Proximal Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea in the OSPREY Study: A Randomized Controlled Trial

Atul Malhotra, MD; Alan R Schwartz, MD; Eric G Lovett, PhD; Nadine Juran, RN; Shaun A Nguyen, MD; Jose E Barrera, MD; Richard K Bogan, MD; Samuel A Mickelson, MD; Haresh Boghara, MD; Mitchell B Miller, MD; Ofer Jacobowitz, MD, PhD; on Behalf of the OSPREY Investigators.
Annals of Internal Medicine. 2026 Apr 21. doi: 10.7326/ANNALS-25-04414. Online ahead of print.

LivaNova

MA-PROACT-OSA-00003-0426

Key Takeaway

Proximal hypoglossal nerve stimulation (pHGNS) greatly reduced breathing interruptions and improved blood oxygen levels during sleep, and improved patient-reported daytime sleepiness symptoms in adults with moderate-to-severe obstructive sleep apnea (OSA). LivaNova has the only pivotal HGNS prospective randomized controlled trial to date.

Abbreviations: AHI, Apnea-Hypopnea Index; BMI, body mass index; CCC, complete concentric collapse; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; GLP-1, glucagon-like peptide-1; OSA, obstructive sleep apnea; pHGNS, proximal hypoglossal nerve stimulation.

Why Was This Study Conducted?

People with OSA globally: 1 billion

Major long-term potential health consequences: cardiovascular events, stroke, metabolic syndrome, cognitive impairment and dementia, injury from accidents due to sleepiness

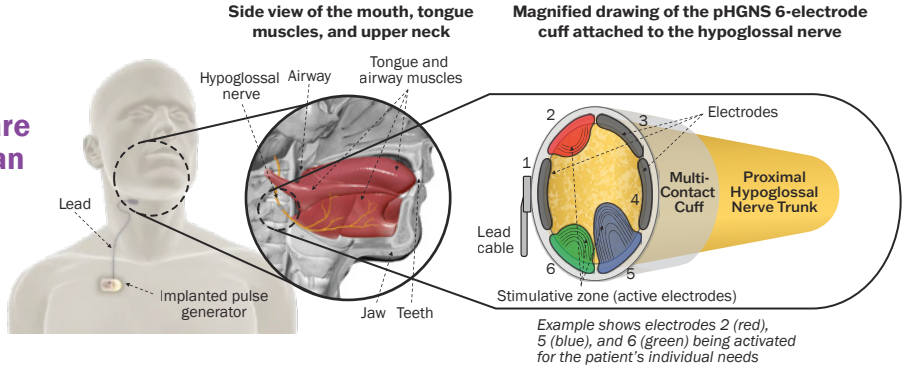
Early treatments: CPAP and weight loss drugs (eg, GLP-1 receptor agonists)

Failure of CPAP: ~50% of patients

For patients who cannot tolerate or are otherwise unable to continue CPAP, an effective and safe therapy is needed

What Is pHGNS?

The **hypoglossal nerve** is a motor nerve that controls tongue movement. **pHGNS** is a medical device to treat OSA containing an electrode cuff with 6 contacts that stimulate the proximal hypoglossal nerve, leading to **tongue and airway muscle toning and stiffening to open the airway during sleep.** The **6 contacts of the electrode cuff** can be activated both individually and simultaneously, which results in a unique combination of technology and physiology and **tailoring of therapy for patient needs.**



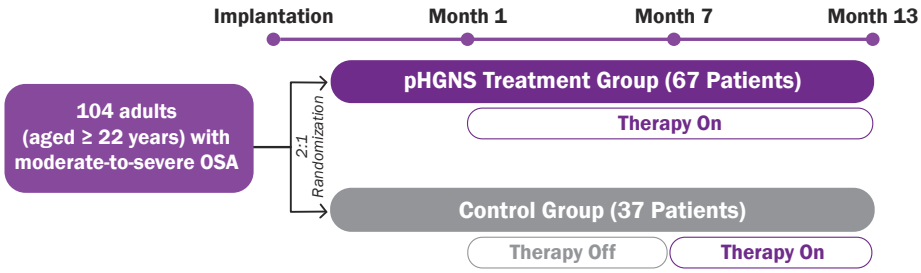
Example shows electrodes 2 (red), 5 (blue), and 6 (green) being activated for the patient's individual needs

