MICHIGAN
OTOLARYNGOLOGIC SOCIETY

Inspire Therapy for Treatment of Obstructive Sleep Apnea

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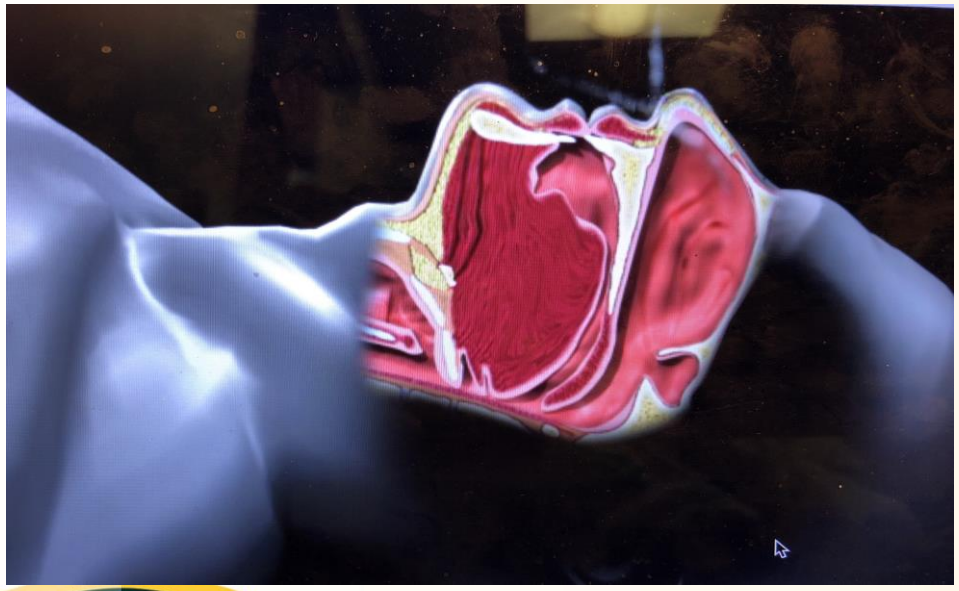
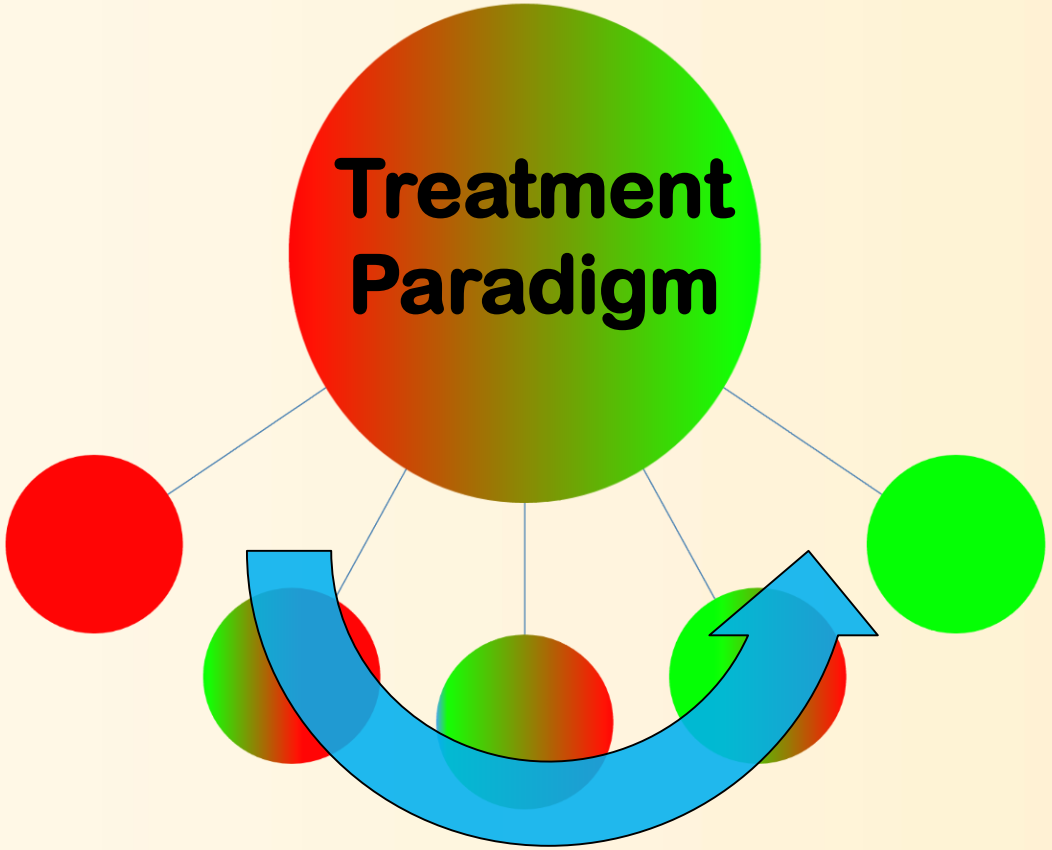
07/19/19

Multi-Level Airway Surgery

-Always ON (swallowing/breathing)
-Permanent (too much vs. too little)
-Very invasive (inpatient, ICU)
-Precise Localization of Site of Obstruction
-Results variable (technique & scar)
-Surgery irreversible

