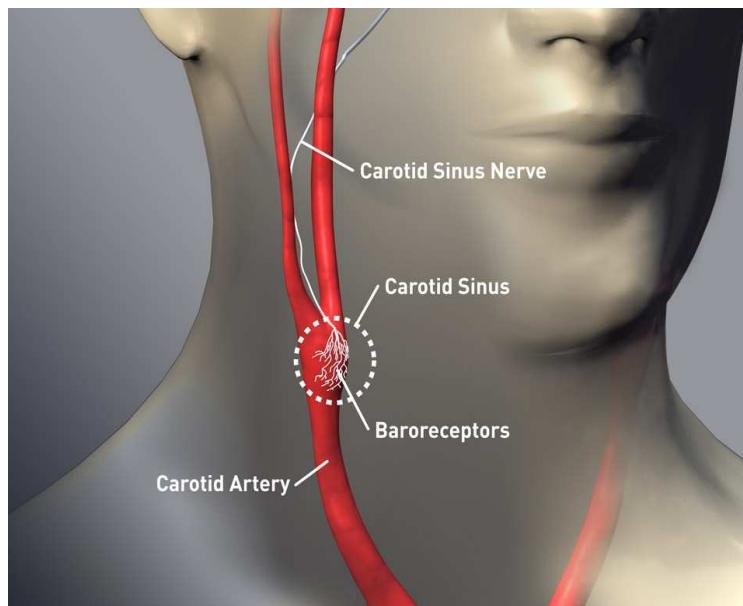


BAROREFLEX ACTIVATION THERAPY: UPDATE OF LONGTERM RESULTS



**37^{es} JHTA, Paris
BEL-NLD-CHE meeting**

Dec 14, 2017

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specialist**



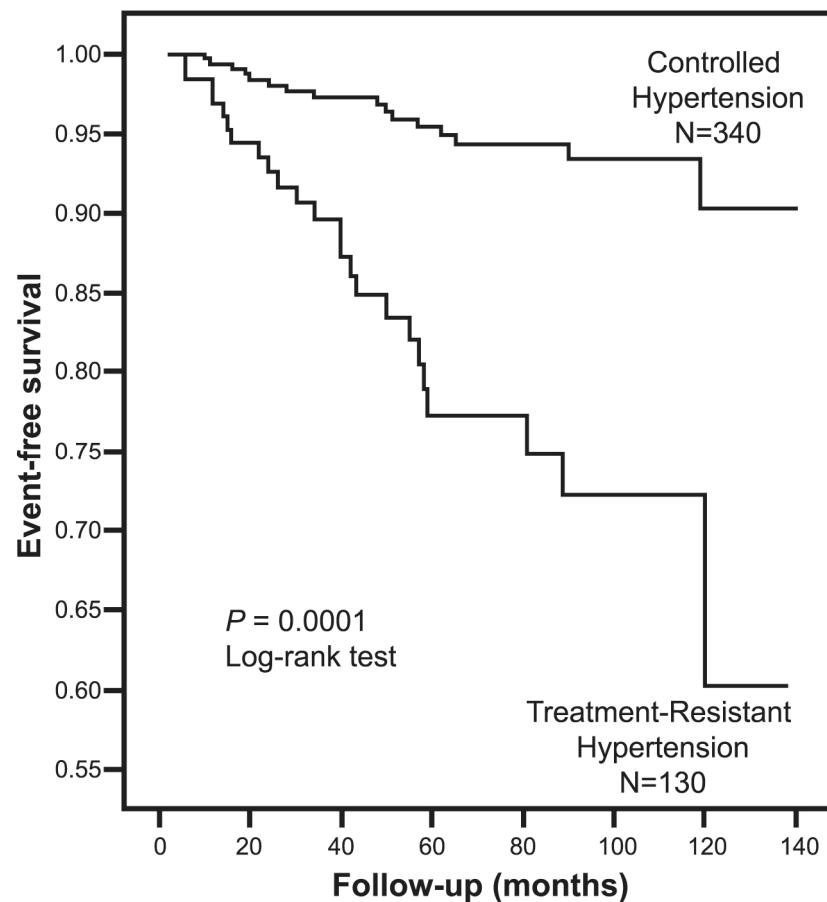
**Maastricht University Medical Center (MUMC+)
Cardiovascular Research Institute Maastricht (CARIM)**



Disclosures A.A. Kroon

- **Research grants:** CVRx, Vascular Dynamics, ReCor
- **Trials:** DEBuT-HT, Rheos-PIVOTAL, BAROSTIM Neo, CALM-studies (3), RADIANCE trials (2)
- **Registry:** BAROSTIM Neo
- **Consultant:** CVRx

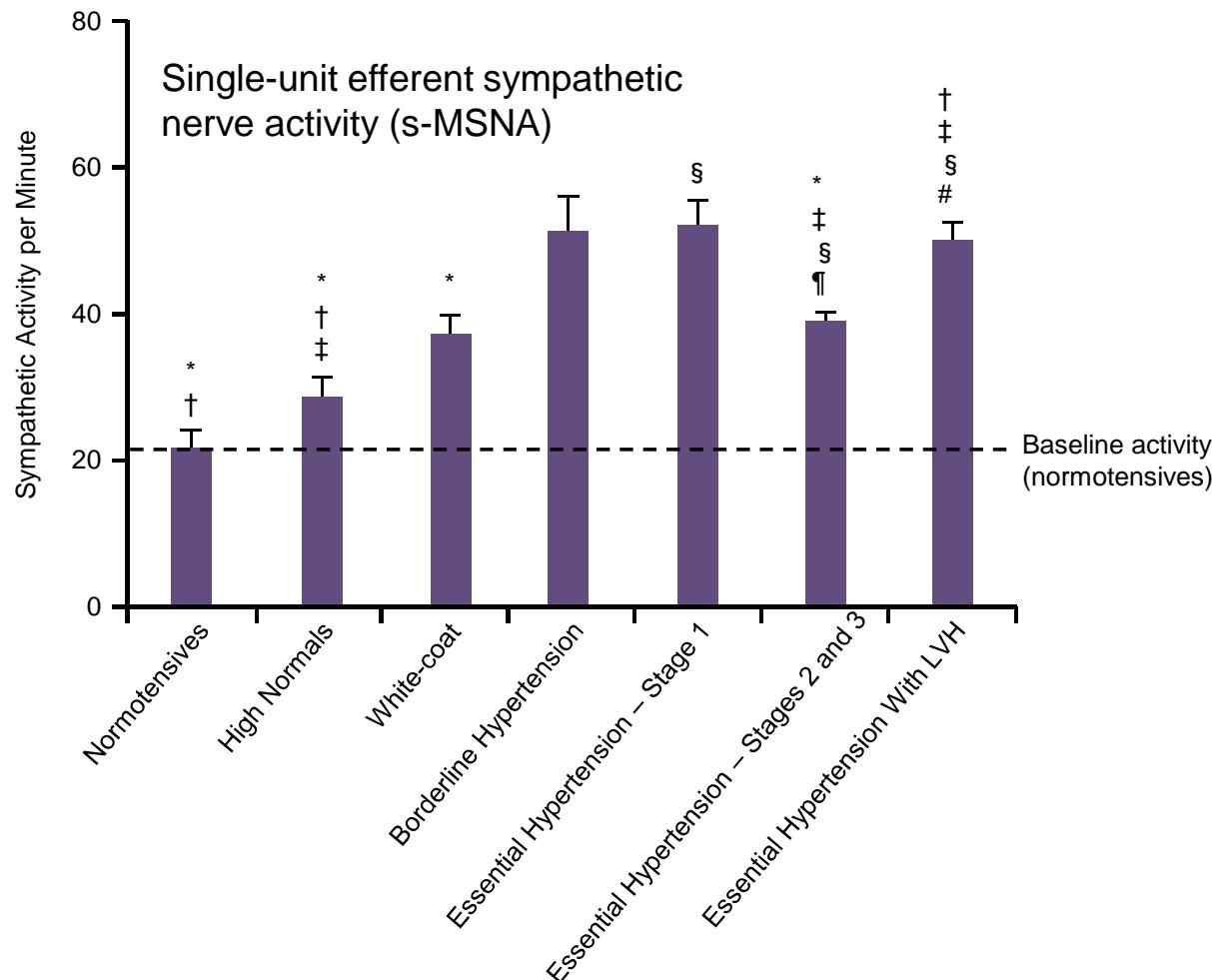
Treatment-resistant hypertension is associated with a substantially increased risk of CV events



CV Event Rate (5-year follow-up)	
Controlled Hypertension	5%
Treatment Resistant	19%

Differences between groups were apparent from very early in the follow-up period, indicating the urgent need for BP control in patients with treatment-resistant hypertension.

