GAYLORD

# [redacted] Neuromodulation Therapy Report

Gaylord Sleep Research and Education
Meir Kryger, MD, FRCPC

I. Investigational Device: Neuromodulation prototype Sleep Apnea Therapy

II. Background:

a. Obstructive Sleep Apnea Syndrome (OSAS), a disease in which people stop breathing repetitively during sleep, is a common disorder affecting at least 4% of adult males and 2% of females. Its prevalence and symptoms (increased cardiovascular risk, severe daytime sleepiness) make it a condition with public health implications. It is also common in the pediatric age group. Apnea occurs when the tone of upper airway muscles is insufficient to maintain an open upper airway.

b. The gold standard for treatment is continuous positive airway pressure (CPAP). This treatment, although effective has major compliance issues with most centers reporting that 30 to 50% of patients are not using the treatment as indicated. The treatment is uncomfortable. Children with OSA are treated surgically; however in some CPAP is the only current option. In children there is the concern that CPAP may affect growth of facial structures. A new treatment would be enthusiastically welcomed by patients and clinicians.

c. Neuromodulation employs implantable and non-implantable medical device technologies to stimulate or suppress activity of the nervous system for the treatment of disease. In the case of the device [redacted] stimulation of the auditory system once apnea is detected is hypothesized to stimulate areas of the brainstem that result in restoration of upper airway patency.

d. Neuromodulation therapy, if found to be effective, would be rapidly adopted as a treatment option. This would have a tremendous game-changing impact in sleep apnea therapy because it is estimated that about 30% of patients already diagnosed are not treated. The device could also perhaps have a role in central sleep apnea. The impact would be felt by clinics such as ours and would have a real positive impact on patient health.

III. Purpose of study is to document:

a. Whether this prototype version of the Neuromodulation system detects apneas,
b. Whether this prototype terminates apneas within up to 9 stimulation pulses, one second apart.
c. Whether findings suggest that changes to the prototype device or algorithms would be helpful.

IV. Research Team:

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

a. Principal Investigator: Meir Kryger, MD, FRCPC
b. Program Coordinator: Valerie Assalone, RN, CCRP
c. Regional Technical Manager: Gary Lavalette, RT, RPSGT
d. Senior Research Technologist: Laurie Skinger, RRT, RPSGT

V. Protocol Procedures:

a. Screening/consenting visit and randomization
b. Sleep study: control night
c. Sleep study: device night

VI. Primary Endpoint:

a. Percentage of total apneas treated successfully by Neuromodulation
    i. Analysis of data examines the percentage of apneas terminated within nine pulses.

VII. Subjects:

a. D1-01: This 50-year-old male has sleep-related symptoms of snoring, restless sleep and excessive daytime sleepiness that occur against the background setting of diabetes, hypertension, obesity, and hypercholesterolemia. The subject endorsed nocturnal sleep-related symptoms of sleep disruption and sleep maintenance insomnia that have been ongoing for approximately 6-7 years and have worsened in both course and severity.

   BMI 38.4, ESS 7, diagnostic AHI 29.8 (9/14/2010).

   Primary endpoint:
   Percentage of total apneas that were treated successfully: 74 %

b. D1-02: This is a 63-year-old female who was diagnosed and treated for sleep apnea 5/20/2002. At that time she was found to have an apnea hypopnea index of 16.7, and she was ultimately prescribed Bilevel 15/11 cmH2O. The subject has been using the same machine since then and has not had another assessment. She has a 15 year history of snoring, 8 year of witnessed apnea, and excessive daytime sleepiness. In spite of treatment, which she uses every day, the subject has an Epworth sleepiness scale score of 10. Past medical history includes: obesity, chronic bronchitis, hay fever, hypertension, irritable bowel syndrome, kidney stones, uterine fibroids, polycystic ovarian syndrome, basal cell cancer, diabetes mellitus, and hypercholesterolemia.

   BMI 43.7, ESS 10, diagnostic AHI 25.1 (10/01/2010).

   Primary endpoint:
   Percentage of total apneas that were treated successfully: 86 %

c. D1-03: This is a 46-year-old male with a 20 year history of snoring, 20 year of witnessed apnea, and excessive daytime sleepiness. In 2000, the subject states that he was diagnosed at another

center as having obstructive sleep apnea. He was started on CPAP treatment and he states that he did well on it. The subject has not been on treatment for approximately 3 years because his equipment broke and/or disappeared during a series of moves. He has the following symptoms when awakening at night: shortness of breath and choking. Past medical history is positive for obesity.

BMI 49.5, ESS 7, AHI 39.3 (10/13/2010), occasional PVC's noted on EKG.