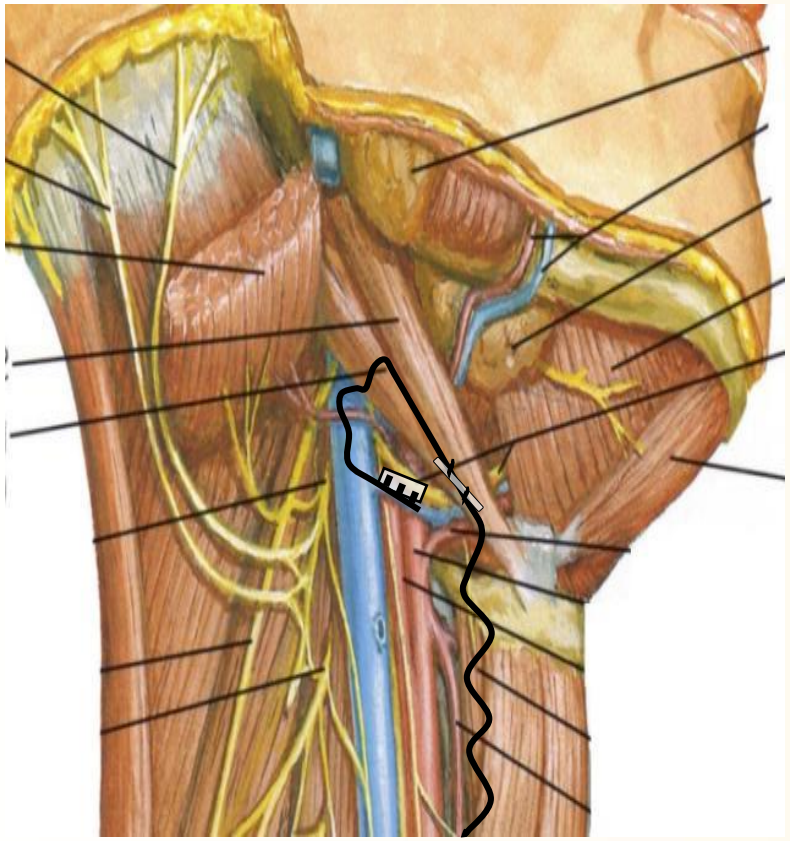


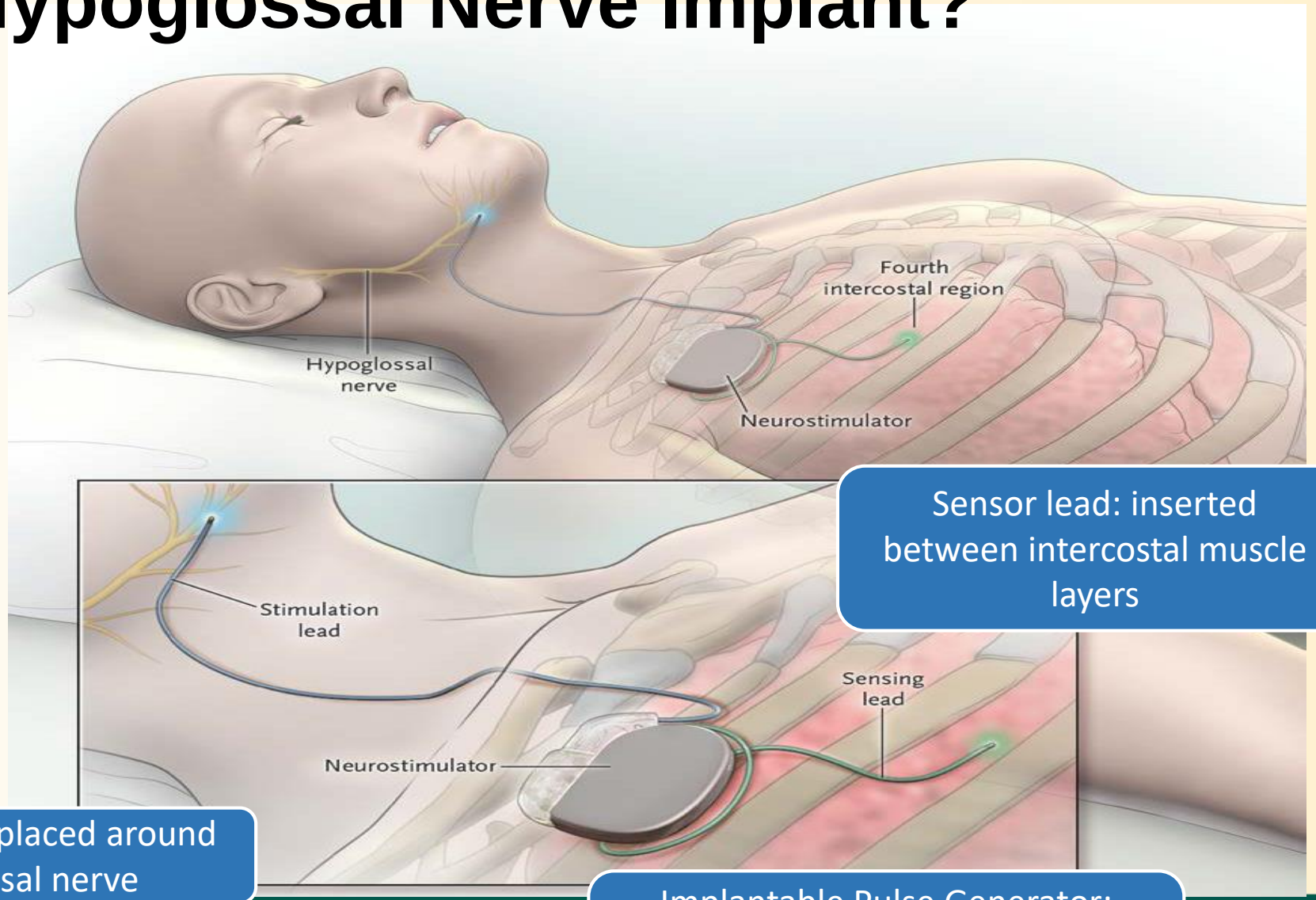


Hypoglossal Nerve Stimulation

-ON and OFF (only use at night)
-Titratable (0V to 5V)
-Minimally Invasive (outpatient)
-Global Effect
-Results highly reproducible & effective
-Surgery reversible

What is Hypoglossal Nerve Implant?





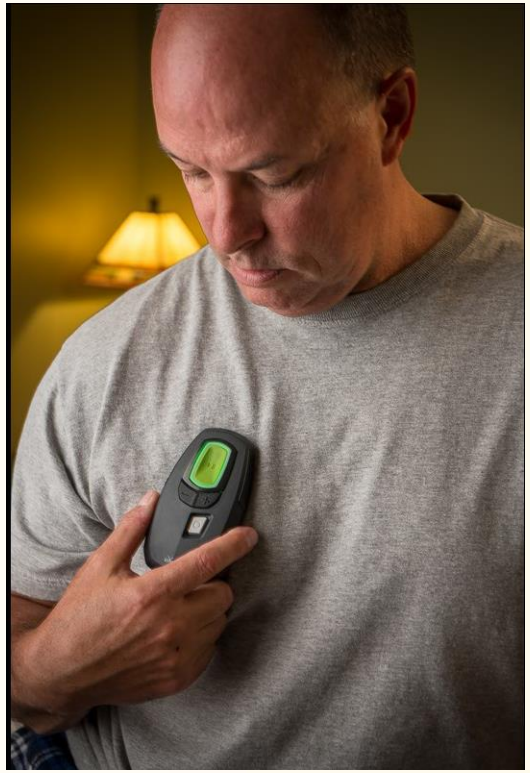
Sensor lead: inserted between intercostal muscle layers

