhesive putty. (It is important to note that had this small gap not been filled, air movement would have interfered with carbon dioxide concentration levels, spirometer data, and other experimental data calculations.)

One final potential source of error arose while measuring the cumulative dead space between the patient's airway and the added dead space from the mask. In order to calculate the dead space volume of the ergonomic mask, it was filled with water, the water was poured into a beaker, and its volume was measured. Unfortunately, each individual has a different physiological make up of his or her airway and oral cavity. As a result, each individual's airway presents unique dead space volumes. These discrepancies make it extremely difficult to accurately calculate the precise amount of dead space volume each individual experience.

Future Work

Several aspects of the design process could be changed or improved if this design and testing procedure were performed again. One of these changes would be to increase the sample size of patient testing in order to more accurately affirm the relationship between hypercapnia and decreased AHI. Similarly, the testing procedure would be slightly modified in that the patient would begin the testing procedure with the control (just the mask itself), and add incremental volumes of dead space throughout testing. Then, using the average AHI (measured as a percentage), statistical analysis could be conducted, specifically a paired t-test, to analyze the validity of the experimental data. Through this statistical analysis

the team could confirm the relationship between hypercanpic conditions, induced through incremental volumes of dead space, and decreased AHI through personal experimental data.

Another change that would be made would be to make minor adjustments to the design prototype itself. The final design utilizes dead space adapters with a wall thickness of 1.026 cm; developing an adapter with thinner walls would serve to cut down materials cost, reduce the weight of the adapters, and create a sleeker, more esthetically pleasing design. The final design also utilizes a prefabricated elevation simulation facemask, composed of a thick silicon rubber mouth/nasal mask. Use of softer, more lightweight plastics would optimize testing functionality, comfort, and marketability. The design also utilizes prefabricated neoprene ear straps used for securing the facemask to the patient's face. Use of a softer, more lightweight, breathable fabric for the straps would minimize the weight of the mask, while also, improving upon comfort and functionality of the design.

Finally, with more time and an extended budget, the development of a "Smart Dead Space Technology" design would be the next task. This technology would utilize algorithms based on measurements of airflow (taken through a spirometer located on the mask), in order to identify and execute necessary changes in dead space volume during sleep. The device would automatically change the lengths of dead space tubing, in order to alter the hypercapnic conditions, and prevent apneas from occurring. The design would also store AHI data within a memory device; this data could be used for follow up care or in clinical settings. Due to numerous technological advancements, data could also be sent directly to personal computers or smart phones for immediate personal accessibility. Two current therapies, "Smart CPAP" and MIR Spirodoc Spiromete, utilize similar self-regulated detecting systems to provide treatment to patients. Advancements in the field of sleep, specifically sleep apnea, continue to grow; the invention of a "Smart Dead Space Technology" may be the treatment of the future.

Appendix

I. Product Design Specifications

Client Requirements

- The device must induce hypocapnic conditions in the bloodstream.
- The device must increase the effective amount of dead space present in the breathing system.
- The device must be comfortable, small, and quiet since it is worn during sleep.
- The device will be used in a home setting; therefore, it must be easy to use and safe for those of all ages.

Design Requirements

1. **Physical and Operational Characteristics**
    a. *Performance Requirements:* The device should be able to withstand repeated nightly use, and maintain extended functionality. The facial mask should cover the nose and mouth while also generating an effective airtight seal through the use of straps, sealants, or individually molded face masks. The device should also increase the amount of dead space available during respiration to maximize an effective treatment
    b. *Safety:* The device's ability to function effectively should continue throughout the duration of the night. In addition to this, if the device should fail, further breathing difficulty should not arise and the patient should be able to maintain a stable and safe respiratory rate. The device should not contain small pieces that pose possible choking hazards for patients of all ages.
    c. *Accuracy and Reliability:* The device must be more effective than the current methods of preventing obstructive sleep apnea. Given the chronic nature of sleep apnea, the device must be able to function accurately and reliably on a daily basis to ensure an effective treatment.
    d. *Life in Service:* The device should remain operational indefinitely over its lifetime. If a carbon dioxide reservoir is used, the reservoir must function for over twelve hours.
    e. *Shelf Life:* The device must be safe to store at room temperature. The device should not contain any biological or perishable items that would suggest that the device has a maximum shelf life. If a carbon dioxide reservoir is required, the carbon dioxide must remain usable for the entirety of its life.
    f. *Operating Environment:* The device will mainly be operated in an individual's home, with many diverse individual users. The device must accommodate individuals of all "shapes and sizes". The use of individual facial molds is most effective in creating an effective seal for individuals with different physical builds. The targeted users are elderly adults and those who are at more risk to suffer from obstructive or central sleep apnea (overweight adults, those exhibiting particular facial features, etc.).
    g. *Ergonomics:* The device must be user friendly (easy to understood and simple to operate for individuals without a medical or technical background) and comfortable (generates an effective seal while not disturbing the user during sleep)
    h. *Size:* The device must be small enough to not be cumbersome or uncomfortable during sleep and all attachments should be portable.

