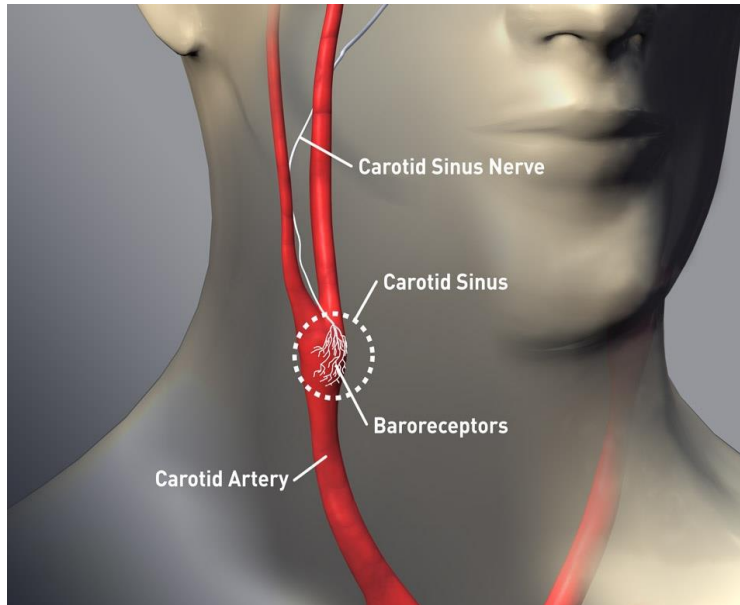


DEVICES HEBBEN ~~GEEN~~ PLAATS IN DE BEHANDELING VAN THERAPIE RESISTENTE HYPERTENSIE



Nationaal Hypertensie
Congres

Pro-Con debat

2 feb 2018

A.A. (Bram) Kroon

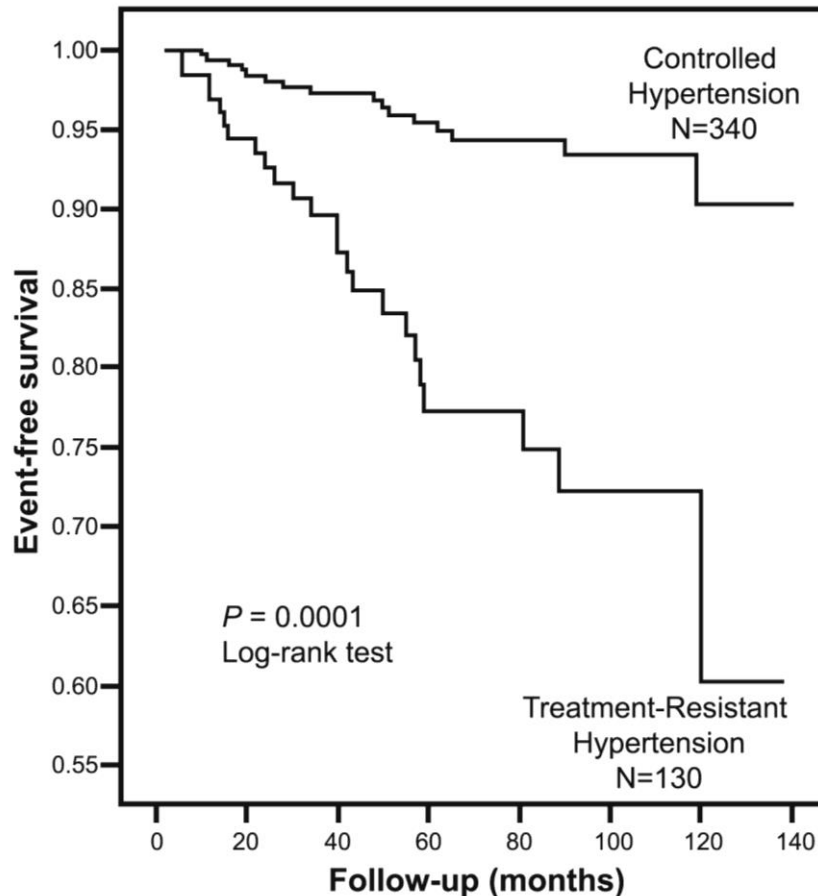
internist - vasculair geneeskundige



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



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

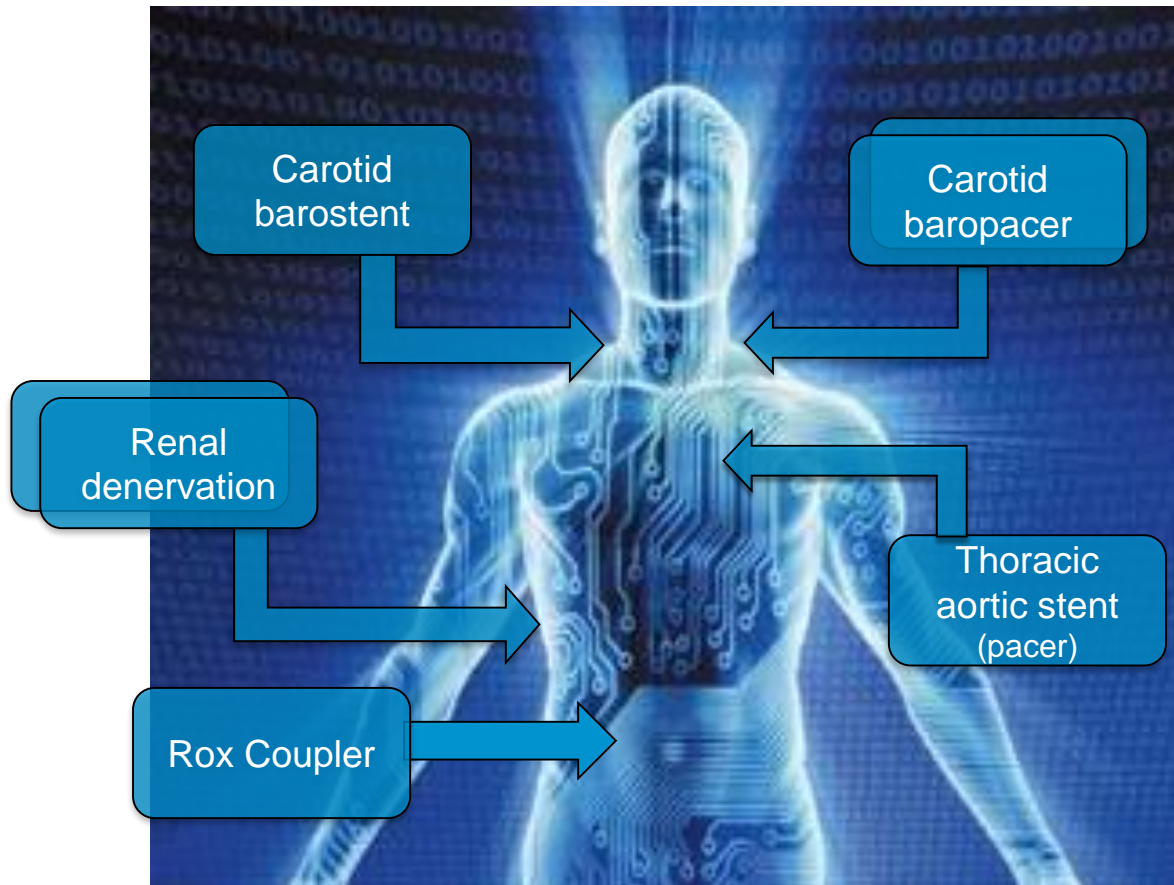


CV Event Rate (5-year follow-up)