Primary endpoint:
Percentage of total apneas that were treated successfully: 94 %

d. D1-04: This is a 19 year old man whose referring physician endorsed sleep-related symptoms of snoring during sleep, witnessed pauses in breathing, episodes of gasping/choking during sleep, mouth breathing, leg kicks during sleep, difficulty remaining asleep, difficulty remaining awake during the day, and daytime fatigue/sleepiness. This occurs against a background setting of hypertension, tonsillar hypertrophy, gastroesophageal reflux, allergies, and obesity. The patient's sleep-related problems and symptoms consist of inadequate sleep hygiene given his practice of television viewing, telephone conversations, video game interaction from 7:30 p.m.-11 p.m. (all conducted prior to his nocturnal bedtime), sleep-onset insomnia, insufficient sleep, probable sleep-disordered breathing given his endorsement of witnessed apnea, awakening from episodes of shortness of breath, loud snoring, sleep disruption, unrefreshing sleep, and moderate-severe daytime somnolence given his practice of napping between 3 p.m. - 8 p.m. He also endorsed experiencing one episode of drowsy driving that occurred approximately 2 years ago. His past medical history includes obesity and asthma. His surgical history includes appendectomy.

BMI 40, ESS 10, diagnostic AHI 49.6 (12/06/2010).

Primary endpoint:
Percentage of total apneas that were treated successfully: 84 %

e. D1-05: This is a 64-year-old woman diagnosed with obstructive sleep apnea about 4 or 5 years ago which she states was classified as severe. She was prescribed CPAP but had trouble tolerating it. She reports loud snoring, waking with a dry mouth, waking with headaches, sleep onset insomnia, nocturnal awakenings, drowsy while driving and falling asleep driving, tooth grinding, and some somniloquy. She notes unrefreshing sleep, needing more than one alarm to get up, excessive daytime sleepiness, some daytime napping, and some rare symptoms that may be consistent with restless legs syndrome. Her past medical history includes obesity, obstructive sleep apnea, asthma, diabetes mellitus, depression, chronic fatigue syndrome, headaches, hypothyroidism, fibromyalgia, total abdominal hysterectomy with bilateral salpingo-oophorectomy, major motor vehicle accident with extensive injuries.
This patient had some hearing difficulties and during the setup for the treatment night loud stimuli were used. Interesting, see below, she had no apneas on the treatment night.

BMI 30.9, ESS 14, diagnostic AHI 30.3 (11/14/2010), occasional PVC's noted on EKG.

Primary endpoint:
Percentage of total apneas that were treated successfully: Subject experienced no apneas during this night.

f. D1-06: This is an 18 year old male noted to snore loudly, have witnessed breathing pauses, gasping arousals, and have significant obesity. Sometimes, if sedentary in the afternoon, he will find himself feeling sleepy. The subject is noted to talk in his sleep. His past medical history includes obesity and seasonal allergies. We believe that the low yield might have been related to the mouth flow sensor being too short. Longer sensors have been supplied.

BMI 39.6, ESS 9, diagnostic AHI 37 (11/16/2010), respiratory sinus arrhythmia noted on EKG.

Primary endpoint:
Percentage of total apneas that were treated successfully: 50 %

g. D1-07: This is a 38 year old man with sleep-related symptoms of loud and socially disruptive snoring, occasional witnessed apnea and unrefreshing sleep that began during the past 15 years. This occurs against a background setting of non-Hodgkin's lymphoma, treated with chemotherapy in 2007.

BMI 31.8, ESS 5, diagnostic AHI 20.6 (12/23/2010), rare wide-complex premature beats were noted on EKG.

Primary endpoint:
Percentage of total apneas that were treated successfully: 88%

h. D1-08: This 63 year old male has a history of witnessed pauses in breathing, daytime, daytime fatigue, nocturia, snoring and difficulty maintaining sleep. He also complains of libido issues which may possibly be associated with OSA. His past medical history includes hypertension, myocardial infarction (1983), kidney stones, gout, skin cancer, cataracts and hypothyroidism. He had a bilateral hernia repair in 2008.

BMI 31.7, ESS 7, diagnostic AHI 26 (1/06/2011)

Primary endpoint:
Percentage of total apneas that were treated successfully: 90%

i. D1-09: This is a 48 year old gentleman with a 30 year history of snoring, witnessed apnea and excessive daytime sleepiness. He takes metoprolol succinate.

BMI 32.9, ESS 16, diagnostic AHI 24.9 (1/17/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 89 %

j. D1-10: This is a 55 year old male with complaints of sleep onset/maintenance insomnia, frequent mind-racing, loud snoring , sleep disruption, sleep bruxism, and daytime somnolence. Although deliberate napping was denied, the subject inadvertently dozes at random times throughout the day.

BMI 32.6, ESS 5, diagnostic AHI 25.1 (2/04/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 89 %

k. D1-11: This 43 year old male complained of frequent awakenings, nonrestorative sleep, and daytime sleepiness. He estimates he gets 5 hours of sleep per night. He will occasionally take a nap on Saturday for 2-3 hours. His past medical history includes asthma, chronic shoulder and jaw pain, migraine, and high cholesterol.

