5 6 7 JUIN 2019

APPAC Ensemble, imaginons la cardiologie de demain

HTA : état actuel et futur

L'interventionnel dans le traitement de l'HTA

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Clinique Pasteur , Toulouse

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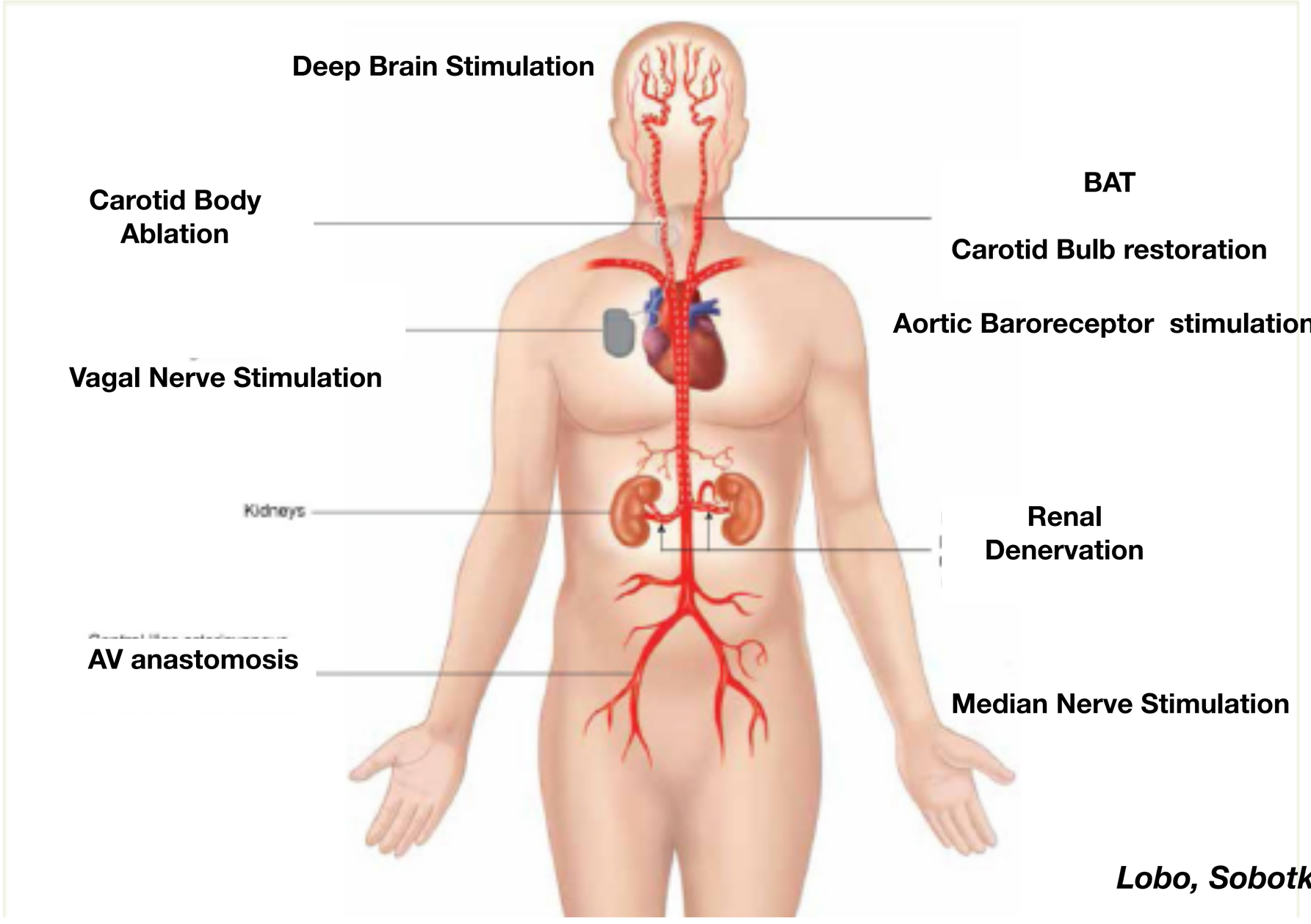
ESH European Hypertension Excellence Center Clinique Pasteur Toulouse/ France

CLINIQUE Pasteur

Les cardiologues interventionnels: Réveillez vous !