Stimulation lead: placed around the hypoglossal nerve

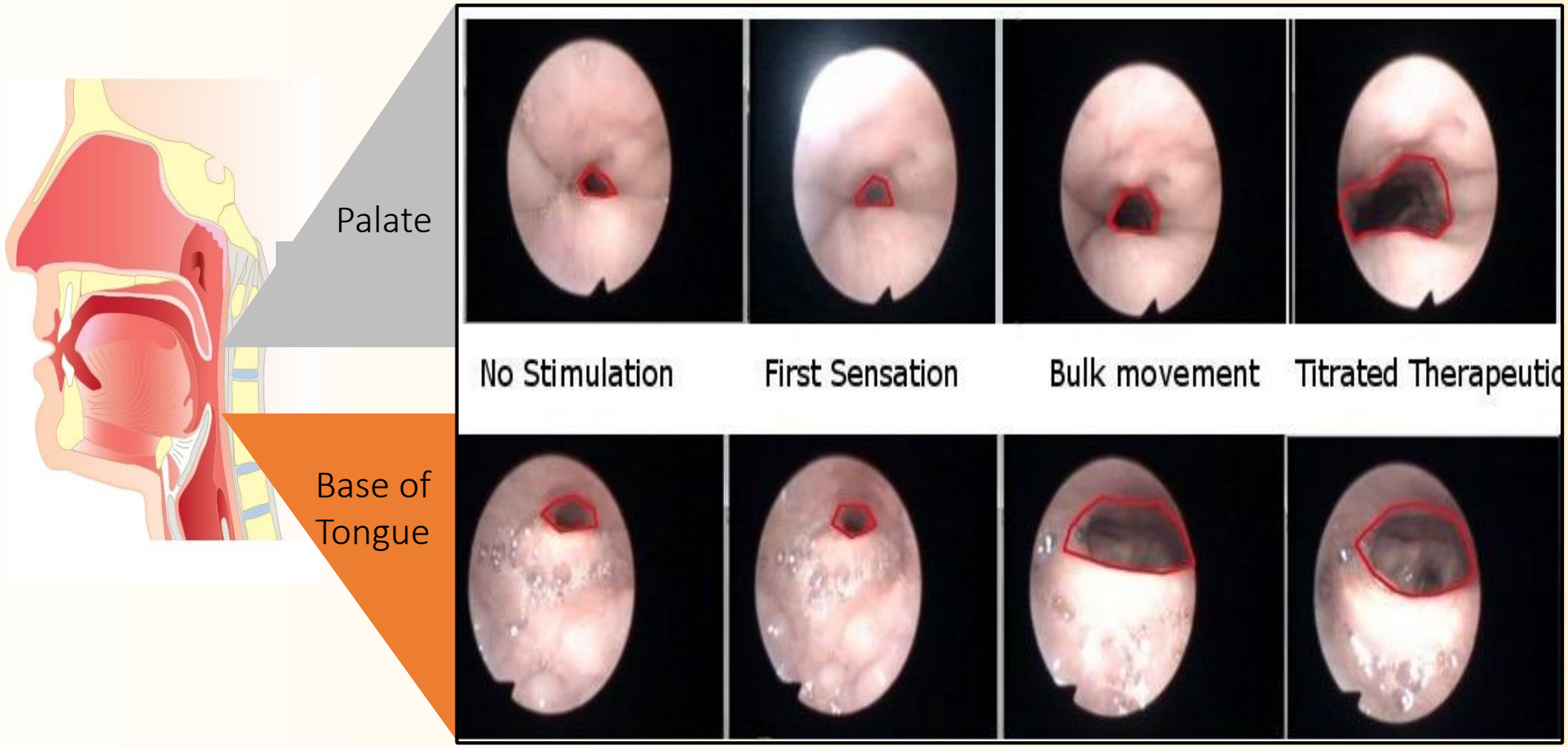
Implantable Pulse Generator: subcutaneous pocket common to pacemakers and neurostimulators

Strollo et al, NEJM 2014

Clinic Visit → Diagnostic Sleep Study → ENT: DISE & Implant → **Therapy Activation (1-mo post-op)** → In Lab Therapy Titration → Routine Follow-Ups (1-2 per year)



Multi-level (Global) Mechanism of Action



Therapeutic effect is evident at both the palate and tongue-base

More prominent response with increasing stimulation energy – within therapeutic range

Saffiruddine et al, ERJ 2015

- 2008 Initial involvement with Inspire
- Feb, 2010 First patient implanted in Detroit VA (Inspire 2 Trial)
- Sep, 2011 First patient implanted in DMC (STAR Trial)
- Jan, 2014 STAR Trial published in NEJM
- May, 2014 FDA approval
- Jul, 2019 Over 100 Active Programs in the US
- Over 4000 Patients Treated
- Over 50 Peer Reviewed Publications

Implanted Upper Airway Stimulation Device for Obstructive Sleep Apnea

*Inspire 2: Feasibility Study

Paul H. Van de Heyning, MD, PhD; M. Safwan Badr, MD; Jonathan Z. Baskin, MD; Michel A. Cramer Bornemann, MD; Wilfried A. De Backer, MD, PhD; Yaniv Dotan, MD; Winfried Hohenhorst, MD; Lennart Knaack, MD; Ho-Sheng Lin, MD; Joachim T. Maurer, MD, PhD; Aviram Netzer, MD; Rick M. Odland, MD; Arie Oliven, MD; Kingman P. Strohl, MD; Olivier M. Vanderveken, MD, PhD; Johan Verbraecken, MD, PhD; B. Tucker Woodson, MD

TABLE II.
Summary of Treatment Effects for Part 1 Responders (n = 6) at Baseline and 6-Month Postimplant Visits.

Measure	Baseline	6 Months	P
AHI	26.1 ± 4.5	7.7 ± 4.1*	<.01
AHI_REM	38.2 ± 9.5	11.1 ± 9.3*	<.01
AHI_NREM	24.2 ± 4.1	7.0 ± 3.8*	<.01
AI	15.3 ± 8.3	2.5 ± 1.4*	.02
HI	10.8 ± 6.6	5.2 ± 3.3	.19
ODI	14.5 ± 7.2	6.7 ± 4.3*	<.05

TABLE III.
Summary of Treatment Effects for Part 1 Nonresponders (n = 14).

Measure	Baseline	6 Months	P
AHI	51.1 ± 16.2	56.1 ± 22.[illegible]	.40
AHI_REM	43.8 ± 22.9	45.4 ± 27.2	.82
AHI_NREM	48.8 ± 18.2	56.9 ± 22.5	.29
AI	33.0 ± 21.5	42.0 ± 24.5	.22
HI	18.1 ± 10.4	14.1 ± 9.6	.27
ODI	36.7 ± 24.7	45.0 ± 27.1	.10

TABLE IV.
Summary of Therapy Responses for Part 2 Subjects (n = 8).