Study Objective

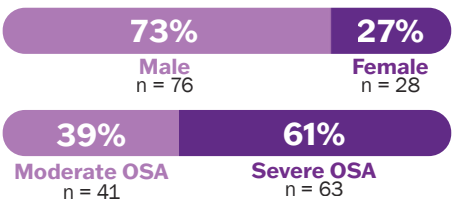
To measure the efficacy and safety of pHGNS in adults with moderate-to-severe OSA

Study Design

The OSPREY study compared sleep measures and oxygen levels between 2 groups of patients: one group had pHGNS turned on ~1 month after implantation, and the other group (control → treatment) at ~7 months after implantation. Patients with complete concentric collapse (CCC) were not excluded and drug-induced sleep endoscopy was not required.



Patients



55.6 years
Mean age

30.6 kg/m²
Mean BMI
(> 30 = obese)

38%
Patients with BMI ≥ 32

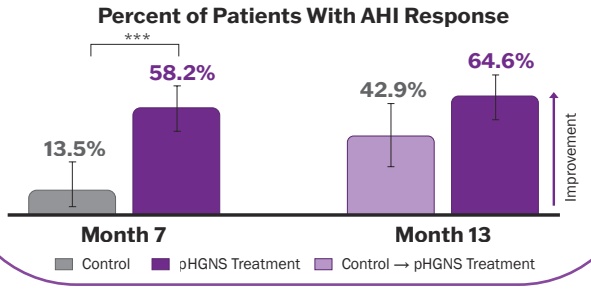
35.7
Mean AHI
(> 30 = severe OSA)

45%
Patients at high risk of CCC[a]

10.1
Mean ESS
(> 10 = excessive daytime sleepiness)

Efficacy

pHGNS greatly reduced breathing interruptions during sleep



AHI = number of times breathing slows or stops each hour during sleep. AHI response was defined as ≥ 50% reduction in AHI from the start of the study and AHI < 20 events/hour. ***P < .001.

Daytime sleepiness (ESS) and other **patient-reported sleepiness symptoms** (FOSQ, PROMIS-SDI, and PROMIS-SRI) **improved at month 7 with pHGNS treatment**

At month 7, more patients in the **pHGNS group had improved symptoms** according to their clinician's assessment and experienced **fewer drops in blood oxygen levels during sleep** than the control group.

Percent of patients at month 7 achieving:	Control	pHGNS Treatment
CGI-I response (much or very much improved)	8.6%	**56.3%**
ODI response (fewer drops in blood oxygen levels)	37.8%	**68.7%**

CGI-I = how much a patient's illness has improved from the start of the study. ODI = drops in blood oxygen levels during breathing interruptions while asleep. ODI response was defined as ≥ 25% improvement in ODI from the start of the study.

At month 13, improvements in all outcome measures at month 7 were maintained in the pHGNS group; patients who switched from the control group to the treatment group experienced substantial improvements in OSA symptoms and sleepiness

Safety

Most common side effects (> 5% of patients in the pHGNS treatment group) were **Headache** | **Implant site pain** | **Difficulty swallowing**

0 serious side effects related to the device or implantation procedure

Most side effects were **mild or moderate** in severity

Abbreviations: CGI-I, Clinician Global Impression of Improvement; FOSQ, Functional Outcomes of Sleep Questionnaire; ODI, Oxygen Desaturation Index; PROMIS-SDI, Patient-Reported Outcomes Measurement Information System Sleep Disturbance Index; PROMIS-SRI, Patient-Reported Outcomes Measurement Information System Sleep-Related Impairment.

[a]Data on file, LivaNova PLC. Based on the recently presented PREDICTOR algorithm (Weiner J. Presented at the 2024 International Surgical Sleep Society Educational Update, September 27, 2024, Miami, FL. https://surgicalsleep.org/wp-content/uploads/2025/11/16253-ISSS-2024-EducationI-Agenda-22.pdf).

