A Randomized Control Trial of Continuous Positive Airway Pressure to Reduce Systolic Blood Pressure in Patients with Obstructive Sleep Apnea and Systemic Hypertension.

Candice Kwan

A. Study Purpose and Rationale

Obstructive sleep apnea (OSA) is the most common sleep associated breathing disorder, affecting 24% and 9% of middle-aged men and women respectively (1), and more than 10 percent of the population over the age of 65 (2). Moreover, in the urban adult population, the 5-year incidence of sleep disordered breathing (SDB) is about 7.5% for moderately severe SDA and 16% for mild to moderately severe SDB (3). During sleep, the upper airway musculature relaxes and leads to a collapse of the "floppy" upper airway upon inspiration. Airway patency is compromised despite vigorous diaphragmatic respiratory efforts. Continuous positive airway pressure (CPAP) during sleep is the treatment of choice in patients with OSA. A pneumatic splint is created by air pressure applied to the upper airway through a nasal or nasal-oral mask. In randomized, placebo-controlled trials, continuous positive airway pressure has been demonstrated to decrease somnolence, and to improve mood, alertness, and quality of life (2, 4, 5).

OSA is thought to be an independent risk factor for daytime systemic hypertension. In a large population-based prospective observational study, the Wisconsin Sleep Cohort Study demonstrated an independent dose-related association between sleep-disordered breathing at baseline and the presence of hypertension four years later. This association was present even after adjustment for other known risk factors for hypertension such as habitus, age, sex, and cigarette and alcohol use (6). The pathophysiologic mechanism for the development of hypertension in obstructive sleep apnea is thought to be multifactorial (1). Intermittent nocturnal hypoxia and hypercapnia leads sympathetic activation and increased nocturnal blood pressure. This activation is hypothesized to increased daytime sympathetic activity and elevated daytime systemic blood pressure. In addition, chemoreceptor resetting, tonic chemoreceptor activation, endothelial dysfunction, increased endothelin, and lower nitric oxide levels have all been hypothesized to lead to diurnal systemic hypertension. Effective CPAP treatment will lower nocturnal hypertension. However, no large prospective cohort studies or randomized control trials have shown that treatment of OSA with CPAP effectively reduces daytime hypertension. Specifically, there have been a handful of small poorly controlled studies with conflicting results on the effect of CPAP treatment on daytime systemic hypertension (5, 7, 8, 9). More recently published data indicates that CPAP may lower daytime blood pressure, but these studies are compromised by poor controls, uneven baseline characteristics between the two groups, and high dropout rates (5,7).

B. Study Design and Statistical Analysis

The study is a 12-week randomized double-blind control trial based at the Sleep Disorders Laboratory at Columbia Presbyterian Medical Center. The goal is to determine the effects of CPAP on daytime blood pressure in patients with OSA and systemic hypertension. Adult patients who qualify for the study and meet the inclusion criteria of hypertension (documented SBP >140 or DBP >90 at 2 clinic visits, or on antihypertensive medication) and OSA (Apnea-hypopnea Index >/= 5 and excessive daytime somnolence, >/= 10 points on Epworth sleepiness 24-point scale) are asked to participate in the study. Participants and their primary care physicians are asked to keep their antihypertensive medications at enrollment unchanged during the three-month course of the study unless SBP>180 or <100. After informed consent has been obtained, participants are randomized to either effective CPAP or non-therapeutic CPAP over a 12-week period. Upon study enrollment, baseline characteristics (age, sex,

weight, BMI, neck/waist circumference) and blood pressure will be obtained, and the participant will be asked to fill out a questionnaire regarding current medications, alcohol use, tobacco use, and exercise frequency. CPAP will be titrated to a therapeutic or subtherapeutic level by a qualified sleep technician during an overnight sleep study. Blood pressure will be measured at 2-week intervals by a blinded study investigator at the sleep disorders laboratory. In addition, counseling regarding diet and lifestyle modifications for HTN and OSA will be given at 2-week intervals. At the end of the study, the participant will be asked to complete the questionnaire again, and will have their weight and BMI recorded.

a. Enrollment Site
Columbia Presbyterian Sleep Disorders Laboratory

b. Intervention
- Effective CPAP vs. non-therapeutic CPAP
- Counseling provided to both groups at biweekly sessions re: lifestyle modification for HTN: salt restriction, diet, weight reduction, need to limit alcohol consumption, smoking cessation, and re: conservative treatment for OSA: use of lateral sleeping position, avoidance of alcohol or sedative medications, weight loss, and caution with driving motor vehicles and heavy machinery.