Measure	Baseline	6 Months	P
AHI	38.9 ± 9.8	10.0 ± 11.0*	<.01
AHI_REM	28.2 ± 17.7	9.0 ± 9.4*	.01
AHI_NREM	39.6 ± 10.8	10.0 ± 12.1*	<.01
AI	22.7 ± 8.2	6.4 ± 9.7*	<.01
HI	16.1 ± 12.5	3.6 ± 3.9*	<.01
ODI	32.1 ± 15.1	9.5 ± 10.2*	<.01

-AHI < 50
-BMI < 32
-Absence of concentric narrowing on DISE

The Laryngoscope

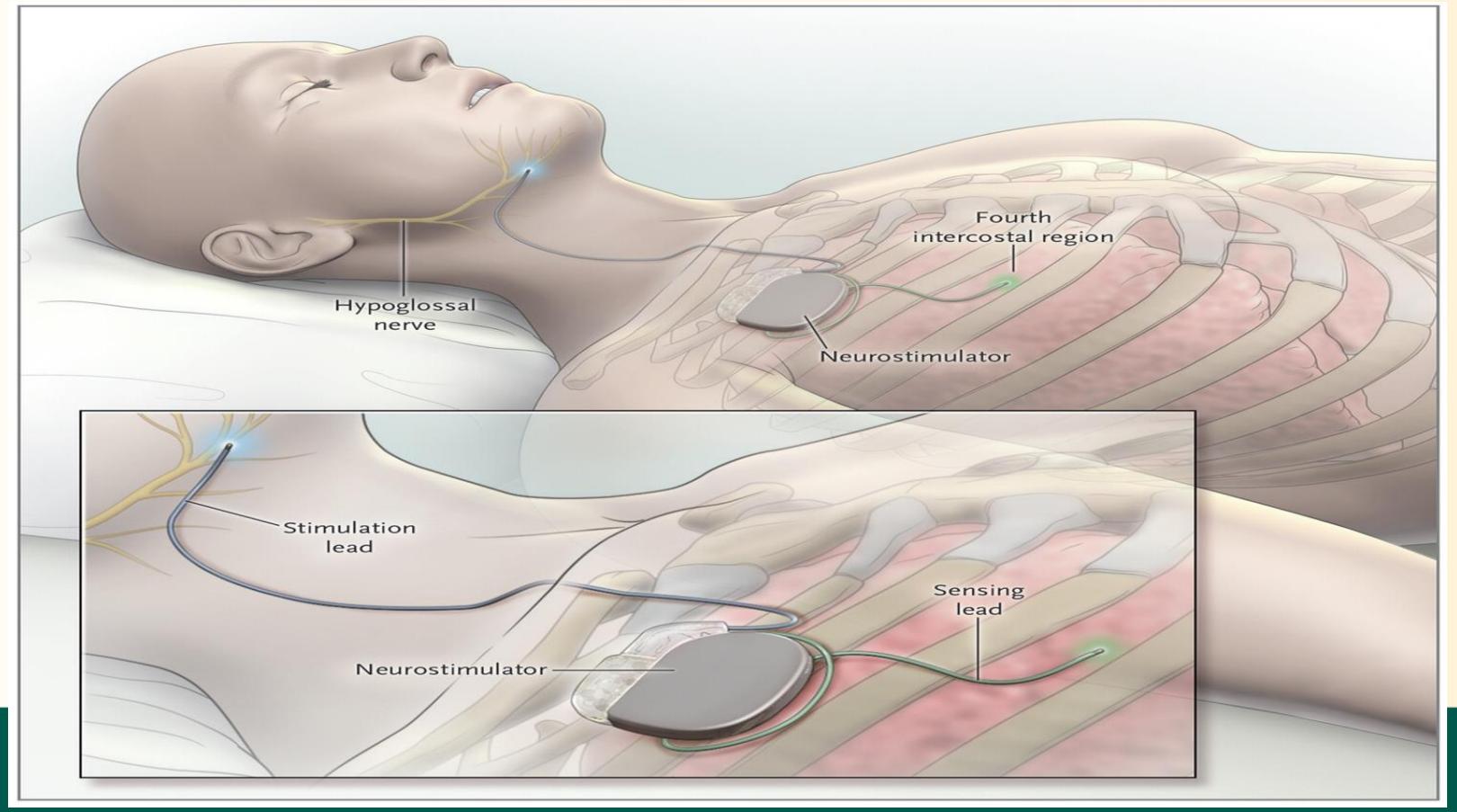
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

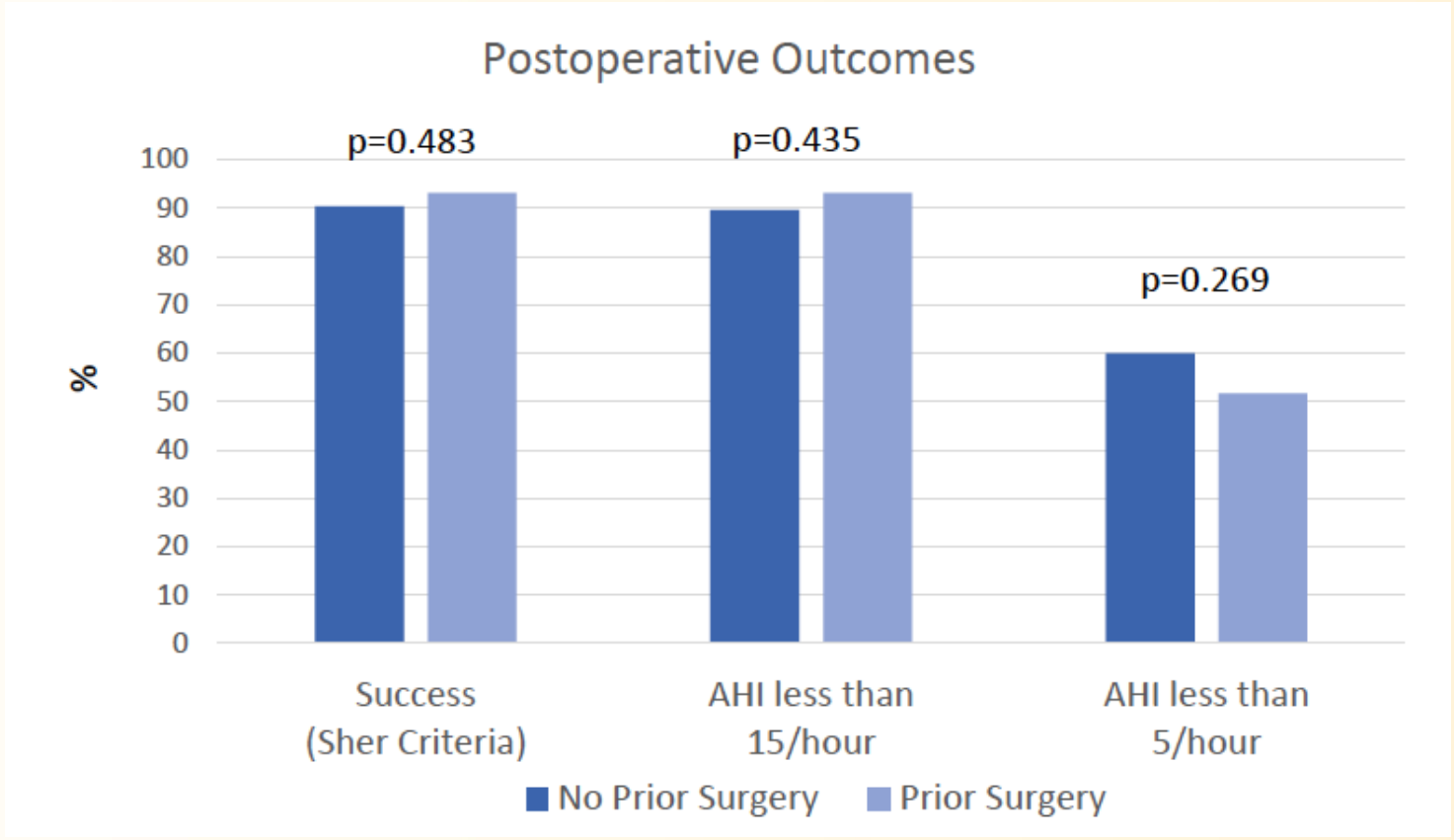
Upper-Airway Stimulation for Obstructive Sleep Apnea

