Inspire Therapy for Obstructive Sleep Apnea

For OSA patients unable to tolerate or get consistent benefit from CPAP

Clinical Data Update

Summary of published long-term 3-year outcomes data

Treatment Goals for OSA Patients

- Reduce Symptoms
- Improve Quality of Life
- Reduce Accident Risk
- Minimize Cardiovascular and Other Health Risks
Consequences of Untreated Obstructive Sleep Apnea (OSA)

**AIRFLOW**

- During sleep, OSA patients experience repetitive airway obstructions followed by oxygen desaturations

**OXYGEN SATURATION LEVEL**

- Moderate to severe OSA patients can experience hundreds of obstructions and desaturations each night

**INCREASED RISK DUE TO UNTREATED OSA**

- Untreated OSA can have devastating effects on heart and brain health, impair quality of life and increase motor vehicle and occupational accident risk

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*Excerpt from a sleep study of an Inspire therapy candidate

OSA Treatment Shown to Reduce Cardiovascular Events

- Untreated severe OSA (AHI of 30+) is associated with an increased risk of both fatal and non-fatal cardiovascular events.

- Consistent treatment with Continuous Positive Airway Pressure (CPAP) or an AHI <15 reduces risk.

Adapted from Spanish Sleep Cohort (n=1,651, mean follow-up of 10 yrs; age ~ 50 yr)

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1 Consistent use - Average daily use more than 4 hours; Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea w/ or w/o treatment with CPAP: an observational study; Marin et al., Lancet 2005
The Hypoglossal Nerve (Cranial Nerve XII)  
The Basis for Inspire Upper Airway Stimulation Therapy

- Motor nerve
- Controls the muscles and movements of the tongue
- Mild stimulation of the distal hypoglossal nerve restores upper airway muscle tone
- Increase in muscle tone can prevent the tongue and other soft tissues from collapsing and obstructing the airway during sleep

Adapted from IVLine.org
Stimulation Synched with Breathing
The Inspire System Delivers Therapy When Airway is Most Vulnerable to Collapse

- Fully implanted system that uses well-established technologies and surgical techniques
- Breathing sensor monitors a patient’s breathing cycle
- Rhythmic, mild stimulation is delivered to the hypoglossal nerve through the stimulation cuff
- Mild stimulation is delivered during inspiration, when the OSA patient’s airway is most vulnerable to collapse
Stimulation Effect on Airway Anatomy

No Stimulation

- Palate
  - Obstructed Airway
  - Tongue Base

Mild Stimulation

- Palate
  - 180% increase in airway dimension
- Tongue Base
  - 130% increase in airway dimension

Open Airway

At therapeutic titrated levels, Inspire therapy prevents the airway from collapsing to facilitate unobstructed breathing

*Endoscopy images of an Inspire therapy recipient

Stimulation Effect During Sleep

- Airflow and breathing stabilized
- Normal SaO₂ levels restored
- Uninterrupted sleep continues without arousals

*Sleep study of an Inspire therapy recipient*
Inspire Therapy
Clinical Evidence Development

12 peer-reviewed publications as of November 2015

<table>
<thead>
<tr>
<th>INSPIRE 1, 2, 3 FEASIBILITY STUDIES</th>
<th>STAR PHASE III TRIAL WITH RANDOMIZED CONTROLLED WITHDRAWAL STUDY</th>
<th>ONGOING STUDIES</th>
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<td>First in Man</td>
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Peer-Reviewed STAR Trial Outcomes Publications:


**Randomized Study:** Randomized Controlled Withdrawal Study of Upper Airway Stimulation on OSA. Woodson et al. *Otolaryngology Head and Neck Surgery*. September 2014

**18 Months:** Upper Airway Stimulation for Obstructive Sleep Apnea—Durability of the Treatment Effect at 18 months. Strollo et al. *SLEEP*. June 2015

**Two Year:** Upper Airway Stimulation for Obstructive Sleep Apnea: Self-Reported Outcomes at 24 months. Soose et al. *Journal of Clinical Sleep Medicine*. July 2015

**Three Year:** Three Year Outcomes of Cranial Nerve Stimulation for Obstructive Sleep Apnea: The STAR Trial. Woodson et al. *Otolaryngology Head and Neck Surgery*. November 2015
Patients using Inspire therapy experienced significant decreases in both AHI and ODI from baseline to 12 months. These significant improvements were maintained over the 36-month follow-up period.

**APNEA HYPOPNEA INDEX (AHI)**

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All p values < 0.01 vs. baseline. Results in median.

**OXYGEN DESATURATION INDEX (ODI)**

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All p values < 0.01 vs. baseline. Results in median.
Patients using Inspire therapy reported significant improvements and normalization of both daytime sleepiness and daytime functioning. These significant improvements were reported at 12 months and were sustained at 36-month follow up.

**EPWORTH SLEEPINESS SCALE (ESS)**

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N=126, N=123, N=123, N=110

All p values < 0.01 vs. baseline. Results in median.

**FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE* (FOSQ)**

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N=126, N=123, N=123, N=110

All p values < 0.01 vs. baseline. Results in median.

* Importantly, all 5 FOSQ subscale variables showed clinically significant improvements. FOSQ subscale variables include (1) activity, (2) productivity, (3) social, (4) intimacy and (5) vigilance.
Sleep apnea affects not only patients but their bed partners as well. Snoring, a common sleep apnea symptom, was significantly impacted in patients using Inspire therapy from baseline. Additionally, fewer partners left the room due to their partner’s snoring.

**PARTER REPORTED SNORING OUTCOMES**

Therapy adherence remained high throughout the three-year follow-up period.

**THERAPY ADHERENCE**
Inspire Therapy
Patient Selection Considerations

Patients use the handheld sleep remote to turn the therapy on before bed and off upon waking.

Inspire therapy is FDA-approved and available at over 50 leading medical centers in the United States. It is intended for people who:

• Have been diagnosed with moderate to severe OSA (AHI 20-65)
• Cannot tolerate or get consistent benefit from CPAP
• Are not significantly overweight

People who meet these basic criteria can be referred to a specialist who can evaluate sleep parameters, assess the airway anatomy and determine if Inspire therapy is right for them.

In addition, Inspire therapy is approved and available in over 8 European countries.

Visit www.inspiresleep.com to review risks, benefits and expectations associated with Inspire therapy. Risks associated with the surgical implant procedure are low but may include infection and temporary tongue weakness. Most patients acclimate well to the presence of the Inspire system and to the therapeutic stimulation. Some patients may require post-implant adjustments to the system’s settings in order to improve effectiveness and ease acclimatization.

Additional Resources:
www.InspireSleep.com
844 OSA HELP (844-672-4357)

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Inspire Medical Systems

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800-132-001 Rev A Nov 2015