BMI 41.6, ESS 13, diagnostic AHI 16.6 (2/12/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 100 %

l. D1-12: This 42 year old male was originally diagnosed with Obstructive Sleep Apnea in 2004. At the time, CPAP therapy was ordered, but the pt did not accept it or return for follow-up. Over the years, his snoring and witnessed apneas continued (his wife uses headphones in bed). He returned to the sleep center in 2011 at the request of his physician who was treating him for hypertension. His past medical history also includes obesity and hyperlipidemia.

BMI 41.3, ESS 11, diagnostic AHI 16 (2/4/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 88 %

m. D1-13: The subject is a 46 year old male with a 1 year history of snoring and excessive daytime sleepiness. Examples of the impact of sleepiness: The patient falls asleep in all low stimuli situation, including lunch breaks, and he has fallen asleep at his job. A second important symptom for patient is that he wakes up frequently at night it is wide awake for long periods of time. The patient often worries about the chest pain he has had at night and this may keep him from falling asleep.

The patient has had the following symptoms when awakening at night: The perception of not breathing, shortness of breath, chest pain, palpitations. The patient denies acid reflux, panic, or night sweats.

The patient denies any history consistent with another primary sleep disorder.

BMI 33.6, ESS 20, diagnostic AHI 16.1 (2/18/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 81 %

n. D1-14: This 60 year old female was originally diagnosed with Obstructive Sleep Apnea 8/21/2008. That study showed she had severe sleep apnea with SaO2 dropping as low as 78%. Therapeutic study done later that year showed that she did well with a pressure of 9 cm H2O. The patient was started on an auto-titrating machine. The patient states that she has never had the expected benefit from CPAP in spite of trying different masks, and adjustments of her machine. The last machine download suggested that AHI was about 30. This subject had another diagnostic polysomnogram 3/2/2011 which displayed an AHI of 40.7. The AHI in REM rose to 51.8. The patient snored for 45.1 percent of the night. Her past medical history includes restless leg syndrome, arthritis, hypertension, depression, anxiety, hypercholesterolemia, facial dystonia and cataracts.

BMI 35.2, ESS 8, diagnostic AHI 40.7 (3/2/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 95 %

o. D1-15: This subject is a 50 year old male who reports difficulty maintaining sleep, unrefreshing sleep, daytime sleepiness, morning headache and pauses in breathing during sleep. He has become more aware of sleep problems since shift changes began at work. He starts work at 4 a.m. now but will likely soon be moving to a 5 a.m. shift. He lists difficulty falling asleep, morning headache and excessive sleepiness during driving as his major concerns and also reports frequent awakenings. He has tried Benadryl in the past without significant effect on sleep quality. He has also tried behavioral therapy with deep breathing exercises which he followed on a CD. He reports a bedtime of 9 p.m., a 10 minute sleep onset latency, 2-3 awakenings per night lasting 5 minutes due to noise, light or unknown reasons. He takes scheduled naps at various times during the day and also falls asleep while watching television without meaning to. Naps occur at various times during the day and may last about 90 minutes.

BMI 30.8, ESS 15, diagnostic AHI 44.2 (11/02/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 88 %

p. D1-16: This 40 year old male has sleep-related problems that consist of sleep onset insomnia, rumination prior to sleep onset, severe restless leg symptoms that occur during periods of inactivity prior to his nocturnal bedtime and are seldom relieved with movement, loud snoring, witnessed pauses in breathing, leg kicks at night, and reflux/somatic pain and nocturia resulting with sleep disruption. There exists evidence of an intrinsic sleep disorder associated with lower back pain that has been ongoing for many years. The patient stated that his sleep-related problems began many years ago and has worsened in both course and severity. He also endorsed having a significant amount of marital and financial related stresses that have been negatively impacting his sleep. His past medical history includes chronic lower back pain, hay fever and hypercholesterolemia.

BMI 31.5, ESS 11, diagnostic AHI 31 (2/25/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 66 %

q. D1-17: This 21 year old female is morbidly obese and complains of excessive daytime sleepiness. Her sleep is not restorative. She does snore and her friends have told her that she does have pauses in her breathing while sleeping. She takes two naps per week in the afternoon of 1-2 hours in duration. Her naps are not refreshing. Past medical history is significant for obesity only.