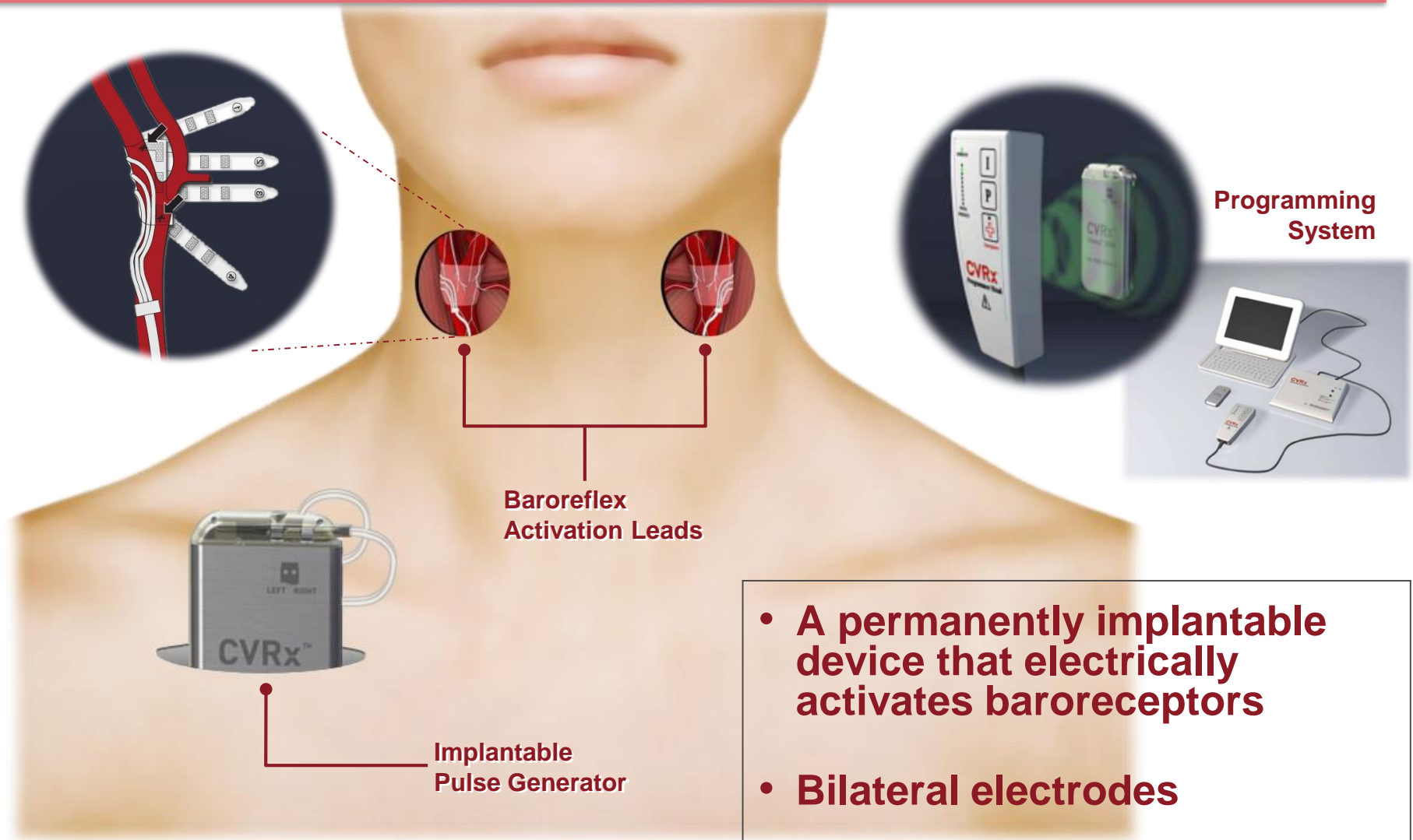
Controlled Hypertension	5%
Treatment Resistant	19%

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.

Different BP lowering devices



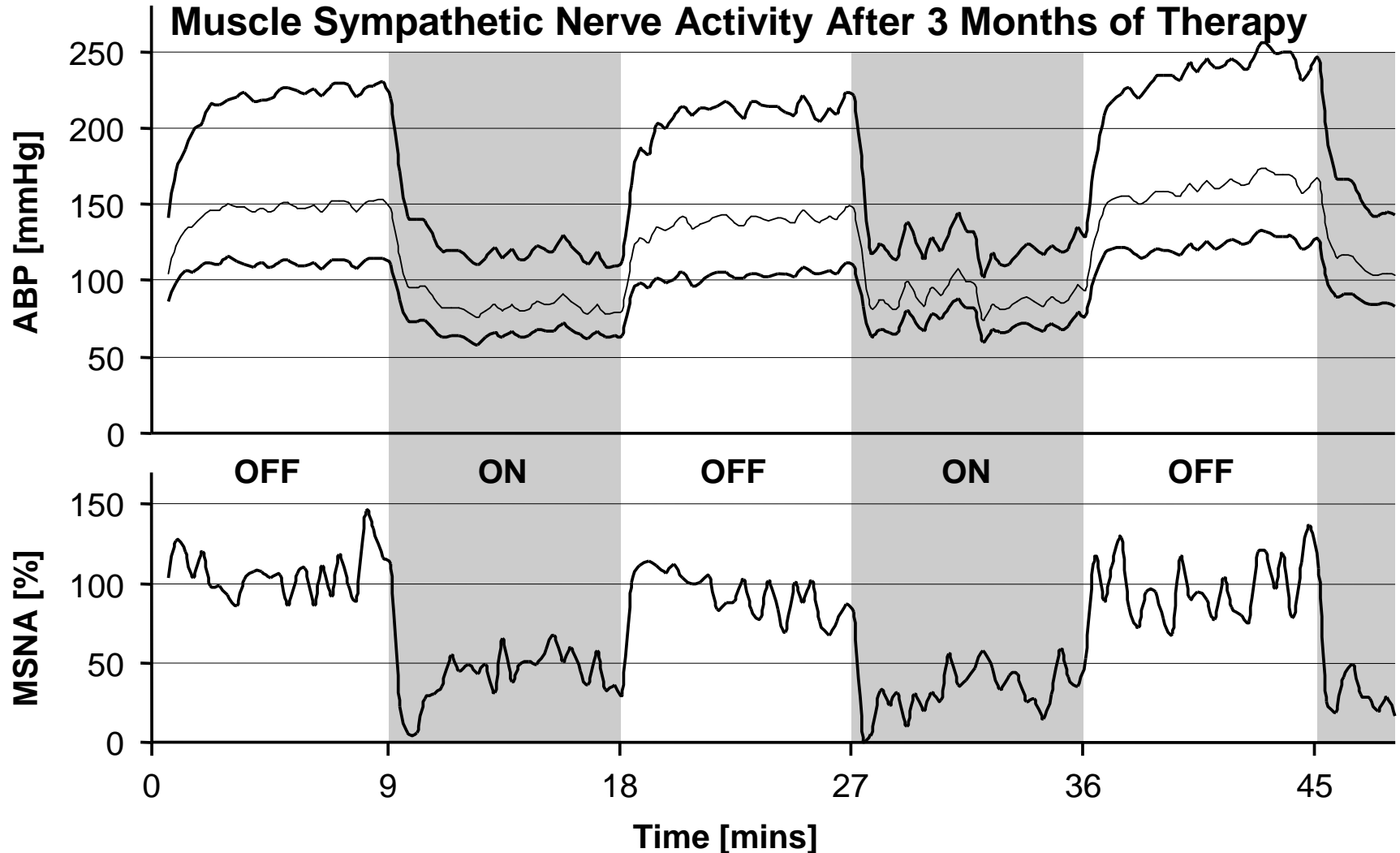
The CVRx[®] Rheos System: 1st generation device



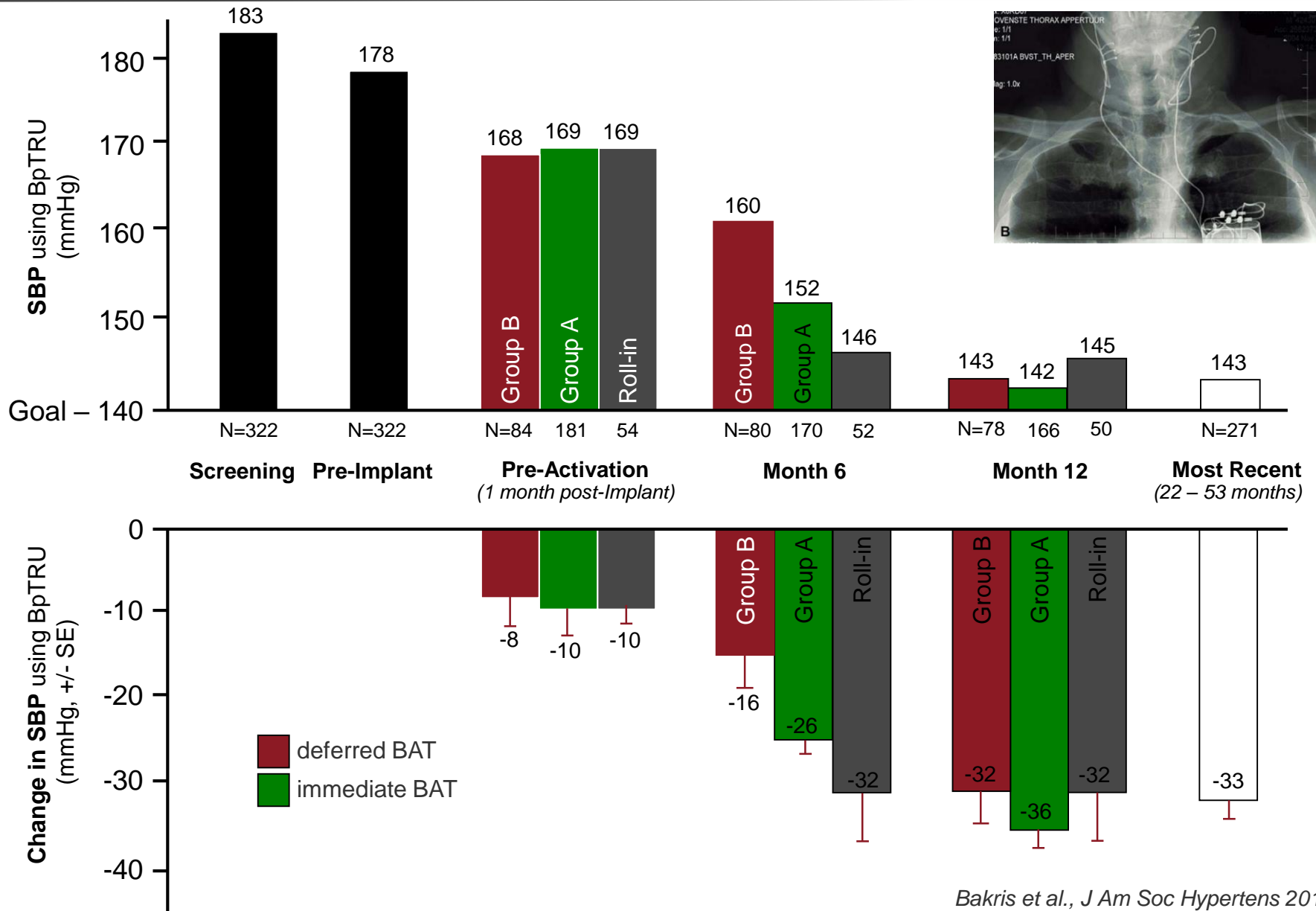
- A permanently implantable device that electrically activates baroreceptors
- Bilateral electrodes
- External programmer