i. *Weight:* The device should be light enough so as not to disturb the user during sleep. The device and its corresponding parts should be easily transferable from location to location to ensure ease of use.
j. *Materials:* The device and the entirety of its parts should not be carbon dioxide permeable, and must not react with relatively high concentrations of carbon dioxide. Materials must be light weight, malleable, and soft as to eliminate any sharp edges that may cause harm to an individual.
k. *Aesthetics, Appearance, and Finish:* The device should look professionally crafted. The device should be comfortable and contain a finish that is hypoallergenic.

2. Production Characteristics:

a. *Quantity:* One product will be needed.
b. *Target Product Cost:* A budget has not yet been proposed. Costs associated with device's construction should try to be minimized.

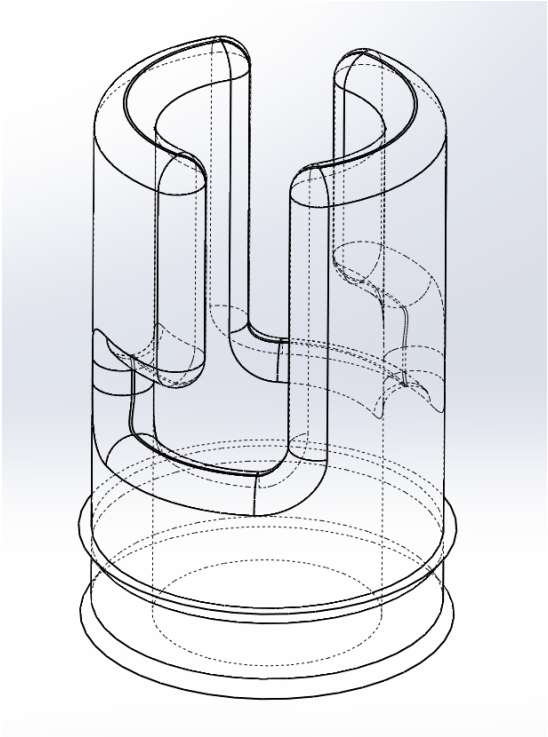
3. Miscellaneous:

a. Standards and Specifications: The device will need to be FDA approved before implementation.
b. Customer: the customers will be those (or the caretakers of those) with central sleep apnea, obstructive sleep apnea, or complex sleep apnea.
c. Patient-Related Concerns: The device must be safe and effective while also maximizing patient comfort. The device must be capable of being sterilized without physical damage; the materials should be non-carcinogenic and not cause allergic reactions or irritation upon contact or association with an individual. The materials should be antimicrobial and antifungal to reduce possible health concerns that may arise from use.
d. Competition: Multiple commercial devices are available, they are as follows:

