The Clinical Outcomes of Implantable Devices for Treatment of Sleep Apnea

10-16-2018

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Conflicts of Interest

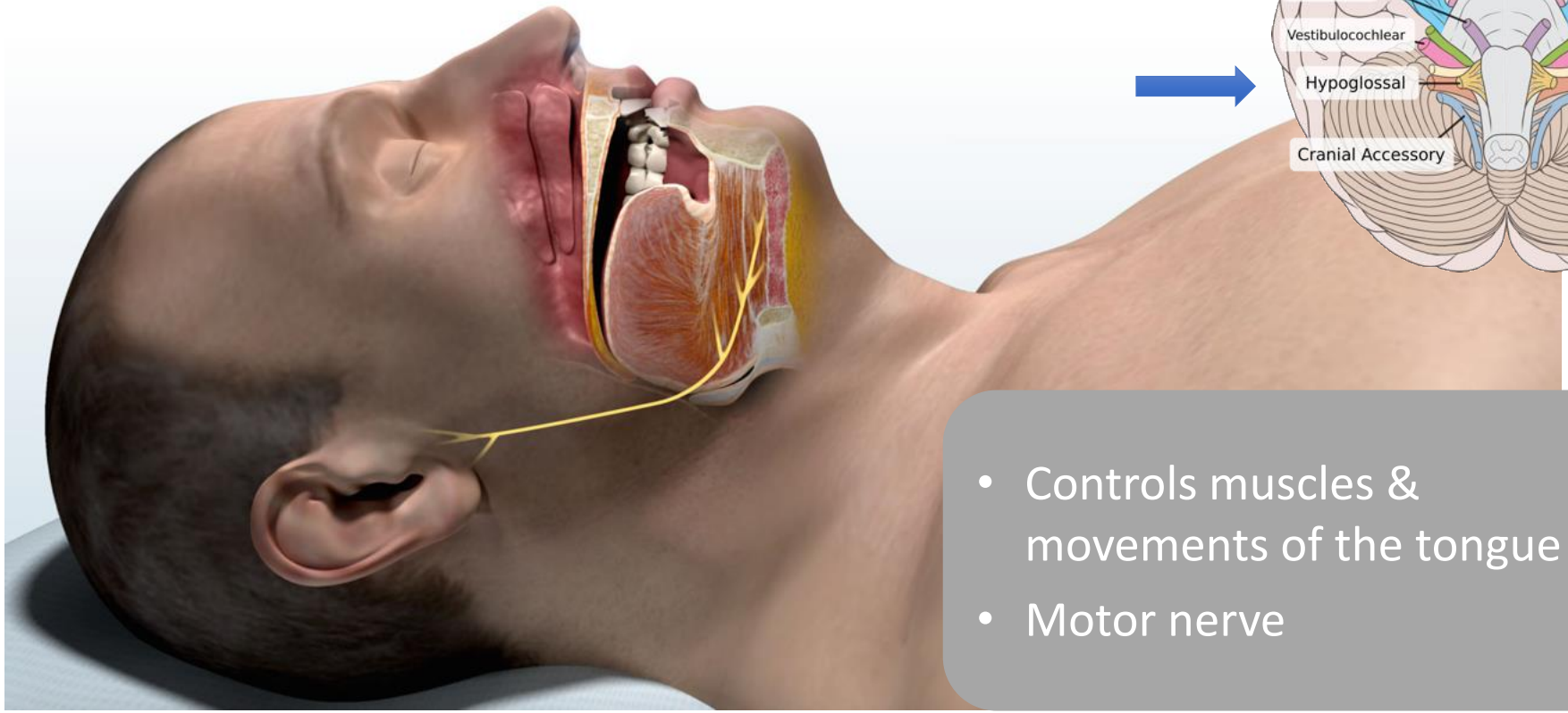
- Senior Therapy Development Program Manager at Inspire Medical Systems

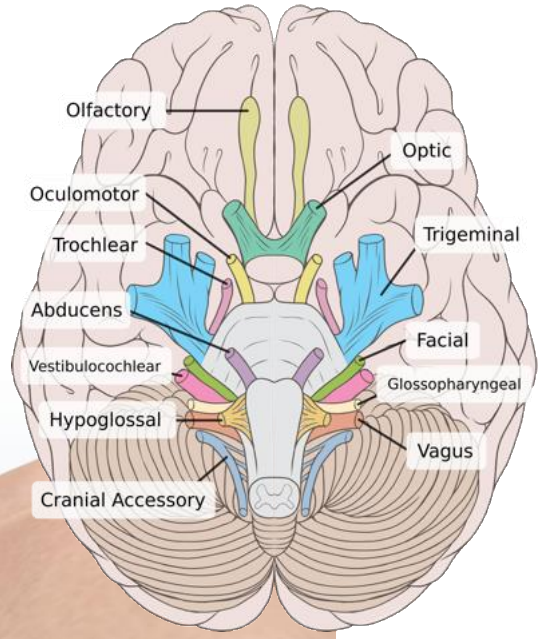
Topics

- Upper Airway Stimulation Basics
- Upper Airway Stimulation Feasibility Research
- STAR Trial Long Term Data (Pivotal Trial)
- New Clinical Data
- Pediatric Research

Upper Airway Stimulation Basics

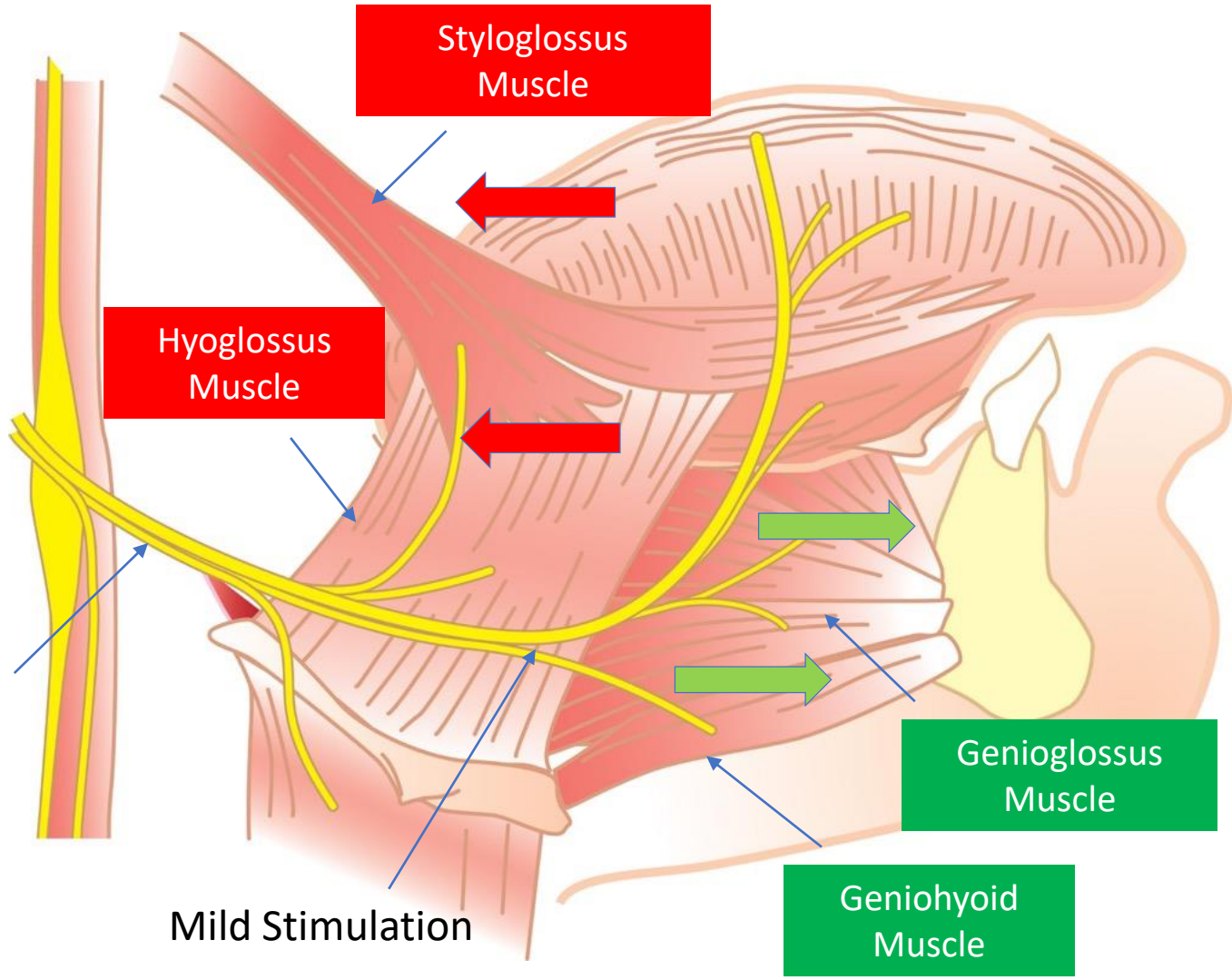
The Hypoglossal Nerve (Cranial Nerve XII)