c. Method of Randomization
Randomization will occur in blocks of four participants.

d. Primary Endpoint
- Change in SBP with treatment from baseline SBP
- Baseline SBP is the average SBP measured on two separate days upon study entry
- SBP on treatment is the average of the last 2 clinic SBP readings at the end of the study
- Each recorded SBP is the average of at least 2 seated BP measured at 5 minute intervals, read with mercury sphygmomanometer, while the patient is at rest for at least 30 minutes.
- Note: 7th JNC 2003 recommends treatment of HTN based on achieving a SBP goal

e. Secondary Endpoints
- mean systolic blood pressure
- mean diastolic blood pressure
- change, if any, in number of antihypertensives being used
- AHI, HI, and AI
- side effects of masked ventilation
- excessive daytime sleepiness (measured on 24 point Epworth sleepiness scale)
- CPAP compliance (defined as at least 3.5 hours of use per night, at least 4 nights/week)

f. Follow up Period
- Week 2, Week 4, Week 6, Week 8, Week 10, Week 12

g. Statistical Analyses
- Effect size of interest: 5mmHg drop in SBP in the CPAP group
- Power Calculation using the unpaired T test shows that 42 patients in each group will be needed to demonstrate a difference of 5 in the two groups. (Power 0.80, a 0.05, SD 10)

h. Data Analysis
- Data will be analyzed on an intention-to-treat basis
- Unpaired T test will be used to measure the primary and secondary endpoints

- The two groups will also be compared for the following variables
  - BMI
  - neck/waist circumference
  - age
  - sex
  - use of ETOH
  - use of TOB
  - DM
  - number of hours of exercise per week
  - Stage of hypertension (Stage 1: SBP140-159 or DBP 90-99; Stage 2: SBP 160-179 or DBP 100-109, Stage 3: SBP>180 or DBP>110)
  - Severity of OSA (mild: AHI5-9; mild-moderate AHI: 10-14, moderate 15 or greater)

C. Study Procedure

a. Measurement of blood pressure

After the participant had been seated for at least 30 minutes, two or three readings of systolic and diastolic blood pressure is obtained at five-minute intervals using a conventional mercury sphygmomanometer, in accordance with the recommendations of the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Participants are asked to refrain from tobacco or caffeine use within 30 minutes prior to blood pressure measurement. The recorded blood pressure will be the average of the two or three seated BP readings.

b. Measurement of habitus

Habitus is assessed with the use of standard procedures including measurements of height (in meters), weight (in kilograms), and neck and waist circumference (in centimeters)

c. Measurement of Apnea-Hypopnea Index

18-channel polysomnography is performed as part of an overnight sleep study by skilled technician in the sleep laboratory. Sleep is recorded and the stage of sleep is determined by electroencephalography, electrooculography and electromyography. Thoracic and abdominal respiratory movements are measured by inductance plthysmography and arterial oxygen saturation is measured using pulse oximetry. In addition, breathing and limb movements and electrocardiographic lead are monitored. Cessation of airflow for at least 10 seconds was defined as an episode of apnea. A discernible reduction in the sum amplitude of the rib-cage plus the abdominal excursions on respiratory inductance plethysmography that lasted at least 10 seconds and that was associated with a reduction in the oxyhemoglobin saturation of at least 4 percent was defined as an episode of hypopnea. The apnea-hypopnea index is defined as the average number of episodes of apnea and hypopnea per hour of objectively measured sleep. Obstructive sleep apnea was diagnosed if the participant has Apnea-Hypopnea index of 5 or greater.

d. CPAP Titration

Polysomnography will be performed to calculate the correct level of CPAP required to restore upper-airway patency. This will be done by trained sleep technicians as recommended by American Thoracic Society.

- Active reinforcement (by sleep technicians) on the night of CPAP titration of the benefits of treatment, use of patient education videotapes on the night of the CPAP titration to promote compliance with CPAP machine.