Short-form Safety Information for Physicians – aura6000™ System for Obstructive Sleep Apnea (US) (April 2026)

DEVICE DESCRIPTION

The aura6000 System for proximal hypoglossal nerve stimulation (pHGNS) consists of an implantable generator, an implantable stimulation lead, and an external programming system to change stimulation settings, which includes the aura6000 Clinical Manager (aCM), Remote Control & Charger (RCC), and Charging Antenna (CA).

INTENDED USE / INDICATION

The aura6000 System is indicated for the reduction of apneas, hypopneas, or both in adult patients with moderate to severe obstructive sleep apnea (OSA), defined as an apnea-hypopnea index (AHI) of ≥ 15 and ≤ 65. The aura6000 System is intended for patients who failed, do not tolerate, or are ineligible to be treated with current standard of care treatments such as positive airway pressure (PAP), oral appliances, or pharmacotherapy.

PAP failure is defined as an inability to eliminate OSA (AHI > 15 despite PAP usage). PAP intolerance is defined as an inability to use PAP > 5 nights per week for > 4 hours per night or an unwillingness to use PAP.

CONTRAINDICATIONS

Not for use in patients with: combined central and mixed AHI ≥ 25% of the total AHI; any functional or structural problem, medical illness, or condition that would prevent or interfere with implantation, activation, or continued use of the aura6000 System; an implantable device which may be susceptible to unintended interaction with the aura6000 System; any condition or procedure that has compromised neurological control of the upper airway; or in patients who are pregnant, planning to become pregnant, or breastfeeding.

Not for use in patients who require diathermy. Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with an aura6000 System. Not for use in patients who require magnetic resonance imaging (MRI). The generator, lead, RCC, and CA are MR Unsafe devices.

WARNINGS & PRECAUTIONS

Product warnings and potential risks and adverse events are discussed in the aura6000 System manufacturer's product labeling. The aura6000 System should only be prescribed and monitored by physicians who are experienced in the diagnosis and treatment of OSA and have specific training and expertise in the management of OSA and the programming and use of this device.

Use of the aura6000 System should be carefully considered in patients who fall outside the studied population, including: patients < 22 or > 75 years of age; patients with body mass index (BMI) > 35 kg/m2; or patients with AHI < 15 or > 65 events/hour. Drug-induced sleep endoscopy (DISE) is not required for patient selection and clinical studies did not exclude patients with complete concentric collapse (CCC) at the velum. However, CCC status was not systematically assessed as a separate subgroup nor characterized during enrollment, therefore clinicians should exercise judgment when evaluating patients with suspected or confirmed CCC. The safety and efficacy of the aura6000 System have not been established for pediatric use.

Do not modify the RCC or CA and do not use the RCC if it has been tampered with. Do not bypass system controls on the aCM computer or connect the aCM computer to insecure networks. Do not connect any non-LivaNova provided devices or accessories to the RCC or aCM computer. The use of non-approved or non-LivaNova components with the aura6000 System may damage the system or its components and increase the risk to the patient, resulting in loss of therapy or patient injury, and may void the product warranty. Device malfunction could cause painful stimulation or direct current stimulation which could cause nerve damage.

ADVERSE EVENTS

The most commonly reported side effects in randomized control trials (≥ 5% of patients) were headache, implant site pain, oropharyngeal pain, and difficulty swallowing. Other adverse events reported (≥ 2% of patients): implant procedure-related events, including pain (tongue, neck, ear), reduced sensation, implant site swelling, and tongue movement disturbance; and stimulation-related events, including discomfort, pain, and speech disorder. Most adverse events were mild or moderate in severity and no serious procedure-related adverse events were reported.

*The information contained in this summary represents partial excerpts of important prescribing information taken from the product labeling. The information is not intended to serve as a substitute for a complete and thorough understanding of the aura6000 System or the material presented in the manufacturer's product labeling, nor does this information represent full disclosure of all pertinent information concerning the use of the product, potential safety complications, or efficacy outcomes.