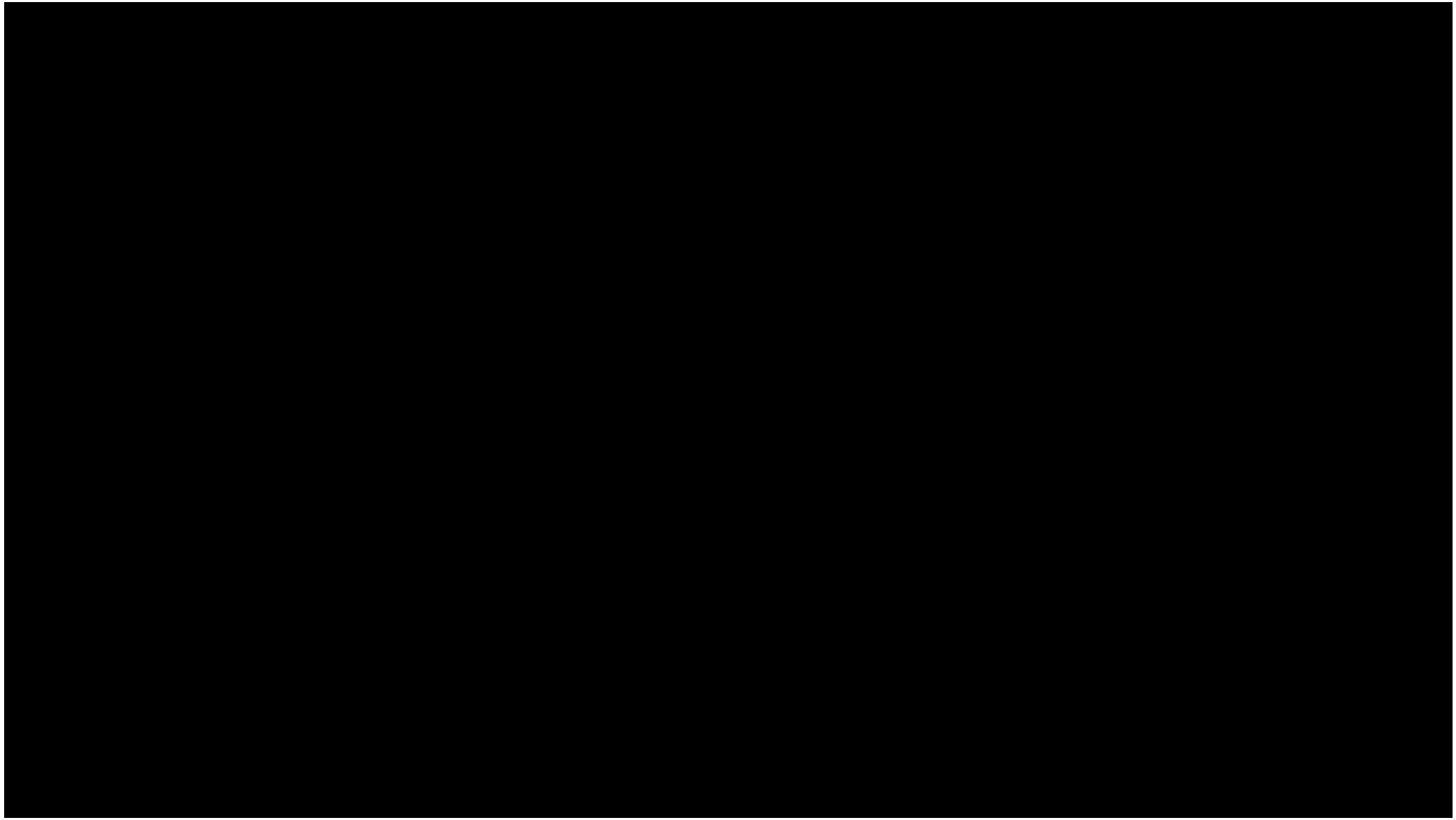




- Controls muscles & movements of the tongue
- Motor nerve

The Distal Hypoglossal Nerve



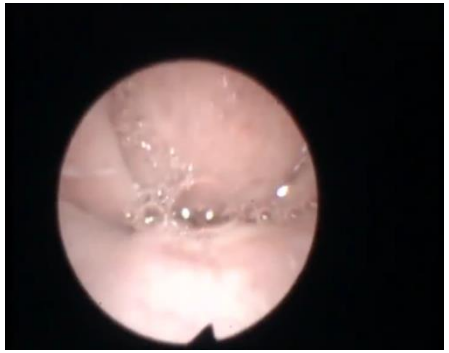


Hypoglossal Nerve Stimulation Effect

No Stimulation

Base of Tongue

Palate



Mild Stimulation

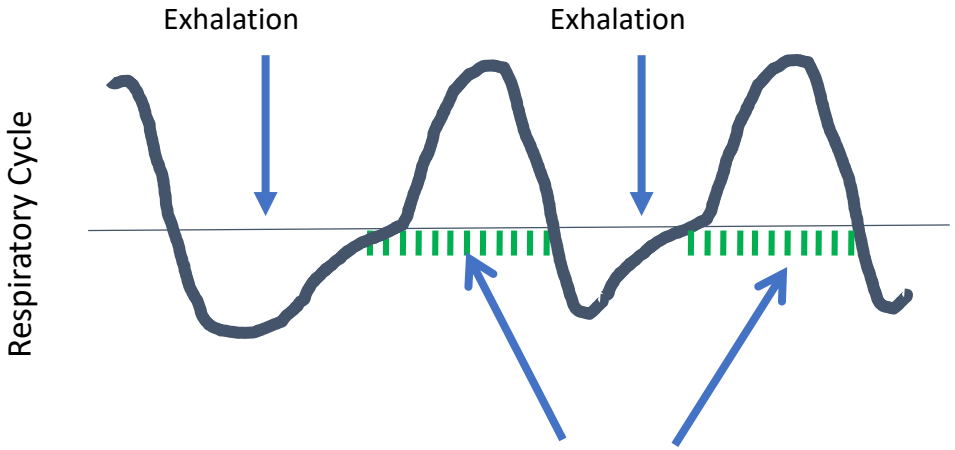
Base of Tongue

Palate

Stimulation Timed With Breathing

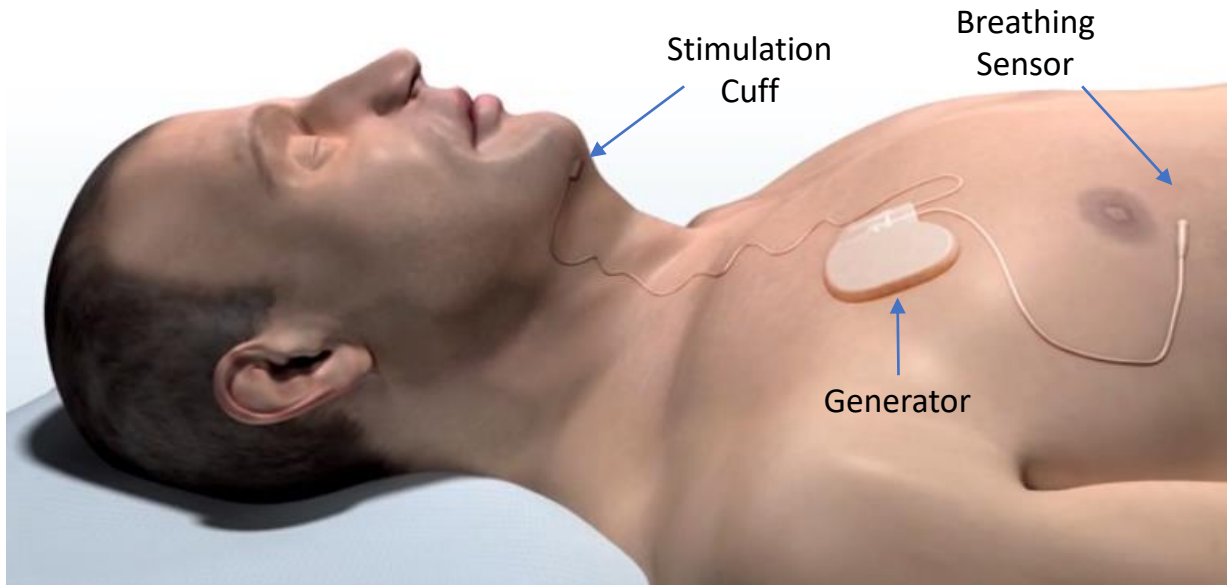
Rhythmic, Preventative Stimulation When Airway is Most Vulnerable to Collapse

Breathing sensor placed in between intercostal muscle layers

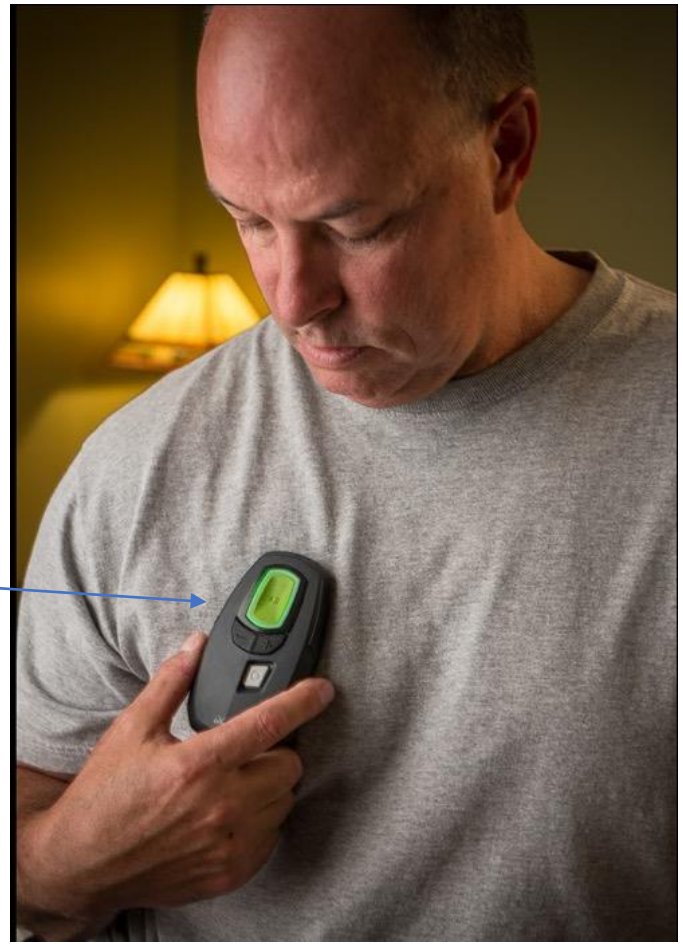


Stimulation delivered during inspiratory period

Upper Airway Stimulation



- Safe outpatient procedure – 3 skin incisions
- Fast recovery; over-the-counter pain meds typical
- MRI conditional labeling
- ~11 year battery longevity