- Participants will be provided written information on OSA and CPAP to encourage compliance with intervention.

e. Measurement of CPAP compliance

- Hour-meter record: data from hour-meter on the assist device is recorded every 2 weeks, and the average hours of device use is calculated (meter hours/number of days)
- Computer Analysis: Actual mask-on compliance data is downloaded from the CPAP machine at biweekly intervals onto a personal computer, and the mean effective usage over the treatment period is calculated.
- some patients find CPAP obtrusive and become frustrated by frequent mask leaks and nasal congestion. Long term use is more likely in patients with history of snoring, a high apnea-hypopnea index, and severe daytime sleepiness. Intensive support of patients when CPAP is initiated is important to maximize the likelihood of long-term use. (Flemons)

f. Schedule of Repeated Measurements and Procedures, Duration of Study

Participants will get BP measured every 2 weeks. They are asked not to change their antihypertensives during the study period of 12 weeks, unless SBP is greater than 160 or less than 100. Standard clinical care for hypertension would require a BP check at the physician's offic every 3 months.

D. Study Drugs

N/A

E. Study Medical Device

CPAP systems will be commercially available ResMed S7 Elite CPAP devices. The ResMed S7 Elite CPAP device is FDA approved for use in CPAP titration studies and as a home CPAP device for the treatment of obstructive sleep apnea in adult patients. The CPAP system is used every night through the night while the participant is asleep. The ResMed S7 Elite CPAP device records and stores data on 365 days of usage, pressure, leak, AHI, HI, and AI. [please see enclosed brochure on ResMed S7 Elite CPAP]

According to the American Thoracic Society Consensus Statement, CPAP is effective in eliminating obstructive sleep apnea, oxyhemoglobin desaturation, and respiratory event-related arousal from sleep. CPAP is also associated with improved morbidity as manifested primarily by reductions in daytime sleepiness and improved cardiopulmonary function. Although the long-term effects of nasal CPAP have not been fully determined, available data suggest a possible reduction in mortality. Common side effects of CPAP use include local skin irritation, drying of the nasal and pharyngeal membranes (~50 percent), nasal congestion/rhinorrhea (~25 percent), and eye irritation (~25 percent). Rare case reports of major complications with CPAP device have been reported and include pneumocephalus, bacterial meningitis, conjunctivitis, massive epistaxis, and atrial arrhythmia. There are no reports of pneumothorax. CPAP is a safe form of therapy with relatively few recorded major complications. Nevertheless, minor discomfort and complaints regarding the mask interface remain relatively common. Severe facial skin irritation due to nasal masks may be avoided by using ADAM nasal pillows.

F. Study Questionnaires

A questionnaire will be administered to study participants at the beginning of the study and at the end of the 3 month study period. The questionnaire will assess the following:

1 The use of antihypertensive medications (current use of alpha-adrenergic antagonists, beta-blockers, calcium-channel blockers, diuretics, angiotensin-converting-enzyme inhibitors, angiotensin receptor blockers)
2 Dietary habits
3 Average amount of exercise per week
4 Use of alcohol (number of drinks/week; duration of ETOH use)
5 Use of tobacco (number of cigarettes per day, duration of tobacco use)
6 Excessive daytime somnolence (Epworth sleepiness scale)
7 Side effects of CPAP (ongoing mask discomfort, nasal congestion, dry nose, dry or red eyes, machine noise, ear pain, facial acne, difficulty exhaling)

G. Study Subjects

a. Inclusion Criteria

- Age>18years and <65 years
- Diagnosis of hypertension.
- Systemic hypertension is defined by a seated SBP>140mmHg or DBP>90 mmHg measured by mercury sphygmomanometer on each of at least two office visits, or self-reported current use of an antihypertensive medication
- Diagnosis of obstructive sleep apnea.
- OSA is defined by an apnea-hypopnea index (total number of episodes of apnea and hypopnea per hour of sleep) of 5 or higher (measured by an overnight sleep study) in association with self-reported excessive daytime somnolence.

b. Exclusion Criteria

- -pregnancy
- -unstable or decompensated cardiopulmonary disease
- -airway carcinoma
- -recent surgery of upper respiratory tract
- -inadequate period of sleep as defined by less than 4 hours per night
- -history of CVA or dementia
- -history of MI within the past 6 months, or current angina
- -history of life-threatening arrhythmias (2^{nd} degree AV Block, complete heart block, V fib, V tach)
- -currently receiving other treatment for sleep disordered breathing (e.g. mandibular and tongue advancement devices)

H. Recruitment of Subjects

Study participants will be recruited through the Sleep Disorders Laboratory at Columbia Presbyterian Medical Center. The patient's primary physician will be contacted by the study investigators in order to ascertain that the patient is suitable for the study, and to discuss the study with the research team prior to approaching the patient for informed consent. In addition, the patient's diagnosis of hypertension and current antihypertensive medications will be confirmed with the primary physician.

