Hypoglossal nerve stimulation for obstructive sleep apnea

Suzanne Stevens, MD, MS, D-ABSM, Subspecialty ABPN
Assistant Professor of Neurology
University of KS Health System

"Some people talk in their sleep. Lecturers talk while other people sleep."
-Albert Camus
A Treatment Option for Some Obstructive Sleep Apnea Patients Who Are Unable to Use CPAP

- Moderate to severe OSA
- Not significantly overweight
- Right airway anatomy profile
Untreated OSA Increases Risk for Comorbidities and Accidents

Increased Risk

1. Stroke
2. Death (severe OSA)
3. Hypertension
4. Motor Vehicle Accidents
5. Heart Failure
6. Occupational Accidents
7. Death (moderate OSA)
8. Type 2 Diabetes
9. Depression
10. Coronary Artery Disease

Top 3

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
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<tbody>
<tr>
<td>3.8</td>
</tr>
<tr>
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<td>2.4</td>
</tr>
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<td>2.4</td>
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<tr>
<td>2.2</td>
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1. Artz et al, Am J Respir Crit Care Med 2005
2. Young et al, Sleep 2008
4. Tregear et al, J Clin Sleep 2009
5. Shahar et al, Am J Respir Crit Care Med 2001
8. Smith et al, CHEST 2002
How it Works
The Hypoglossal Nerve (Cranial Nerve XII)

- Controls muscles and movements of the tongue
- Motor nerve
- Mechanical coupling with palate is very common
LAUGH AND THE WORLD LAUGHS WITH YOU, SNORE AND YOU SLEEP ALONE.

Anthony Burgess
English Novelist
The Distal Hypoglossal Nerve

Hypoglossal Nerve (CN XII)

Styloglossus Muscle

Hyoglossus Muscle

Geniohyoid Muscle

Genioglossus Muscle

Mild stimulation
Hypoglossal Nerve Stimulation Effect

No Stimulation

Base of Tongue

Palate

Mild Stimulation

Base of Tongue

Palate
Stimulation Timed With Breathing

1. Mild stimulation of HGN
2. Sense Breathing
3. Computer & Battery

Timing
Stimulation delivered during inspiration

Respiratory Cycle
The Inspire Upper Airway Stimulation System
(Adjustable, Titratable, Adherence Monitoring)

Several million patients receive implantable stimulation therapies annually
- Cardiac conditions (Bradycardia, Tachycardia, Heart failure)
- Pain management
- Other neuro-related conditions (Urologic disorders, Parkinson’s Disease)
Inspire Therapy Amplitude Titration Algorithm for PSG*

- Increase amplitude by 0.1 to 0.2 volts if ≥ 5 obstructive apneas or hypopneas or loud, unambiguous snoring. May also increase for RERAs and to explore the therapeutic amplitude range.

- ≥ 10 min

- Start at: FT - 0.2 V

- Turn off Inspire, and reduce amplitude by 0.1 to 0.2 volts if stimulation causes persistent arousals or is poorly tolerated.

- No arousal threshold

- Therapeutic Amplitude Range: ≥ 30 minutes in the patient’s preferred sleep position with minimum occurrence of events, preferably with REM sleep observed

- Minimum Therapeutic Amplitude

- *Adapted from current practice guidelines established for CPAP titration by the American Academy of Sleep Medicine, ref: Journal of Clinical Sleep Medicine, Vol. 4, No 2, 2008

Implant Procedure → Therapy Activation in the Office (1-mo post-op) → In Lab Therapy Titration (following 1 month of home use)
Inspire Therapy: Sleep Study Illustration

Airflow, breathing and normal oxygen levels restored
Inspire therapy turned on at titrated therapeutic level

Airflow

SpO2

Severe OSA Events

OSA Events Resolved
Patient Experience
Inspire Therapy Procedure Overview

• Typically an Outpatient Procedure
  – General anesthesia

• Pain Management
  – Mild discomfort and swelling at the incision sites for a few days after the procedure, usually managed with over-the-counter pain medication

• Recovery
  – Return to regular diet and most activities of daily living immediately after the procedure
  – Avoid strenuous activities for a few weeks
Incisions After Healing is Complete

- Incision on neck for stimulation lead
- Incision and device under collarbone
- Incision on chest for sensor lead

*Photos used with patient consent
Inspire 2500 Sleep Remote
Designed for an enhanced patient experience
I love you so much.