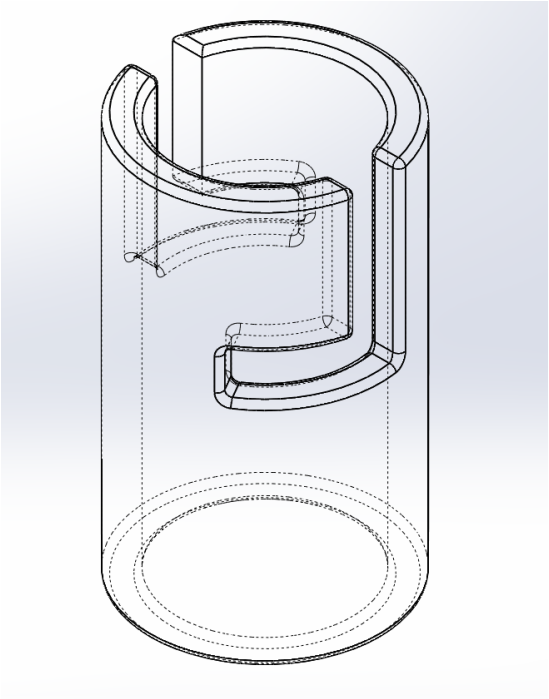
i. Continuous Positive Airway Pressure (CPAP): A machine that delivers air pressure through a facial mask placed over the nose and mouth during sleep. The air pressure provided is slightly greater than the surrounding air pressure, causing the upper airway passage of the patient to remain open, allowing for the movement of air. This is the most common and reliable treatment method, but can be uncomfortable and cumbersome to patients.
ii. Adjustable airway pressure device: A device that automatically adjusts air pressure during sleep.
iii. Automatic Positive Airway Pressure (APAP): A device that decreases air pressure when the upper airway is stable, and increases air pressure when the upper airway is blocked.
iv. Bilevel Positive Airway Pressure (BPAP): A device that provides more air pressure during inhalation and decreases air pressure during exhalation.
v. Expiratory Positive Airway Pressure (EPAP): A small, single use device that is placed over each nostril before sleep; device allows unrestricted air flow in, but restricts airflow out, thus increasing air pressure in the dead space.
vi. Oral Device: A device that keeps the airway open by 1.) Pushing the lower jaw forward using a mandibular advancement device, 2.) Preventing the tongue from falling back over the airway using a tongue retaining device, or 3.) A combination of the previous devices.

II. SolidWorks Schematics

Female Adapter for Facemask:



Female Adapter – General:



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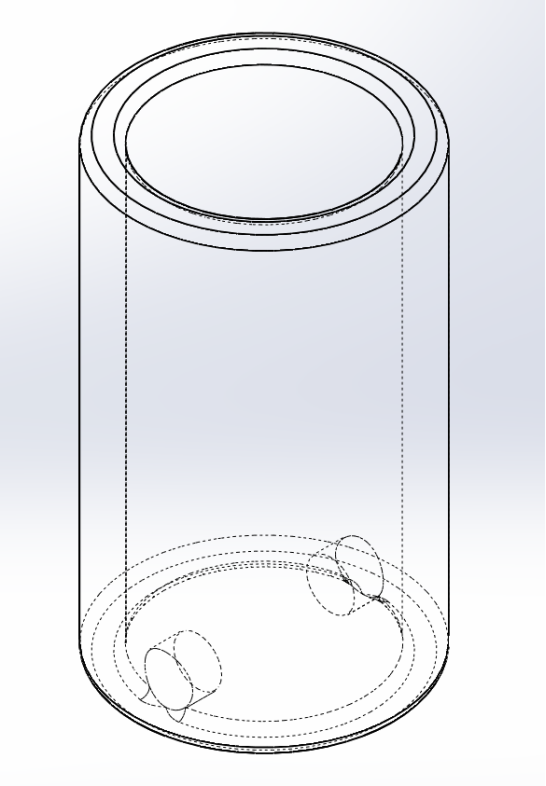
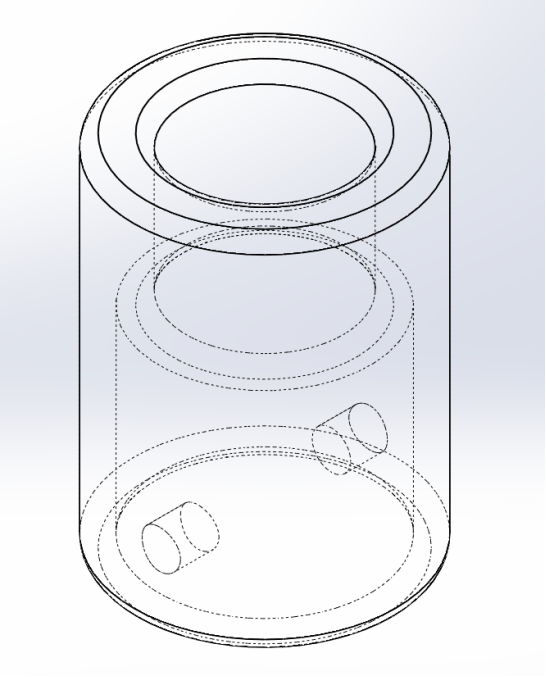