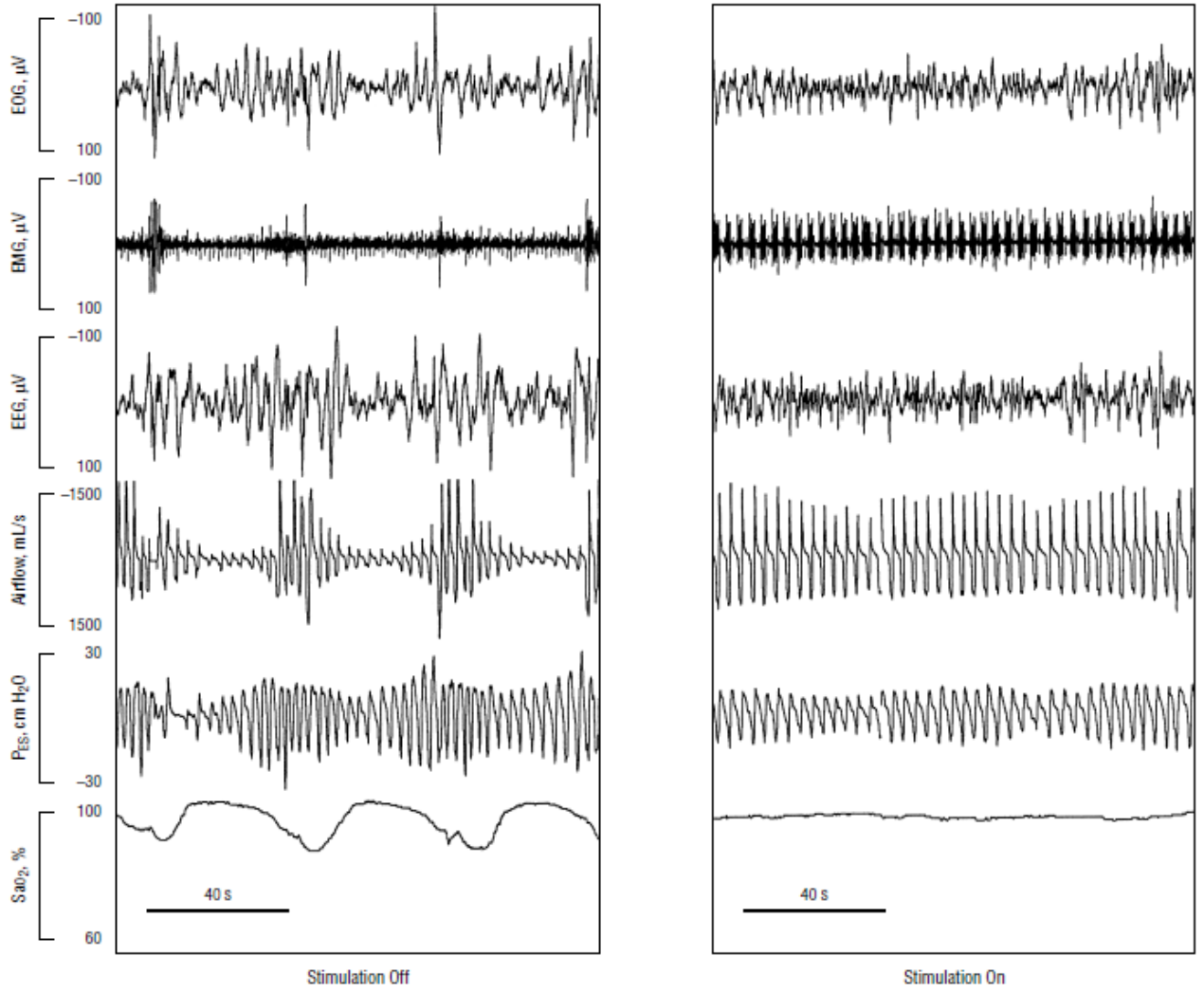
- Adjustable
- Titratable
- Daily adherence monitoring

What Does Stimulation Feel Like?

- Patients describe a mild tongue movement when UAS is on
- Adjustable for patient comfort
- Most patients acclimate well within the first month of use

Upper Airway Stimulation Feasibility Research

Feasibility of Hypoglossal Nerve Stimulation



Augmented muscle tone

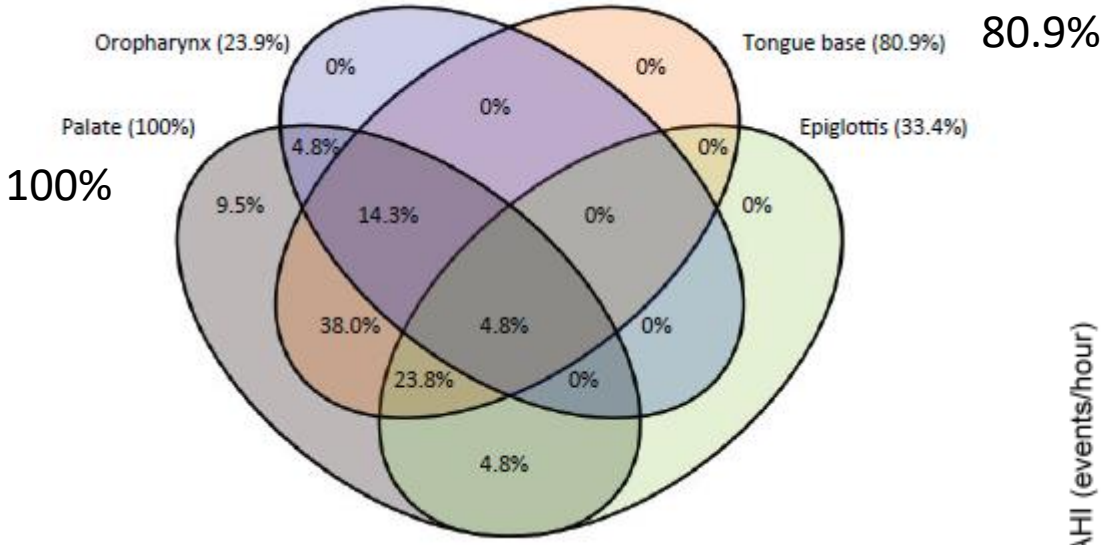
Without causing arousals

Immediately stabilized airway

Improved Oxygenation

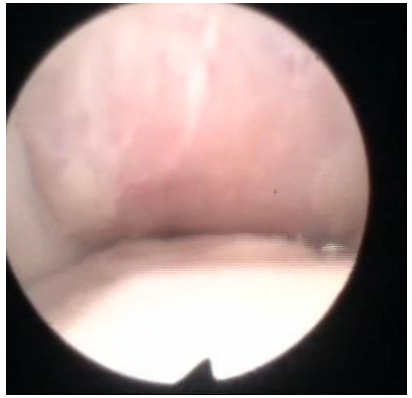
Schwartz et al, Arch Oto Head Neck Surg 2001