Patrick J. Strollo, Jr., M.D., Ryan J. Soose, M.D., Joachim T. Maurer, M.D., Nico de Vries, M.D., Jason Cornelius, I
D. Hanson, M.D., Tapan A. Padhya, M.D., David L. Steward, M.D., M. Boyd Gillespie, M.D., B. Tucker Woodson, M
Ph.D., Mark G. Goetting, M.D., Oliver M. Vanderveken, M.D., Ph.D., Neil Feldman, M.D., Lennart Knaack, M.D., an
STAR Trial Group

N Engl J Med 2014; 370:139-149 | January 9, 2014 | DOI: 10.1056/NEJMoa1308659



How Effective is this Treatment?



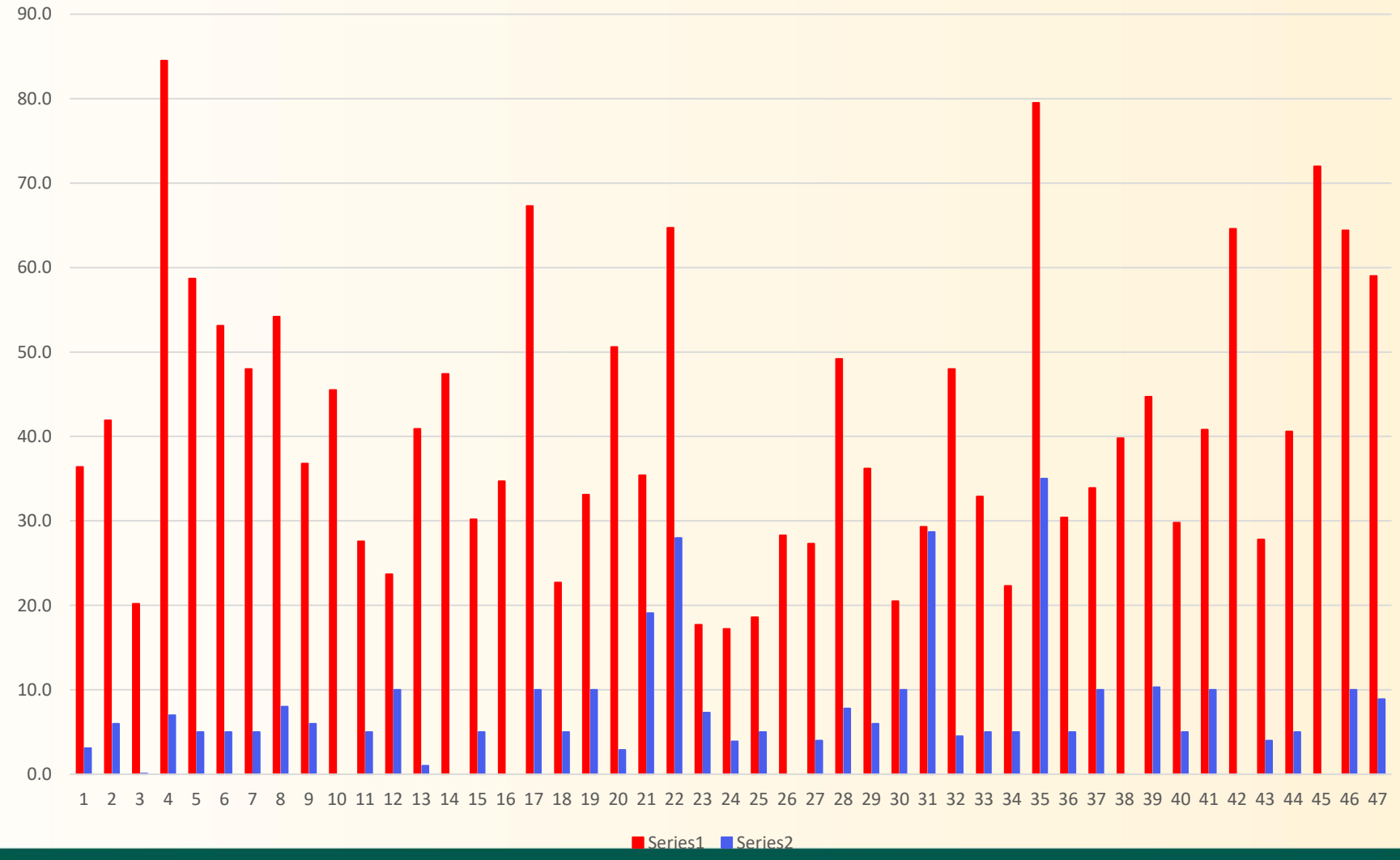
Thomas Jefferson (n=81) and Germany (n=83)