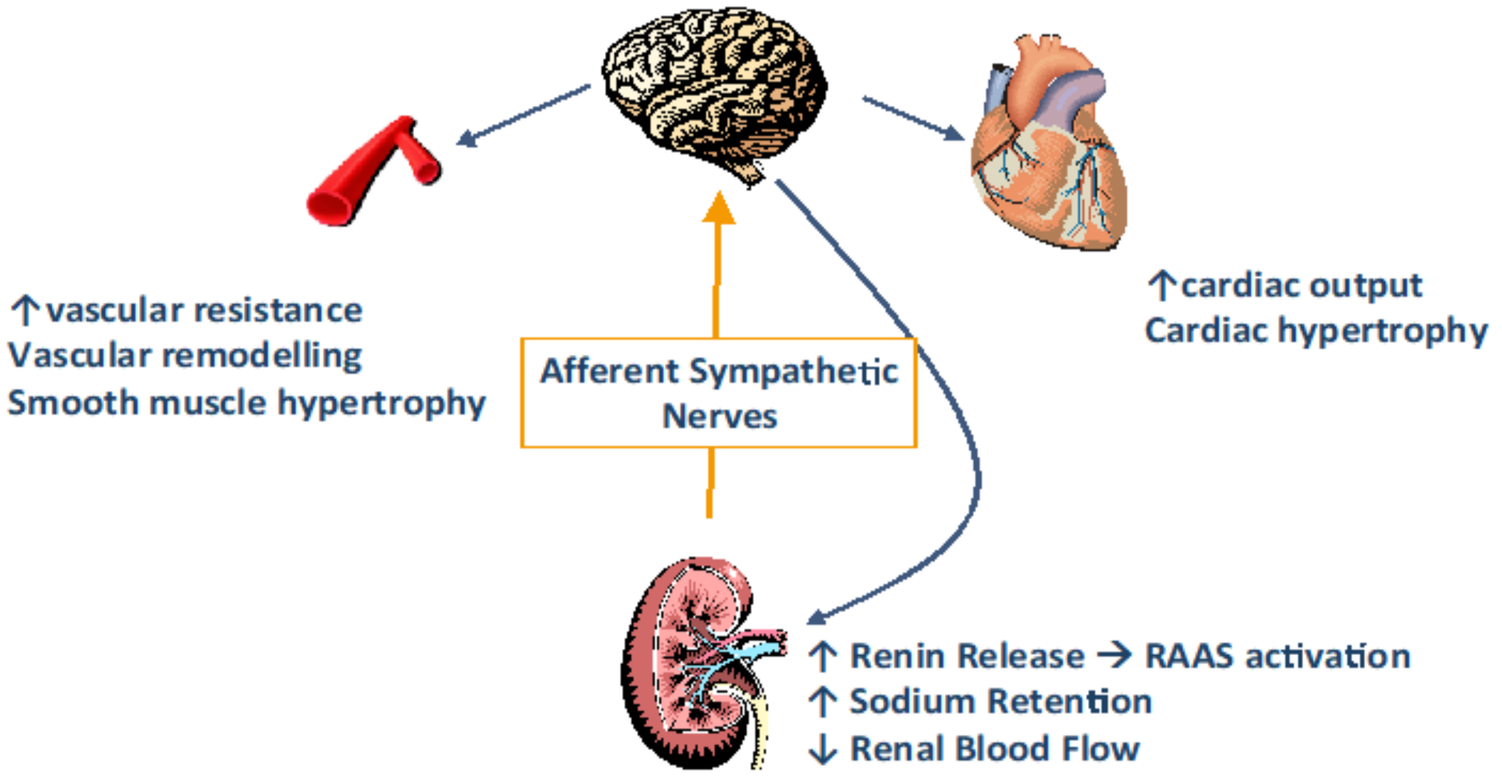


Lobo, Sobotka, Pathak. EHJ 2016

Target : the Renal Nerve

Sympathetic modulation and the scientific basis for RDN

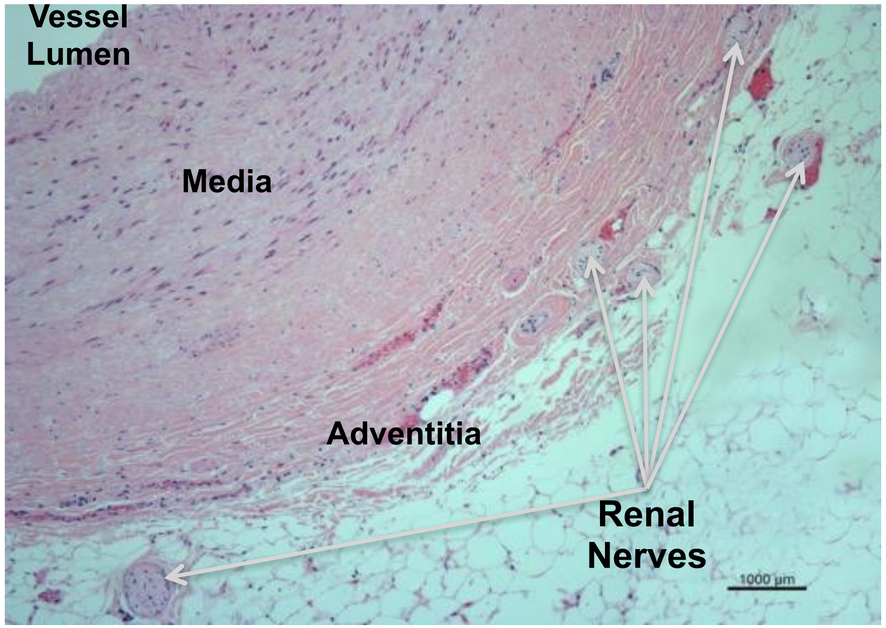
SNS Role in Hypertension



Thomas P and Dasgupta I. *Pediatr Nephrol* 2015; 30 (4): 549-60

Sympathetic modulation and the scientific basis for RDN