Except when you snore and then I just want to punch you in the face.
Inspire Therapy Clinical Evidence Development

Over 20 Peer-Reviewed Publications as of June 2016

**INSPIRE 1, 2, 3 FEASIBILITY STUDIES**
- First Human Implant
- Patient Selection
- Implant Technique
- Safety/Efficacy

**STAR PHASE III TRIAL WITH RANDOMIZED CONTROLLED WITHDRAWAL STUDY**
- Safety/Efficacy
- FDA Approval
- Long-Term Follow-Up
- Cost Effectiveness

**ONGOING STUDIES**
- European Post-Market Study
- US Post-Approval Study
- Single Center Experience Projects
- Global Registry (2nd half of 2016)

Peer Reviewed Publications — STAR Trial Outcomes


18 MONTHS: Strollo et al. *SLEEP*. June 2015


STAR Trial Safety Summary
126 Patients

Serious adverse events/side effects within the first year

• One elective device removal requested by patient
• Two device repositionings to resolve patient discomfort

Serious adverse events/side effects after the first year

• Device removal due to insomnia and other psychological issues (N=2)
• Device removal due to septic arthritis of right shoulder; no device-related infection found with implanted pulse generator (IPG) pocket (N=1)
• IPG and sense lead replacement due to unstable sensing performance (N=1)
• IPG replacement and stimulation lead reposition due to lack of therapy response (N=1)
Inspire Therapy Long-Term Objective Outcomes: AHI

12 Month Data: Strollo et al NEJM 2014
18 Month Data: Strollo et al SLEEP 2015
36 Month Data: Woodson et al OTO-HNS 2015

Results in median, p < 0.01
Inspire Therapy Long-Term Objectives Outcomes: ODI

Oxygen Desaturation Index

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Median ODI</th>
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<tbody>
<tr>
<td>Baseline</td>
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<tr>
<td>18 Month</td>
<td>8.6</td>
</tr>
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<td>36 Month</td>
<td>4.8</td>
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Results in median, p < 0.01

12 Month Data: Strollo et al NEJM 2014
18 Month Data: Strollo et al SLEEP 2015
36 Month Data: Woodson et al OTO-HNS 2015
Inspire Therapy Long-Term Subjective Outcomes: FOSQ*

*All 5 FOSQ subscale variables showed clinically significant improvements. FOSQ subscale variables include (1) activity, (2) productivity, (3) social, (4) intimacy, and (5) vigilance.

Results in median, p < 0.01

<table>
<thead>
<tr>
<th>Time</th>
<th>N</th>
<th>Score</th>
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<tr>
<td>Baseline</td>
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<tr>
<td>36 Month</td>
<td>110</td>
<td>18.8</td>
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Normalized daytime functioning
Inspire Therapy Long-Term Subjective Outcomes: ESS

Epworth Sleepiness Scale

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>12 Month</th>
<th>18 Month</th>
<th>36 Month</th>
</tr>
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<tr>
<td>N</td>
<td>126</td>
<td>123</td>
<td>123</td>
<td>110</td>
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<tr>
<td>Median</td>
<td>11.0</td>
<td>6.0</td>
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Normalized daytime functioning

Results in median, p < 0.01
Inspire Therapy Adherence

Patient Self-Reported

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Use every night (%)</th>
<th>Use at least 5 nights a week (%)</th>
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<tbody>
<tr>
<td>12 Month</td>
<td>86%</td>
<td>93%</td>
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<tr>
<td>N = 124</td>
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<tr>
<td>24 Month</td>
<td>81%</td>
<td>86%</td>
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<tr>
<td>N = 117</td>
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<tr>
<td>36 Month</td>
<td>81%</td>
<td>87%</td>
</tr>
<tr>
<td>N = 108</td>
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From STAR database
Partner Reported Snoring Outcomes