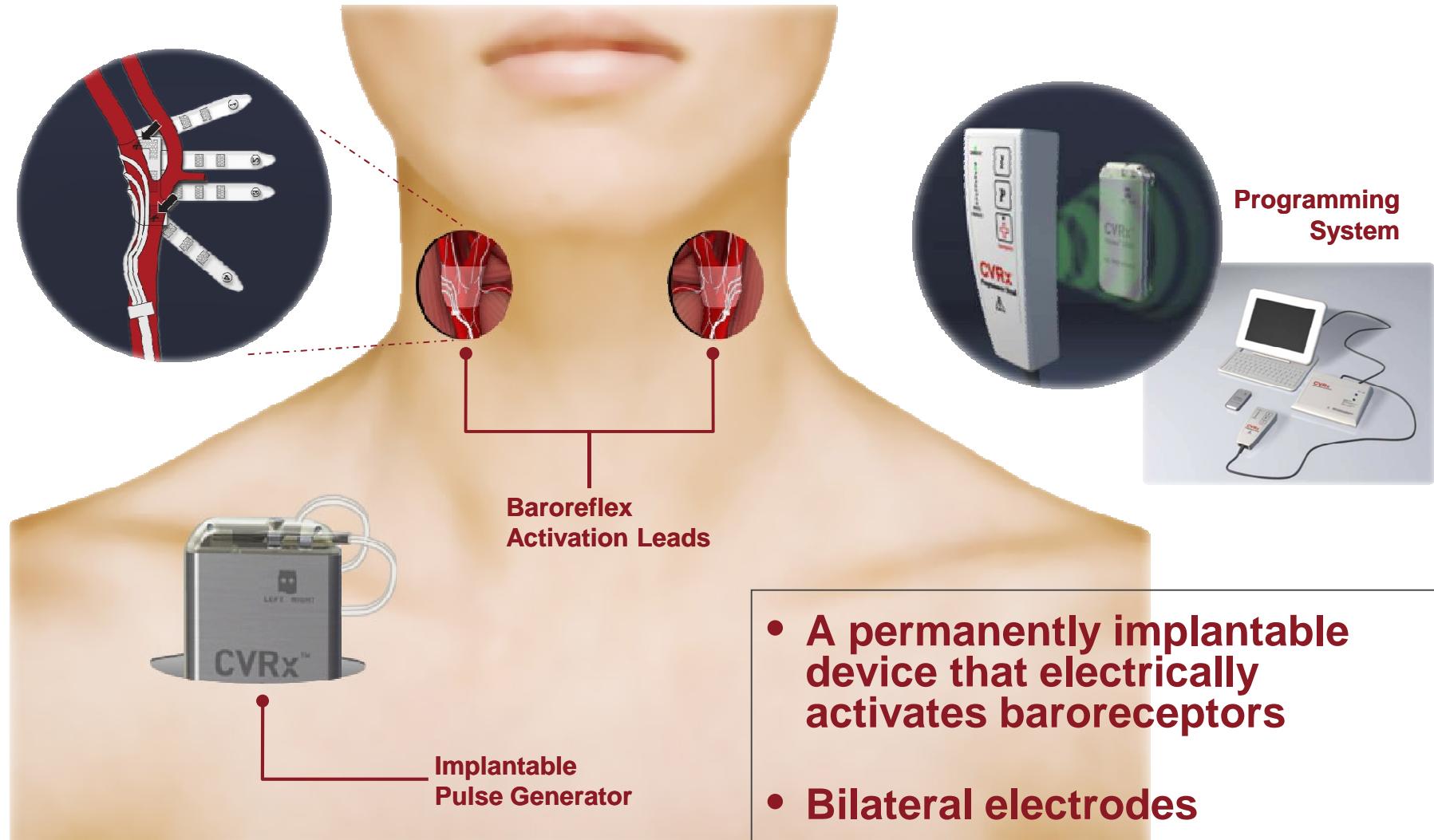
Sympathetic drive is elevated in multiple types of hypertension



* $P<0.05$ Compared with borderline hypertension. / † $P<0.05$ Compared with white-coat hypertension. / ‡ $P<0.05$ Compared with normal pressure.

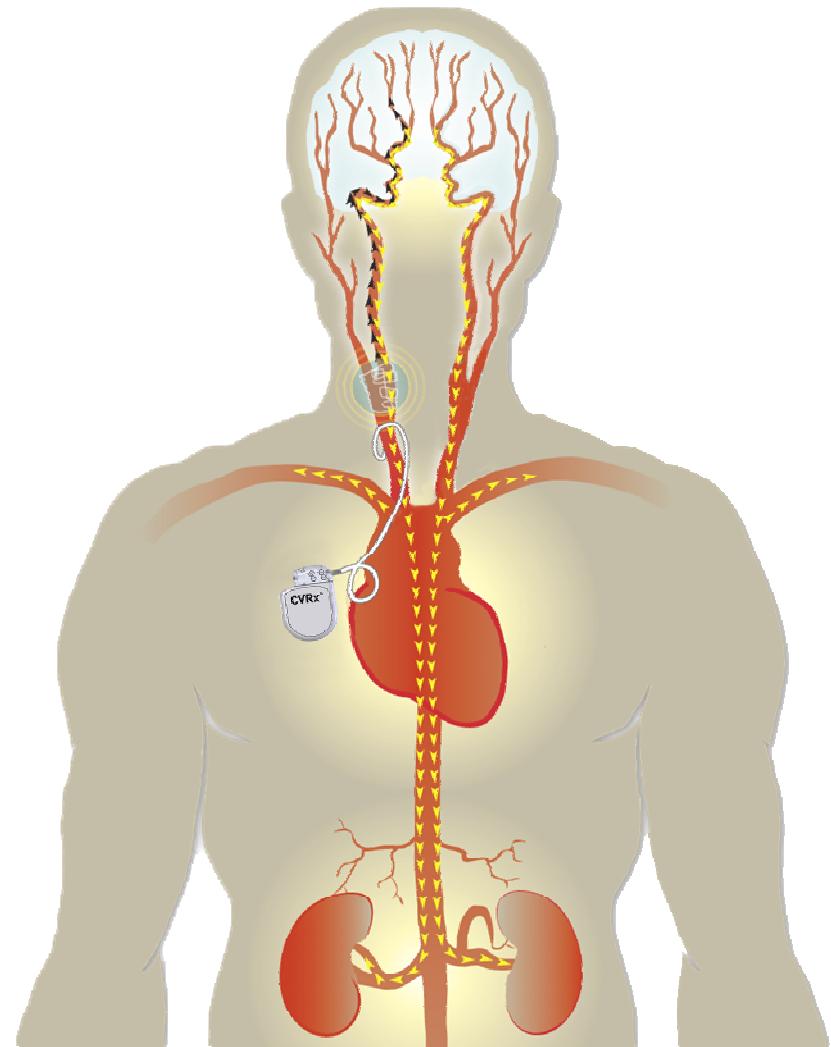
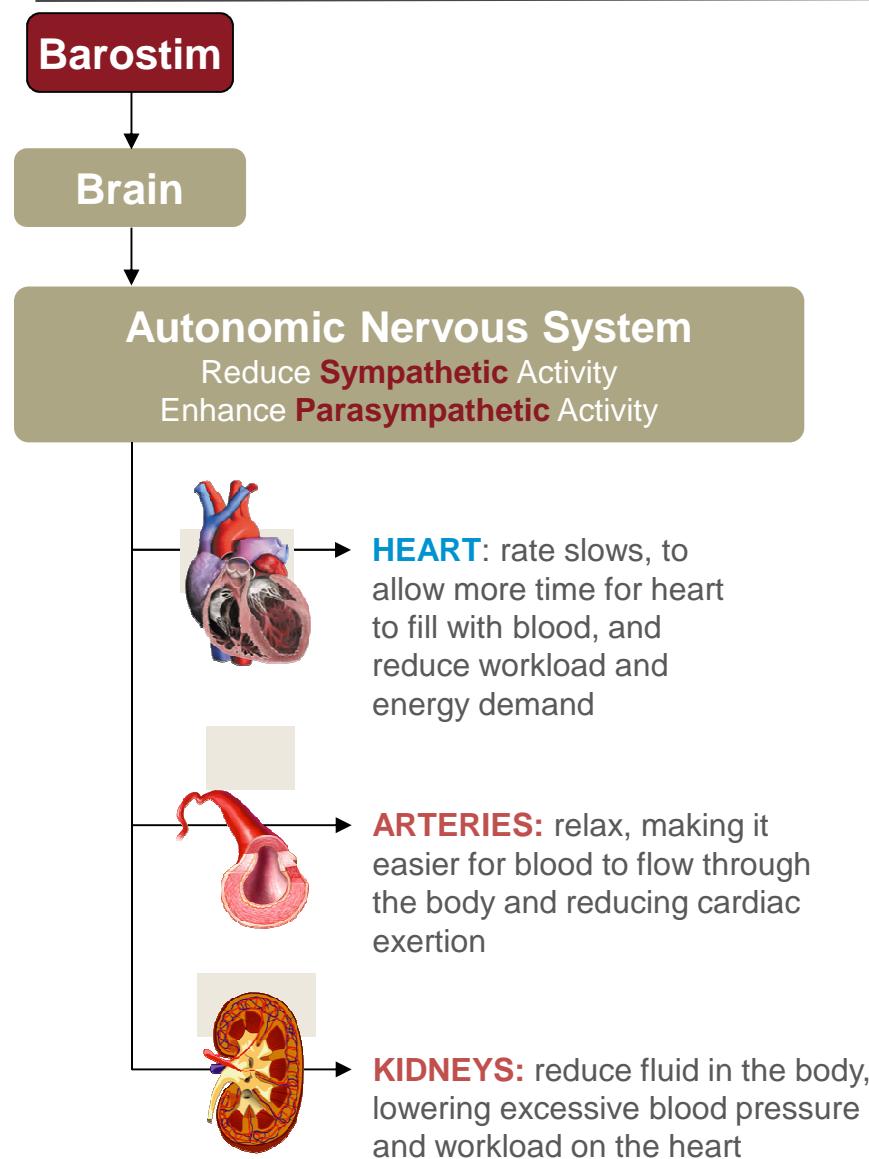
§ $P<0.05$ Compared with high-normal pressure. / ¶ $P<0.05$ Compared with essential hypertension–stage 1. / # $P<0.05$ Compared with essential hypertension–stages 2 and 3.