Renal Nerves as a Therapeutic Target



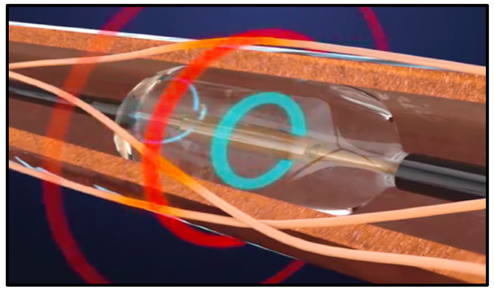
Arise from T10-L1, Follow the renal artery to the kidney

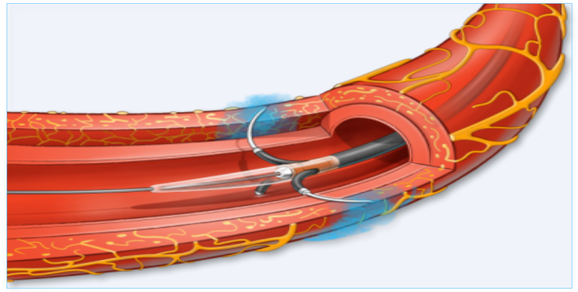
3 techniques

2 types d’essai

1 résultat !

3 techniques





2 types d’essai

1 résultat !

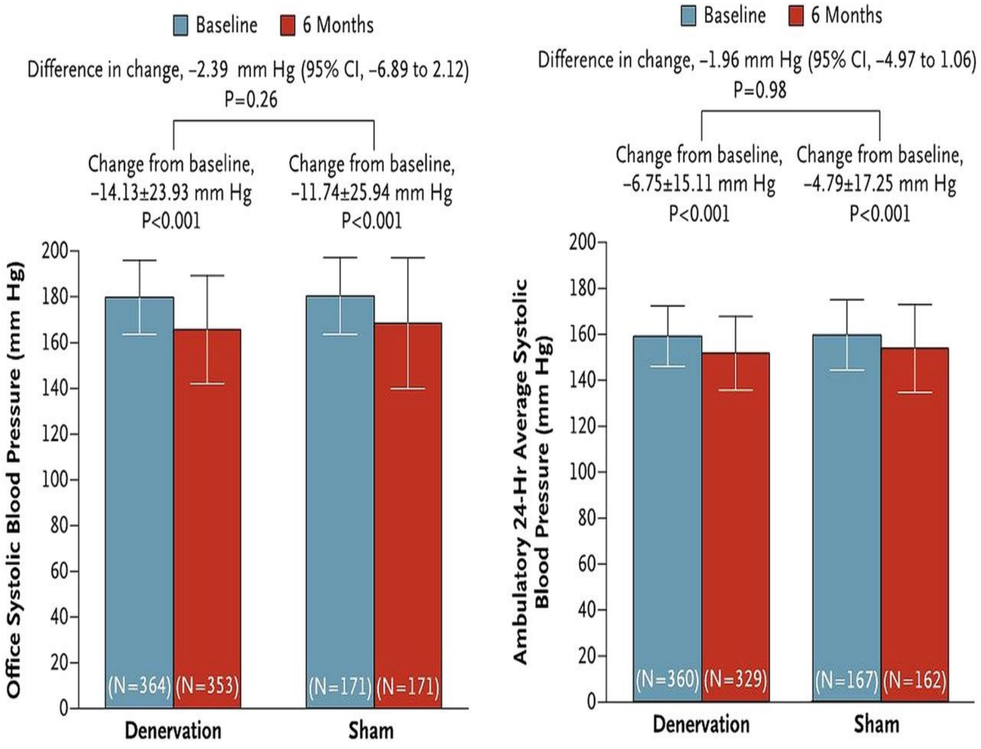
3 techniques

2 types d’essai

1 résultat !