BMI 61.1, ESS 12, diagnostic AHI 15.5 (3/12/2011)
Primary Endpoint:
Percentage of total apneas that were treated successfully: 25 %

r. D1-18: The patient presented today with sleep-related symptoms consisting of loud snoring that began many years ago, witnessed apnea as per his spouse, sleep disruption that he associated with shortness of breath that began during the past year, acid reflux resulting with sleep disruption, mind racing, sleep talking and sleep-related bruxism which is not being treated with the use of a mouth guard. This occurs against a background setting of seasonal allergies, hemochromatosis - phlebotomy, cold uticaria, borderline proteinuria, and a previous polysomnographic exam that was conducted at an outside laboratory and did not reveal evidence of sleep disordered breathing. The Epworth Sleepiness Scale score which is a self-administered test representing a patient's perception of their own daytime drowsiness is 14, which is suggestive of moderate daytime drowsiness.

The patient's typical nocturnal bedtime during weekdays is 10:30 p.m. and on weekends is 11:30 p.m. Sleep onset latency was endorsed at 5 minutes. The patient also endorsed experiencing one episode of sleep disruption because of urination. His weekday and weekend rise time is 6 a.m. and 7:30 a.m. respectively. He endorsed accruing 7.5 hours of sleep during weekdays and 8 hours of sleep on weekends. He typically prefers to sleep laterally. If and when having difficulty achieving sleep, he watches television.

BMI 28.9, ESS 14, diagnostic AHI 44.8 (3/17/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 100 %

s. D1-19 This 47 year old male presented with sleep-related symptoms consisting of frequent sleep disruption associated with his own snoring, awakening from sleep unrefreshed and moderate to severe excessive daytime sleepiness that is best characterized by his need to nap in his car during lunch breaks on 2-3 occasions per week. He stated that past naps provided relief from sleepiness however; he has not been experiencing the same outcome during the past year. He has also gained approximately 50 pounds during the past year. He did not endorse severe depressed moods or anxiety.

BMI 45.4, ESS 13, diagnostic AHI 38.2 (3/02/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 88 %

t. D1-20: This is a 41-year-old female with a 20 year history of snoring. The patient states that she had a sleep study done in 2003, but never followed up on that test and does not know what it showed. Family history is positive. The patient's mother was diagnosed with sleep apnea and treated with a CPAP machine. She has an older son who snores.

BMI 31.6, ESS 3, diagnostic AHI 17.5 (3/18/2011)

Primary Endpoint:
Percentage of total apneas that were treated successfully: 92 %

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

| | D1-01 | | D1-02 | | D1-03 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Female | | Male | |
| Age | 50 | | 63 | | 46 | |
| Height (in.) | 66 | | 66 | | 71 | |
| Weight (lbs) | 238 | | 271 | | 355 | |
| BMI | 38.4 | | 43.7 | | 49.5 | |
| ESS | 7 | | 10 | | 7 | |
| Dx AHI | 29.8 | | 25.1 | | 39.3 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 84.8 % | 80.1 % | 86.3 % | 84.9 % | 82 % | 80.7 % |
| % N1 | 10.9 % | 17.2 % | 10.9 % | 14.5 % | 17.1 % | 16.8 % |
| % N2 | 78 % | 74.6 % | 72.3 % | 67.9 % | 62 % | 66.8 % |
| % N3 | 0.8 % | 3.1 % | 3.6 % | 0.8 % | 11.2 % | 13.1 % |
| % REM | 10.3 % | 5.1 % | 13.2 % | 16.8 % | 9.7 % | 3.4 % |
| Arousal Index (AI) | 37.7 | 46.5 | 28.5 | 33.5 | 33.7 | 39 |
| Nadir SaO2 | 73 % | 80 % | 66 % | 64 % | 77 % | 84 % |
| % Apneas Detected | N/A | 77 % | N/A | 98 % | N/A | 96 % |
| % Apneas Treated Successfully | N/A | 74 % | N/A | 86 % | N/A | 94 % |

| | D1-04 | | D1-05 | | D1-06 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Female | | Male | |
| Age | 19 | | 66 | | 18 | |
| Height (in.) | 68.5 | | 64.5 | | 74 | |
| Weight (lbs) | 267 | | 189 | | 308.5 | |
| BMI | 40 | | 30.9 | | 39.6 | |
| ESS | 10 | | 14 | | 9 | |
| Dx AHI | 49.6 | | 30.3 | | 37 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 93.2 % | 90.3 % | 68.1 % | 62 % | 84.5 % | 74.7 % |
| % N1 | 10.6 % | 14.9 % | 12.5 % | 9.1 % | 9.6 % | 12.4 % |
| % N2 | 59.5 % | 50.9 % | 57.5 % | 69.2 % | 80.4 % | 79.6 % |
| % N3 | 14.7 % | 14.6 % | 5.8 % | 10.2 % | 1.2 % | 1.1 % |
| % REM | 15.3 % | 19.7 % | 24.1 % | 11.5 % | 8.9 % | 6.9 % |
| Arousal Index (AI) | 43.7 | 73.6 | 37.9 | 29.4 | 28.2 | 50.1 |
| Nadir SaO2 | 64 % | 65 % | 82 % | 83 % | 84 % | 86 % |
| % Apneas Detected | N/A | 87 % | N/A | N/A | N/A | 50 % |
| % Apneas Treated Successfully | N/A | 84 % | N/A | No Apneas | N/A | 50 % |