Male Adapter – General



Works Cited

1. Ailiang, X., Teodorescu, M., Pegelow, D., Teodorescu, M., Gong, Y., Fedie, J., & Dempsey, J. (2013). Effects of stabilizing or increasing respiratory motor outputs on obstructive sleep apnea. *Journal of Applied Physiciology*, (115), 22-33. Retrieved from http://jap.physiology.org/content/early/2013/04/15/japplphysiol.00064.2013
2. Aronson, D. C. (2013). *Cpap alternatives*. Retrieved from www.vacavilledentistry.com/cpap-alternatives.html
3. Berry, R. B., Kryger, M. H., & Massie, C. A. (2011). A novel nasal expiratory positive airway pressure (epap) device for the treatment of obstructive sleep apnea: A randomized controlled trial. *Sleep*, *34*(4), 479-485. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065258/
4. Brown DL; Anderson CS; Chervin RD; Kushida CA; Lewin DS; Malow BA; Redline S; Goldman EB. Ethical issues in the conduct of clinical trials in obstructive sleep apnea. *J Clin Sleep Med* 2011;7(1):103-108.
5. Dempsey, J., Xie, A., Patz, D., & Wang, D. (2013). Physiology in medicine: Obstructive sleep apnea pathogenesis and treatment – considerations beyond airway anatomy. Unpublished manuscript, Department of Population Health Science, University of Wisconsin - Madison, Madison, WI.
6. Gay, P. (2008). Complex sleep apnea: it really is a disease. *Journal of Clinical Sleep Medicine*, *15*(4(5)), 403-405. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2576323/
7. Kryger MH, Berry RB, Massie CA. Long term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea. SLEEP Abstract Supplement, 2011 (34):A118.
8. Louis R. Chanin, M. (n.d.). Retrieved from http://www.webmd.com/sleep-disorders/sleep-apnea/sleep-apnea
9. Mayo Clinic Staff. (n.d.). Retrieved from http://www.mayoclinic.com/health/obstructive-sleep-apnea/DS00968
10. Neighmond, P. (n.d.). Retrieved from http://www.npr.org/2011/03/14/134467782/how-to-beat-sleep-apnea-cut-it-out-surgically
11. ResMed (2013). *VPAP Adapt SV and Adaptive Servo-Ventilation.* Retrieved from <http://www.resmed.com/us/clinicians/treatment/adapt_sv.html?nc=clinicians.
12. "Snoring, Sleep Apnea, and Travel." *Sleep Right Australia, Specialists in Sleep, Sleep Apnea, and Snoring*. Sleep Right Australia, 7 June 2013. Web. 07 Oct. 2013. <http://sleepright.com.au/sleeping-disorders>.

13. Staff, Healthwise. "Uvulopalatopharyngoplasty Surgery for Snoring." *WebMD*. WebMD, 03 Jan. 0000. Web. 07 Oct 2013. http://www.webmd.com/sleep-disorders/uvulopalatopharyngoplasty-for-snoring
14. “Uvulopalatopharyngoplasty." *Wikipedia*. Wikimedia Foundation, 29 Aug. 2013. Web. 07 Oct. 2013. <http://en.wikipedia.org/wiki/Uvulopalatopharyngoplasty>. http://en.wikipedia.org/wiki/Uvulopalatopharyngoplasty
15. Weaver , T., & Grunstein, R. (2008). Adherence to continuous positive airway pressure therapy:the challenge to effective treatment. *Proceedings of the American Thoracic Society*, (5), 173-178.