The CVRx® Rheos System: 1st generation device



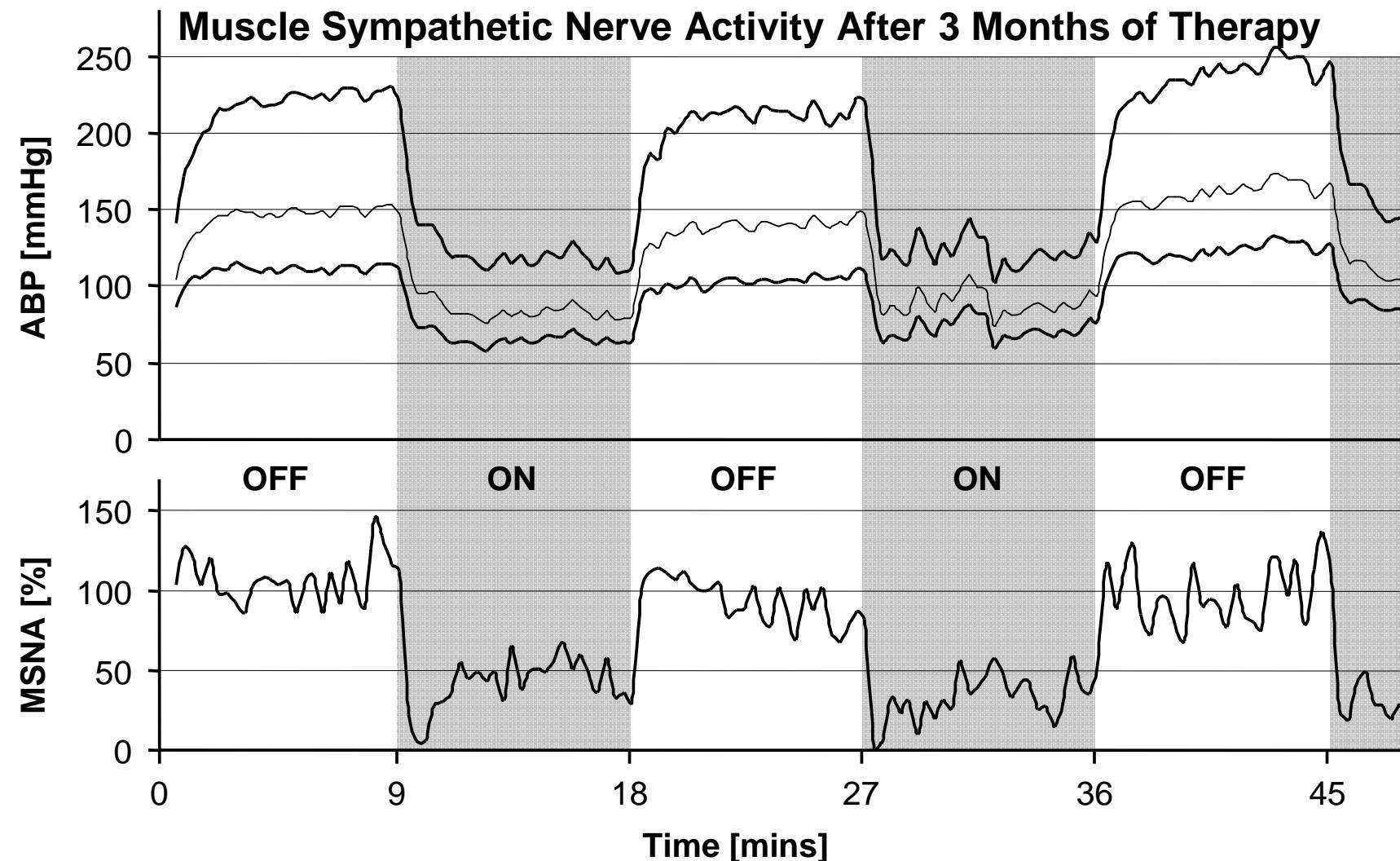
- A permanently implantable device that electrically activates baroreceptors
- Bilateral electrodes
- External programmer

Baroreflex activation therapy (BAT)



Inhibition of Sympathetic Activity – acute effects

Heusser et al., J Hypertens 2009;27(suppl):S288



Indications & Ideal Patient Profiles for BAROSTIM THERAPY

Indications

Resistant hypertension (rHTN)

- SBP > 140/90 mmHg + 3(4) antihypertensive drugs

Heart failure (HF)

- NYHA Class III, LVEF ≤ 35%
- Premium effect in patients not indicated for CRT

Examples of Ideal Patient Types

rHTN & HF

Classical treatment-resistant hypertension (TRH)

