CAROTID BARORECEPTOR STIMULATION (BAROREFLEX ACTIVATION THERAPY – BAT)

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Last reviewed: October 2026

I INTRODUCTION AND DEFINITION

- **Definition:** Baroreflex Activation Therapy (BAT) is a surgical device-based neuromodulation therapy (**Barostim Neo system**) that delivers continuous, programmable electrical stimulation to the mechanoreceptors of the carotid sinus.
- **Therapeutic Objective:** Directly restores autonomic **sympathovagal balance** by suppressing maladaptive central sympathetic overdrive and augmenting vagal (parasympathetic) activity—targeting the shared neurohormonal driver of **Heart Failure with Reduced Ejection Fraction (HFrEF)** and **Resistant Hypertension**.

II PATHOPHYSIOLOGY AND NEURAL MECHANISM OF ACTION

- **Afferent Neural Pathway:** A miniature 2-mm extravascular electrode is sutured onto the adventitia of the carotid sinus (typically unilaterally on the right side). Electrical impulses activate carotid sinus baroreceptor afferents, which transmit action potentials along the **Carotid Sinus Nerve of Hering** (a branch of the **Glossopharyngeal Nerve, CN IX**) to the **Nucleus Tractus Solitarius (NTS)** in the medulla oblongata.
- **Central Medullary Integration:** The NTS interprets this sustained afferent input as elevated arterial stretch/pressure, activating caudal ventrolateral medullary inhibitory interneurons that **suppress the Rostral Ventrolateral Medulla (RVLM — the sympathetic vasomotor center)** while **stimulating the Nucleus Ambiguus and Dorsal Motor Nucleus of the Vagus**.
- **Efferent Physiological Triad (Heart, Vasculature, Kidneys):**
  - **Cardiac Effects:** Restored parasympathetic vagal tone and reduced beta-1 sympathetic drive **lower resting heart rate**, reduce myocardial oxygen consumption, reverse beta-receptor downregulation, and **increase the ventricular fibrillation threshold**.
  - **Vascular Effects:** Sympathetic withdrawal induces **arterial vasodilation** (lowering **Systemic Vascular Resistance [SVR]** and LV afterload) and **splanchnic venodilation** (increasing venous capacitance and lowering cardiac filling pressures).
  - **Renal Effects:** Inhibits renal efferent sympathetic nerve activity to the **juxtaglomerular apparatus** and proximal tubules, **suppressing renin-angiotensin-aldosterone system (RAAS) activation** and promoting pressure-independent natriuresis.

III LANDMARK CLINICAL TRIALS AND CURRENT STATUS

A Heart Failure with Reduced Ejection Fraction (HFrEF) — The BeAT-HF Trial

- **Trial Design and Target Population:** Randomized 408 patients (264 in the expedited phase; 323 in the extended long-term phase) with **symptomatic HFrEF (LVEF <=35%)**, **NYHA Functional Class III** (or Class II with recent HF hospitalization), **NT-proBNP <1,600 pg/mL**, and **ineligibility for Cardiac Resynchronization Therapy (CRT; QRS <130 ms)** to **BAT + Optimal GDMT versus GDMT Alone**.
- **Primary Outcomes:**
  - **6-Month Functional and Biomarker Endpoints (*JACC* 2020):** Demonstrated highly significant improvements in **6-Minute Walk Distance (+60 meters; p < 0.001)**, **Quality of Life (MLWHFQ score -14.1 points; p < 0.001)**, and a **25 percent reduction in NT-proBNP (p = 0.004)**, with **97 percent freedom from MANCE complications**.
  - **Long-Term Post-Market Phase (*Eur J Heart Fail* 2024):** While the primary composite of CV death and HF morbidity was neutral (RR 0.94; p = 0.82), BAT maintained durable 24-month functional/QoL gains; post hoc analyses suggested fewer deaths, LVAD implants or transplants (hypothesis-generating only).
  - **FDA Regulatory Status: FDA-approved** for improving symptoms and functional status in patients with **LVEF <=35%, NYHA Class III (or II), NT-proBNP <1,600 pg/mL, and no Class I indication for CRT**.

B Resistant Hypertension — The Rheos Pivotal Trial and Barostim Neo Registries

- **First-Generation Rheos Pivotal Trial (*JACC* 2011):** Double-blind randomized trial (n = 265) of the first-generation bilateral device; met long-term 12-month efficacy (53% achieved SBP <=140 mmHg with a ~26 to 35 mmHg SBP drop), but **failed its co-primary 6-month acute responder endpoint and 30-day procedural nerve-safety endpoint** (due to cranial nerve injuries from bilateral circumferential carotid dissection).
- **Second-Generation Unilateral Barostim Neo:** Eliminates posterior carotid dissection and achieves a **>95% complication-free safety profile** with sustained **25 to 30 mmHg office SBP reductions** in European registries; however, due to the requirement for surgical generator implantation and lack of a new sham-controlled RCT, it remains an **investigational / last-resort therapy** behind **Renal Denervation (RDN)** in the **2024 ESC / 2023 ESH Hypertension Guidelines**.

Parameter	BAT in HFrEF (BeAT-HF Phenotype)	BAT in Resistant Hypertension
Eligibility Criteria	**LVEF <=35%, NYHA Class III, NT-proBNP <1,600 pg/mL**, and **NO CRT indication (QRS <130 ms)** despite optimal Quadruple GDMT	True drug-refractory hypertension (**>=4–5 drugs including Spironolactone**) failing or unsuitable for **Renal Denervation**
Primary Proven Benefit	**+60 m 6MWD, -14.1 pt MLWHFQ QoL, -25% NT-proBNP** (**BeAT-HF**, *JACC* 2020)	**-25 to -30 mmHg office SBP** & **-8 to -13 mmHg 24-h ABPM** in Barostim Neo registries
Guideline & FDA Status	**FDA Approved** for symptoms/QoL; **no formal class** in 2021 ESC / 2022 AHA-ACC HF Guidelines	**Not FDA approved for HTN** (humanitarian exemption only for prior Rheos responders); **Investigational in ESC 2024**

IV CLINICAL GUIDELINES, PATIENT SELECTION AND CONTRAINDICATIONS

- **Strict HFrEF Selection Checklist (The Four Criteria):**
  - **Left Ventricular Ejection Fraction <= 35 percent** on maximally tolerated Quadruple GDMT.
  - **Persistent NYHA Class III symptoms** (or Class II with recent Class III decompensation).
  - **Ineligible for Cardiac Resynchronization Therapy (CRT)**—specifically **QRS duration < 130 ms** (or non-LBBB <150 ms).
  - **Baseline NT-proBNP < 1,600 pg/mL** (identifying patients before irreversible end-stage pump failure).
  - **Contraindications:**
  - **Carotid Artery Stenosis (>50%) or Ulcerative/Calcific Plaque at the Carotid Bifurcation** (risk of perioperative embolic stroke during lead suturing).
  - **Prior Neck Surgery, Tracheostomy, or Cervical Radiation** obliterating the carotid anatomical plane.
  - **Bilateral Carotid Body Paragangliomas, Baroreflex Failure, or Severe Autonomic Neuropathy**.
  - **Symptomatic Bradyarrhythmias (Sick Sinus Syndrome or High-Grade AV Block)** unless protected by a permanent pacemaker.

KEY REFERENCES

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- **Heidenreich PA, Bozkurt B, Aguilar D, et al.:** 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure, *Circulation*, 2022.