BMI	Implanted	PSG preop	PSG w/Tx
29.0	02/08/10	36.4	3
24.0	9/15/11	41.9	6
31.0	11/03/16	20.2	0
37.0	12/08/16	84.5	7
25.7	02/16/17	58.7	5
28.2	02/24/17	53.1	5
32.3	03/02/17	48.0	5
31.0	03/20/17	54.2	8
33.9	04/10/17	36.8	6
21.3	06/01/17	45.5	0
24.3	08/21/17	27.6	5
28.0	08/03/17	23.7	10
25.0	08/21/17	40.9	1
31.1	09/14/17	47.4	0
28.6	09/14/17	30.2	5
23.4	09/28/17	34.7	0
27.9	10/30/17	67.3	10
29.3	11/09/17	22.7	5
32.0	12/11/17	33.1	10
24.9	02/22/18	50.6	3
30.7	01/11/18	35.4	19
28.9	05/03/18	64.7	28
25.1	11/23/18	17.7	7
33.1	05/24/18	17.2	4

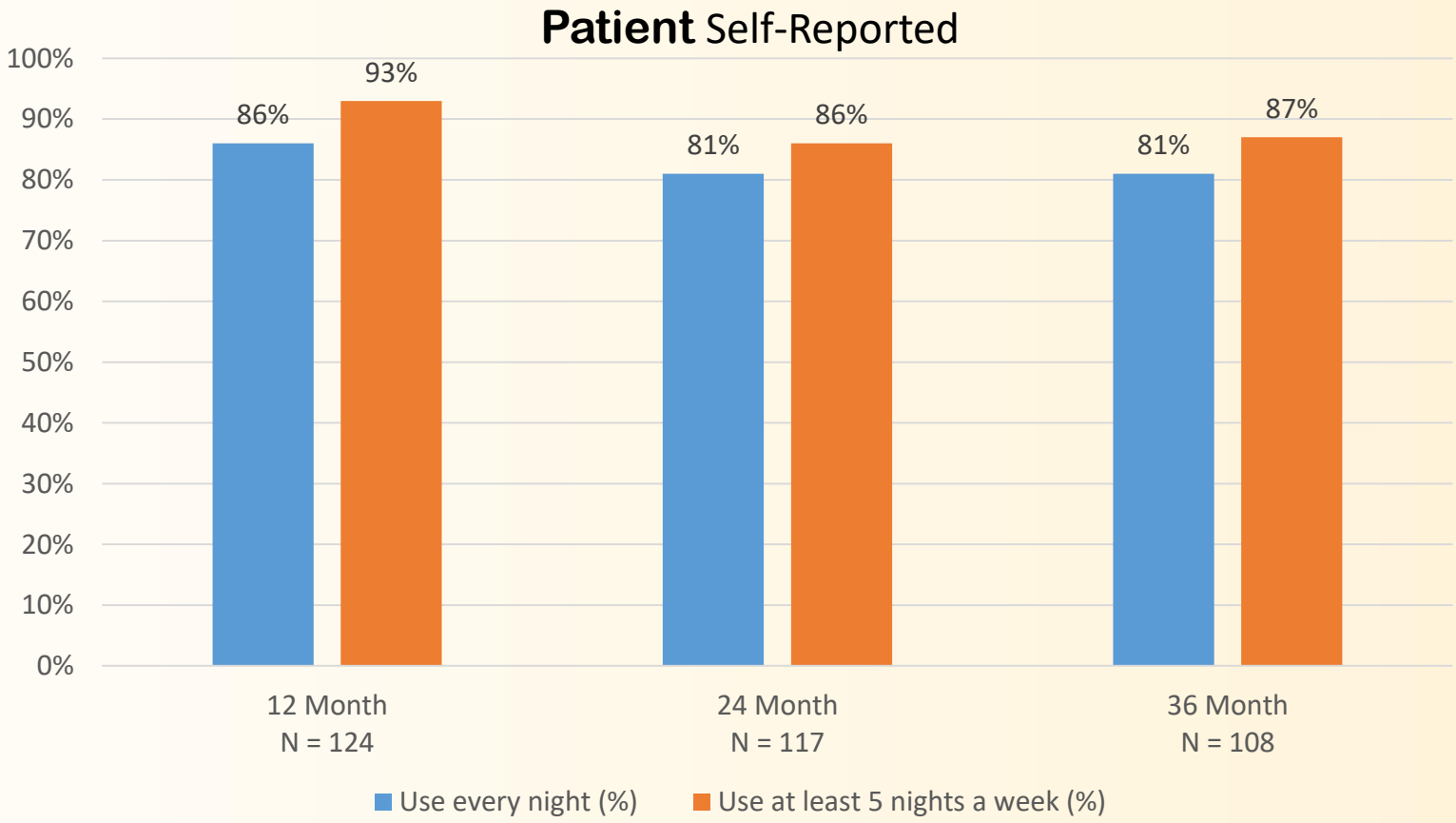
BMI	Implanted	PSG preop	PSG w/Tx
31.0	06/18/18	18.6	5
31.8	06/21/18	28.3	0
26.5	06/22/18	27.3	4
27.2	06/29/18	49.2	8
29.0	06/21/18	36.2	6
33.3	07/27/18	20.5	10
29.0	08/02/18	29.3	29
23.8	08/02/18	48.0	5
31.6	08/09/18	32.9	5
25.5	9/21/18	22.3	5
31.1	10/15/18	79.5	35
27.6	09/13/18	30.4	5
31.0	9/27/18	33.9	10
30.0	10/19/18	39.8	0
32.7	11/15/18	44.7	10
29.6	10/18/18	29.8	5
32.5	11/23/18	40.8	10
24.9	12/07/18	64.6	0
26.0	11/23/18	27.8	4
26.4	12/07/18	40.6	5
34.3	12/13/18	72.0	0
33.0	01/17/19	64.4	10
31.8	02/07/19	59.0	9

Success rate (AHI <10) of 91% (43/47)