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

| | D1-07 | | D1-08 | | D1-09 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Male | | Male | |
| Age | 38 | | 63 | | 48 | |
| Height (in.) | 69 | | 72 | | 67 | |
| Weight (lbs) | 215 | | 220 | | 210 | |
| BMI | 31.8 | | 29.8 | | 32.9 | |
| ESS | 5 | | 0 | | 16 | |
| Dx AHI | 20.6 | | 26 | | 24.9 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 94.6 % | 88.1 % | 78 % | 85.8 % | 78 % | 81.7 % |
| % N1 | 8.8 % | 13.3 % | 9.9 % | 10.8 % | 9.5% | 24.2 % |
| % N2 | 66.3 % | 67.6 % | 68.6 % | 55.1 % | 62 % | 47.4 % |
| % N3 | 9.5 % | 4.9 % | 6.9 % | 11.5 % | 8.8 % | 1.8 % |
| % REM | 15.4 % | 14.2 % | 14.6 % | 22.6 % | 19.6 % | 26.7 % |
| Arousal Index (AI) | 17.6 | 30.1 | 27.3 | 30.1 | 34.5 | 66.6 |
| Nadir SaO2 | 90 % | 87 % | 83 % | 85 % | 82 % | 80 % |
| % Apneas Detected | N/A | 92% | N/A | 99% | N/A | 89 % |
| % Apneas Treated Successfully | N/A | 88% | N/A | 90% | N/A | 89% |

| | D1-10 | | D1-11 | | D1-12 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Male | | Male | |
| Age | 55 | | 43 | | 42 | |
| Height (in.) | 69 | | 69 | | 66 | |
| Weight (lbs) | 221 | | 282 | | 256 | |
| BMI | 32.6 | | 41.6 | | 41.3 | |
| ESS | 5 | | 13 | | 11 | |
| Dx AHI | 25.1 | | 16.6 | | 16 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 80.4 % | 85.4 % | 94.5 % | 89.7 % | 88.7 % | 79.8 % |
| % N1 | 7.6 % | 9 % | 9 % | 13.1 % | 12.5 % | 24.9 % |
| % N2 | 72.3 % | 80.2 % | 67.3 % | 68 % | 70.4 % | 62.5 % |
| % N3 | 3 % | 0 | 1.2 % | 0 | 4.8 % | 0 |
| % REM | 17 % | 10.8 % | 22.5 % | 18.9 % | 12.3 % | 12.6 % |
| Arousal Index (AI) | 23.2 | 19.1 | 21.2 | 23.6 | 29.1 | 49.3 |
| Nadir SaO2 | 79 % | 84% | 69 % | 75 % | 73 % | 72 % |
| % Apneas Detected | N/A | 99 % | N/A | 100 % | N/A | 88 % |
| % Apneas Treated Successfully | N/A | 89 % | N/A | 100 % | N/A | 88 % |

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

| | D1-13 | | D1-14 | | D1-15 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Female | | Male | |
| Age | 46 | | 60 | | 50 | |
| Height (in.) | 70 | | 64 | | 71 | |
| Weight (lbs) | 234 | | 205 | | 221 | |
| BMI | 33.6 | | 35.2 | | 30.8 | |
| ESS | 20 | | 8 | | 15 | |
| Dx AHI | 16.1 | | 40.7 | | 44.2 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 88.4 % | 82.3 % | 92.7 % | 77.7 % | 87 % | 89.5 % |
| % N1 | 5.1 % | 14.5 % | 10.2 % | 8.4 % | 13.2 % | 19.2 % |
| % N2 | 65.1 % | 64.3 % | 83.7 % | 83.3 % | 71.3 % | 67.6 % |
| % N3 | 15 % | 10.2 % | 0 | 2.6 % | 0.3 % | 0 |
| % REM | 14.8 % | 11 % | 6.2 % | 5.7 % | 15.2 % | 13.2 % |
| Arousal Index (AI) | 19.5 | 38.1 | 17.1 | 29.2 | 30.3 | 32.5 |
| Nadir SaO2 | 84 % | 85 % | 74 % | 75 % | 74 % | 78 % |
| % Apneas Detected | N/A | 81 % | N/A | 95 % | N/A | 89 % |
| % Apneas Treated Successfully | N/A | 81 % | N/A | 85 % | N/A | 88 % |