**No or Soft Snoring**

- Baseline: 17% (N=108)
- 12 Month: 86% (N=103)
- 18 Month: 87% (N=103)
- 36 Month: 80% (N=97)

**Bed Partner Leaves Room**

- Baseline: 30% (N=108)
- 12 Month: 5% (N=103)
- 18 Month: 4% (N=103)
- 36 Month: 3% (N=97)

12 Month Data: Strollo et al NEJM 2014
18 Month Data: Strollo et al SLEEP 2015
36 Month Data: Woodson et al OTO-HNS 2015
UPMC Single-Center Experience Study*

Results from first 20 consecutive implanted patients:

• Average AHI reduction from 33 to 5
  • 70% with AHI < 5, 85% with AHI < 10, and 95% with AHI < 15
• Average ESS improvement from 10 to 6
• Average use of 7 hours/night
  • After mean follow-up of 230 days

*OTO-HNS. Kent D, Lee J, Strollo PJ, Soose R.J. March 2016 (online)
University of Pennsylvania: Single Center Study

Summary:

• 8 of 8 patients with post-treatment AHI < 10
• AHI reduced from 67 to 4.7
• Same-day surgery
• No complications
Patient Selection and Education
Hearing you snore does the exact opposite of turning me on.
AHI = apnea hypopnea index

- Events per hour
- AHI <5 normal
- AHI 5-15 mild
- AHI 15-30 moderate
- AHI >30 severe

- Apnea = central + obstructive
Inspire Therapy Indications*

• Adults 22 years of age and older

• Diagnosed OSA with an AHI range of 20-65 per hour

• CPAP failure or inability to tolerate CPAP treatment:
  – PAP failure is defined as an inability to eliminate OSA (AHI of greater than 20 despite PAP usage)
  – PAP intolerance is defined as inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night)
  – Unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)

• Appropriate airway anatomy

* Indications approved by the United States Food & Drug Administration, April 2014
Inspire Therapy Contraindications*

- Screening sleep study shows < 25% central+mixed apneas
- Anatomical assessment findings that could compromise the performance of Inspire such as complete concentric collapse (CCC) at the palate
- Pre-existing conditions that have compromised neurological control of the upper airway
- Patients who are unable or do not have the necessary assistance to operate Inspire therapy
- Patients who are pregnant or plan to become pregnant
- Patients who will require MRI
- Patients with another implantable device (i.e. pacemaker) should consult the device manufacturer to assess possibility of interaction

*Indications approved by the United States Food & Drug Administration, April 2014
Inspire Therapy Warnings and Precautions*

- **Body Mass Index ≤ 32**
  - BMI > 32 may be associated with decreased likelihood of response to treatment
- **Diathermy (primarily used in physical therapy)**
  - Do not use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy on patients with a neurostimulation system
- **MRI can cause tissue damage as well as damage to the Inspire system and components**
- **Electromagnetic compatibility and interference (EMI).** Extremely strong sources of EMI could interfere with normal IPG operation
  - Electrocautery, irradiation, lithotripsy, RF-ablation, x-ray, and fluoroscopy are typical EM disturbance sources. Treatments that use ultrasonics, defibrillation, or radiation can adversely affect the Inspire System.

*Indications approved by the United States Food & Drug Administration, April 2014*
Pre-op Anatomical Assessment
Drug Induced Sleep Endoscopy (DISE)
Examples

Complete AP collapse at palate
Good candidate

Complete concentric collapse at palate
Not a good candidate
It's funny you blame your snoring for the reason I hate you. Your snoring only proved you could also annoy me while you slept.
Patient flow

• Once has seen ENT (Chris Larsen)
  – Schedule for DISE
  – Insurance prior authorization (weeks)
  – Schedule for OR implant
  – 2 week follow up with surgeon for incision check
  – 30 days after implant activate device
  – 60 days after implant in lab PSG titration
  – 80 days after implant see sleep specialist