I. Confidentiality of Study Data

All study data will be coded. Once enrolled, patients will be identified with a number. Only the principal investigator will have information regarding which number represents which patient. Data will be stored in a secure location, accessible only to the investigators.

J. Potential Conflict of Interest

None of the investigators associated with this study has a proprietary interest in any device that might be used in this study. None of the investigators stands to benefit financially from the results of the study.

K. Location of Study

The Sleep Disorders Laboratory at Columbia Presbyterian Medical Center.

L. Potential Risks

Participants may get randomized into receiving subtherapeutic CPAP that is not as effective as therapeutic CPAP. Common side effects of CPAP use include local skin irritation, drying of the nasal and pharyngeal membranes (~50 percent), nasal congestion/rhinorrhea (~25 percent), and eye irritation (~25 percent). Rare case reports of major complications with CPAP device have been reported and include pneumocephalus, bacterial meningitis, conjunctivitis, massive epistaxis, and atrial arrhythmia.

M. Potential Benefits

Participants may experience decreased somnolence, and improved mood, alertness, and quality of life. Participants will receive intensive counseling for diet and lifestyle modification over the study period.

N. Alternative Therapies

N/A

O. Compensation to Subjects

Participants will be pain $25 dollars as compensation for time and travels costs for participating in this study.

P. Costs to Subjects

N/A

Q. Minors as Research Subjects

N/A

R. Radiation or Radioactive Substances

N/A

S. References

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Additional Notes

1. Lifestyle Modifications and approximate SBP reduction.
    - Weight reduction (to maintain normal body weight; BMI 18.5-24.9): 5-20mmHg/10kg weight loss
    - Adopt DASH eating plan: 8-14mmHg
    - Dietary sodium reduction: 2-8mmHg
    - Physical Activity: 4-9mmHg
    - Moderation of alcohol consumption: 2-4mmHg

2. Focus on Systolic Blood Pressure
    - According to the 7th Report of JNC, in persons older than 50 years, systolic blood pressure greater than 140mmHg is a more potent cardiovascular disease risk factor than diastolic blood pressure. Since the achievement of goal SBP is associated with the achievement of goal diastolic BP, the current recommendation on primary treatment for hypertension is to focus on achieving the SBP goal.

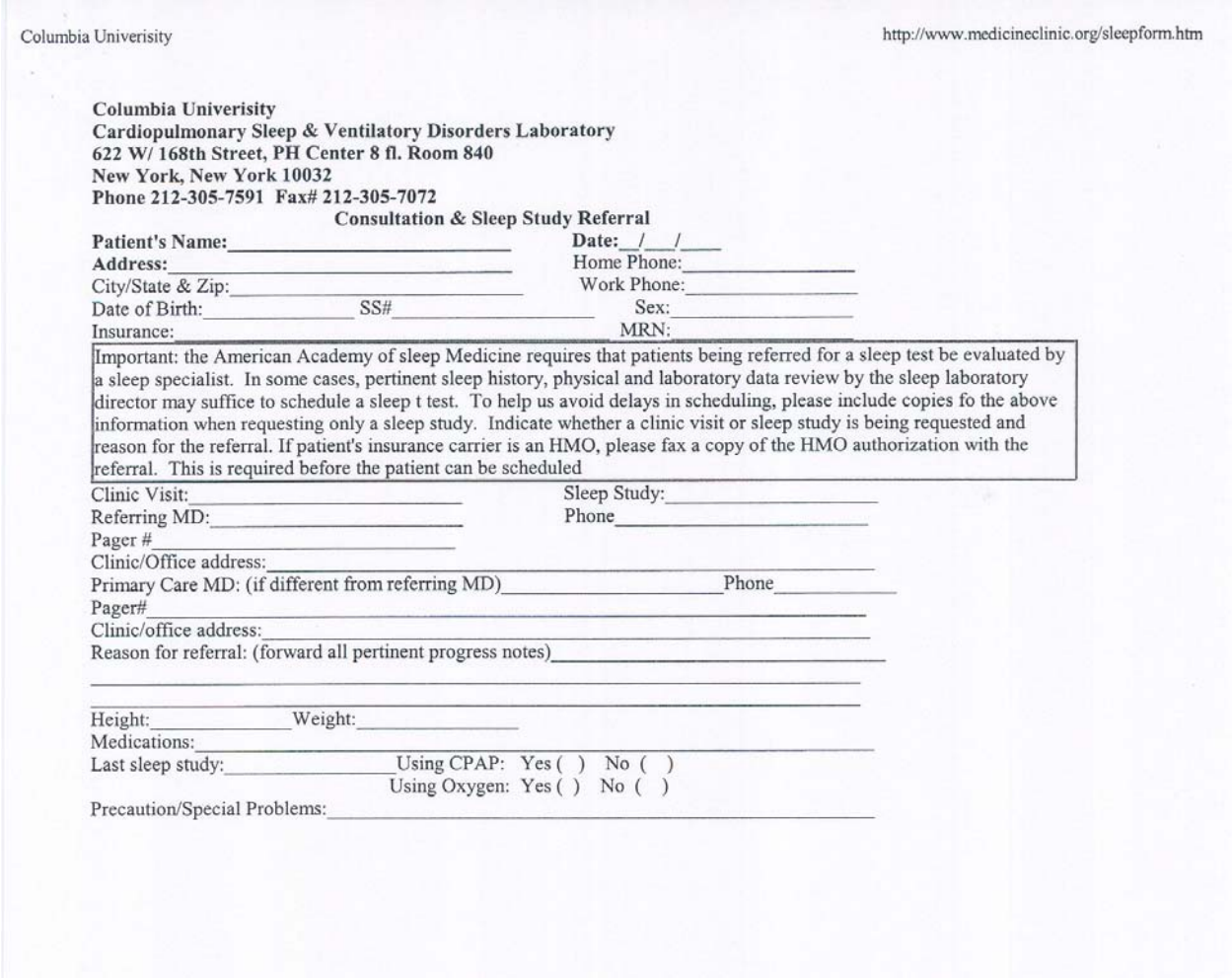
3. Blood Pressure and Cardiovascular Risk