| | D1-16 | | D1-17 | | D1-18 | |
|---|---|---|---|---|---|---|
| Gender | Male | | Female | | Male | |
| Age | 40 | | 21 | | 46 | |
| Height (in.) | 71 | | 68 | | 69 | |
| Weight (lbs) | 226 | | 402 | | 196 | |
| BMI | 31.5 | | 61.1 | | 28.9 | |
| ESS | 11 | | 12 | | 14 | |
| Dx AHI | 31 | | 15.5 | | 44.8 | |
| PSG | Control | Device | Control | Device | Control | Device |
| Sleep Efficiency | 82.3 % | 91.2 % | 97 % | 95.5 % | 92.4 % | 84.6 % |
| % N1 | 20.9 % | 12.2 % | 7.4 % | 6.6 % | 11.9 % | 9.3 % |
| % N2 | 70.2 % | 64.2 % | 69.2 % | 57.2 % | 76.1 % | 65.3 % |
| % N3 | 0.2 % | 5 % | 22.3 % | 22.7 % | 0.1 % | 11.3 % |
| % REM | 8.7 % | 18.6 % | 1 % | 13.5 % | 11.8 % | 14.1 % |
| Arousal Index (AI) | 37.1 | 43.3 | 16.2 | 17.4 | 25.6 | 32.4 |
| Nadir SaO2 | 82 % | 79 % | 79 % | 75 % | 83 % | 84 % |
| % Apneas Detected | N/A | 73 % | N/A | 25 % | N/A | 100 % |
| % Apneas Treated Successfully | N/A | 66 % | N/A | 25 % | N/A | 100 % |

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

| | D1-19 | | D1-20 | |
|---|---|---|---|---|
| Gender | Male | | Female | |
| Age | 47 | | 41 | |
| Height (in.) | 72 | | 65 | |
| Weight (lbs) | 335 | | 190 | |
| BMI | 45.4 | | 31.6 | |
| ESS | 13 | | 3 | |
| Dx AHI | 38.2 | | 17.5 | |
| PSG | Control | Device | Control | Device |
| Sleep Efficiency | 73.2 % | 86.2 % | 89.6 % | 91.2 % |
| % N1 | 15.1 % | 10.2 % | 7.1 % | 5.1 % |
| % N2 | 64.7 % | 71.3 % | 74.3 % | 71.8 % |
| % N3 | 0 | 0 | 0.6 % | 0.4 % |
| % REM | 20.2 % | 18.6 % | 18.1 % | 22.7 % |
| Arousal Index (AI) | 32.9 | 20.5 | 21.7 | 17.9 |
| Nadir SaO2 | 87 % | 88 % | 90 % | 92 % |
| % Apneas Detected | N/A | 50 % | N/A | 74 % |
| % Apneas Treated Successfully | N/A | 67 % | N/A | 74 % |

Across the 20 subjects investigated using the neuromodulation sleep apnea device, there was a total of 1464 apneas identified during device night. Of those, 1217 obstructive and mixed apneas were appropriately resolved by the neuromodulation device and 44 central apneas were appropriately resolved by it.

The 2 subjects of interest chose to have the polysomnograms back-to-back AND both were randomized to Device night, followed by Control night.

Subject D1-05 had a (pre-research) **diagnostic AHI of 30 with 14 apneas**.
She had a Neuromodulation Device psg, followed by a Control night psg on the very next night.
It would be reasonable to expect that the Control night psg would display results similar to the Diagnostic psg; however, this subject had an **AHI of 15.5 with 0 apneas on the Control night**.

Subject D1-07 had a (pre-research) **diagnostic AHI of 20.6 with 13 apneas**.
Again, he had a Neuromodulation Device psg, followed by a Control night psg on the very next night.
This subject had an **AHI of 0.5 with 0 apneas on the Control night**.
It would be reasonable to expect that the Control night psg would display results similar to the Diagnostic psg, but interestingly, the Control night psg occurring *the night after* Neuromodulation Device night therapy, displayed a *normal* AHI with *no apneas*.

