CAROTID BARORECEPTOR ACTIVATION THERAPY (BAT): CURRENT EVIDENCE

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I MECHANISM OF ACTION AND AUTONOMIC PATHOPHYSIOLOGY

- **The Device System (Barostim Neo):** A second-generation implantable neuromodulation system consisting of a programmable **subcutaneous pectoral pulse generator** connected to a single **2-mm sutureless/sutured platinum-iridium extravascular disk electrode** surgically attached to the outer adventitial surface of the **unilateral (typically right) carotid sinus** at the carotid bifurcation.
- **Afferent and Central Neural Pathway:** Continuous, titratable electrical stimulation depolarizes mechanosensitive **carotid sinus baroreceptor nerve endings** without mechanical stretch. Action potentials travel via the **Carotid Sinus Nerve of Hering** (a branch of the **Glossopharyngeal Nerve, Cranial Nerve IX**) to the **Nucleus Tractus Solitarius (NTS)** in the dorsal medulla oblongata.
- **Efferent Autonomic Rebalancing (Counteracting Neurohormonal Toxicity):** The NTS integrates this afferent signal as elevated arterial pressure, inhibiting the rostral ventrolateral medulla (RVLM) and activating the nucleus ambiguus:
- **Sympathetic Withdrawal:** Markedly reduces central sympathetic nerve traffic (measured by a 30% reduction in muscle sympathetic nerve activity), lowering **Systemic Vascular Resistance (SVR / LV afterload)**, increasing **venous capacitance (reducing preload/pulmonary congestion)**, and inhibiting renal **juxtaglomerular renin secretion (downregulating RAAS)**.
- **Parasympathetic (Vagal) Augmentation:** Restores cardiac vagal tone, slows resting heart rate, improves **Heart Rate Variability (HRV)**, inhibits inflammatory cytokine release, and raises the ventricular fibrillation threshold.

II CLINICAL EVIDENCE AND INDICATIONS IN HEART FAILURE (HFREF)

- **Target Clinical Niche ("The No-CRT-Option HFrEF Patient"):** Designed for patients with symptomatic **HFrEF (LVEF 35 percent or less)** who remain in **NYHA Functional Class III** (or Class II with recent Class III hospitalization) despite maximally tolerated **Quadruple GDMT** and who are **NOT candidates for Cardiac Resynchronization Therapy (CRT)** because they have a **narrow QRS complex (<130 ms) or non-LBBB morphology (QRS <150 ms)**.
- **The Pivotal Trial: BeAT-HF (Zile et al., *JACC* 2020 [Expedited Phase] & *European Journal of Heart Failure* 2024 [Long-Term Post-Market Phase]):**
- **Trial Design:** Prospective multicenter randomized controlled trial comparing **Barostim Neo (BAT) + Optimal GDMT versus GDMT Alone** in patients with **LVEF <=35%, NYHA Class III (or II), NT-proBNP <1,600 pg/mL (in the FDA cohort), 6MWD 150 to 400 meters, and NO Class I indication for CRT**.
- **6-Month Symptomatic & Biomarker Endpoints (*JACC* 2020 — Basis of FDA Approval):** BAT produced highly significant improvements in **6-Minute Walk Distance (+60 meters vs. GDMT; p < 0.001)**, **Quality of Life (Minnesota Living with Heart Failure Questionnaire [-14.1 points; p < 0.001])**, **NYHA Functional Class (34% more patients improved by >=1 class)**, and a **25 percent reduction in NT-proBNP (p = 0.004)**, with a **97 percent freedom from major adverse neurological and cardiovascular system/procedure-related events (MANCE)**.
- **Long-Term Morbidity and Mortality Phase (*Eur J Heart Fail* 2024):** Over median 3.6-year follow-up (n = 323), the primary composite endpoint of **Cardiovascular Mortality and Heart Failure Morbidity** did not reach statistical significance (Rate Ratio 0.94; p = 0.82); however, BAT demonstrated sustained 24-month functional/QoL durability, and post hoc analyses suggested fewer deaths, LVAD implants or transplants (hypothesis-generating only).
- **Current Guideline Status (ESC 2021 HF & AHA/ACC/HFSA 2022 HF Guidelines):**
  - **FDA Approved (2019; Expanded Label 2023/2024):** Approved for improving symptoms, functional capacity, and quality of life in patients with **NYHA Class III (or Class II with recent III), LVEF <=35%, NT-proBNP <1,600 pg/mL, and no Class I indication for CRT**.
  - **Guideline Stance:** BAT has **no formal class recommendation** in the **2021 ESC or 2022 AHA/ACC/HFSA Heart Failure Guidelines**; it is regarded as an emerging device that improves exercise capacity and quality of life in CRT-ineligible HFrEF without proven mortality benefit.