Inhibition of Sympathetic Activity – acute effects

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



Rheos Pivotal Study (RCT, 1st generation)



Sustained Reduction of Blood Pressure With Baroreceptor Activation Therapy

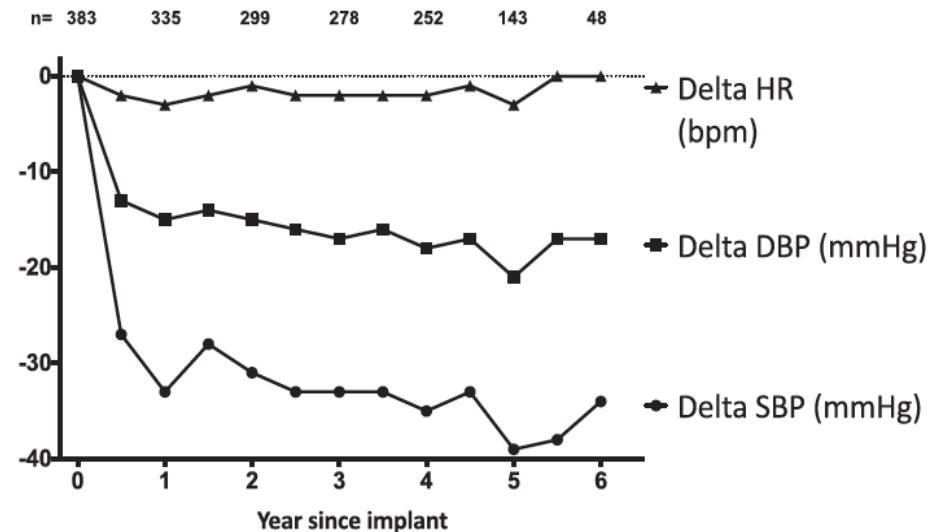
Results of the 6-Year Open Follow-Up

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)

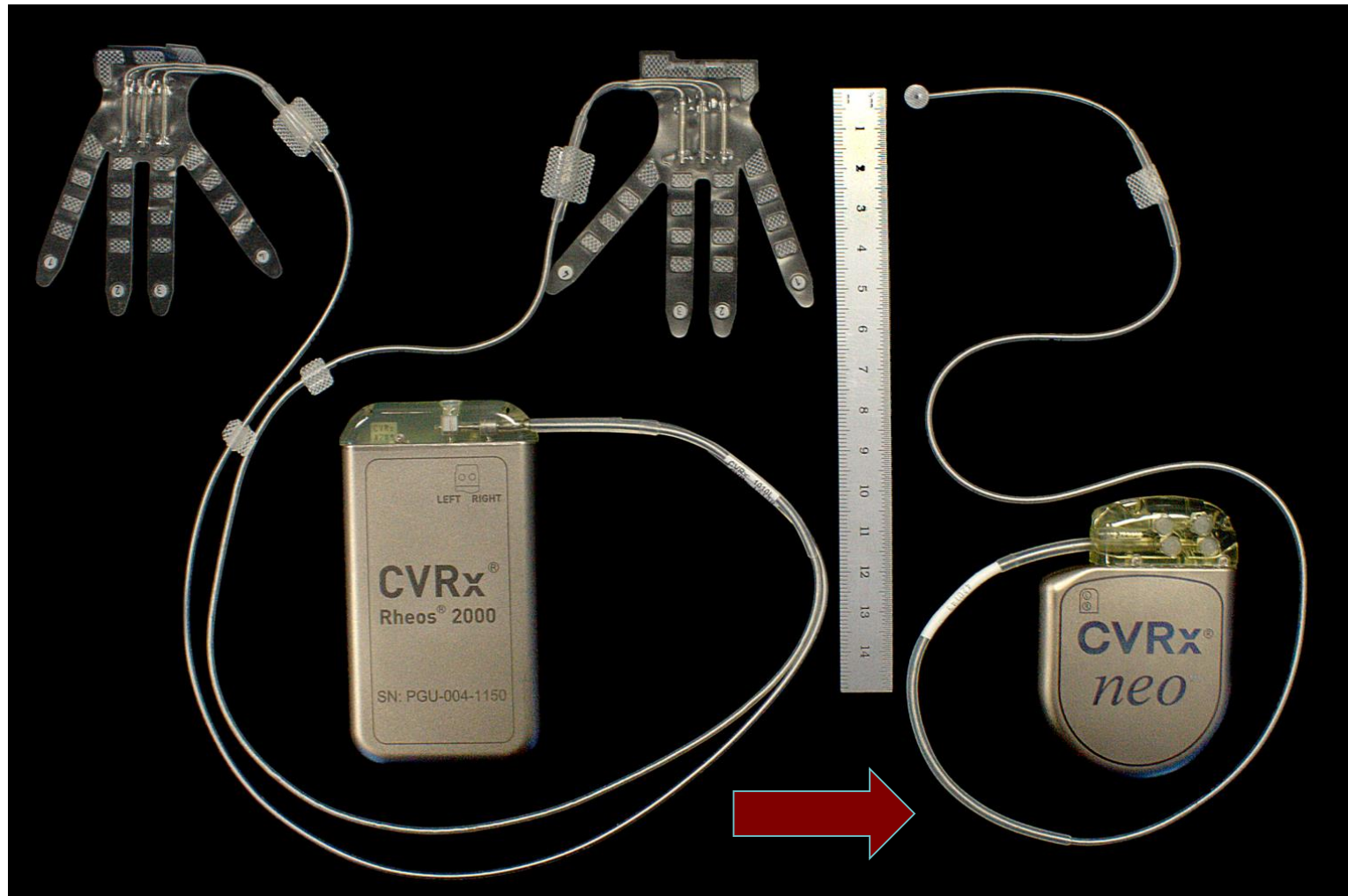


Baseline BP: 179/103 mmHg, HR 74 bpm
6-yrs f.u. BP: 144/ 85 mmHg, HR 71 bpm



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

Evolution of BAROSTIM THERAPY Delivery System



1st generation

RHEOS (obsolete)

