Hypoglossal Nerve Stimulation for Sleep Apnea

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Disclosures

• Inspire Medical Research/consulting
• Medtronic Consultant/royalty
• Lingualflex Consultant/Research
• Cryosa
  – Consultant
• Nyxoah
  – Research / Consultant
Effect of upper-airway stimulation for obstructive sleep apnoea on airway dimensions

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- Stimulation affects both lower and upper pharynx anatomy
- Palatal changes are most critical to outcomes
- Mechanism of palatoglossal coupling still poorly understood
Primary Tongue Base versus Multilevel Obstruction

- N=25  AHI 39.8 to 16.8  (responder n=11, 40%)
- Non-responder
  - Higher AHI (46 vs 30 events/hr)
  - Higher % velar obstruction  54% versus 17%
Inspire UAS effect during DISE

Reference: 2 slices

Palate Therapy OFF

Tongue Base Therapy OFF

Palate Therapy ON

Tongue Base Therapy ON

Posterior oropharyngeal wall

Posterior Uvula

Epiglottis

Lingual Tonsils

Courtesy Pat Strollo MD, University Pittsburgh
Stimulator and Sensing Leads

- 3 lead cuff wire electrode with micro-selective dissection and is placed on the medial (protrusive) division
  - Ground settings can change movement patterns
  - Beware apraxia or other factors in inclusion/exclusion
- Sensory lead placed at intercostal space timed with ventilation (timing has not shown to help, 50% + non-timed stimulation)
AHI – Raw Data

- Lot of scatter in data
- Adherence is not accounted for
- Titration AHI used for many studies not actual treatment effects (potentially large differences)
OSA Phenotypes (Testlemans 2021)

- Phenotypes affect outcome (survival) more than AHI
Serious Related Adverse Events: 8 of 126 (6%) participants in 5 years

- Device revision (N = 4)
  - IPG repositioning (2)
  - IPG and sensing lead repositioning (1)
  - Stimulation lead reposition (1)

- Device replacement (N=4)
  - IPG and sensing lead replacement (3)
  - Full system replacement (1)

- Anecdotal reports: pneumothorax, facial nerve placement, broken / nonfunctional leads
Multiple Post Market Studies

• Multiple Post Market Studies (inspire sponsored)
  – German trial
  – Adhere registry

• Several case series

• Effect RCT Trial
- RCT n=85 (therapy responders)
- Only one week therapy or off
- 95% patients correctly guessed blinding
German Post Market Study

Steffen et al Laryngoscope 2017
Limitations

- Titration versus treatment AHI
- Standard should be full-night efficacy (ie, single device setting)
- Home sleep apnea test (HSAT) or in-laboratory polysomnography (PSG)
- Titration effectiveness 91% versus 52% treatment
- Only 1/3 Adhere with treatment AHI
Older patients or lower BMI may be predictors

- **Age**: 1-year increase associated with 4% increased odds of success
- **BMI**: 1-unit increase associated with 9% decreased odds of success
Patterns Tongue Protrusion and Stimulation Grounding Lead Parameters

- **3 Primary Protrusion Patterns**
  - Bilateral
  - Right Based
  - Mixed activation

- Can change with electrode configuration

Steffen A, Tongue Motion Variability With Changes of Upper Airway Stimulation, *Laryngoscope* 2017

Pattern change M2 to M12
Advanced Titration/Impulse Configuration

• Concept of changing stimulation parameters to improve tolerance or efficacy

• Settings
  – Default = Pulse width 90 msec  Frequency 33 HZ
  – Alternative = Pulse width 120 msec  Frequency 40 HZ
  – Measure at Sensation/ Functional Threshold/ Subdiscomfort

  – Allows drop in voltage to achieve same degree muscle activity
  – Follows normal strength duration physiology curve

• Does this improve tolerance or effectiveness?
• N=85 patients > 1 year follow up
• AHI 30.0 to 18.6 (27 to 13.6)
• No improvement in Sensation/Functional Threshold/Subdiscomfort range
• No measurable improvement in tongue movement at different settings

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**Table 2.** Comparison of Amplitude Thresholds (FT and SDT) Between Two Pulse Widths and Frequency Configurations, 90 μsec 33 Hz and 120 μsec 40 Hz, at Three Different Electrode Configurations.

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Pulse width and frequency configuration</th>
<th>Electrode configuration</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bipolar [+−+] (n = 73)</td>
<td>Broad unipolar [−−] (n = 76)</td>
<td>Focal unipolar [o−o] (n = 75)</td>
</tr>
<tr>
<td>FT</td>
<td>90 μsec 33 Hz</td>
<td>1.5 (0.5–3.4)</td>
<td>0.6 (0.1–1.5)</td>
</tr>
<tr>
<td>FT</td>
<td>120 μsec 40 Hz</td>
<td>1.3 (0.3–3)</td>
<td>0.4 (0.1–1.3)</td>
</tr>
<tr>
<td>SDT</td>
<td>90 μsec 33 Hz</td>
<td>2.2 (0.7–5)</td>
<td>0.8 (0.3–2.5)</td>
</tr>
<tr>
<td>SDT</td>
<td>120 μsec 40 Hz</td>
<td>1.9 (0.5–3.8)</td>
<td>0.7 (0.2–2.0)</td>
</tr>
</tbody>
</table>
Association between anxiety, depression, and emotional distress and hypoglossal nerve stimulator adherence

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<table>
<thead>
<tr>
<th>Variable</th>
<th>Metric (mild, moderate, severe)</th>
<th>Adherence &lt; 28 h (n=11)</th>
<th>Adherence ≥ 28 h (n=22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHQ-9</td>
<td>Anxiety (0-4,5-9,10-14)</td>
<td>10.09 ± 7.53</td>
<td>6.15 ± 4.31</td>
<td>0.118</td>
</tr>
<tr>
<td>GAD7</td>
<td>Depression (0-4,5-9,10-14)</td>
<td>8.27 ± 6.69</td>
<td>3.90 ± 3.98</td>
<td>0.049</td>
</tr>
<tr>
<td></td>
<td>(15-19,19-24)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-ADS</td>
<td>Emotional Distress (&gt;10, &gt;20, &gt;30)</td>
<td>19.20 ± 9.80</td>
<td>10.05 ± 7.49</td>
<td>0.035</td>
</tr>
</tbody>
</table>

- N=33 All PSG responders
- Mood disorder associated with outcomes
- Even Mild abnormalities associated with poorer outcomes
UPPP Tonsillectomy for Salvage CN XII

- Using Sher criteria success 81%
13 Patients (7 responders, 6 non-responders)
• Wake CT scans stimulation ON / OFF
• Hyoid movement predictive. Other data strongly suggests more movement more effect
• Discriminant analysis demonstrated CPAP opening < 8 cm H2O with higher success rates, greater change AHI, sleepiness, snoring (consistent with hypopnea being more responsive)
Conclusions

• UAS demonstrates long term clinically significant improvements in
  – Single time point AHI and ODI
  – Self reported symptoms sleepiness, sleep related quality of life, and snoring
• Low rate of adverse events
• Lacking much relevant clinical outcomes
  – Blood pressure
  – Objective sleepiness
  – Heart and metabolic disease
Conclusions - Future

- Advocate for interventions with low morbidity
- Ancillary Procedures
  - Bilateral stimulation
  - Combined with other surgery/medications/devices
- Biggest challenge is integrating procedure with care of the complicated OSA patient