Mechanism of Action: Site of Obstruction



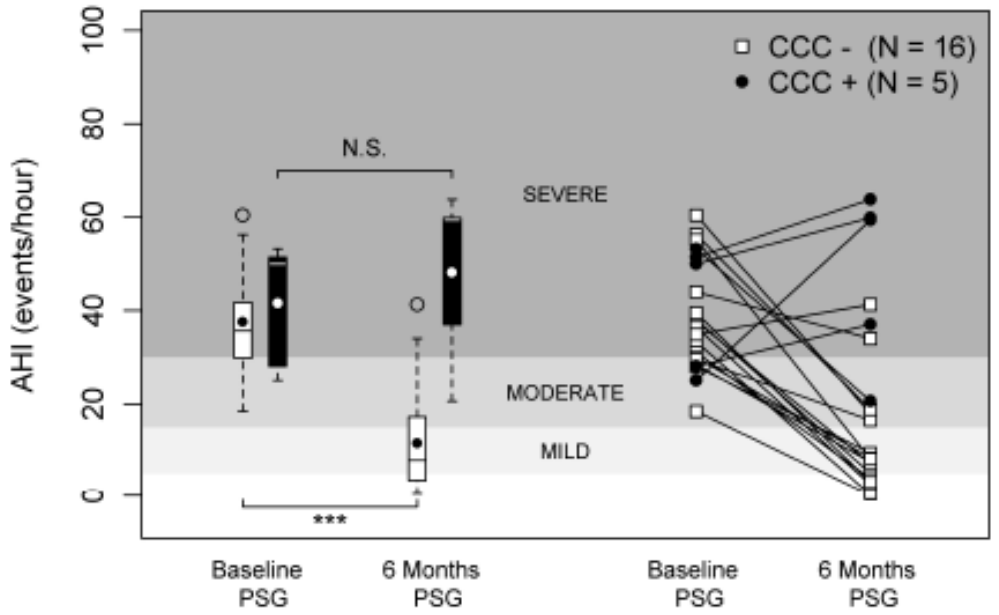
80.9%

100%



AP Collapse

Concentric Collapse



Exclusion of complete concentric collapse (CCC) at palate for improved response

Vanderveken et al, J Clin Sleep Med 2013

Stimulation Therapy for Apnea Reduction (STAR) Pivotal Trial - Long Term Data

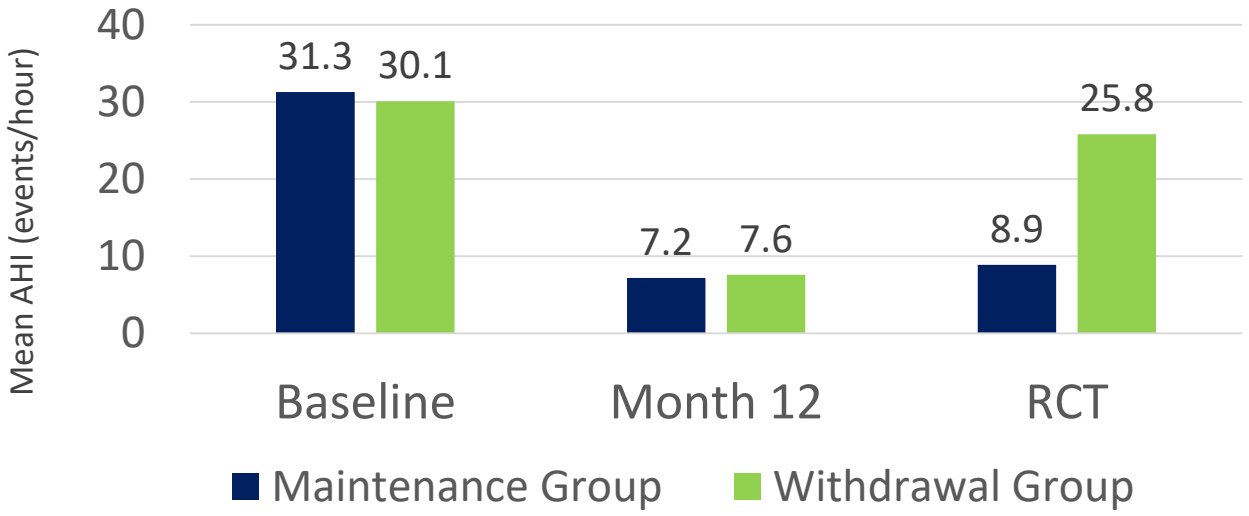
STAR Trial Overview – 5 Year Follow-Up Complete

STAR Trial Design

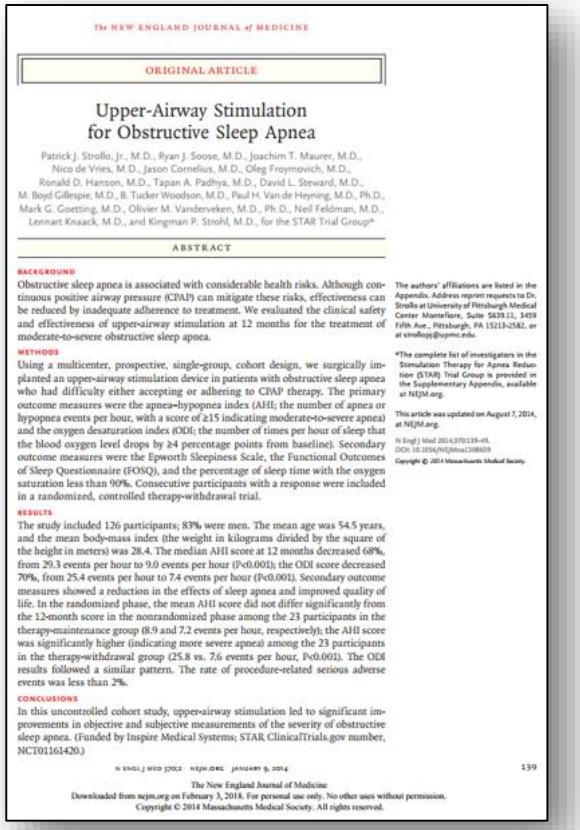
- Multi-center, prospective, Phase III pivotal trial
- 126 patients at 22 centers across US & Europe

Randomized Control Therapy Withdrawal

- Withdrawal of UAS resulted in reversal of therapeutic benefit



12 month STAR results published in the *New England Journal of Medicine, 2014*



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Upper-Airway Stimulation for Obstructive Sleep Apnea

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ABSTRACT

BACKGROUND

Obstructive sleep apnea is associated with considerable health risks. Although continuous positive airway pressure (CPAP) can mitigate these risks, effectiveness can be reduced by inadequate adherence to treatment. We evaluated the clinical safety and effectiveness of upper-airway stimulation at 12 months for the treatment of moderate-to-severe obstructive sleep apnea.

METHODS

Using a multicenter, prospective, single-group, cohort design, we surgically implanted an upper-airway stimulation device in patients with obstructive sleep apnea who had difficulty either accepting or adhering to CPAP therapy. The primary outcome measures were the apnea–hypopnea index (AHI; the number of apnea or hypopnea events per hour, with a score of ≥15 indicating moderate-to-severe apnea) and the oxygen desaturation index (ODI; the number of times per hour of sleep that the blood oxygen level drops by ≥4 percentage points from baseline). Secondary outcome measures were the Epworth Sleepiness Scale, the Functional Outcomes of Sleep Questionnaire (FOSQ), and the percentage of sleep time with the oxygen saturation less than 90%. Consecutive participants with a response were included in a randomized, controlled therapy-withdrawal trial.

RESULTS

The study included 126 participants; 83% were men. The mean age was 54.5 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 28.4. The median AHI score at 12 months decreased 68%, from 29.3 events per hour to 9.0 events per hour (P<0.001); the ODI score decreased 70%, from 25.4 events per hour to 7.4 events per hour (P<0.001). Secondary outcome measures showed a reduction in the effects of sleep apnea and improved quality of life. In the randomized phase, the mean AHI score did not differ significantly from the 12-month score in the nonrandomized phase among the 23 participants in the therapy-maintenance group (8.9 and 7.2 events per hour, respectively); the AHI score was significantly higher (indicating more severe apnea) among the 23 participants in the therapy-withdrawal group (25.8 vs. 7.6 events per hour, P<0.001). The ODI results followed a similar pattern. The rate of procedure-related serious adverse events was less than 2%.

CONCLUSIONS

In this uncontrolled cohort study, upper-airway stimulation led to significant improvements in objective and subjective measurements of the severity of obstructive sleep apnea. (Funded by Inspire Medical Systems; STAR ClinicalTrials.gov number, NCT01161420.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Strollo at University of Pittsburgh Medical Center Montefiore, Suite 5639.11, 3459 Fifth Ave., Pittsburgh, PA 15213-2582, or at strollopj@upmc.edu.

*The complete list of investigators in the Stimulation Therapy for Apnea Reduction (STAR) Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

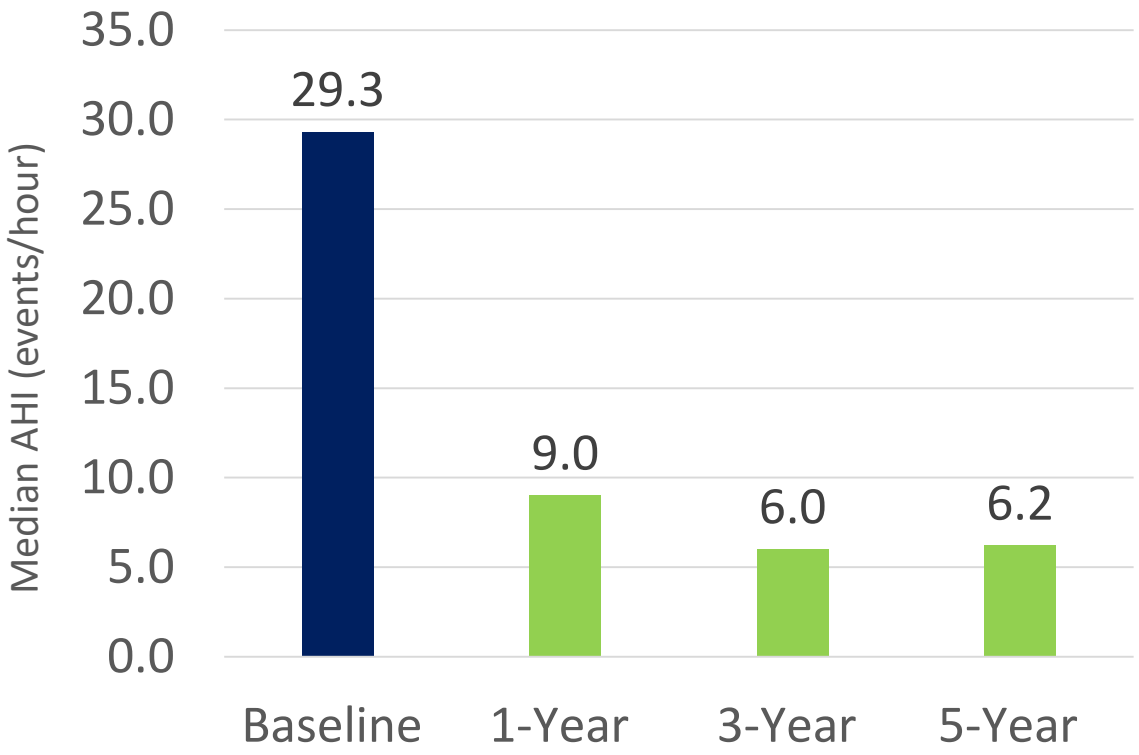
This article was updated on August 7, 2014, at NEJM.org.