2nd generation

BAROSTIM NEO™

First and second generation device

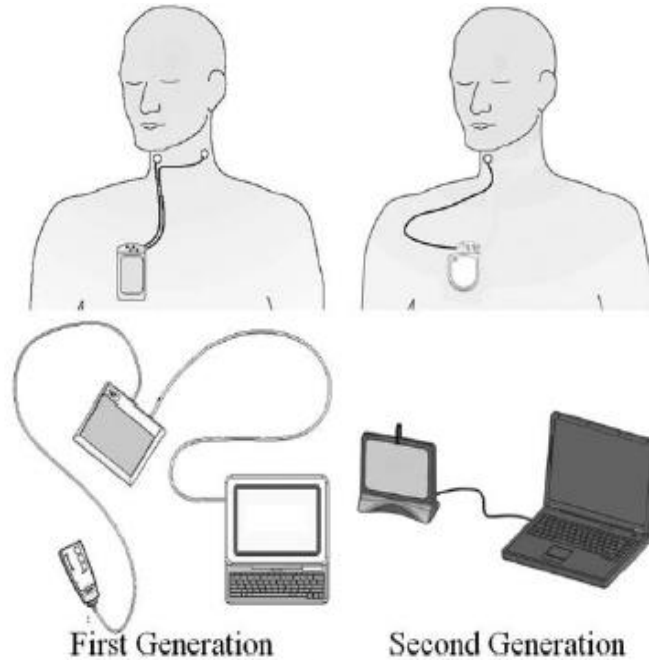
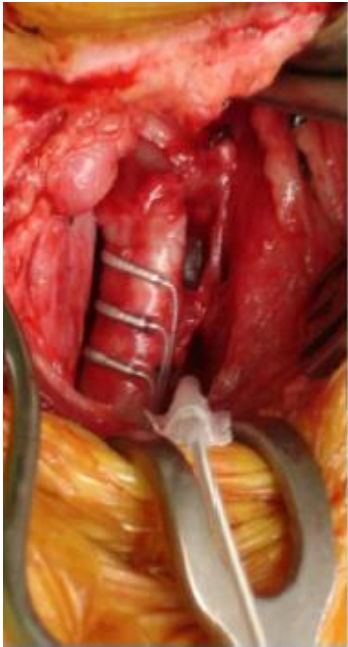
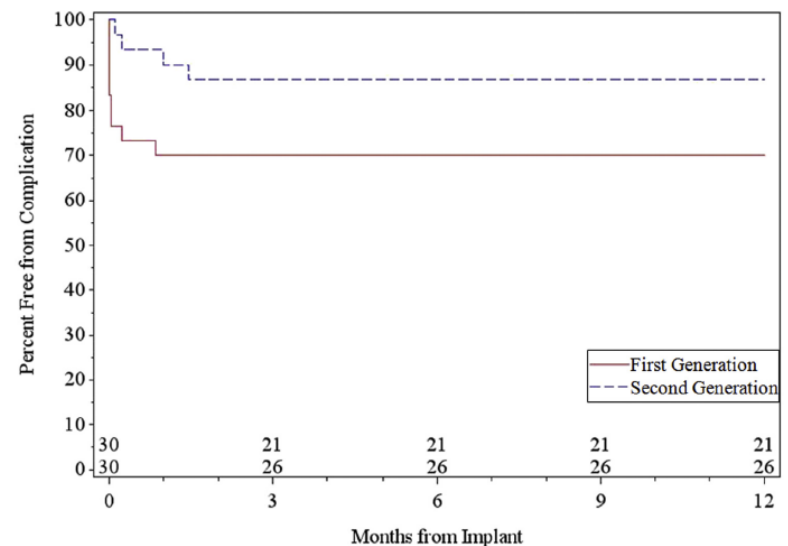
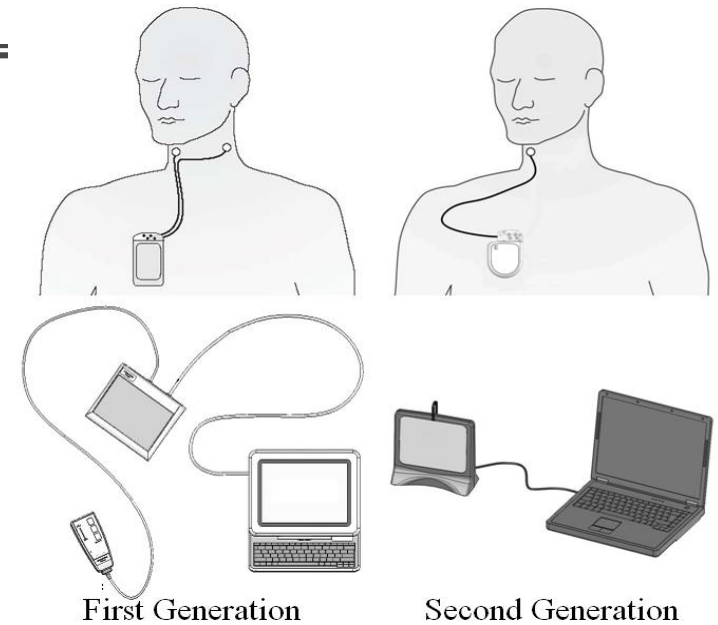
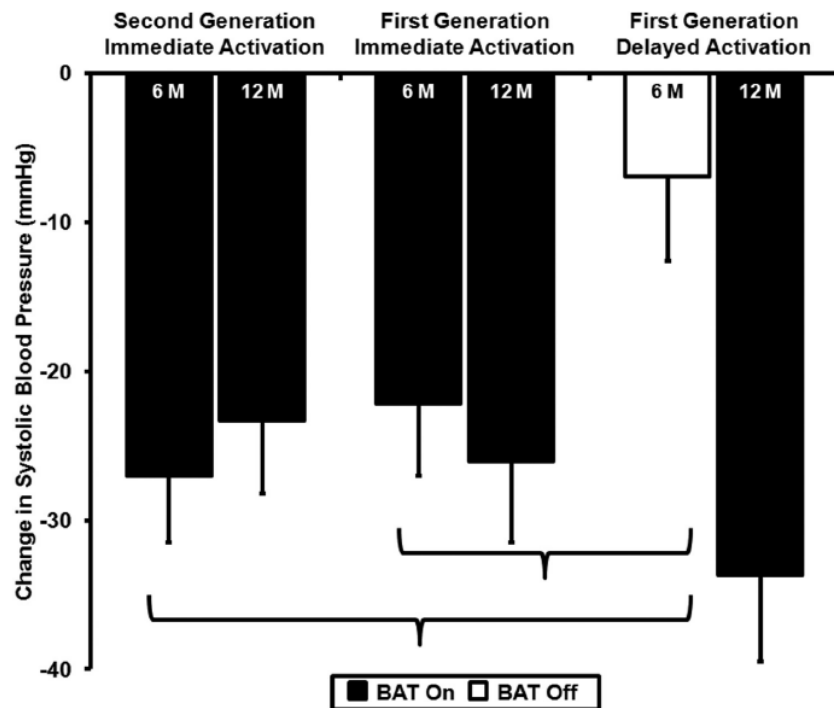


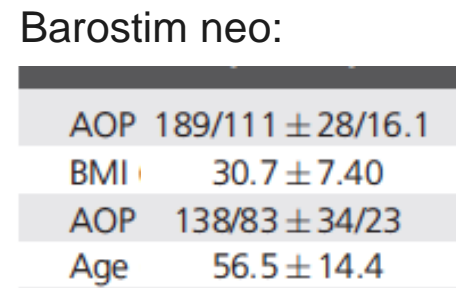
Figure 1. Schematic illustration of the first- (Rhoes, left) and second-generation (Barostim neo) BAT systems. The second-generation system is smaller, less invasive, more efficient, and more easily programmable than the first. BAT, baroreflex activation therapy.

Safety & Efficacy of 2nd Generation Device

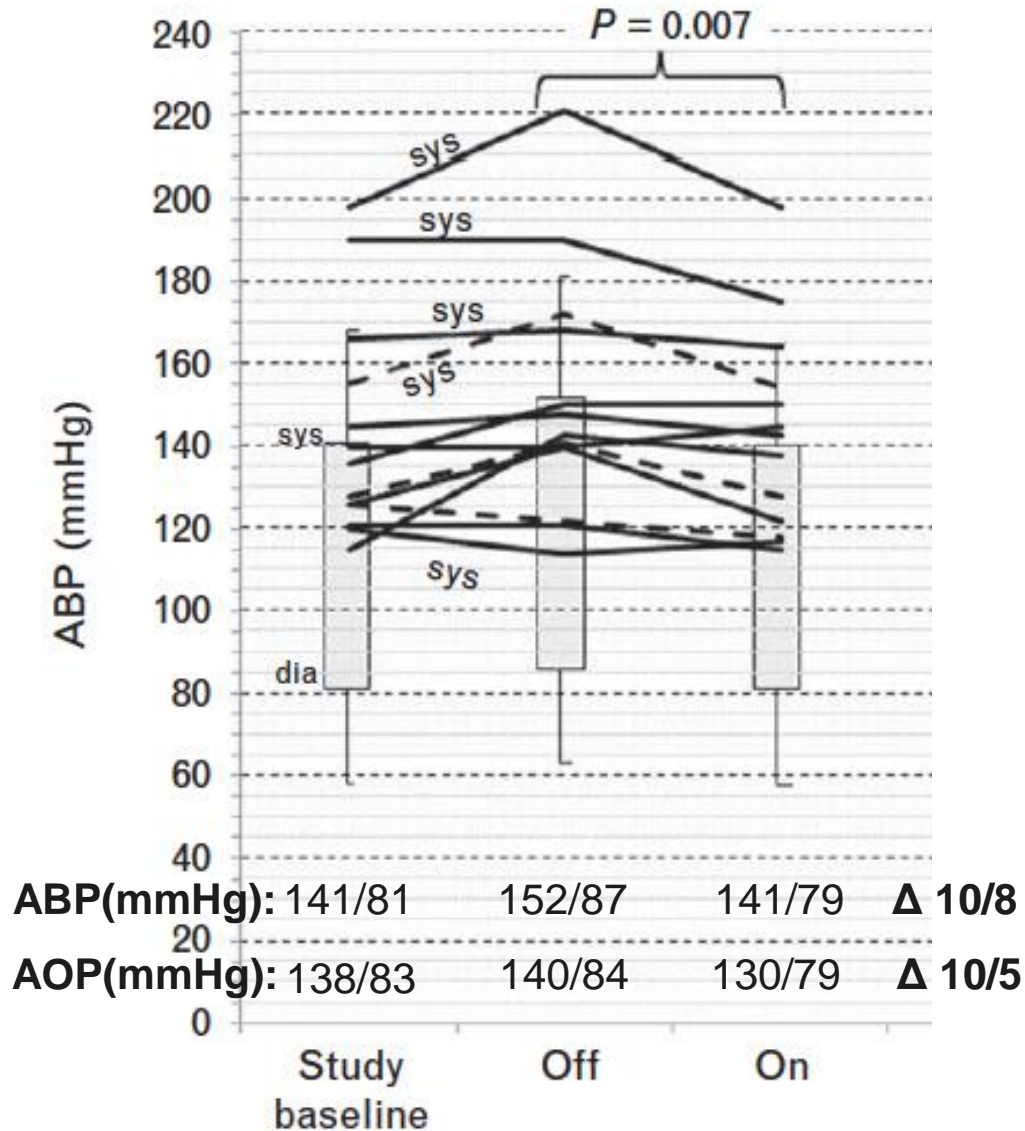
Research Article

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



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

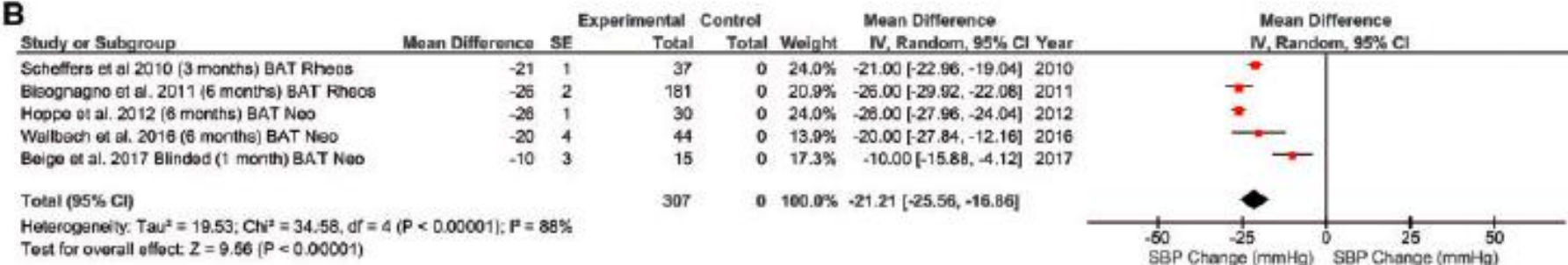
Nephrol Dial Transplant (2017) 1–9
doi: 10.1093/ndt/gfx279