According to the 7th Report of JNC, death from both ischemic heart disease and stroke increases pogressively and linearly from BP levels as low as 115mmHg SBP and 75mmHg DBP upward. For every 20mmHg systolic or 10mmHg diastolic increase in BP, the is a two-fold increase in mortality from both ischemic heart disease and stroke. A reduction of 5mmHg in SBP is estimated to result in 14% overall reduction in mortality due to stroke, a 9% reduction in mortality due to CHD, and a 7% decrease in all-cause mortality.

4. Frequency Distribution of SBP
    - NHANES III Study: SBP for ages 60 to 74 years, 1988-1991. Median 130mmHg, 90% percentile 160mmHg.
    - For Gaussian distribution, about 2/3 (68%) fall within 1 standard deviation of the mean, and about 95% fall within 2 standard deviations.

5. Current Classification and Recommended Management of Blood Pressure for Adults Aged 18 Years or Older (based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure)

- Stage 1 Hypertension (SBP140-159)
    - Lifestyle modification
    - Without compelling indication: thiazide-type diuretic; consider ACE-I, ARB, BB, CCB, or combination.
    - With compelling indication: Medication(s) for the compelling indications. Other antihypertensive medications as needed.
- Stage 2 Hypertension (SBP >/= 160)
    - Lifestyle modification
    - Without compelling indication: 2-medication combination for most
    - With compelling indication: Medication(s) for the compelling indications. Other antihypertensive medications as needed.



Columbia Univerisity http://www.medicineclinic.org/sleepform.htm

Columbia Univerisity
Cardiopulmonary Sleep & Ventilatory Disorders Laboratory
622 W/ 168th Street, PH Center 8 fl. Room 840
New York, New York 10032
Phone 212-305-7591 Fax# 212-305-7072

Consultation & Sleep Study Referral

Patient's Name:_____ **Date:**__/___/____
Address:_____ Home Phone:_____
City/State & Zip:_____ Work Phone:_____
Date of Birth:_____ SS#_____ Sex:_____
Insurance:_____ MRN:_____

Important: the American Academy of sleep Medicine requires that patients being referred for a sleep test be evaluated by a sleep specialist. In some cases, pertinent sleep history, physical and laboratory data review by the sleep laboratory director may suffice to schedule a sleep t test. To help us avoid delays in scheduling, please include copies fo the above information when requesting only a sleep study. Indicate whether a clinic visit or sleep study is being requested and reason for the referral. If patient's insurance carrier is an HMO, please fax a copy of the HMO authorization with the referral. This is required before the patient can be scheduled