Preop vs. Postop AHI

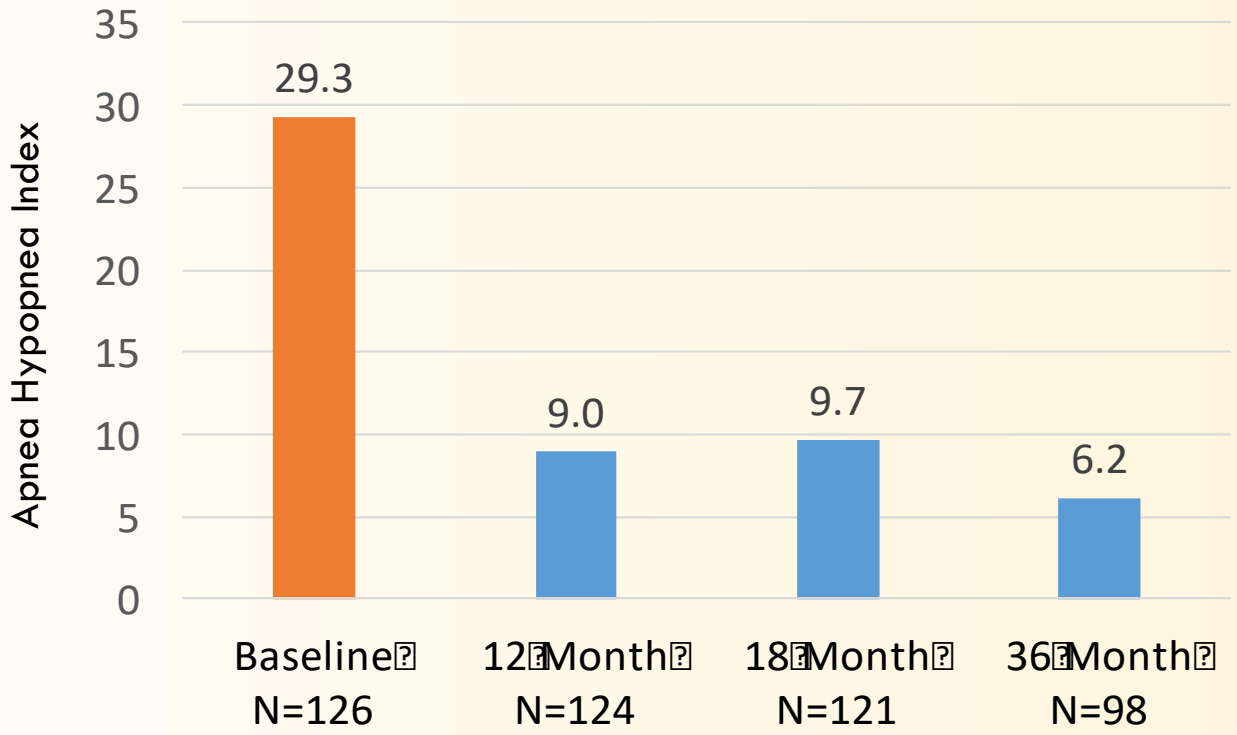


Are patients using the therapy?



From STAR database

Is the therapy long lasting?

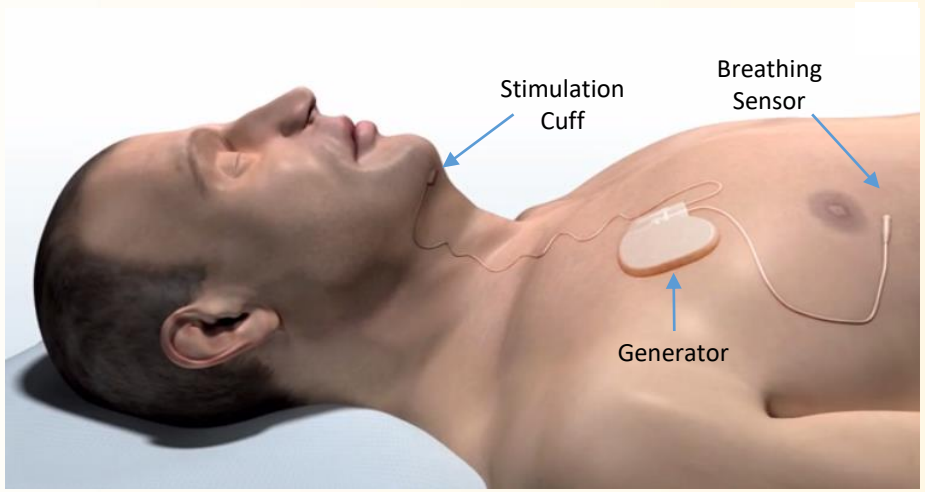


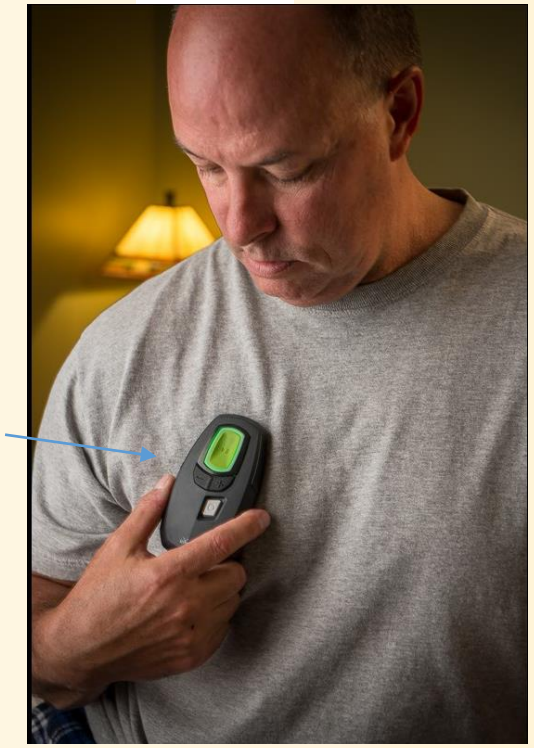
Results in median, $p < 0.01$

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*

Long-Term Objective Outcomes

Is the implant safe?





<u>Several million patients receive implantable stimulation therapies annually</u>

- Cardiac conditions (Bradycardia, Tachycardia, Heart failure)
- Pain management
- Other neuro-related conditions (Urologic disorders, Parkinson's Disease)

What are the Potential Side Effects?

Table 3. Nonserious Adverse Events over 48 Months of STAR Trial.

Adverse Events	Events, n					Participants with Event, %[a] (n)
	0-12 mo	12-24 mo	24-36 mo	36–48 mo	Total	
Procedure-related nonserious adverse events						
Postoperative discomfort related to incisions	47	1	2	1	51	29.4 (37)
Postoperative discomfort independent of incisions	41	0	1	0	42	27.0 (34)
Temporary tongue weakness	34	0	0	0	34	18.3 (23)
Intubation effects	18	0	0	0	18	11.9 (15)
Headache	8	0	0	0	8	6.3 (8)
Other postoperative symptoms	22	0	0	0	22	11.1 (14)
Mild infection	1	0	0	0	1	0.8 (1)
Device-related nonserious adverse events						
Discomfort due to electrical stimulation	81	23	25	7	136	57.9 (73)
Tongue abrasion	28	12	4	3	47	26.0 (33)
Dry mouth	10	5	2	0	17	12.7 (16)
Mechanical pain associated with presence of the device	7	2	4	0	13	9.5 (12)
Temporary internal device usability or functionality complaint	12	8	1	3	24	15.9 (20)
Temporary external device usability or functionality complaint	11	11	8	9	39	23.8 (30)
Other acute symptoms	21	14	1	2	38	23.1 (30)
Mild infection	1	0	0	0	1	0.8 (1)

Abbreviation: STAR, Stimulation Therapy for Apnea Reduction.
[a]Percentage based on original cohort of implanted participants, N = 126.