Manuel Wallbach and Michael J. Koziolk

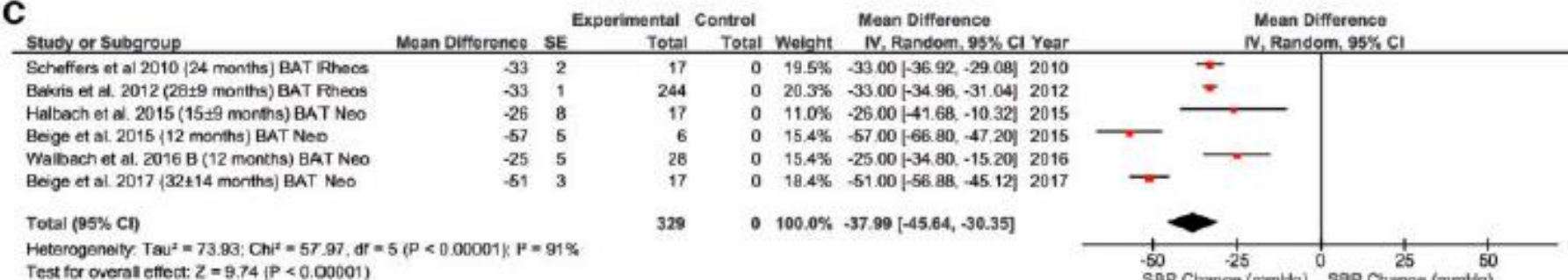
Department of Nephrology and Rheumatology, University Medical Center Göttingen, Göttingen, Germany

REVIEW

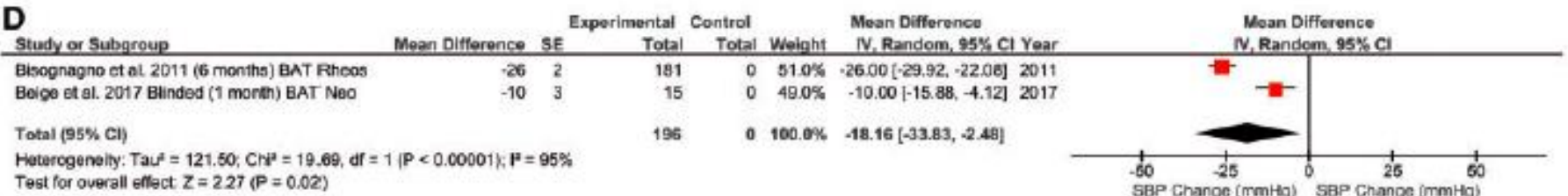
B



C



D



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

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)

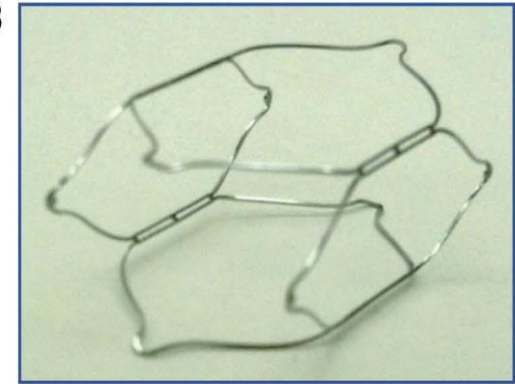
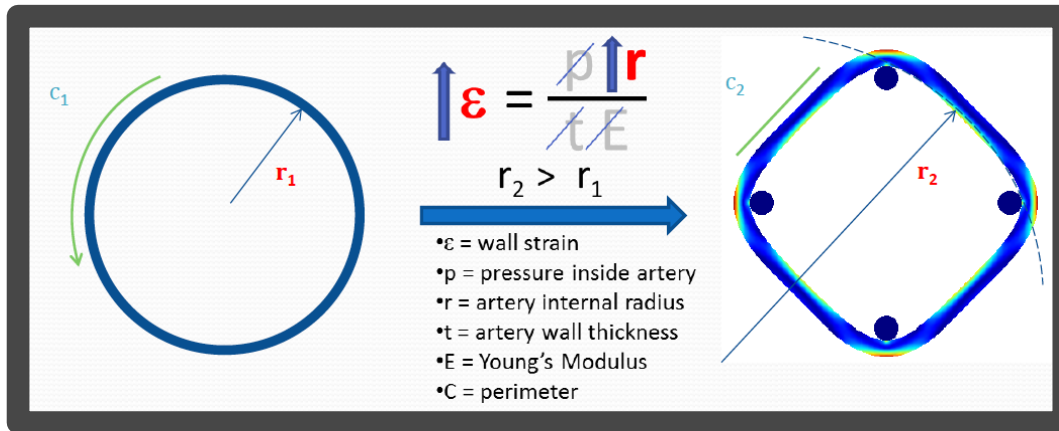


Richtlijnen
database

NEW KID ON THE BLOCK?

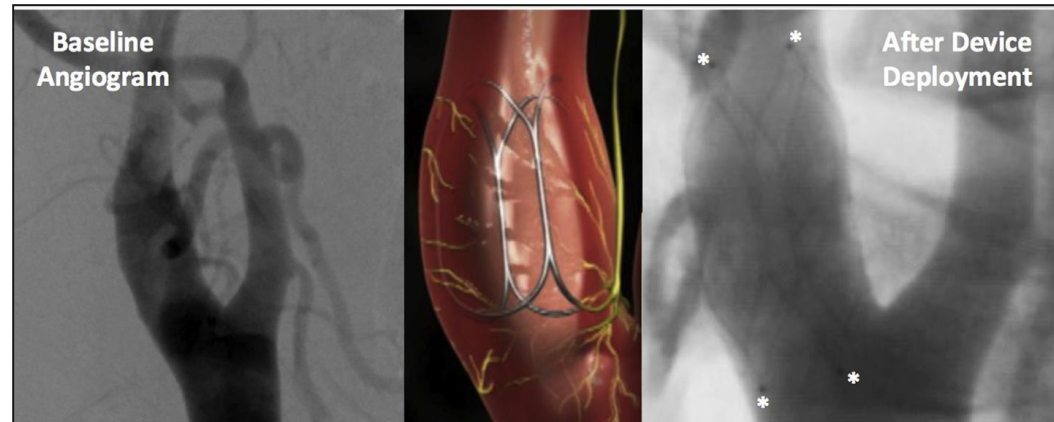
EBA with MobiusHD™ device

Endovascular prosthesis for amplification of the carotid baroreceptor signal



Mechanism of Action

- Deployment of the device reshapes the artery
- The reshaped artery leads to an increased effective radius of curvature of the artery
- The increased effective radius amplifies the signals detected by the baroreceptors



Endovascular baroreflex amplification for resistant hypertension: a safety and proof-of-principle clinical study



Wilko Spiering, Bryan Williams, Jan Van der Heyden, Monique van Kleef, Rob Lo, Jorie Versmissen, Adriaan Moelker, Abraham Kroon, Hannes Reuter, Gary Ansel, Gregg W Stone, Mark Bates, for the CALM-FIM_EUR investigators*

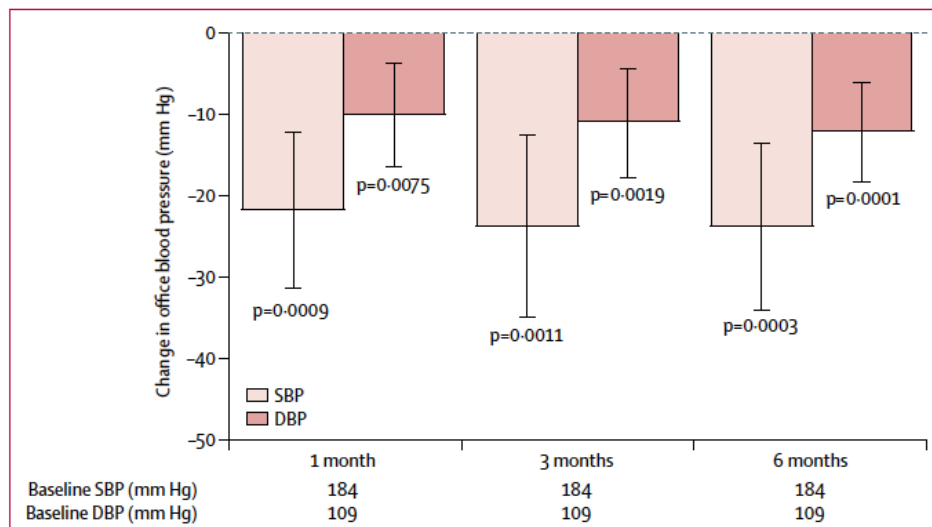
Lancet 2017;390:2655

Summary

Background Carotid baroreflex activation lowers blood pressure and might have potential application for the treatment of resistant hypertension. We did a proof-of-principle trial with a novel endovascular baroreceptor amplification device, MobiusHD (Vascular Dynamics, Mountain View, CA, USA), in patients with resistant hypertension.

