Upper Airway Stimulation For Obstructive Sleep Apnea

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• International Surgical Sleep Society
  – Sleep and Breathing Meeting, October 24-25, 2014
  Detroit Michigan www.surgicalsleep.org
Disclosure

- Consultant
  - Medtronic
  - Siesta Medical
  - Inspire Medical

- Research
  - Inspire Medical

- Royalty/Patent
  - Medtronic Ent
  - Phillips-Respironics
Goals of Sleep Surgery

• Cure
  – Infrequent with current soft tissue techniques
    • Specific pathologic obstructive lesions
  – Skeletal Surgery

• Salvage
  – Most common

• Ancillary
  – Nasal to improve device outcomes
Options to Improve Sleep Surgery

1. Better “patient selection”

2. Development of better techniques
   – Already have 2 of the most successful treatments for OSA
   – MMA
   – Tracheotomy
“GRADE” Scale to Compare Options

How physicians and patients select treatments

“Grade” = Benefit versus Risk versus Cost
Highly effective treatments do currently exist
Infrequently used due to excess morbidity
• Unlikely in creating new high morbidity highly effective treatments
• Lower morbidity is critical
Surgical Concepts to Enlarge Airway

Airway volume = Skeletal Enclosure – soft tissue volume

(1) Expand box
(2) Reduce tissue
(3) Rearrange soft tissue
Alternative is to modify physiology

1. Sleep/ Wake
2. Negative pressure reflex
3. CO2 mediated respiratory drive
Upper Airway Stimulation (UAS)

- Distal hypoglossal nerve
- Avoids hyoglossus and styloglossus effects
Electrical Stimulation has Long History

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guillemiault 1978</td>
<td>transcutaneous submental and intraoral electrical stimulation</td>
<td>Failure</td>
</tr>
<tr>
<td>Miki 1989</td>
<td>intramuscular stimulation</td>
<td>AH1 from 53.8 to 27.3 (p&lt;0.05) and persistence of sleepiness</td>
</tr>
<tr>
<td>Schwartz 1996</td>
<td>Genioglossus protrusor Hyoglossus retrusor</td>
<td>Vlmax 288.1ml/s to 501.4 ml/s Vlmax worse</td>
</tr>
<tr>
<td>Inspire I system 1996</td>
<td>Unilateral hypoglossal nerve sensor / stimulator system AHI from 52.0 to 22.6 events/hr</td>
<td>No tongue atrophy, hypertrophy or fasciculations, No discomfort during sleep Device malfunction</td>
</tr>
<tr>
<td>Inspire II, Apnex, Imthera 2009-2011</td>
<td>US Clinical Trials</td>
<td>Inspire successful, Apnex no longer available, Imthera pending</td>
</tr>
</tbody>
</table>

- Hypoglossal nerve pure motor does not create sensory stimulation ....No Arousal or sleep disruption
Inspire™ II

1) Implantable Pulse Generator (IPG),
2) Self-Sizing Cuff Stimulation Lead, and
3) Differential Pressure Sensing Lead (differential pressure placed near the pleural space to sense thoracic pressure
Inspire™ II

1) Physician Programmer (non-invasively interrogate and program the IPG conduct a limited system self-test, monitor respiratory waveforms, program stimulation modes, adjust stimulation parameter values) and

2) Patient Programmer
Stimulator Lead

- Cuff wire electrode
- Programmable
- Initially placed on main trunk
- Currently placed on the medial branch of the distal nerve beyond bifurcation to styloglossus muscle
Pressure Sensing Lead

- Pressure sensor at intercostal 4-5 (Inspire)
- Impedence lead (Apnexit)
- No sensor (Imthera)
Stimulation: Basic Parameters

- **Amplitude (V)** – primary stimulation strength adjustment
- **Rate (Hz)** – default 33 Hz
- **Pulse Width (µsec)** – default 90 µsec

![Diagram showing stimulator pulses with onset, offset, expiratory, and inspiratory phases.](image)
Pilot Study Publications