QRS < 130 ms

Post-renal nerve ablation

Chronic kidney disease

Non-LBBB and QRS 130-149 ms

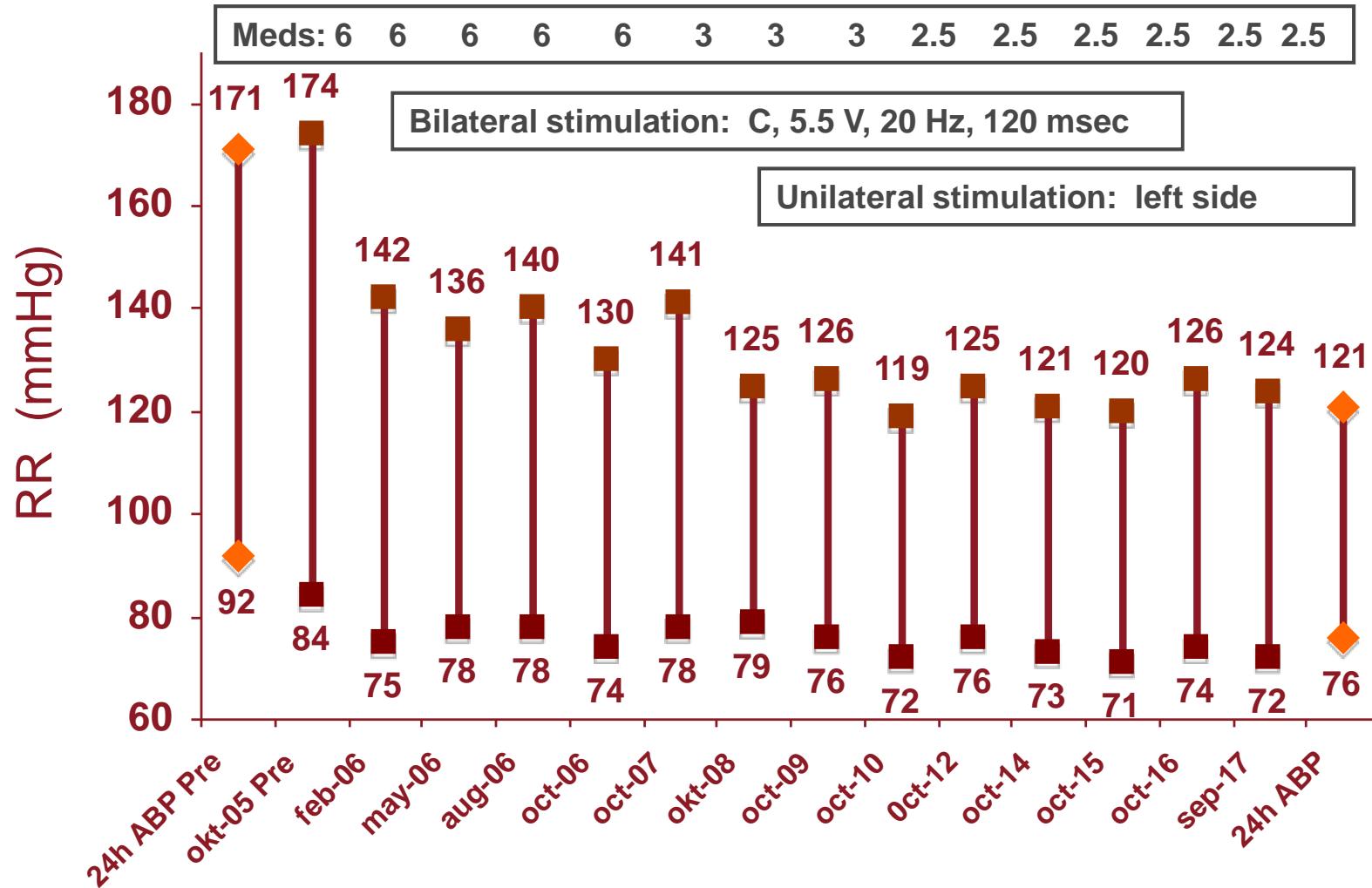
Cardiorenal syndrome

- **Medical history:**

- 1985: Hypertension
- 1993: Ischemic stroke (start antihypertensive medication)
- 2003: Acute MI, recurrent (minor) stroke
- 2005: Referral Maastricht UMC: resistant hypertension
 - An: headache, intermittent claudication (± 200 m); 6 antihypertensives
 - RF: smoking+ (>20 p.yrs), fam.+ (Htn), abdominal obesity (BMI 29)
 - OBP 190/105 mmHg, HR 72/min; ABP 189/100 mmHg, HR 68/min
 - TOD: kreatinine 104 μ mol (eGFR $_{[\text{MDRD}]}$ 55 ml/min/1.73 m^2), microalbuminuria (150 mg/24 h)
 - ACC: OSAS (R/ C-PAP); aorto-iliac atherosclerosis (no renal artery stenosis)



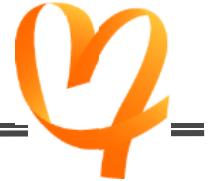
Female, 1953: BAROSTIM THERAPY (1ST generation device)



Office Blood Pressure

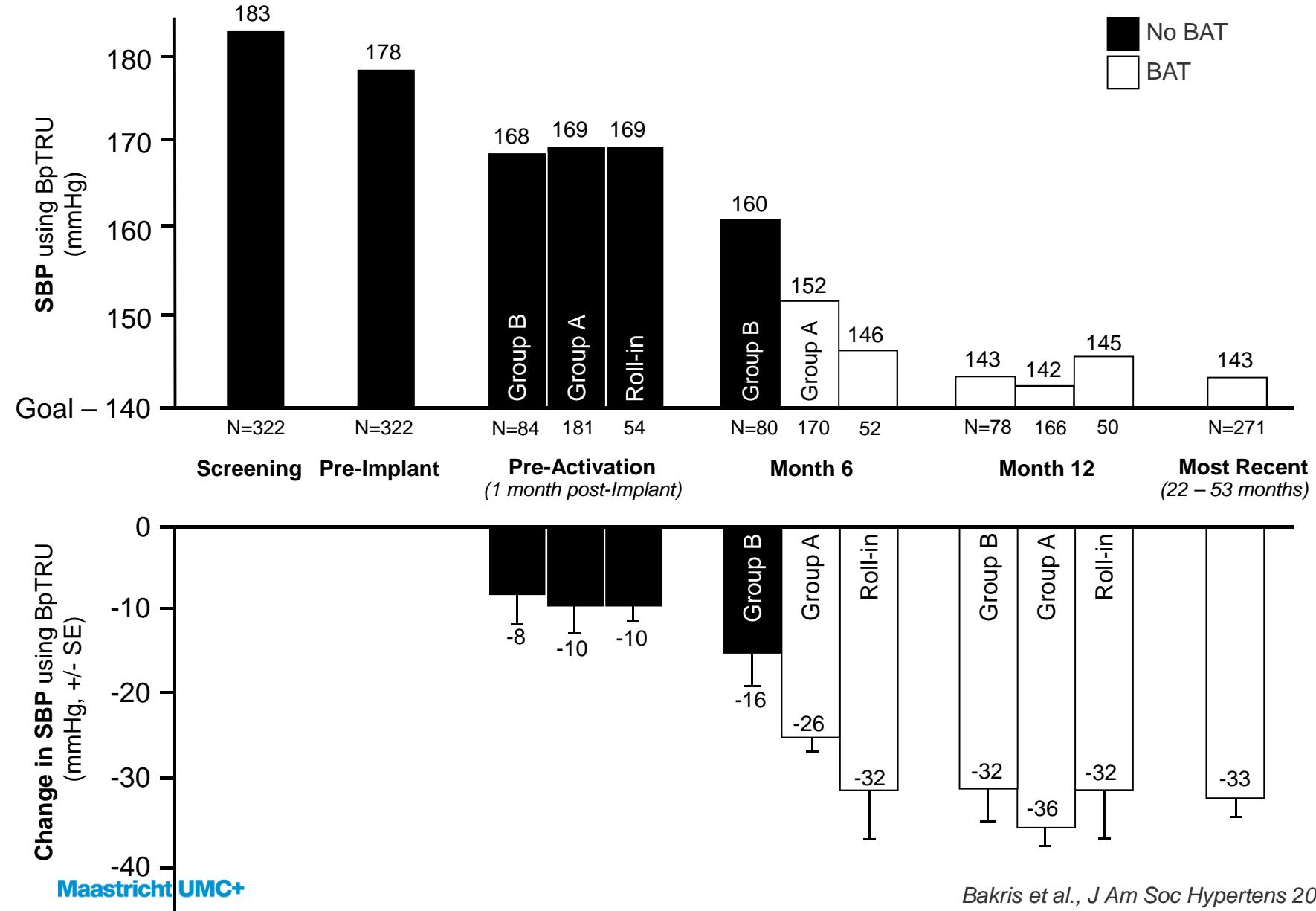


Female, 1953, long term follow up



- Lab-results (2005 → 2017)
 - Kreatinine: 104 uM → 98 uM
 - m-albuminurie: 150 → 23 mg/24u
 - LVH: 14/14 mm → 10/9 mm
- Number of battery replacements
 - 2007 (one-sided), 2010, 2013, 2016
- Medication
 - olmesartan 40 mg, amlodipine 10 mg, HCTZ 12.5 mg
- Risk factors
 - stopped smoking (2009)

RCT: Rheos Pivotal Study

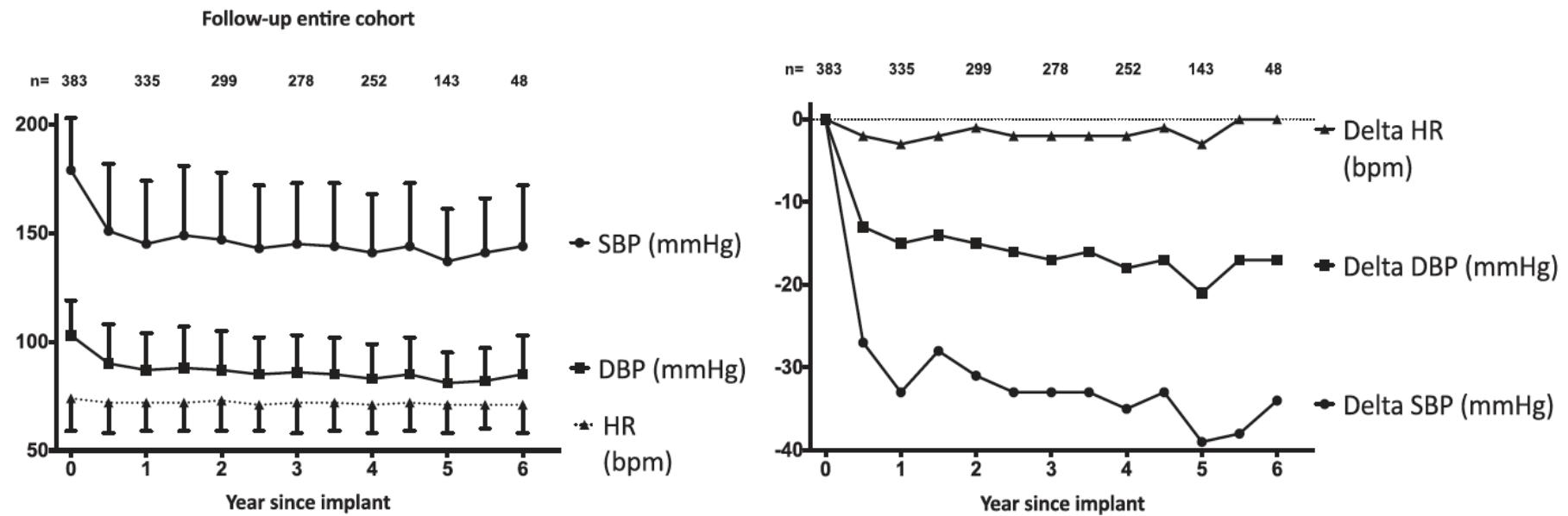


Sustained Reduction of Blood Pressure With Baroreceptor Activation Therapy

Results of the 6-Year Open Follow-Up

Peter W. de Leeuw, John D. Bisognano, George L. Bakris, Mitra K. Nadim, Hermann Haller, Abraham A. Kroon; on behalf of the DEBuT-HT and Rheos Trial Investigators