Published Online
September 1, 2017
[http://dx.doi.org/10.1016/S0140-6736\(17\)32337-1](http://dx.doi.org/10.1016/S0140-6736(17)32337-1)

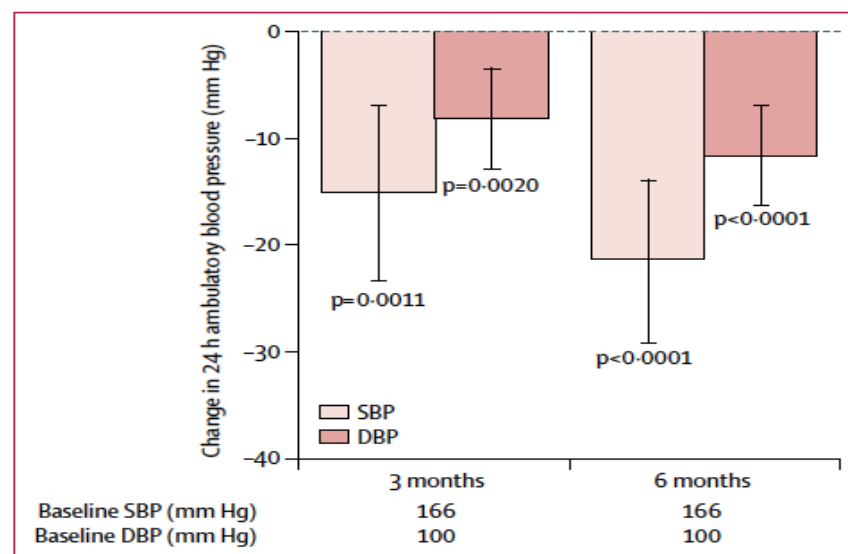
Office BP



- Number of meds: - 0.5

- OBP: 22(73%) \geq 10 mmHg
- ABP: 25(83%) \geq 5 mmHg

Ambulatory BP



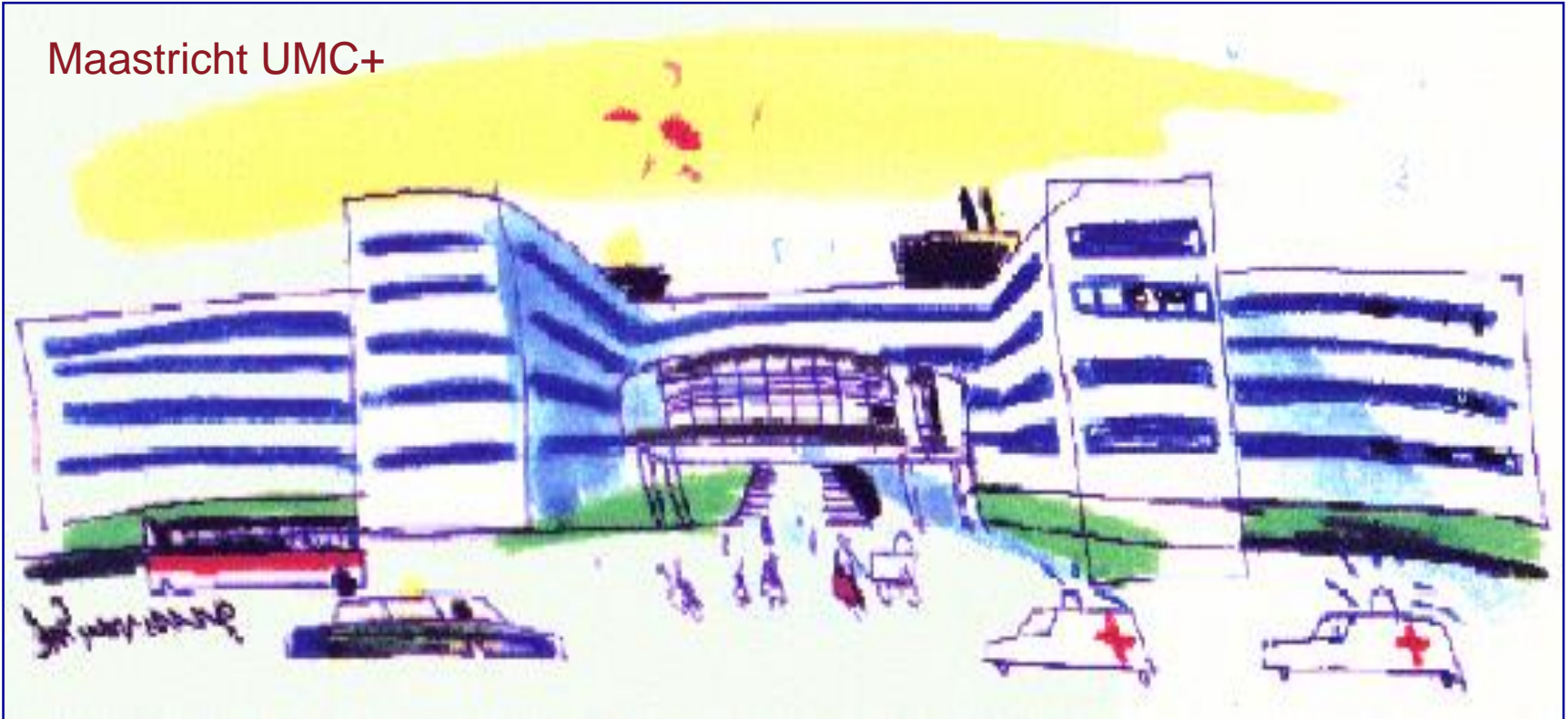
Summary – baropacing

- Baroreflex activation therapy
 - sustained BP lowering for at least 5-6 yrs
 - safety comparable to pacemaker implantations
- \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: reduces target organ damage
- BAT is a cost-effective therapy in resistant hypertension in Europe

Device Treatment in Resistant Hypertension



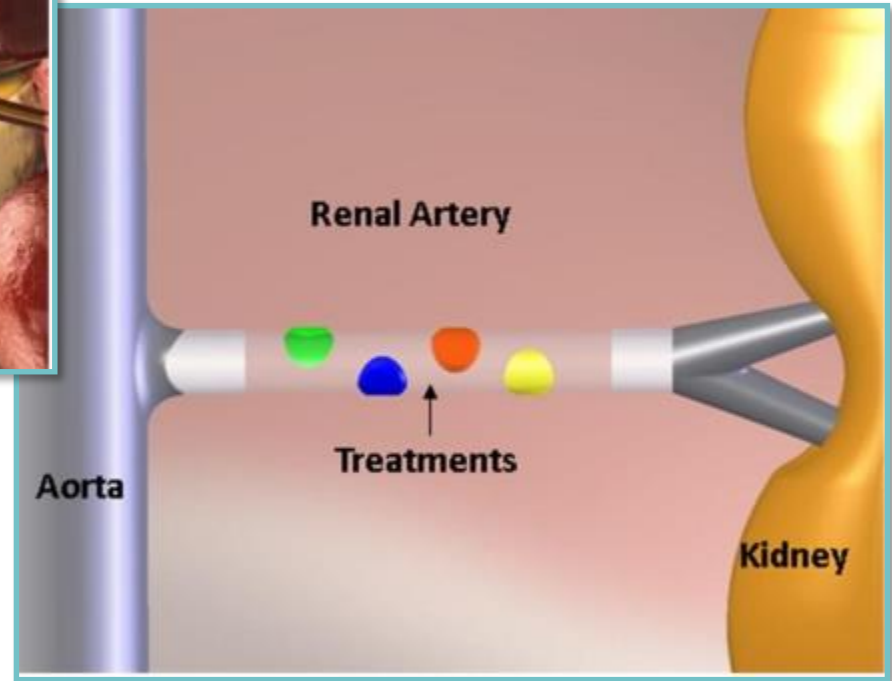
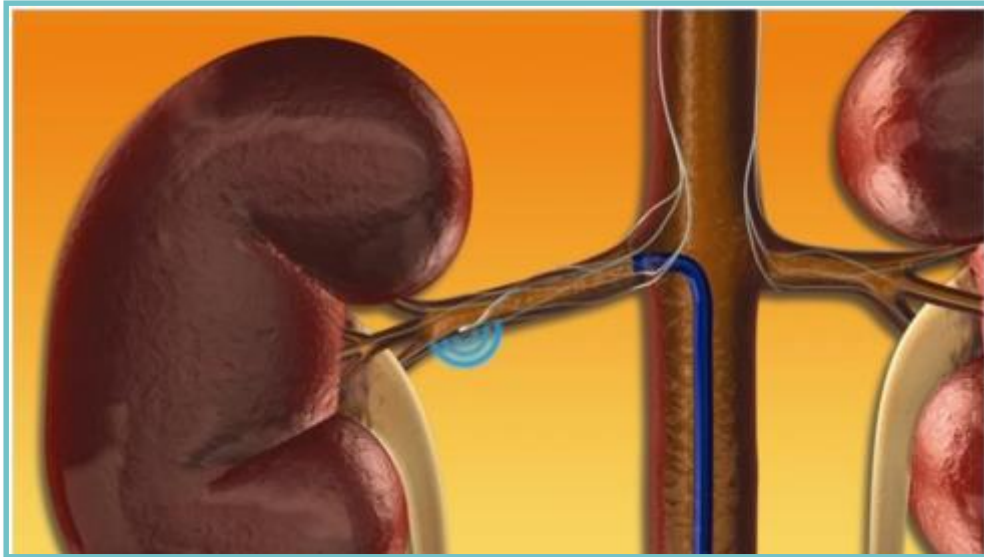
Maastricht UMC+