Clinical Domain	Device Generation & Trial	Key Efficacy & Safety Outcomes	Current Clinical & Regulatory Positioning
HFrEF Without CRT Indication (**LVEF <=35%, QRS <130 ms, NYHA III**)	**2nd-Gen Barostim Neo** (Unilateral single-button lead) — **BeAT-HF Trial** (2020 / 2024)	**+60 m in 6MWD**, **-14.1 pts in MLWHFQ**, **-25% in NT-proBNP**, **97% MANCE-free safety**; neutral long-term CV death/HF morbidity (rate ratio 0.94)	**FDA Approved** for symptomatic/functional improvement in **CRT-ineligible HFrEF** (**NT-proBNP <1,600 pg/mL**)
Resistant Hypertension	**1st-Gen Rheos** (Bilateral tripolar cuffs) — **Rheos Pivotal Trial** (2011) vs. **2nd-Gen Barostim Neo** Registries	**Rheos (2011)** missed acute 6-month responder & procedural nerve-safety endpoints (**25% procedural complications**); **2nd-Gen Barostim Neo** lowers SBP by **~25–30 mmHg** safely in registries	**Not recommended outside trials (ESC 2024)**; investigational in **ESH 2023**; positioned **behind percutaneous Renal Denervation (RDN)**

III CLINICAL EVIDENCE AND POSITIONING IN RESISTANT HYPERTENSION

- **First-Generation Failure (Rheos Pivotal Trial, *JACC* 2011):** Evaluated the bulky first-generation **Rheos** device (requiring **bilateral** neck dissections and circumferential tripolar cuffs wrapped around both carotid sinuses) in 265 patients with resistant hypertension. The trial **missed 2 of its 5 co-primary endpoints**—specifically **6-month acute BP responder rate** (54% vs. 46%; p = 0.97) and **30-day procedural safety** (only 74.8% complication-free due to transient/permanent **facial/hypoglossal nerve injury** during bilateral carotid dissection)—though 12-month sustained SBP reduction reached 26 to 35 mmHg.
- **Second-Generation Unilateral Barostim Neo (Wallbach et al. / Hoppe et al. Registries):** Redesigning the lead to a **unilateral 2-mm miniature disk** sutured only to the anterior carotid sinus without posterior carotid dissection reduced surgical time to <1 hour and raised procedural safety to **>95 percent**, maintaining an office SBP reduction of **25 to 30 mmHg** and 24-hour ambulatory SBP reduction of **8 to 13 mmHg** in open-label registries.
- **Current Guideline Positioning (2024 ESC / 2023 ESH Hypertension Guidelines):** Positioned **behind catheter-based Renal Denervation (RDN)** because BAT requires surgical neck incision, a permanent subcutaneous generator with periodic battery replacement (every 3 to 5 years), and lacks a sham-controlled randomized trial with the second-generation device (**Class III/not recommended for routine use in ESC 2024; investigational/salvage in ESH 2023**).

IV CONTRAINDICATIONS AND COMPLICATIONS

- **Anatomical and Clinical Contraindications:**
  - **Carotid Bifurcation Atherosclerosis (>50% Stenosis or Ulcerated Plaque at Implant Site):** Strictly contraindicated (mandatory pre-operative Carotid Duplex Ultrasound screening) due to the risk of **plaque embolization and perioperative ischemic stroke** during surgical exposure and suturing.
  - **Prior Radical Neck Surgery or Cervical Radiation Therapy** (scarred carotid sheath).
  - **Baroreflex Failure or Autonomic Neuropathy** (destroyed afferent/central reflex loop).
  - **Baseline NT-proBNP >= 1,600 pg/mL or INTERMACS 1–3 End-Stage Heart Failure:** In BeAT-HF, patients with severely elevated NT-proBNP (>1,600 pg/mL) had advanced structural pump failure that no longer responded to autonomic modulation alone.
  - **Complications:** Pocket hematoma or infection (~1–2%), perioperative cranial nerve injury (**hypoglossal nerve [CN XII], marginal mandibular branch of facial nerve [CN VII], or glossopharyngeal/vagus nerve** causing transient dysphagia, dysphonia, or tongue deviation—reduced from ~9% with first-gen Rheos to **<1 to 2 percent** with second-gen Barostim Neo), and stimulation-related neck paresthesia (resolved by reprogramming pulse width/amplitude).

KEY REFERENCES

- **Zile MR, Lindenfeld J, Weaver FA, et al. (BeAT-HF Investigators):** Baroreflex Activation Therapy in Patients With Heart Failure With Reduced Ejection Fraction, *Journal of the American College of Cardiology*, 2020.
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- **McDonagh TA, Metra M, Adamo M, et al.:** 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, *European Heart Journal*, 2021.