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

Clinic Visit → Diagnostic Sleep Study → ENT: DISE & Implant → **Therapy Activation (1-mo post-op)** → In Lab Therapy Titration → Routine Follow-Ups (1-2 per year)

- **Age > 22**
- **AHI = 15-65, central/mixed < 25% total**
- **BMI < 32**
- **CPAP failure or inability to tolerate CPAP**
- **Appropriate airway anatomy (DISE)**
- **Insurance coverage**
- **No contraindications**

Contraindications for Inspire Therapy

- **PSG: > 25% central + mixed apneas**
- **DISE: Concentric collapse at the palate level**
- **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**

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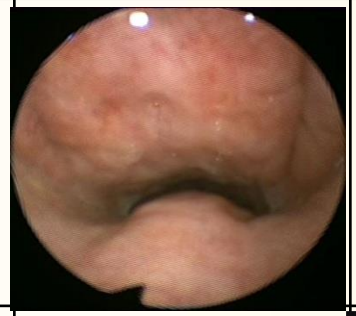
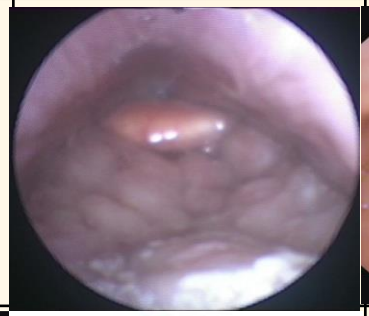
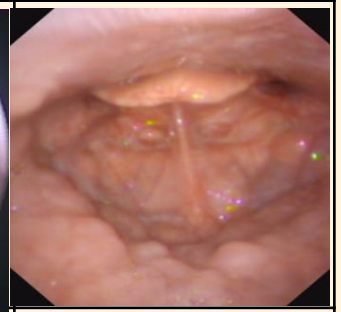
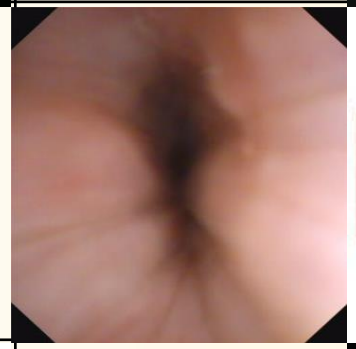
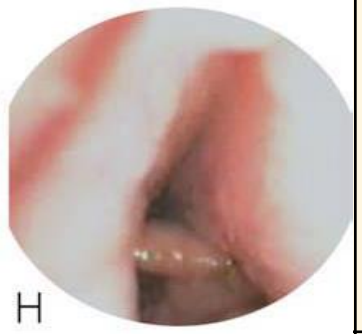
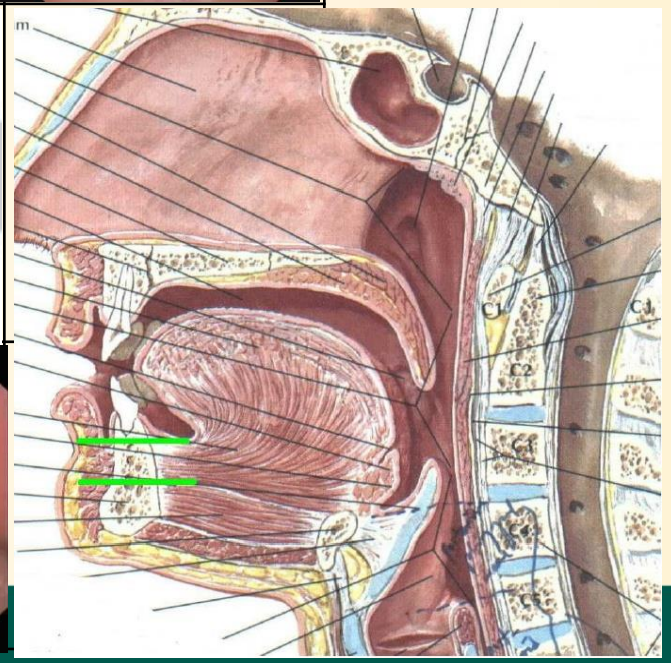
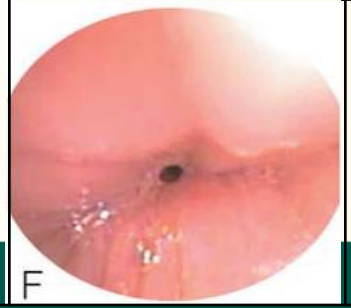
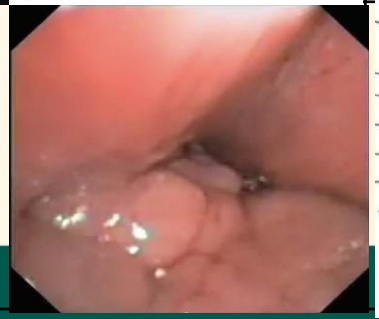
	Velopharynx	Oropharynx	Base of Tongue	Epiglottis
Anterior Posterior Collapse		X		
Lateral Collapse	X			
Concentric Collapse		X		

- **Typically an Outpatient Procedure**
  - **General anesthesia x 2-3 hours**
- **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- Celebrex and Tylenol**
- **Recovery**
  - **Return to regular diet and most activities of daily living immediately after the procedure**
  - **Avoid strenuous activities for a few weeks**

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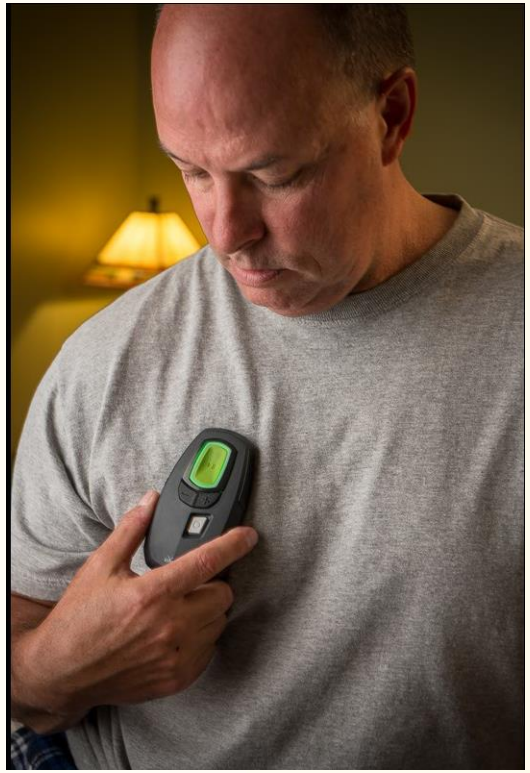

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