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

## Group Data

Table 1. Demographics

| Subject | Gender | Age | Height (in.) | Weight (lbs) | BMI | ESS | Dx AHI |
|---|---|---|---|---|---|---|---|
| D1-01 | Male | 50 | 66 | 238 | 38.4 | 7 | 29.8 |
| D1-02 | Female | 63 | 66 | 271 | 43.7 | 10 | 25.1 |
| D1-03 | Male | 46 | 71 | 355 | 49.5 | 7 | 39.3 |
| D1-04 | Male | 19 | 68.5 | 267 | 40 | 10 | 49.6 |
| D1-05 | Female | 66 | 64.5 | 189 | 30.9 | 14 | 30.3 |
| D1-06 | Male | 18 | 74 | 308.5 | 39.6 | 9 | 37 |
| D1-07 | Male | 38 | 69 | 215 | 31.8 | 5 | 20.6 |
| D1-08 | Male | 63 | 72 | 220 | 29.8 | 0 | 26 |
| D1-09 | Male | 48 | 67 | 210 | 32.9 | 16 | 24.9 |
| D1-10 | Male | 55 | 69 | 221 | 32.6 | 5 | 25.1 |
| D1-11 | Male | 43 | 69 | 282 | 41.6 | 13 | 16.6 |
| D1-12 | Male | 42 | 66 | 256 | 41.3 | 11 | 16 |
| D1-13 | Male | 46 | 70 | 234 | 33.6 | 20 | 16.1 |
| D1-14 | Female | 60 | 64 | 205 | 35.2 | 8 | 40.7 |
| D1-15 | Male | 50 | 71 | 221 | 30.8 | 15 | 44.2 |
| D1-16 | Male | 40 | 71 | 226 | 31.5 | 11 | 31 |
| D1-17 | Female | 21 | 68 | 402 | 61.1 | 12 | 15.5 |
| D1-18 | Male | 46 | 69 | 196 | 28.9 | 14 | 44.8 |
| D1-19 | Male | 47 | 72 | 335 | 45.4 | 13 | 38.2 |
| D1-20 | Female | 41 | 65 | 190 | 31.6 | 3 | 17.5 |
| | low | 18 | 64 | 189 | 28.9 | 0 | 15.5 |
| | high | 66 | 74 | 402 | 61.1 | 20 | 49.6 |
| | **Mean** | **45.1** | **68.6** | **252.08** | **37.51** | **10.2** | **29.415** |

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

Table 2. Sleep architecture

| Subject | Sleep Efficiency | | % N1 | | % N2 | | % N3 | | % REM | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | Device | Control | Device | Control | Device | Control | Device | Control | Device |
| D1-01 | 84.8% | 80.1% | 10.9% | 17.2% | 78% | 74.6% | 0.8% | 3.1% | 10.3% | 5.1% |
| D1-02 | 86.3% | 84.9% | 10.9% | 14.5% | 72.3% | 67.9% | 3.6% | 0.8% | 13.2% | 16.8% |
| D1-03 | 82% | 80.7% | 17.1% | 16.8% | 62% | 66.8% | 11.2% | 13.1% | 9.7% | 3.4% |
| D1-04 | 93.2% | 90.3% | 10.6% | 14.9% | 59.5% | 50.9% | 14.7% | 14.6% | 15.3% | 19.7% |
| D1-05 | 68.1% | 62% | 12.5% | 9.1% | 57.5% | 69.2% | 5.8% | 10.2% | 24.1% | 11.5% |
| D1-06 | 84.5% | 74.7% | 9.6% | 12.4% | 80.4% | 79.6% | 1.2% | 1.1% | 8.9% | 6.9% |
| D1-07 | 94.6% | 88.1% | 8.8% | 13.3% | 66.3% | 67.6% | 9.5% | 4.9% | 15.4% | 14.20% |
| D1-08 | 78% | 85.8% | 9.9% | 10.8% | 68.6% | 55.1% | 6.9% | 11.5% | 14.6% | 22.60% |
| D1-09 | 78% | 81.7% | 9.5% | 24.2% | 62% | 47.4% | 8.8% | 1.8% | 19.6% | 26.7% |
| D1-10 | 80.4% | 85.4% | 7.6% | 9% | 72.3% | 80.2% | 3% | 0.0% | 17% | 10.8% |
| D1-11 | 94.5% | 89.7% | 9% | 13.1% | 67.3% | 68% | 1.2% | 0 | 22.5% | 18.9% |
| D1-12 | 88.7% | 79.8% | 12.5% | 24.9% | 70.4% | 62.5% | 4.8% | 0 | 12.3% | 12.6% |
| D1-13 | 88.4% | 82.3% | 5.1% | 14.5% | 65.1% | 64.3% | 15% | 10.2% | 14.8% | 11% |
| D1-14 | 92.7% | 77.7% | 10.2% | 8.4% | 83.7% | 83.3% | 0 | 2.6% | 6.2% | 5.7% |
| D1-15 | 87% | 89.5% | 13.2% | 19.2% | 71.3% | 67.6% | 0.3% | 0 | 15.2% | 13.2% |
| D1-16 | 82.3% | 91.2% | 20.9% | 12.2% | 70.2% | 64.2% | 0.2% | 0.2% | 8.7% | 18.6% |
| D1-17 | 97% | 95.5% | 7.4% | 6.6% | 69.2% | 57.2% | 22.3% | 22.7% | 1.0% | 13.5% |
| D1-18 | 92.4% | 84.6% | 11.9% | 9.3% | 76.1% | 65.3% | 0.1% | 11.3% | 11.8% | 14.1% |
| D1-19 | 73.2% | 86.2% | 15.1% | 10.2% | 64.7% | 71.3% | 0 | 0 | 20.2% | 18.6% |
| D1-20 | 89.60% | 91.20% | 7.10% | 5.10% | 74.30% | 71.80% | 0.60% | 0.40% | 18.10% | 22.70% |
| | | | | | | | | | | |
| Low | 68.10% | 62.00% | 5.10% | 5.10% | 57.50% | 47.40% | 0.00% | 0.00% | 1.00% | 3.40% |
| High | 97.00% | 95.50% | 20.90% | 24.90% | 83.70% | 83.30% | 22.30% | 22.70% | 24.10% | 26.70% |
| Mean | 85.79% | 84.07% | 10.99% | 13.29% | 69.56% | 66.74% | 5.50% | 5.43% | 13.95% | 14.33% |