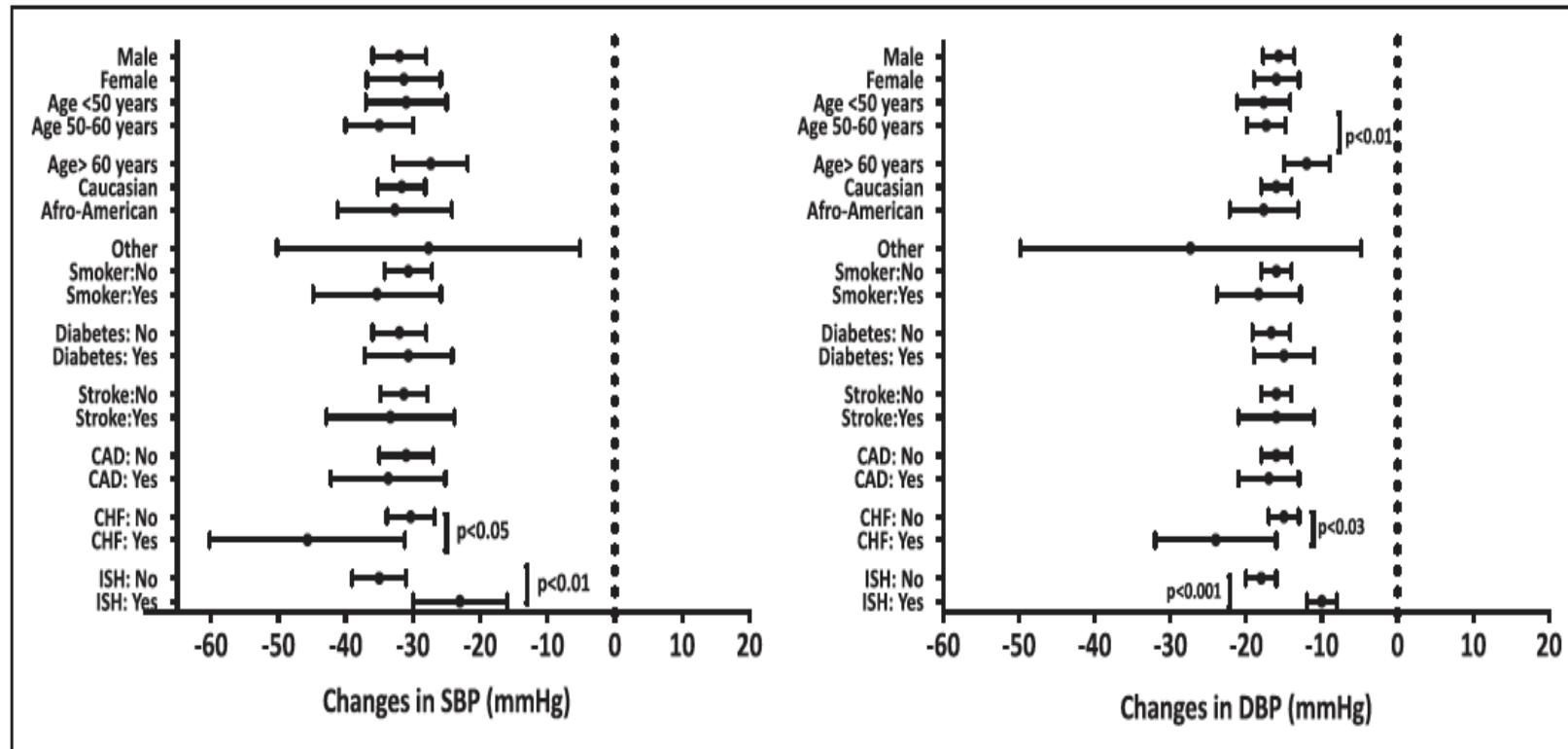
Rheos system: US-Rheos (n=16), DEBuT-HT(n=45), Pivotal (n=322)



Baseline BP: 179/103 mmHg, HR 74 bpm
6-yrs f.u. BP: 144/ 85 mmHg, HR 71 bpm

Pts with BP < 140/90 mmHg: 161 (42%)
Non-responders ($\Delta < 10$ mmHg): 26 (7%)

Longterm follow up Rheos system: subgroup analysis



Overall mean Δ BP 32/16 mmHg
 + HF(pEF): Δ BP 46/24 mmHg
 - ISH: Δ BP 23/8 mmHg

Medication use:

- mean n of meds 5
- 109 (27%) reduction, 139 (34%) no change, 149(39%) increase

Original Article

OPEN

Cost-effectiveness of Barostim therapy for the treatment of resistant hypertension in European settings

Oleg Borisenko^a, Joachim Beige^b, Eric G. Lovett^c, Uta C. Hoppe^d, and Staffan Bjessmo^e

- *Additional life-years gained = +1.66 vs. optimal medical therapy*
- *Additional Quality-Adjusted Life-years gained = +2.17 vs. optimal medical therapy*
- *Cost per QALY gained: EUR 7,797 vs. standard threshold of EUR 35,000 per QALY*
- *Deemed cost effective relative to optimal medical therapy*

QALY Gain +2.17

Reduces rate of: By:

Myocardial Infarction 19%

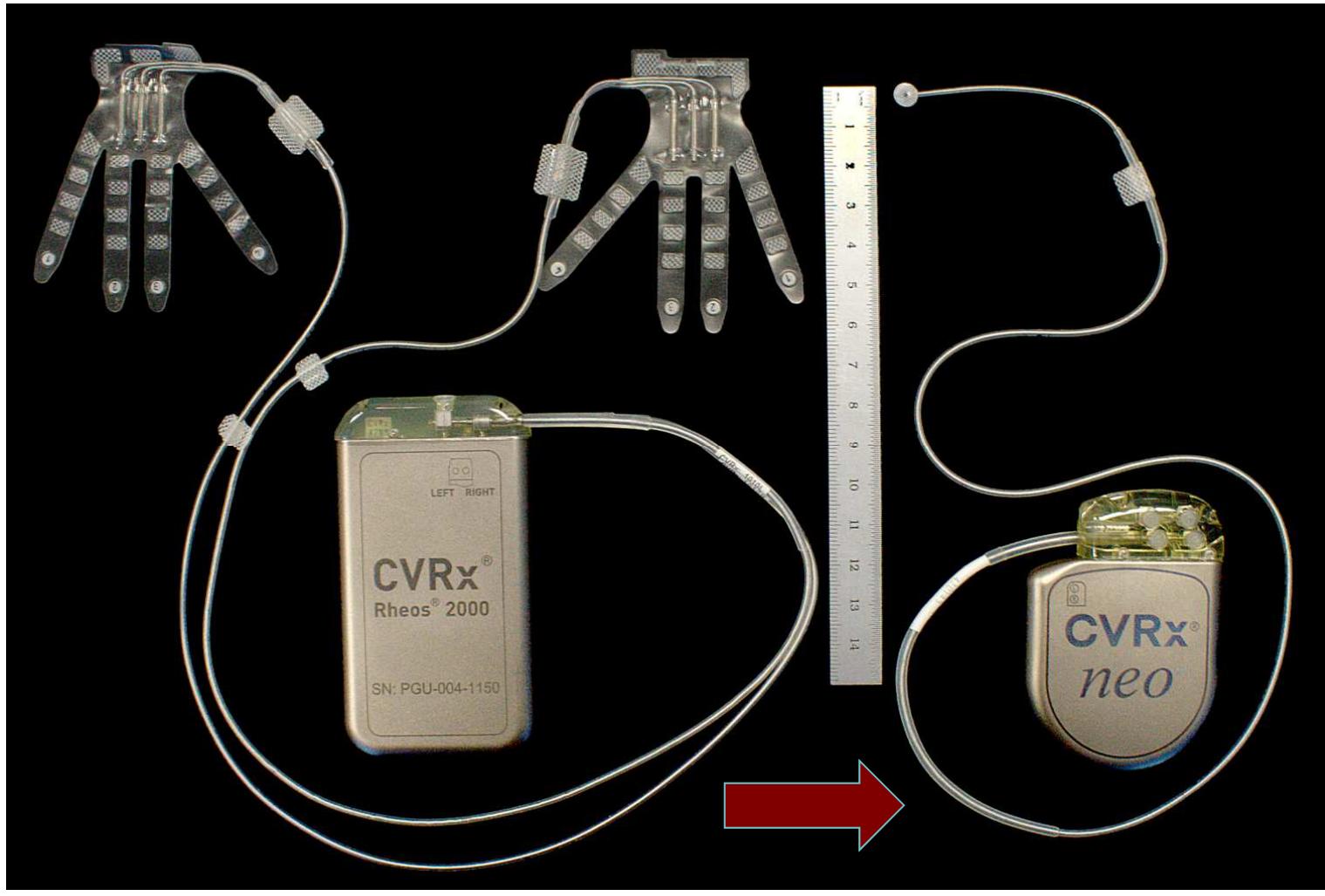
Stroke 35%

Heart Failure 12%

End Stage Renal Disease 23%

Barostim is a Cost-Effective Therapeutic Option Over the Long-Term compared to optimal medical therapy