Clinic Visit:_____ Sleep Study:_____
Referring MD:_____ Phone_____
Pager #_____
Clinic/Office address:_____
Primary Care MD: (if different from referring MD)_____Phone_____
Pager#_____
Clinic/office address:_____
Reason for referral: (forward all pertinent progress notes)_____
_____
_____
Height:_____Weight:_____
Medications:_____
Last sleep study:_____Using CPAP: Yes ( ) No ( )
Using Oxygen: Yes ( ) No ( )
Precaution/Special Problems:_____

Product information for patients & families

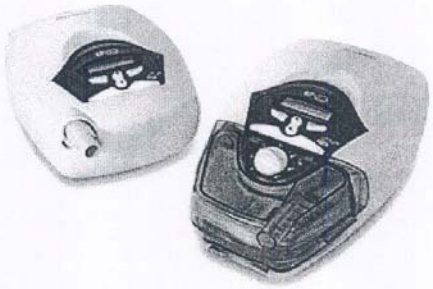
Where to buy

ResMed S7™ Elite CPAP

S7Elite Specifications

We added more than just water . . . We added you.

ResMed's S7 Elite CPAP combines integrated humidification, compliance and efficacy data for both patients and clinicians, and a number of other features that produce optimal comfort, convenience, and patient involvement in CPAP therapy. The S7 Elite software even allows users to upgrade to AutoSet Spirit technology without purchasing a new system. (Right: S7 Elite with and without HumidAire 2i™ heated humidifier)



Features & Benefits

- Optional HumidAire 2i integrated heated humidifier provides a highly effective and highly affordable upgrade path for patients who require heated humidification.
- HumidAire 2i humidifier has a warm-up feature for patients who want full humidification the moment they start therapy.
- All electronic components are isolated from the water chamber to ensure safety.
- Smart Data™ has been designed specifically for patients who want to access the compliance data recorded by the S7 Elite CPAP (each device comes with a Smart Data diary for patient tracking of therapy).
- User-friendly LCD display with an intuitive menu makes accessing data and setting treatment specifications simple.
- SmartStart® automatically starts and stops the S7 Elite CPAP.
- Ramp setting allows patients to select a time interval for the gradual commencement of CPAP therapy.
- Automatic internal power converter enables trouble-free international travel.
- High-tech sound baffling makes the S7 Elite CPAP an extremely quiet device.
- Internal pressure sensor accommodates for altitude changes when traveling.
- Small, lightweight, modular design makes the S7 Elite perfect for travel.
- The S7 Elite fits comfortably on a small nightstand, even with a humidifier attached.

Compatibility

- HumidAire 2i and 2iC humidifiers
- AutoScan™ 4.0 software
- Embla® and Embletta™ diagnostic devices
- ResControl™ clinical assistant

Product Numbers

S7 Elite CPAP	30002
HumidAire 2i heated humidifier	30902
HumidAire 2iC passover humidifier	30927
S7 Elite to AutoSet Spirit Upgrade Kit	30932
AutoScan 4.0 software	31051

Product information for clinicians & dealers

Where to buy

S7™ Elite CPAP

Specifications

We added more than just water . . . We added you.

ResMed's S7 Elite CPAP combines integrated humidification, data for both patients and clinicians, and a number of other features that produce optimal comfort, convenience, and patient involvement in CPAP therapy. (Right: S7 Elite CPAP with and without HumidAire 2i™ humidifier)

Features & Benefits

- Optional HumidAire 2i integrated heated humidifier provides a highly effective and highly affordable upgrade path for patients who require heated humidification.
- HumidAire 2i humidifier has a warm-up feature for patients who want full humidification the moment they start therapy.
- All electronic components are isolated from the water chamber to ensure safety.
- Data for clinicians, including trends in pressure, leak, AHI, AI, and HI, are available through the LCD interface, so downloading data to AutoScan™ software is not necessary for a snapshot of patient therapy.
- User-friendly LCD display with an intuitive menu makes accessing data and setting treatment specifications simple.
- Smart Data™ has been designed specifically for patients who want to access the compliance data recorded by the S7 Elite CPAP (each device comes with a Smart Data diary for patient tracking of therapy).
- SmartStart® automatically starts and stops the S7 Elite CPAP.
- Ramp setting allows patients to select a time interval for the gradual commencement of CPAP therapy.
- Automatic internal power converter enables trouble-free international travel.
- High-tech sound baffling makes the S7 Elite CPAP an extremely quiet device.
- Internal pressure sensor accommodates for altitude changes when traveling.
- Comprehensive data can be viewed using AutoScan 4.0 software (365 sessions Summary Data and 5 sessions Night Profile data).
- Small, lightweight, modular design makes the S7 Elite perfect for travel.
- The S7 Elite CPAP fits comfortably on small night tables, even with a humidifier attached.