Gaylord Hospital
P.O. BOX 400
WALLINGFORD, CT 06492
Tel: 203-741-3410

Table 3. Sleep disordered breathing and apnea detection

| Subject | Arousal/Awakening Index (AAI) | | Nadir SaO2 | | % Apneas Detected | % Apneas Treated Successfully |
|---|---|---|---|---|---|---|
| | Control | Device | Control | Device | Device | Device |
| D1-01 | 37.7 | 46.5 | 73% | 80% | 77% | 74% |
| D1-02 | 28.5 | 33.5 | 66% | 64% | 98% | 86% |
| D1-03 | 33.7 | 39 | 77% | 84% | 96% | 94% |
| D1-04 | 43.7 | 73.6 | 64% | 65% | 87% | 84% |
| D1-05 | 37.9 | 29.4 | 82% | 83% | N/A | No Apneas |
| D1-06 | 28.2 | 50.1 | 84% | 86% | 50% | 50% |
| D1-07 | 17.6 | 30.1 | 90% | 87% | 92% | 88% |
| D1-08 | 27.3 | 30.1 | 83% | 85% | 99% | 90% |
| D1-09 | 34.5 | 66.6 | 82% | 80% | 89% | 89% |
| D1-10 | 23.2 | 19.1 | 79% | 84% | 99% | 89% |
| D1-11 | 21.2 | 23.6 | 69% | 75% | 100% | 100% |
| D1-12 | 29.1 | 49.3 | 73% | 72% | 88% | 88% |
| D1-13 | 19.5 | 38.1 | 84% | 85% | 81% | 81% |
| D1-14 | 17.1 | 29.2 | 74% | 75% | 95% | 85% |
| D1-15 | 30.3 | 32.5 | 74% | 78% | 89% | 88% |
| D1-16 | 37.1 | 43.3 | 82% | 79% | 73% | 66% |
| D1-17 | 16.2 | 17.4 | 79% | 75% | 25% | 25% |
| D1-18 | 25.6 | 32.4 | 83% | 84% | 100% | 100% |
| D1-19 | 32.9 | 20.5 | 87% | 88% | 50% | 67% |
| D1-20 | 21.7 | 17.9 | 90% | 92% | 74% | 74% |
| | | | | | 82% | |
| Low | 16.2 | 17.4 | 64.00% | 64.00% | 25.00% | 25.00% |
| High | 43.7 | 73.6 | 90.00% | 92.00% | 100.00% | 100.00% |
| Mean | 28.15 | 36.11 | 78.75% | 80.05% | 82% | 80.00% |

## Conclusions

The subjects in the research represented a fairly typical cohort of sleep apnea. Age, BMI, gender distribution, and Apnea-hypopnea index were representative of patients referred to a sleep clinic.

This research evaluated an early prototype of the [redacted] device and software that asked two key questions:

*1. Did the [redacted] device detect apneas?*

On the average the device the device detected more than 80% of scored apneas. The means were skewed by two subjects (D-17 and D-06) in whom apneas were not detected reliably (25 and 50%). In 17 of the 20 subjects more than 80% of the apneas were detected.

*2. Did the [redacted] device terminate apneas?*

On the average the device the device treated 80% of scored apneas. Again, the means were skewed by two subjects (D-17 and D-06) in whom apneas had not been detected reliably (25 and 50%). In 17 of the 20 subjects more than 80% of the apneas were detected.

The iteration of the device we tested was not designed to detect or treat hypopneas which are commonly seen in patients with obstructive sleep apnea syndrome. This it is not surprising that we did not see significant changes in sleep architecture. There was an increase in arousal index and this was driven by large changes in some of the subjects. The group sizes are too small to draw conclusions.

These results are encouraging and suggest that a device that detects and treats both apneas and hypopneas at the same rate as in this study would result in a significant reduction in apnea-hypopnea index.

**Future directions**

It is important that a device that tests both apneas and hypopneas be developed and tested. Such future research may also indicate which patients are the most likely to respond. Once a reliable device has been designed and tested in a larger feasibility study, a multicenter pivotal study would be a suggested next step. Devices that also test patients with central apneas would be of great interest.