Evolution of BAROSTIM THERAPY Delivery System



1st generation

RHEOS (obsolete)

2nd generation

BAROSTIM NEO™

First and second generation device

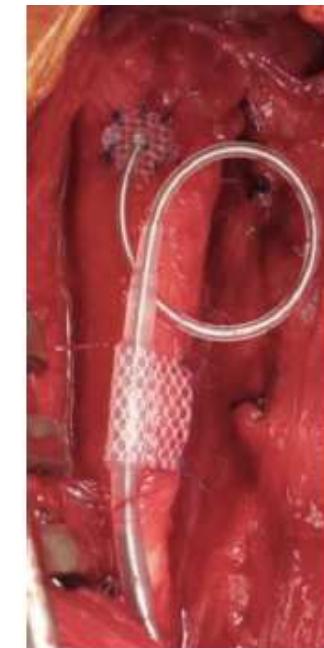
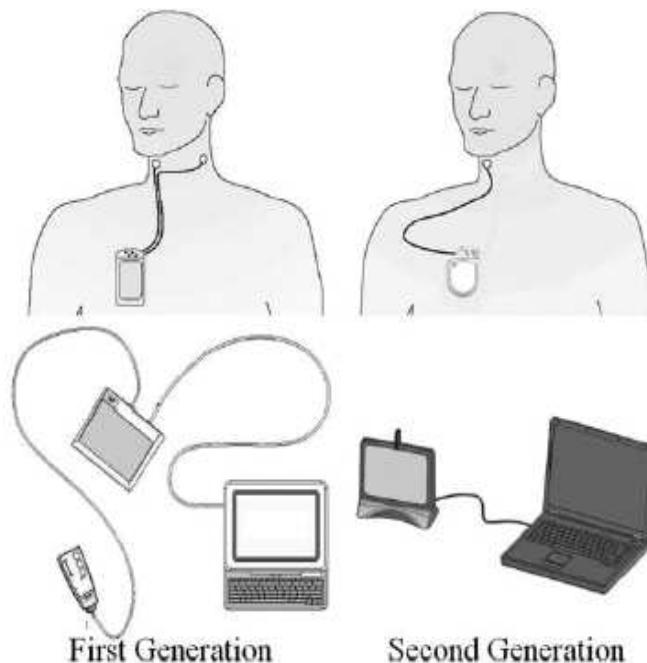
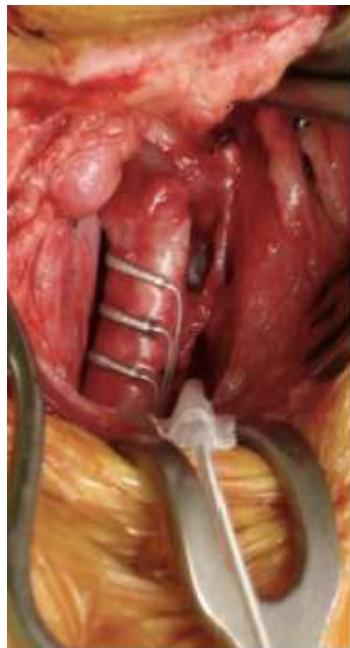
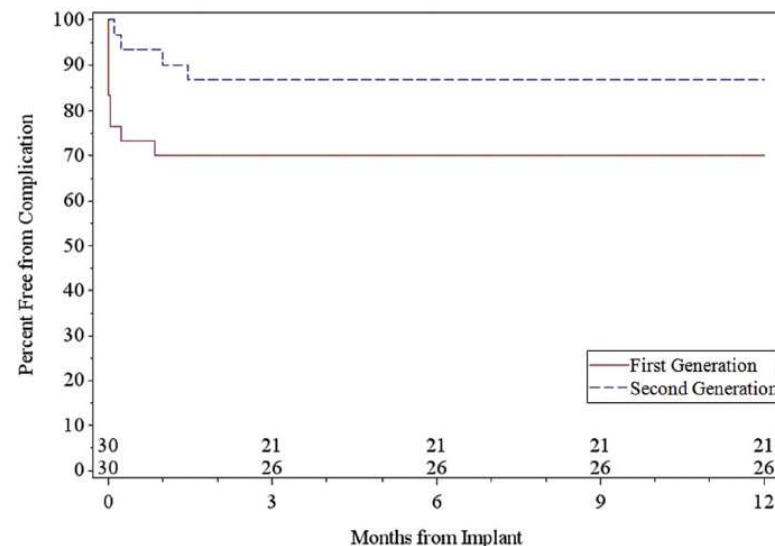
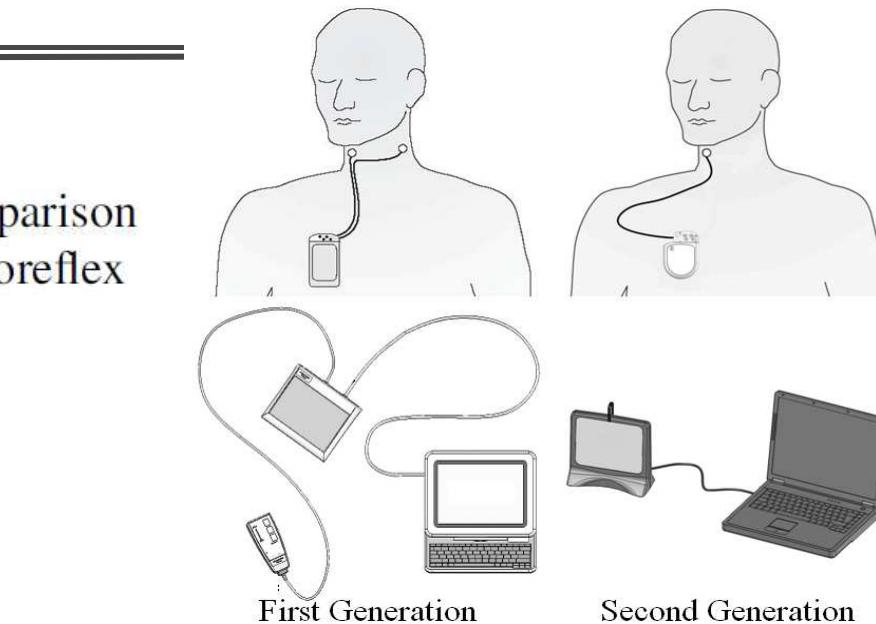
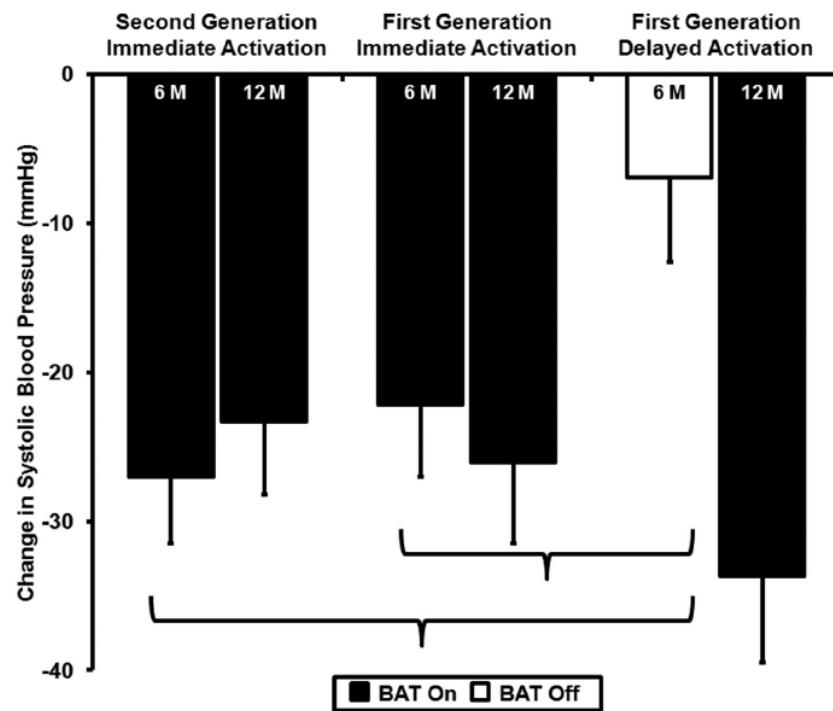


Figure 1. Schematic illustration of the first- (Rhoes, left) and second-generation (Barostim *neo*) BAT systems. The second-generation system is smaller, less invasive, more efficient, and more easily programmable than the first. BAT, baroreflex activation therapy.