Compatibility

- HumidAire 2i humidifier
- AutoScan 4.0 software
- Embla® and Embletta™ diagnostic devices
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AutoScan 4.0 software	31051

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2. Safety and Effectiveness (Summary)

2.1 Indications for Use

The S7™ *Elite* CPAP System is for the treatment of Obstructive Sleep Apnea (OSA) in adult patients. The optional integrated humidifier (HumidAire® 2i™) is indicated for the humidification and warming of air from the S7 Elite flow generator device. The S7 *Elite* CPAP flow generator and HumidAire 2i are for home and hospital use.

2.2 Brief Device Description

The S7 *Elite* CPAP System is a non-invasive Continuous Positive Airway Pressure (CPAP) system, including the following system components:

- Flow generator device
- Integrated Humidifier (HumidAire 2i)
- Mask and air tubing
- Clinical Interface (AutoScan) Software

The flow generator device incorporates a blower (motor/fan assembly), sensors and processing electronics. The blower supplies pressurized air to the patient via the air tubing and a mask.

The S7 *Elite* CPAP Flow Generator has one (1) mode of operation (CPAP fixed-pressure mode). In this mode the flow generator provides a single fixed-pressure as set by the clinician.

AutoScan software allows adjustment of parameter settings and viewing of flow generator-stored treatment data via a PC.

2.3 Substantial Equivalence

This submission demonstrates Substantial Equivalence of the S7 *Elite* CPAP System (including the integrated humidifier) with the predicate ResMed Sullivan AutoSet CPAP System (K980721)[1] and the predicate ResMed Sullivan HumidAire Heated Humidifier (K971260). (The Sullivan AutoSet CPAP System was cleared for use with the Sullivan HumidAire Heated Humidifier.)

[1] The Sullivan AutoSet CPAP System was subsequently marketed in the USA under the name "AutoSet T".

The S7 *ELITE* CPAP flow generator and the HumidAire 2i integrated humidifier are developments from the predicate Sullivan AutoSet flow generator and Sullivan HumidAire devices and share many design features. The predicate Sullivan AutoSet flow generator can operate in two modes (1) fixed-pressure CPAP mode and (2) auto-titrating (AutoSet) mode. The S7 *ELITE* CPAP flow generator operates in fixed-pressure CPAP mode only. However, the S7 *ELITE* CPAP flow generator incorporates some of the features from Sullivan AutoSet flow generator, such as storing patient usage, treatment pressure, mask leak and incidence of apneas and hypopneas. These features are used for Clinician review only.

In AutoSet mode the predicate Sullivan AutoSet flow generator adjusts pressure on a breath-by-breath basis to suit patient needs as they vary throughout the night. As a result, the patient receives the appropriate pressure required for effective therapy. The AutoSet algorithm in the Sullivan AutoSet flow generator responds to three key respiratory parameters: Inspiratory flow limitation, Snore and Apnea.

Note that the S7 *ELITE* CPAP flow generator does not operate in AutoSet mode for providing therapy to the patient as described above.

The S7 *ELITE* CPAP System has been tested to the following standards and guidance documents:

EN 60601-1	*Medical electrical equipment. Part 1: General requirements for safety.*
EN 60601-1-2	*Medical electrical equipment - Part 1: General requirements for safety - 2. Collateral standard: Electromagnetic compatibility.*
IEC 529: *1989*	*Degrees of protection provided by enclosures (Code IP).*
ISO 8185:1997	Humidifiers for medical use - General requirements.
PrEN ISO 17510	*Sleep Apnoea Therapy Devices* (1998).
Reviewer Guidance for Premarket Notification Submissions, November 1993, ARDB, CDRH, FDA.	
FDA *Heated Humidifier Review Guide*, Shelf # 780, 8/30/91 (applicable requirements)	

This submission presents the results of bench testing, and together with detailed descriptions demonstrates Substantial Equivalence of the S7 *ELITE* CPAP System to the predicate devices.

END – Traditional 510(k) Summary of Safety and Effectiveness