contact: aa.kroon@mumc.nl



RENAL DENERVATION



A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D.,
for the SYMPPLICITY HTN-3 Investigators*

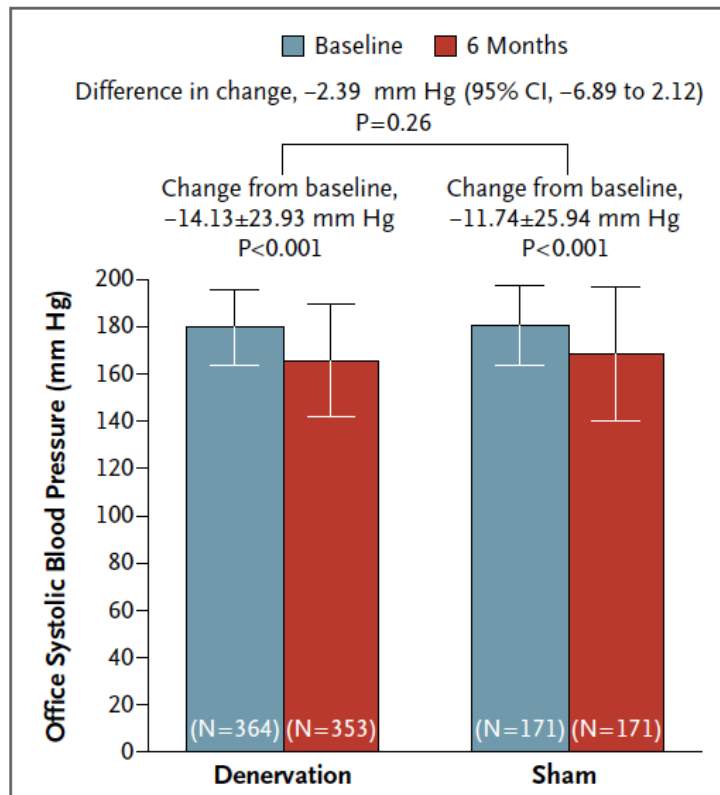


Figure 1. Primary Efficacy End Point.

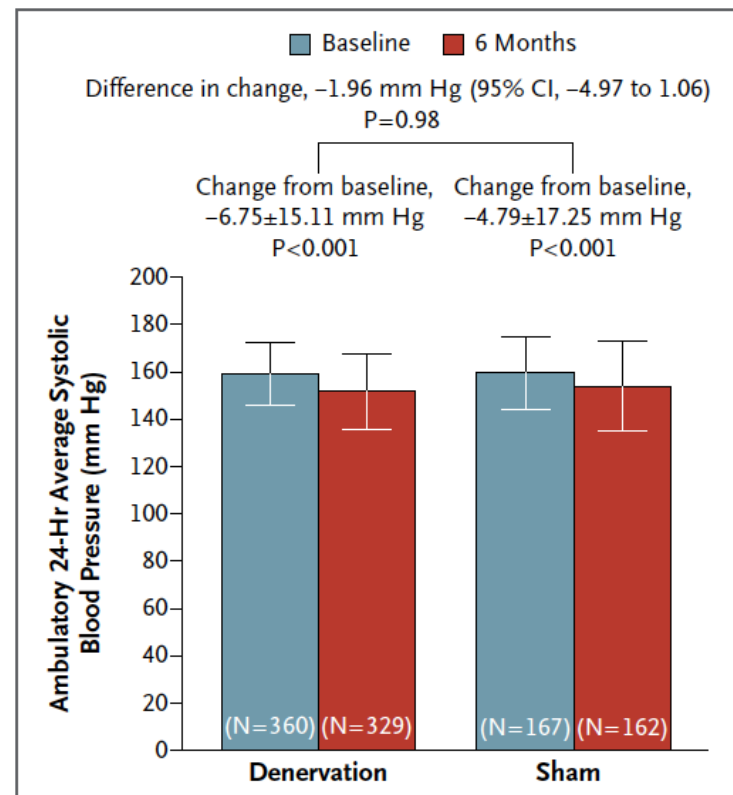
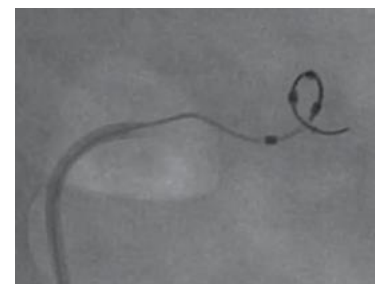


Figure 2. Secondary Efficacy End Point.



Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial



Raymond R Townsend, Felix Mahfoud, David E Kandzari, Kazuomi Kario, Stuart Pocock, Michael A Weber, Sebastian Ewen, Konstantinos Tsioufis, Dimitrios Tousoulis, Andrew S P Sharp, Anthony F Watkinson, Roland E Schmieder, Axel Schmid, James W Choi, Cara East, Anthony Walton, Ingrid Hopper, Debbie L Cohen, Robert Wilensky, David P Lee, Adrian Ma, Chandan M Devireddy, Janice P Lea, Philipp C Lurz, Karl Fengler, Justin Davies, Neil Chapman, Sidney A Cohen, Vanessa DeBruin, Martin Fahy, Denise E Jones, Martin Rothman, Michael Böhm, on behalf of the SPYRAL HTN-OFF MED trial investigators*

Summary

Background Previous randomised renal denervation studies did not show consistent efficacy in reducing blood pressure. The objective of our study was to evaluate the effect of renal denervation on blood pressure in the absence of antihypertensive medications.

Methods SPYRAL HTN-OFF MED was a multicentre, international, single-blind, randomised, sham-controlled, proof-of-concept trial. Patients were enrolled at 21 centres in the USA, Europe, Japan, and Australia. Eligible patients were drug-naïve or discontinued their antihypertensive medications. Patients with an office systolic blood pressure (SBP) of 150 mm Hg or greater and less than 180 mm Hg, office diastolic blood pressure (DBP) of 90 mm Hg or greater, and a mean 24-h ambulatory SBP of 140 mm Hg or greater and less than 170 mm Hg at second screening underwent renal angiography and were randomly assigned to renal denervation or sham control. Patients, caregivers, and those assessing blood pressure were blinded to randomisation assignments. The primary endpoint, change in 24-h blood pressure at 3 months, was compared between groups. Drug surveillance was done to ensure patient compliance with absence of antihypertensive medication. The primary analysis was done in the intention-to-treat population. Safety events were assessed at 3 months. This study is registered with ClinicalTrials.gov, number NCT02439749.

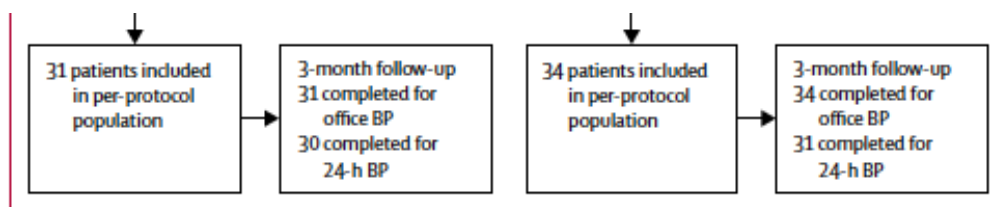
Published Online
August 28, 2017
[http://dx.doi.org/10.1016/S0140-6736\(17\)32281-X](http://dx.doi.org/10.1016/S0140-6736(17)32281-X)

See Online/Comment
[http://dx.doi.org/10.1016/S0140-6736\(17\)32293-6](http://dx.doi.org/10.1016/S0140-6736(17)32293-6)

*SPYRAL HTN-OFF MED trial investigators are listed at the end of the Article

Perelman School of Medicine,
University of Pennsylvania,
Philadelphia, PA, USA
(Prof R R Townsend MD,
D L Cohen MD, R Wilensky MD);
Department of Internal