Safety & Efficacy of 2nd Generation Device

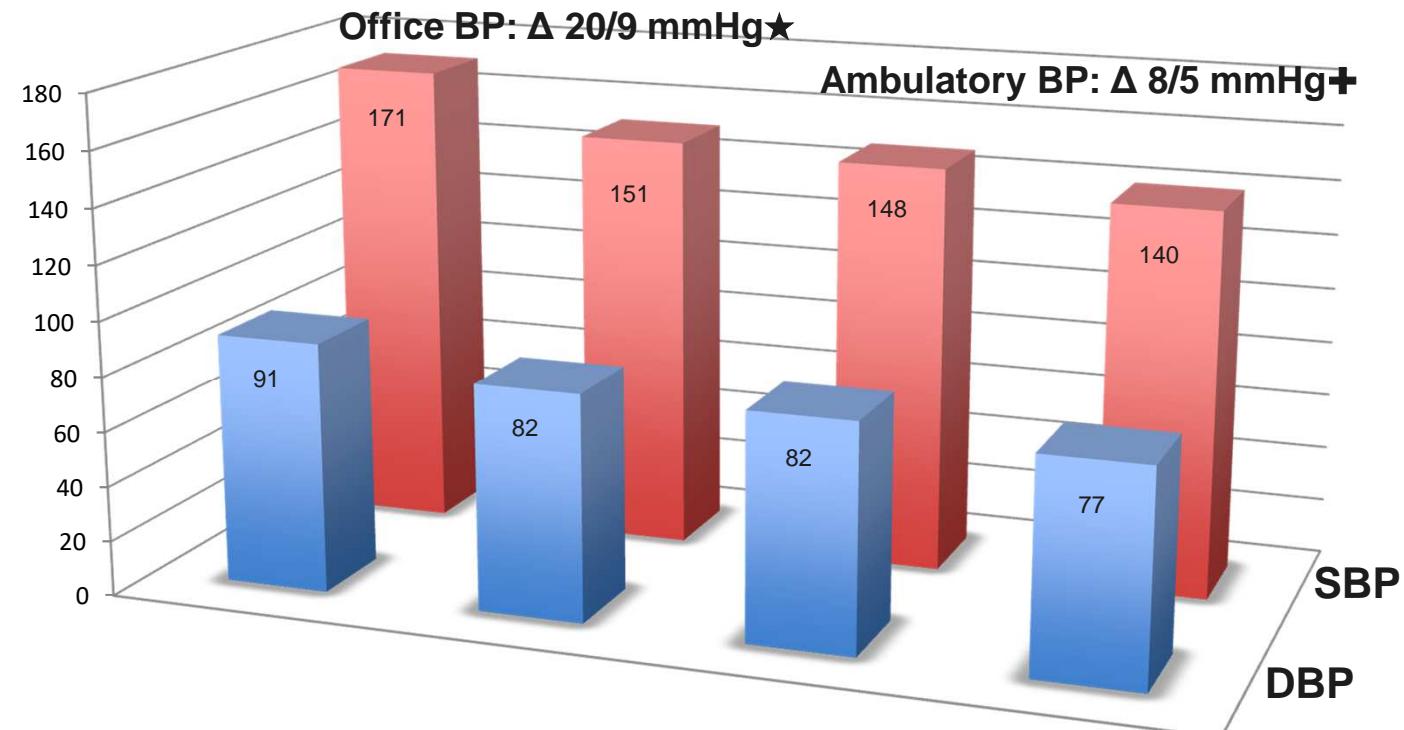
Research Article

An exploratory propensity score matched comparison of second-generation and first-generation baroreflex activation therapy systems



Effects of Baroreflex Activation Therapy on Ambulatory Blood Pressure in Patients With Resistant Hypertension

Manuel Wallbach, Luca-Yves Lehnig, Charlotte Schroer, Stephan Lüders, Enrico Böhning,
Gerhard A. Müller, Rolf Wachter, Michael J. Kozolek