N Engl J Med 2014;370:139–49.
DOI: 10.1056/NEJMoa1308659

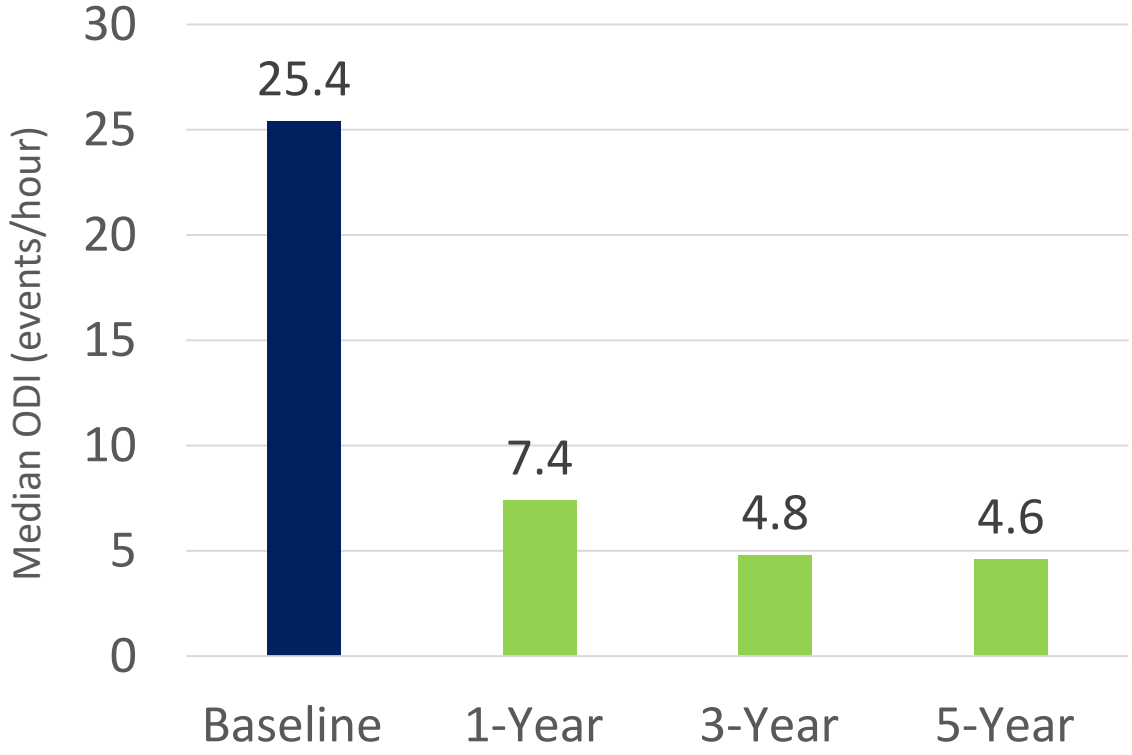
Strollo et al NEJM 2014

Sustained AHI & ODI Reduction Over 5 Years

Apnea Hypopnea Index (AHI)



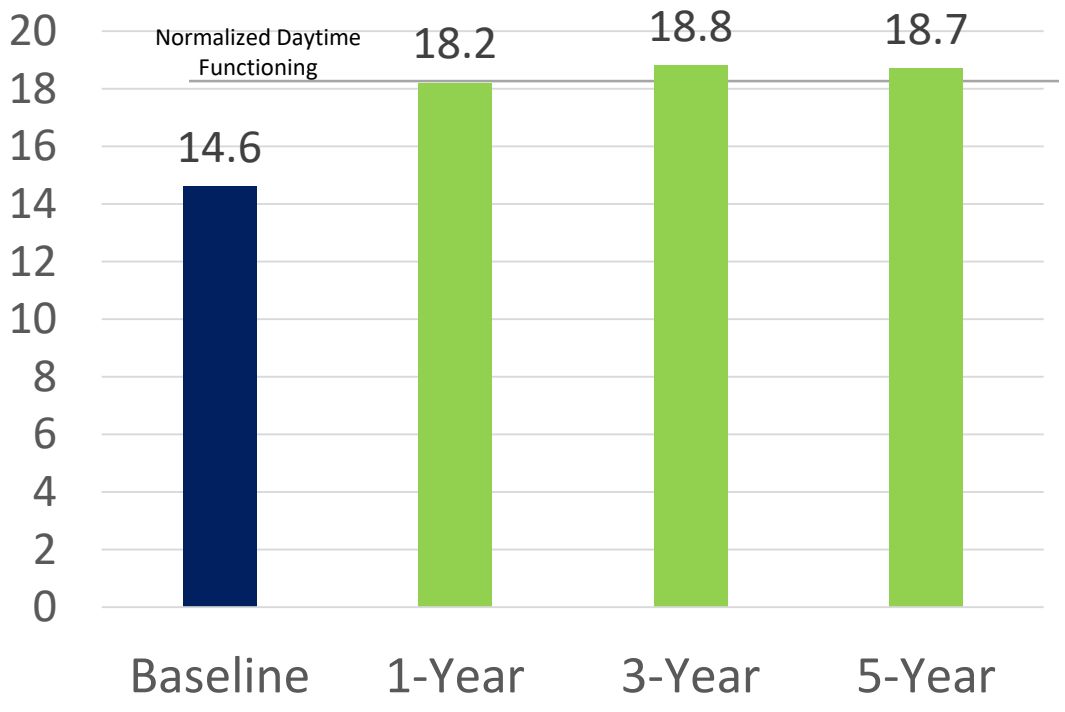
Oxygen Desaturation Index (ODI)



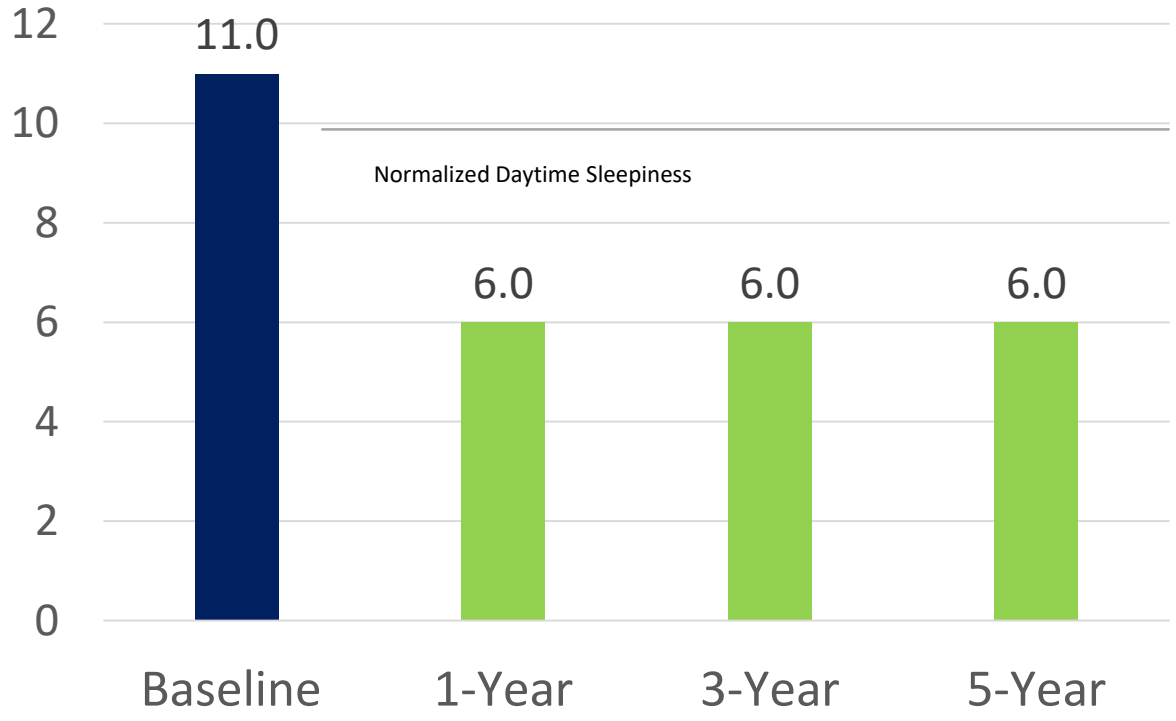
1-Year Data: Strollo et al NEJM 2014
3-Year Data: Woodson et al OTO-HNS 2015
5-Year Data: Woodson et al OTO-HNS 2018

Improved Quality of Life Over 5 Years

Functional Outcomes of Sleep Questionnaire (FOSQ)



Epworth Sleepiness Scale (ESS)

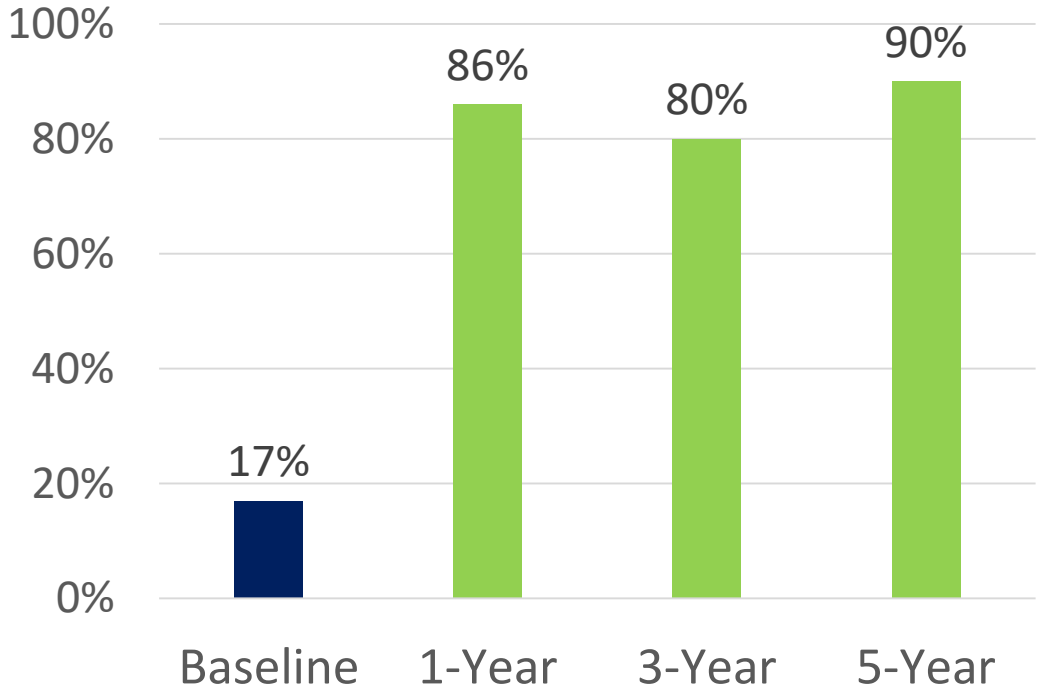


1-Year Data: Strollo et al NEJM 2014
3-Year Data: Woodson et al OTO-HNS 2015
5-Year Data: Woodson et al OTO-HNS 2018