TREATING OSA WITH HYPOGLOSSAL NERVE STIMULATION

Treating Obstructive Sleep Apnea with Hypoglossal Nerve Stimulation

Peter R. Eastwood, PhD¹; Maree Barnes, MBBS²; Jennifer H. Walsh, PhD¹; Kathleen J. Maddison, BSc¹; Geoffrey Hee, MBBS; Alan R. Schwartz, MD³;
Feasibility Clinical Trial

- Multicenter
  - Europe
  - Israel
  - US

- 61 patients enrolled
- 30 excluded
- 22 in first phase of study
- 9 in second stage

Poor Response
AHI Response (post Hoc)
Patients met Selection Criteria (N=18)

Phase 2 =
1. BMI < 32,
2. AHI < 50,
3. Distal electrode site

Responder Rate: 78% (14/18)
STAR Trial

Enrollment Exclusions (205)
- Did not meet inclusion/exclusion criteria (108, 13.4%)
- Participants withdrawal of consent (60, 7.5%)
- Study implant limit complete – Participants withdrawn (21, 2.6%)
- Participants lost to follow-up prior to implant (13, 1.6%)
- Other withdrawals prior to implant (3, 0.4%)

Screen Exclusions (598)
- PSG
  - AHI < 20 (347, 43.2%)
  - AHI > 50 (87, 10.8%)
  - Central sleep apnea (50, 6.2%)
  - Positional OSA (45, 5.6%)
- Surgeon Consultation
  - Tonsil size 3 or 4 (4, 0.5%)
  - Other unfavorable anatomy (9, 1.1%)
- Sleep Endoscopy
  - Complete concentric palatal collapse (54, 6.7%)
  - Others (2, 2.5%)
- 1 Unrelated participant death
- 1 Participant with elective device removal
# Primary Outcomes Star Trial

## Table 2. Primary and Secondary Outcome Measures

<table>
<thead>
<tr>
<th>Primary Outcome Measures</th>
<th>Baseline Mean (SD), N Median (IQR)</th>
<th>12 Month Mean (SD), N Median (IQR)</th>
<th>Change (BL-12M) Mean(SD), N Median (IQR)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>32.0 (11.8), 126 29.3 (23.7, 38.6)</td>
<td>15.3 (16.1), 124* 9.0 (4.2, 22.5)</td>
<td>16.4 (16.7), 124 17.3 (9.3, 26.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ODI</td>
<td>28.9 (12.0), 126 25.4 (19.5, 36.6)</td>
<td>13.9 (15.7), 124 7.4 (3.5, 20.5)</td>
<td>14.6 (15.8), 124 15.7 (8.6, 24.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Secondary Outcome Measures

| FOSQ                     | 14.3 (3.2), 126 14.6 (12.1, 17.1) | 17.3 (2.9), 123 18.2 (16.2, 19.5) | -2.9 (3.1), 123 -2.4 (-4.7, -0.7) | <0.0001 |
| ESS                      | 11.6 (5.0), 126 11.0 (8.0, 15.0) | 7.0 (4.2), 123 6.0 (4.0, 10.0) | 4.7 (5.0), 123 4.0 (1.0, 8.0) | <0.0001 |
| Percentage Sleep Time SaO₂ <90% | 8.7 (10.2), 125 5.4 (2.1, 10.9) | 5.9 (12.4), 124 0.9 (0.2, 5.2) | 2.5 (11.1), 124 2.2 (0.3, 6.6) | 0.01 |

*Note: New data for AHI and ODI at 12 months compared to baseline.*
Complications/Adverse Events

- Use on 86% of nights
- Average use calculated at > 5 hrs/night
18 Month Data from Randomized Trial