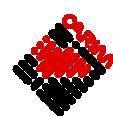


BAROSTIM neo: n=44, f.u. 6 months

- responders (Δ Ambulatory-SBP ≥ 5 mmHg): 55%
- Δ BP day time = Δ BP night time

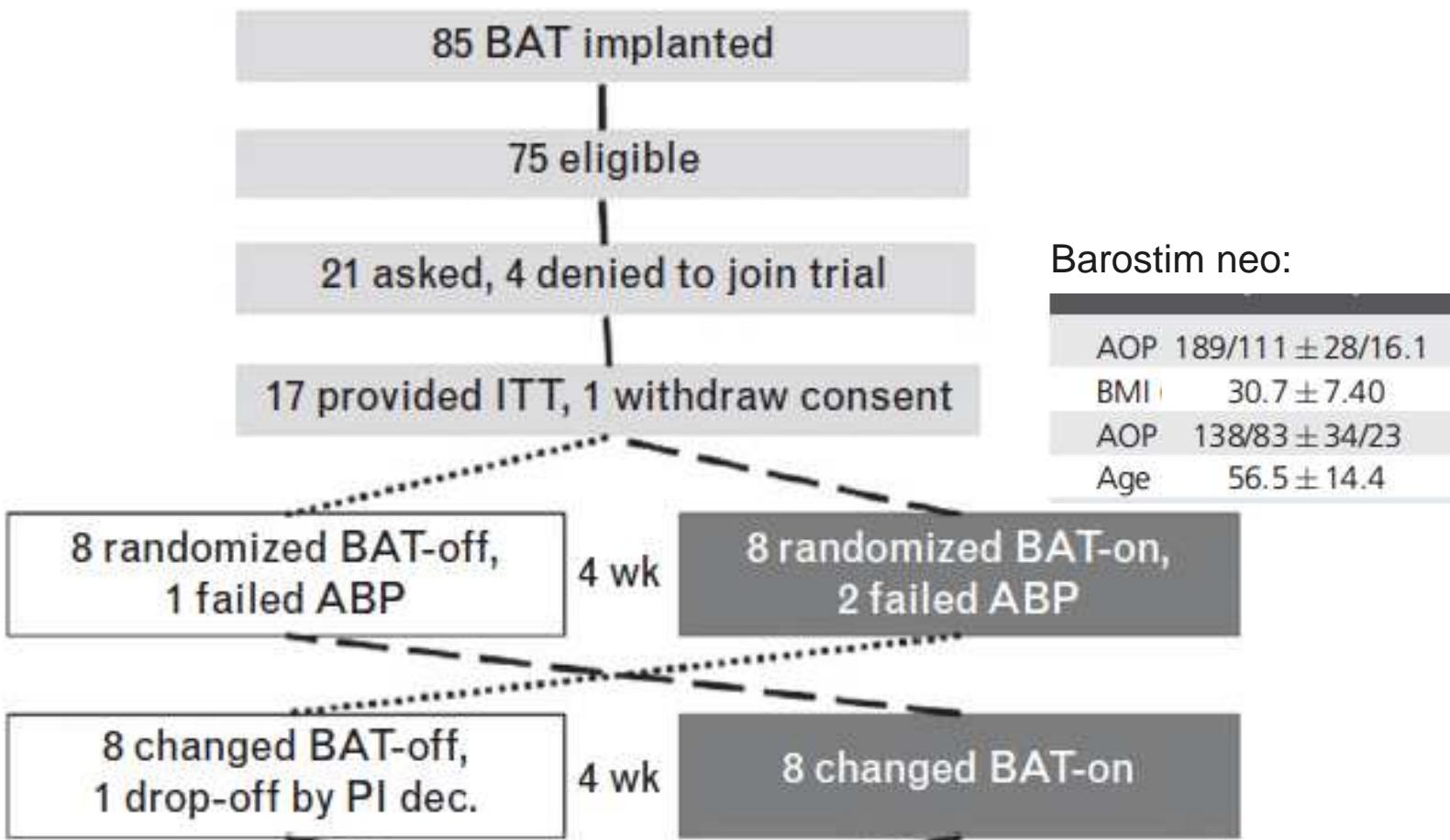
$\star p < 0.05$; $+ p < 0.01$

Hypertension. 2016;67:701-709

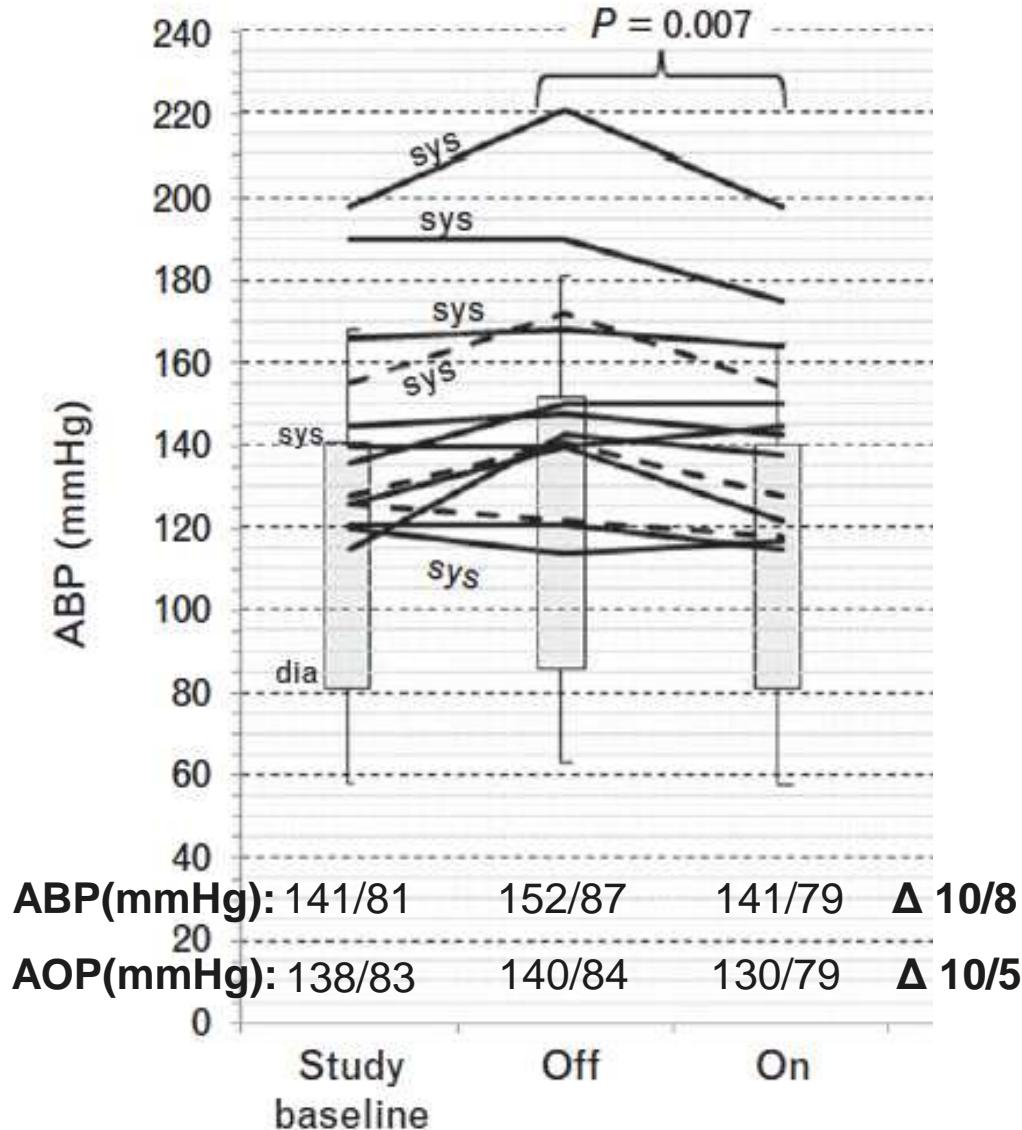


Blood pressure after blinded, randomized withdrawal, and resumption of baroreceptor-activating therapy

Joachim Beige^{a,*}, Theresa Jentzsch^{a,*}, Ralph Wendt^a, Gert Hennig^b, Michael Koziolek^c, and Manuel Wallbach^c



Blinded randomized withdrawal & resumption



- No change in medications
- Barostim treatment: 2.7 yrs
- No large increase in SBP during BAT-off: n=3 > 10 mmHg
- BP does not return to pre-implant
- Randomized significant decrease in BP using Barostim neo
- ? structural or humoral changes due to long term BAT.

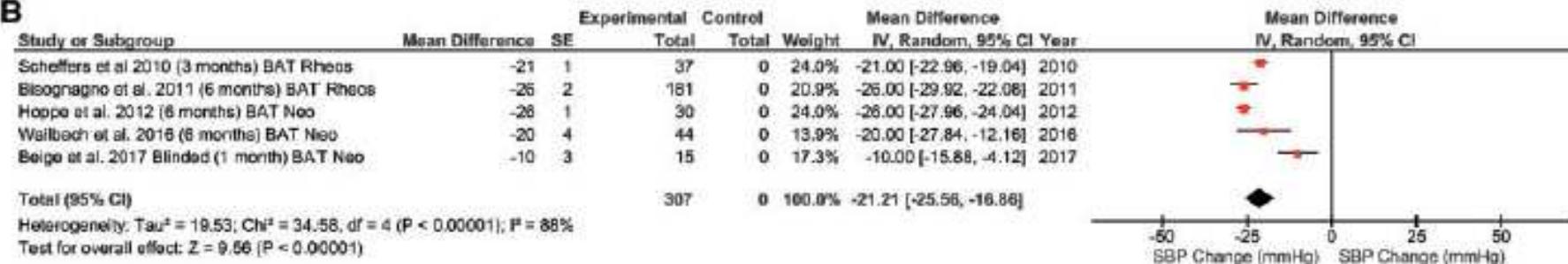
Baroreceptors in the carotid and hypertension—systematic review and meta-analysis of the effects of baroreflex activation therapy on blood pressure

Nephrol Dial Transplant (2017) 1–9
doi: 10.1093/ndt/gfx279

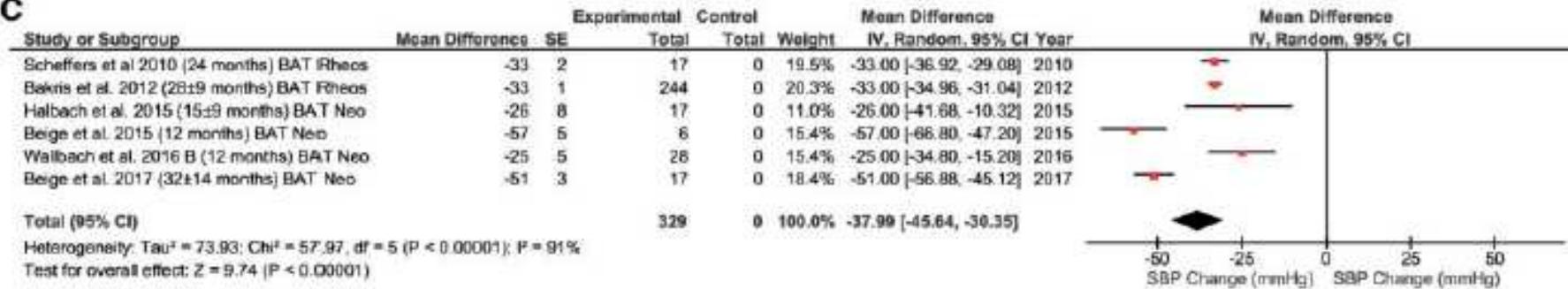
Manuel Wallbach and Michael J. Koziolek

Department of Nephrology and Rheumatology, University Medical Center Göttingen, Göttingen, Germany

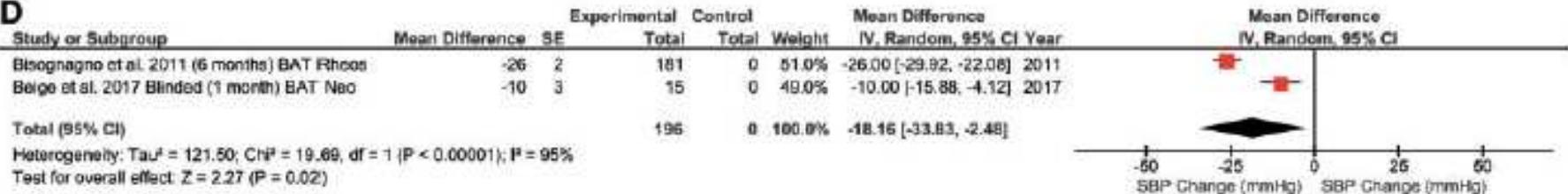
B



C



D



**The effects of baroreflex activation therapy
on blood pressure and sympathetic function
in patients with refractory hypertension: the
rationale and design of the Nordic BAT study***

n=100 pts
fu 16 mos
n=6 centers

ESTIM-rHTN has been granted by the French Ministry of Health & is sponsored by Nancy University Hospital, France

ESTIM-rHTN:
medicoEconomic evaluation of baroreceptor STIMulation
for the treatment of resistant HyperTensioN

A multicenter, randomized, PROBE design trial of baroreceptor stimulation with BAROSTIM NEO™ vs. usual care

n=128 pts
fu: 12 mos
n=16 centers

ClinicalTrials.gov Identifier:
NCT02364310

P. Rossignol, PI
M. Azizi, co-PI

Patient Selection



- BAT should be considered in patients with **resistant hypertension**
 - office cuff BP > 160/90 mmHg
 - after lifestyle modification and
 - at least **3 antihypertensive drugs** (incl. diuretics)
 - initiation of MRA treatment (**i.e. spironolacton**) prior to BAT evaluation
- **End organ damage**
 - BAT in heart failure: symptomatic improvement
 - BAT in renal failure: potentially nephroprotective
- **Exclusion**
 - pseudoresistance and/or secondary causes
 - carotid artery disease (> 50% stenosis)



Summary – baropacing



- BAT – sustained effect for 5-6 yrs
- Largest drop in BP is in the first 12 months
- \pm 50% of TRH patients reach SBP threshold <140 mmHg
- Efficacy of 2nd generation device is likely to be identical to 1st generation
- Barostim neo: significant ambulatory Δ BP \pm 10/5 mmHg
- Longterm treatment: may induce structural changes
- BAT may offer a new addition to treatment in HFrEF
- BAT is a cost-effective therapy in resistant hypertension in Europe



Baroreflex Activation Therapy in Resistant Hypertension



Internal Medicine

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B. Mees
J-W. Daemen

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