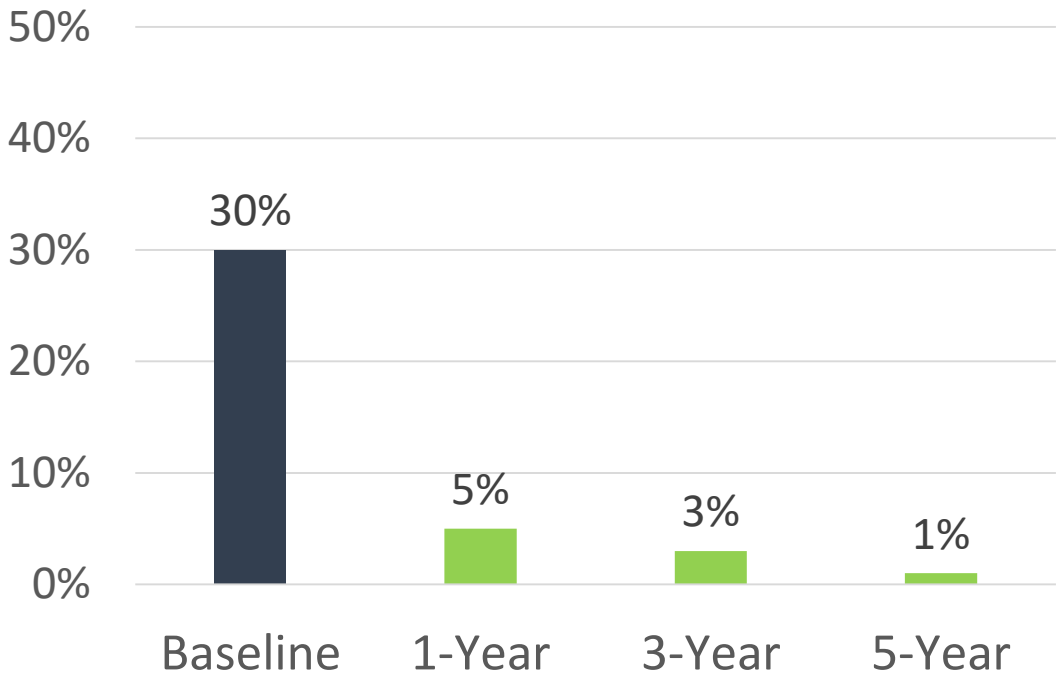
Snoring Reduction

Based on Bed Partner Reporting

No or soft snoring increased from 17% to 90%



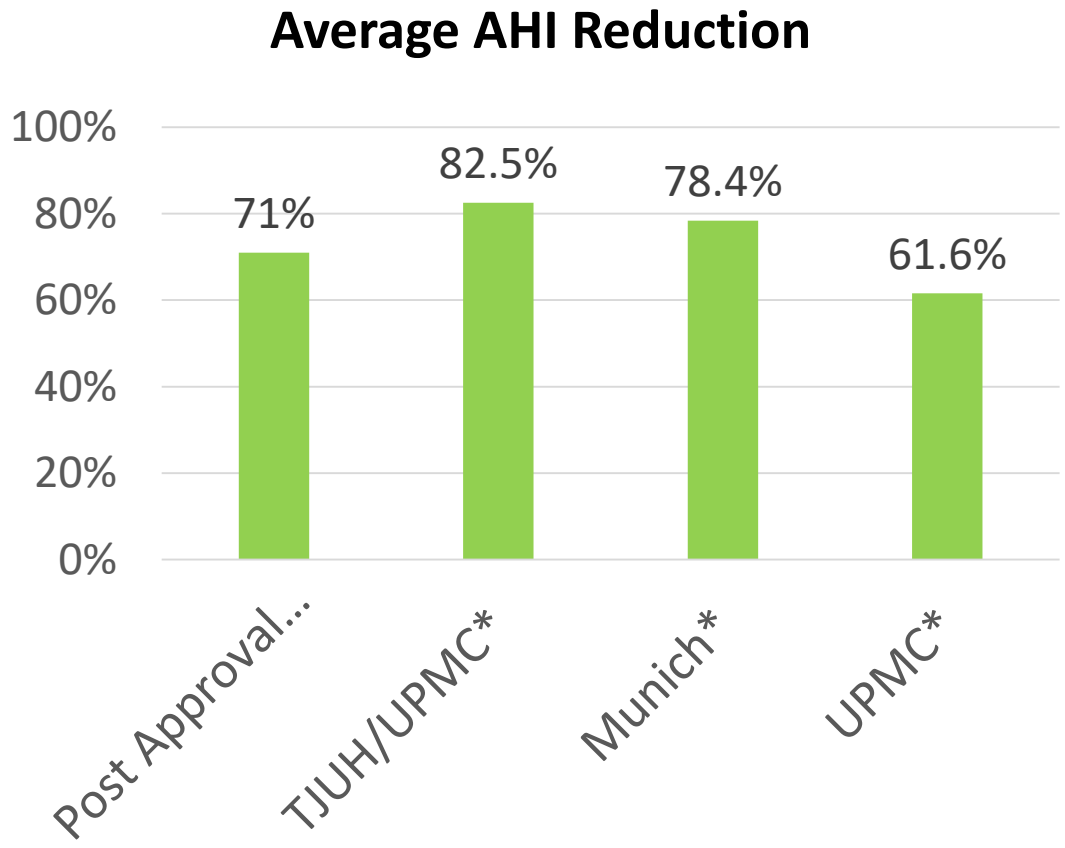
Bed partner leaving room reduced from 30% to less 5%

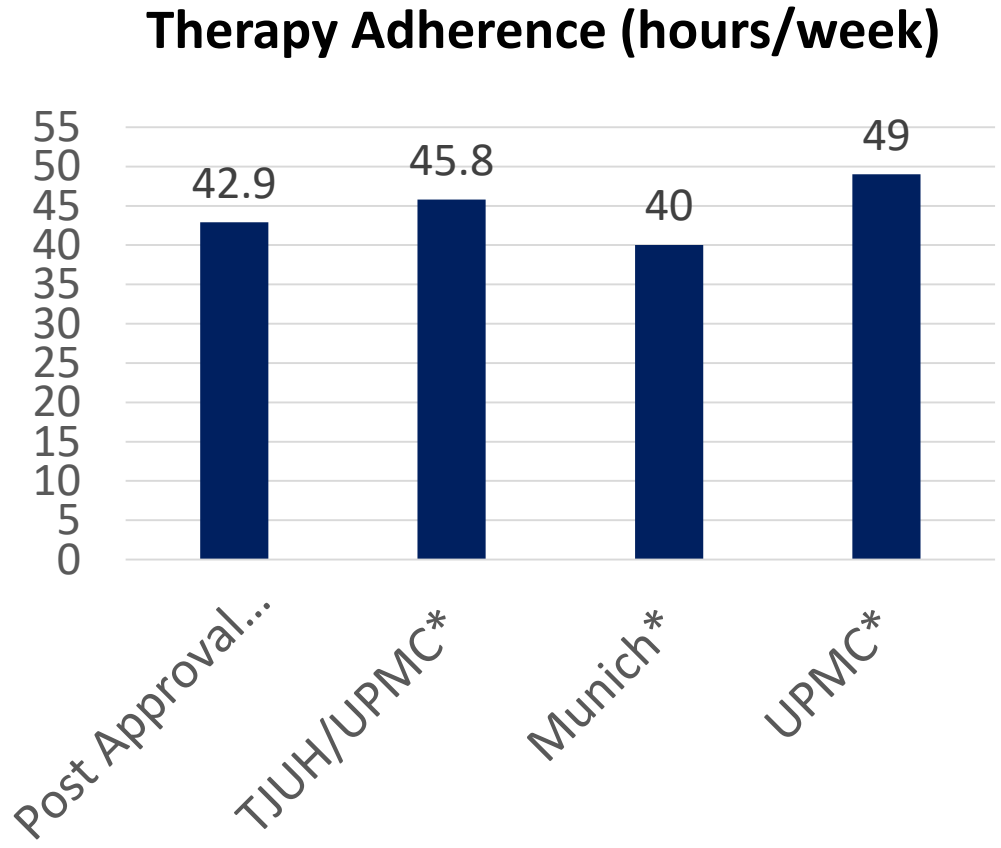


1-Year Data: Strollo et al NEJM 2014
3-Year Data: Woodson et al OTO-HNS 2015
5-Year Data: Woodson et al OTO-HNS 2018