- 18 Month improvement in both AHI and snoring
18 Sleep and Quality of Life

<table>
<thead>
<tr>
<th>Parameters</th>
<th>‘ON’ Group</th>
<th>‘OFF’ Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOSQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>15.1 ± 3.1</td>
<td>13.9 ± 2.6</td>
<td>0.15</td>
</tr>
<tr>
<td>12 month</td>
<td>17.9 ± 2.9*</td>
<td>17.0 ± 3.5*</td>
<td>0.36</td>
</tr>
<tr>
<td>RCT</td>
<td>17.9 ± 2.9*</td>
<td>15.0 ± 4.0</td>
<td>0.008</td>
</tr>
<tr>
<td>18 month</td>
<td>18.0 ± 2.9*</td>
<td>17.1 ± 2.9*</td>
<td>0.29</td>
</tr>
<tr>
<td>Change (12M-RCT)</td>
<td>0.0 ± 1.0</td>
<td>2.3 ± 3.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Change (12M-18M)</td>
<td>-0.1 ± 1.6</td>
<td>0.0 ± 2.3</td>
<td>0.91</td>
</tr>
<tr>
<td>ESS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11.2 ± 5.3</td>
<td>11.3 ± 5.0</td>
<td>0.97</td>
</tr>
<tr>
<td>12 month</td>
<td>5.9 ± 3.4*</td>
<td>6.9 ± 4.6*</td>
<td>0.43</td>
</tr>
<tr>
<td>RCT</td>
<td>5.6 ± 3.9*</td>
<td>10.0 ± 6.0</td>
<td>0.005</td>
</tr>
<tr>
<td>18 month</td>
<td>6.0 ± 3.7*</td>
<td>8.0 ± 4.4*</td>
<td>0.09</td>
</tr>
<tr>
<td>Change (12M-RCT)</td>
<td>0.3 ± 1.8</td>
<td>-3.8 ± 4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change (12M-18M)</td>
<td>-0.1 ± 2.4</td>
<td>-1.3 ± 4.6</td>
<td>0.26</td>
</tr>
</tbody>
</table>

- **Normalized** both quality of life (FOSQ) and sleepiness (ESS)
Historical Concept of Tongue Collapse

- Hypopharyngeal obstruction considered the primary cause of OSA
Jaw Thrust and Tongue Movements on Airway Size

Critical effect is on velopharynx

Isono et al
JAP, 79:2132,1995

Fergeuson et al
AJRCCM
155:1748,1997
Morphologic Effects of CN XII Stimulation

Baseline

Stimulation
MECHANICAL EFFECTS STIMULATION

- Apnex™ Study Flouroscopy during implantation

Hypoglossal Nerve Stimulation and Airway Changes under Fluoroscopy

George S. Goding Jr, MD1, Wondimeneh Tesfayesus2, and
# Mechanical Effects of CN XII Stimulation

- **N=26**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>41.8 events/hr</td>
</tr>
<tr>
<td>Low SAO2</td>
<td>81.8%</td>
</tr>
<tr>
<td>BMI</td>
<td>32.4 kg/M²</td>
</tr>
<tr>
<td>Lower Pharynx</td>
<td>9(3) mm</td>
</tr>
<tr>
<td>Pre-Palate</td>
<td>9(3) mm</td>
</tr>
<tr>
<td>Post-Palate</td>
<td>5(3) mm Seen in 65%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effect</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palatal Thinning</td>
<td>70%</td>
</tr>
<tr>
<td>Anterior Palate Displacement</td>
<td>52%</td>
</tr>
<tr>
<td></td>
<td>½ Major, ½ Minor</td>
</tr>
</tbody>
</table>

- Patients have variable effect on the palate
• Pattern of palatal collapse most predictive of effect
Summary

- Hypoglossal nerve stimulation
  - Stimulation tolerated
  - Few major adverse effects
  - Effectively displaces the tongue and opens lower pharynx
  - Physiologically improves airflow
  - Clinically reduces AHI
  - Clinically reduces snoring, sleepiness and improves quality of life (case series data with large effect sizes)
  - Selection factors may relate to velopharyngeal versus lower pharyngeal factors