SPYRAL HTN-OFF MED



	Renal denervation group (n=38)	Sham control group (n=42)
Age, years	55.8 (10.1)	52.8 (11.5)
Men	26 (68.4%)	31 (73.8%)
BMI, kg/m ²	29.8 (5.1)	30.2 (5.1)
Office SBP (mm Hg)	162.0 (7.6)	161.4 (6.4)
Office DBP (mm Hg)	99.9 (6.8)	101.5 (7.5)
24-h SBP (mm Hg)	153.4 (9.0)†	151.6 (7.4)
24-h DBP (mm Hg)	99.1 (7.7)†	98.7 (8.2)
Office heart rate (bpm)	71.1 (11.0)	73.4 (9.8)
24-h heart rate (bpm)	72.3 (10.9)†	75.5 (11.5)

Table 1: Patient characteristics and blood pressure measurements at baseline

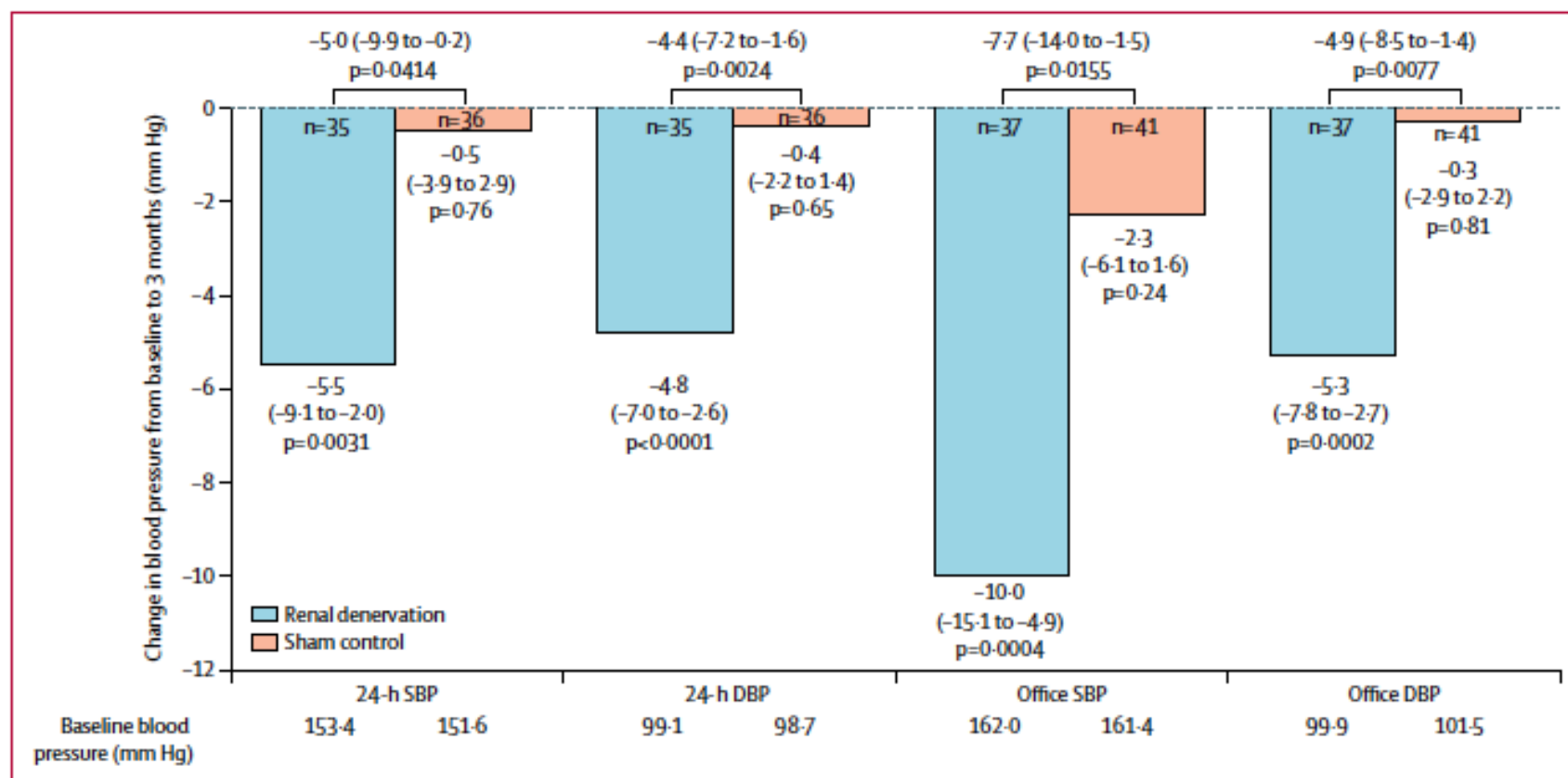
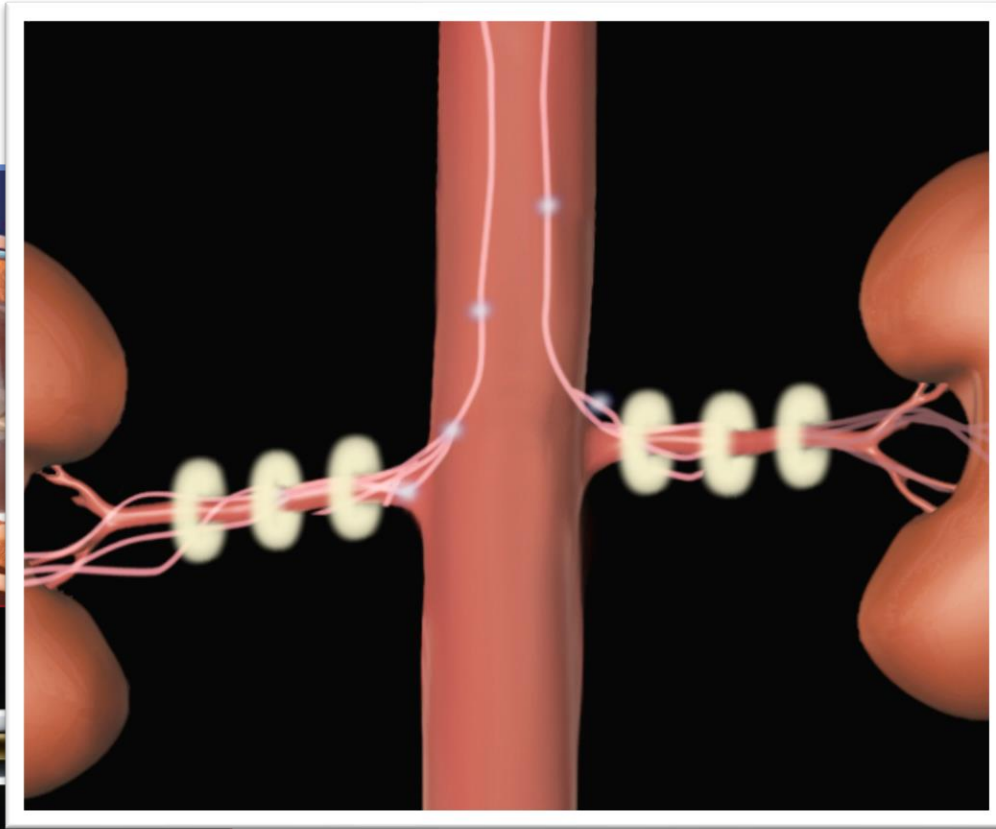
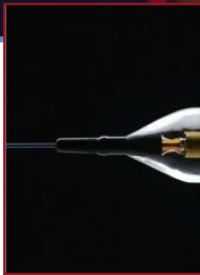
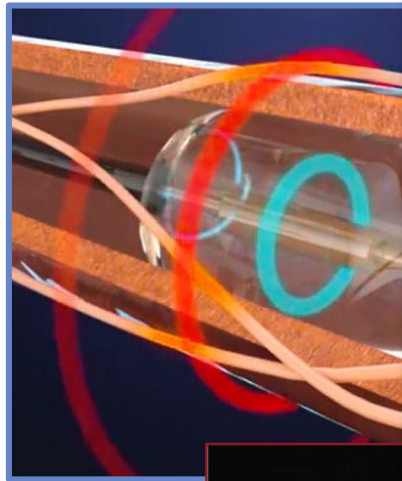


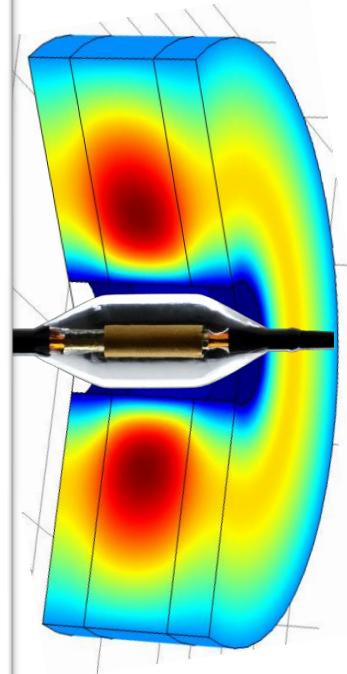
Figure 3: Changes at 3 months in office and ambulatory SBP and DBP for renal denervation and sham control groups

Renal denervation using ultrasound

Paradise system[®] (Recor Medical)



Thermal Profile



- **Heat** – ablate the renal nerves on the outside