New Clinical Data

Consistent AHI Reduction & Therapy Adherence Across Multiple Studies



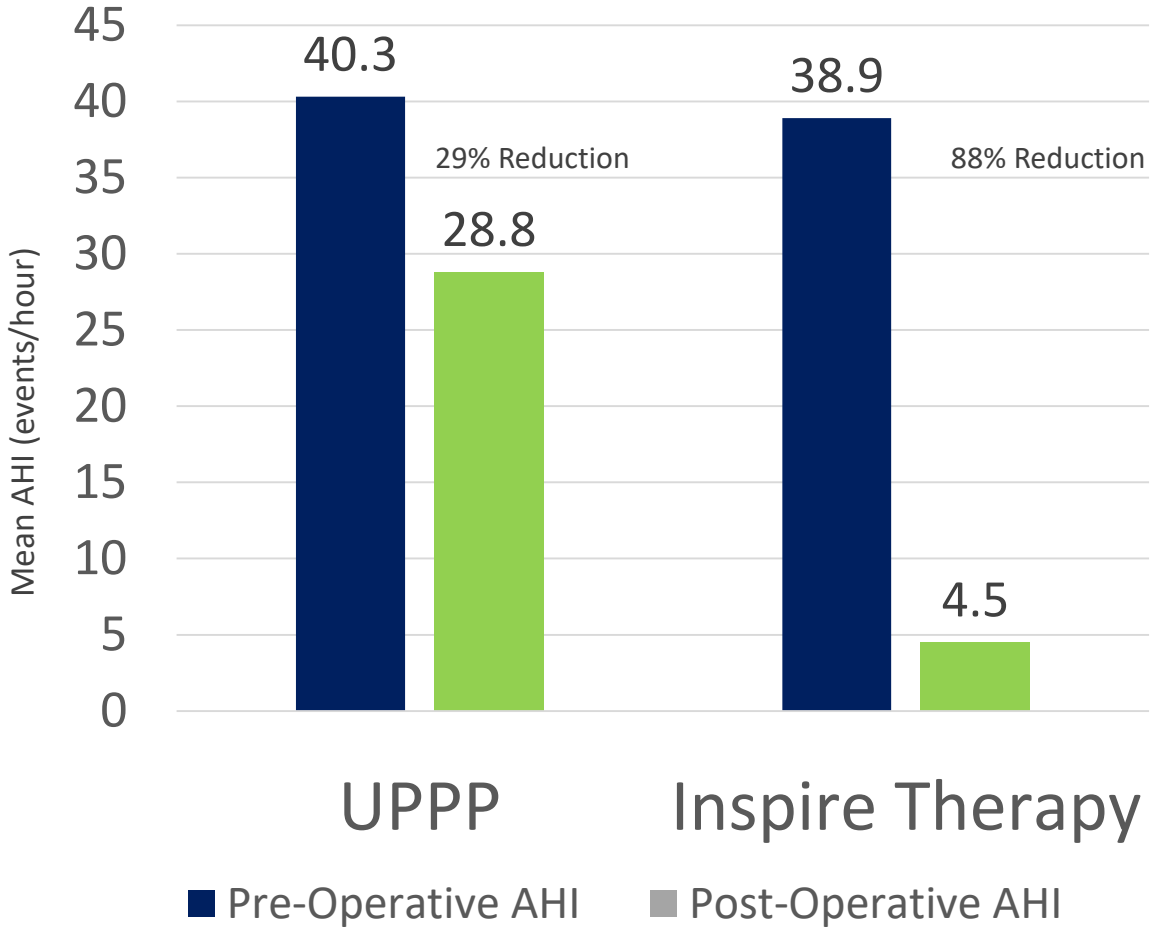


**Independent center publications*

German PAS Study; Heiser et al, OTO-HNS 2016
TJUH/UPMC; Huntley et al, JCSM 2017
Munich; Hofauer et al., Chest 2018
UPMC: Kent et al., OTO-HNS 2016

Independent Cleveland Clinic Study: UPPP vs UAS

- Independent study conducted by multi-disciplinary team of physicians from the Cleveland Clinic
- Study compared outcomes for both UAS therapy and UPPP in patients with moderate to severe OSA (n=20 in each cohort)
- 65% of UAS patients had a treatment AHI < 5

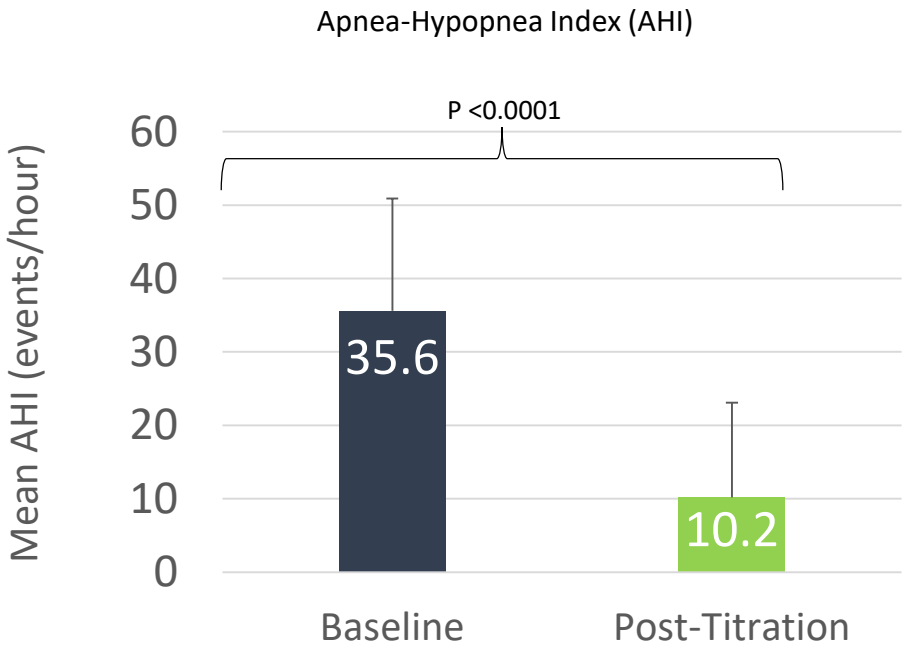


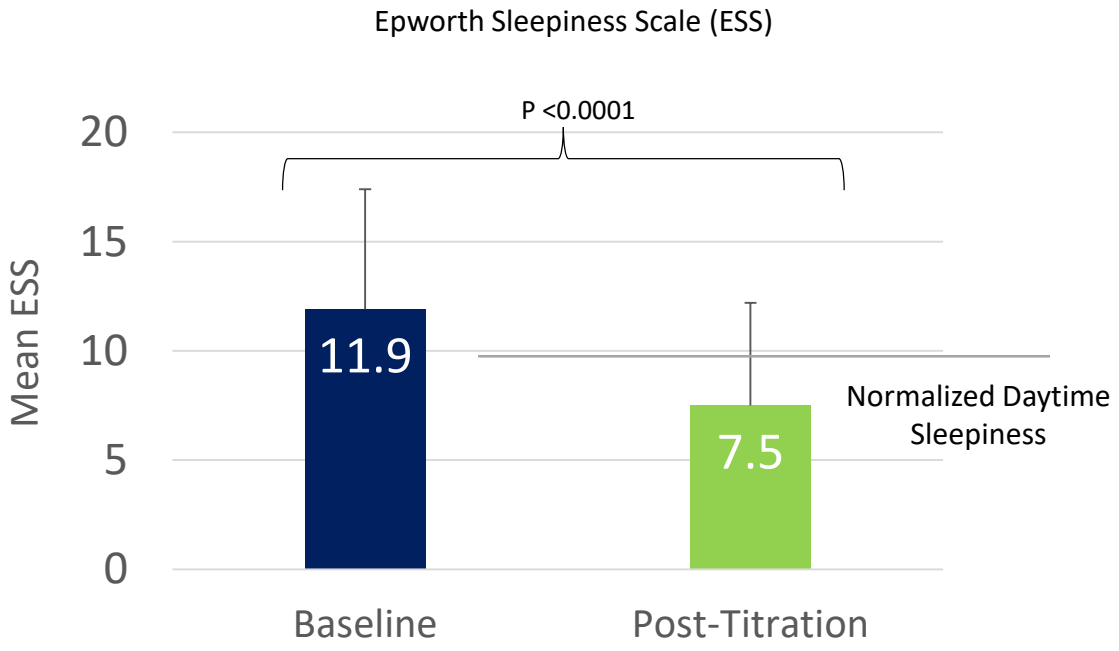
UPPP vs Inspire: Shah et al, Am J Otolaryngol 2018

ADHERE Registry – Real World Clinical Practice

Enrollment Goal: 2,500 patients

- First publication on 301 patients
- Average therapy adherence of 45 hours/week





ADHERE Registry: Boon et al, OTO-HNS 2018

Upper Airway Stimulation: Pediatric Research

Upper Airway Stimulation and Pediatrics

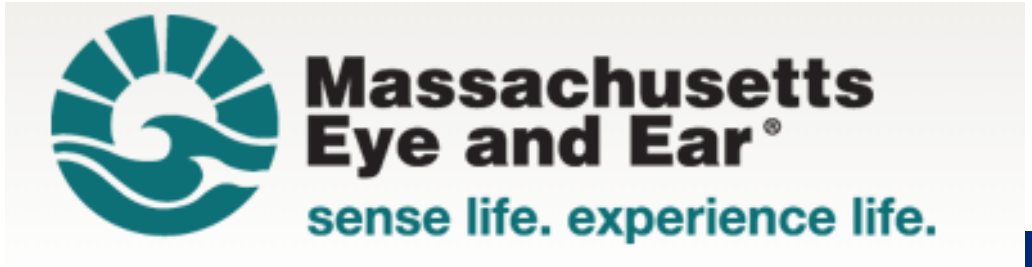
- **Upper Airway Stimulation is only FDA approved for adults who are 22 years and older**

- There is no upper age limit

- Pediatric use is only in the research phase

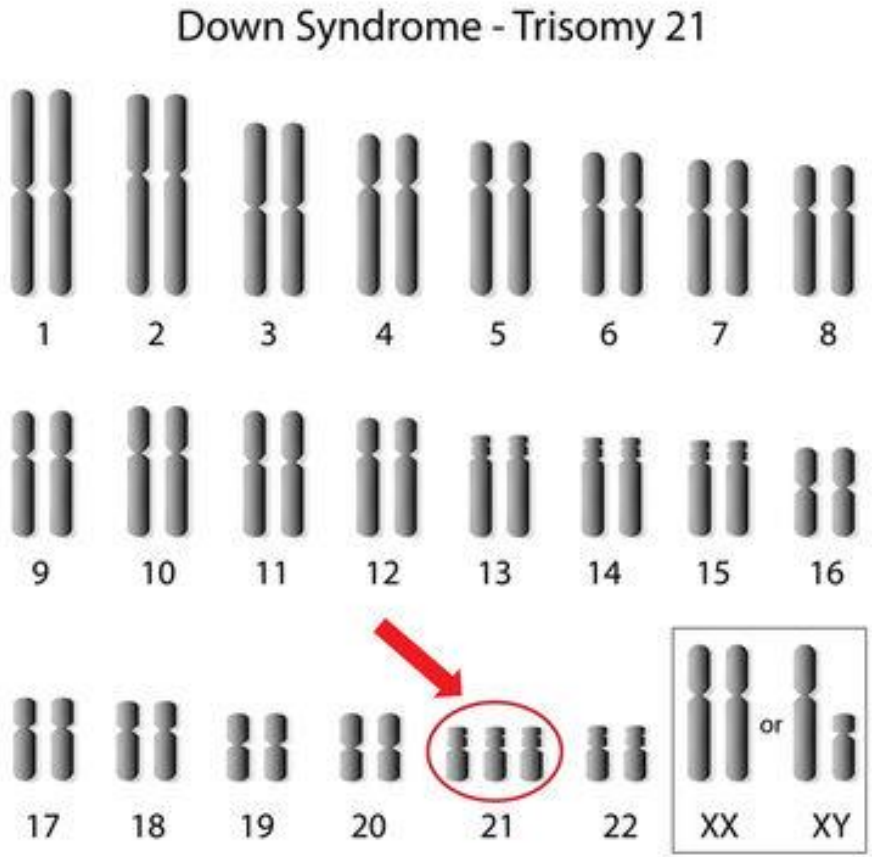
Multi-Center Ongoing Clinical Trial

- Massachusetts Eye and Ear Infirmary (1st implant) & Mass General Hospital
- Cincinnati Children's Hospital
- Emory University
- Ensure Safety & Evaluate Efficacy



Downs Syndrome (Trisomy 21)

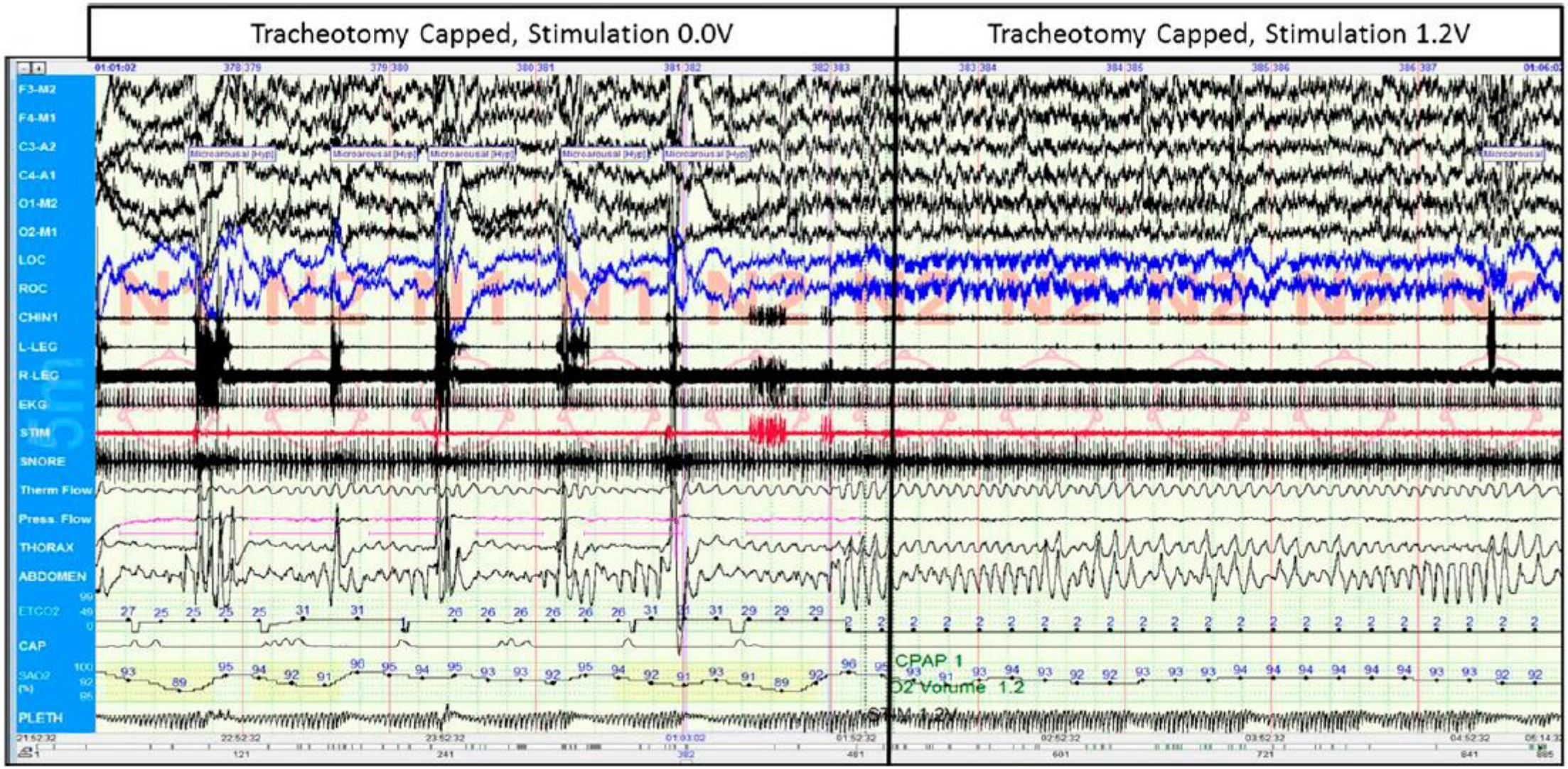
- OSA affects up to 60% of children with Down Syndrome
- Post T&A, up to 50% have residual disease
- CPAP is poorly tolerated
- Large tongues, narrow airway, cranial-facial abnormalities



Case Review – First Implanted Pediatric

- 14 year old boy
- Translocation DS
- Long standing tracheotomy due to severe OSA despite prior T&A and lingual tonsillectomy
- BMI 24.6 (90th percentile, overweight but not obese)
- AHI of 48.5/hour with trach capped (studied 4 months prior to implant)
- AHI of 0.9/hour with trach uncapped

FIGURE 3
Postoperative chest radiograph showing excellent placement of the impulse generator over the right chest, pleural sensing electrode (*), and stimulation electrode (arrow). L, left.


Tracheotomy Capped, Stimulation 0.0V
Tracheotomy Capped, Stimulation 1.2V
F3-M2
F4-M1
C3-A2
C4-A1
O1-M2
O2-M1
LOC
ROC
CHIN1
L-LEG
R-LEG
EKG
STIM
SNORE
Therm Flow
Press. Flow
THORAX
ABDOMEN
ETCO2
CAP
SAO2 (%)
PLETH
CPAP 1
O2 Volume 1.2

Results – 1st 6 Patients

Table 1. Patient Characteristics and Baseline Polysomnogram Findings

Patient No.	Sex	Age, y	BMI	Baseline, Events/h	
				AHI	CAI
1	M	14	24.6	48.5[a]	2.4
2	M	15	26.1	17.1[b]	0.8[b]
3	M	13	19.2	30.7	0.0
4	F	12	20.3	22.7	4.7
5	M	17	28.8	13.9	2.9
6	F	18	25.8	25.6[b]	6.3[b]

Abbreviations: AHI, apnea hypopnea index; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; CAI, central apnea index.

[a] Measured with tracheostomy tube capped.

[b] Values obtained from therapeutic portion of a split-night polysomnogram. The remainder of the patients underwent full-night studies for baseline value.

Results – 1st 6 Patients

Table 3. Polysomnogram Results Before and After Implantation

Patient No.	Preimplantation AHI, Events/h	Follow-up, mo	Stimulator Parameters, V	Postimplantation AHI, Events/h	Device Use, Mean, h/Night
1	48.5[a]	12	1.7-1.9	7.4[b]	9.6
2	17.1	12	1.9	2.7	10.0
3	30.7	12	1.5	4.6	9.3
4	22.7	12	1.5	4.7	5.6
5	13.9	6	1.5-1.7	6.1[c]	9.0
6	25.6	12	1.9-2.3	4.7[d]	9.4

Abbreviation: AHI, apnea hypopnea index.

[a] Measured with tracheostomy tube capped.

[b] Patient 1: overall AHI, 7.4 events/h at 1.7-1.9V; AHI, 5.0 events/h at 1.9V (90% reduction compared with baseline).

[c] Patient 5: overall AHI, 6.1 events/h at 1.5-1.7V; AHI, 5.4 events/h at 1.5V.

[d] Patient 6: overall AHI, 4.7 events/h at 1.9-2.3V; AHI, 1.5 events/h at 2.3V.

Final Notes on UAS with Pediatrics

- Goals: Reduce symptoms and minimize risk by reducing disease burden
- Quality of life improvements for both the patient and the parents
- Cognitive and behavioral improvements

Questions?