Denervation Rénale: apprendre du passé

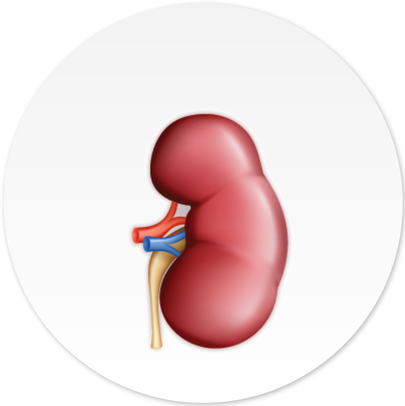
HTN-3: End Points



N Engl J Med 2014;370:1393-401

Medication

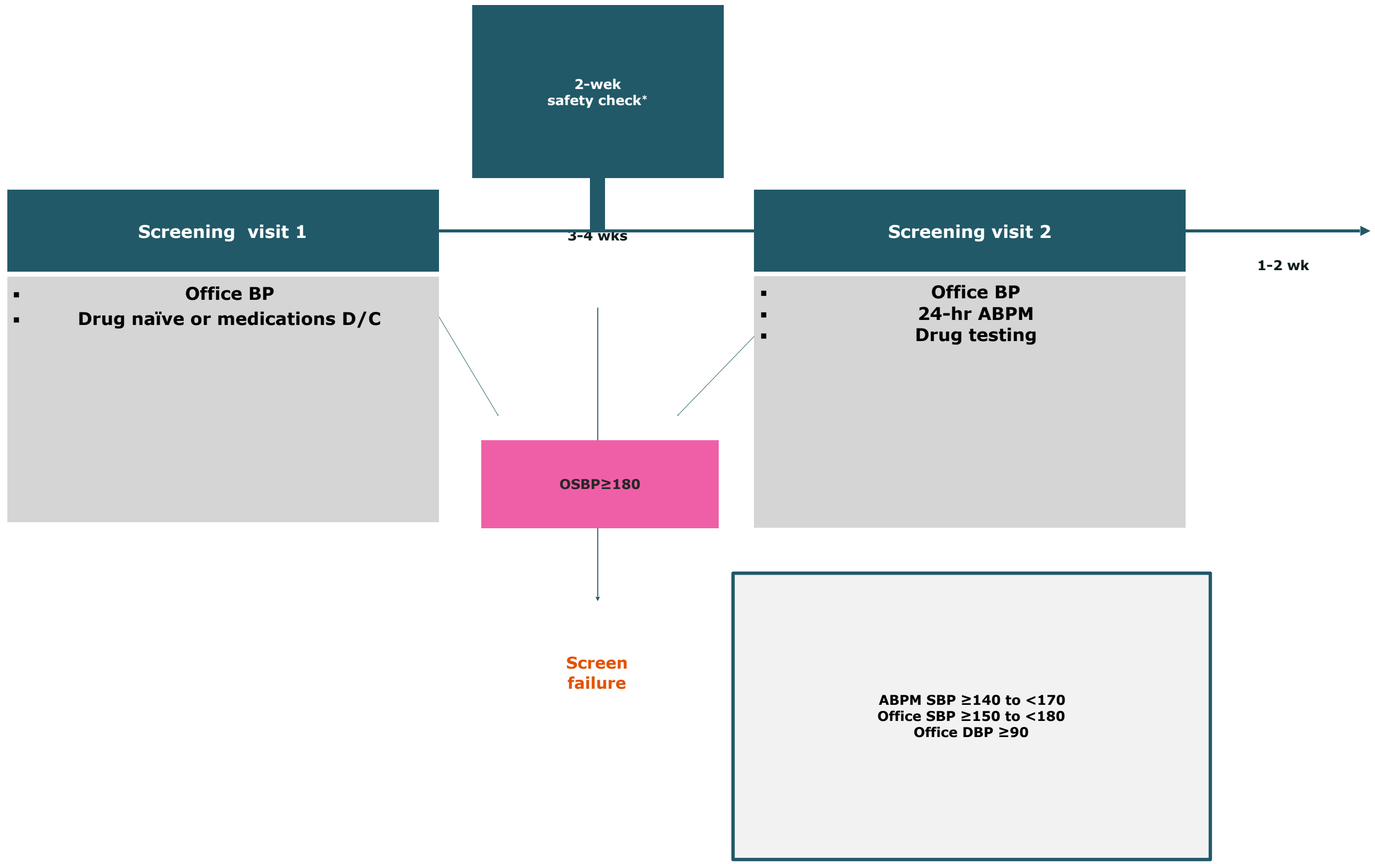
Study Population

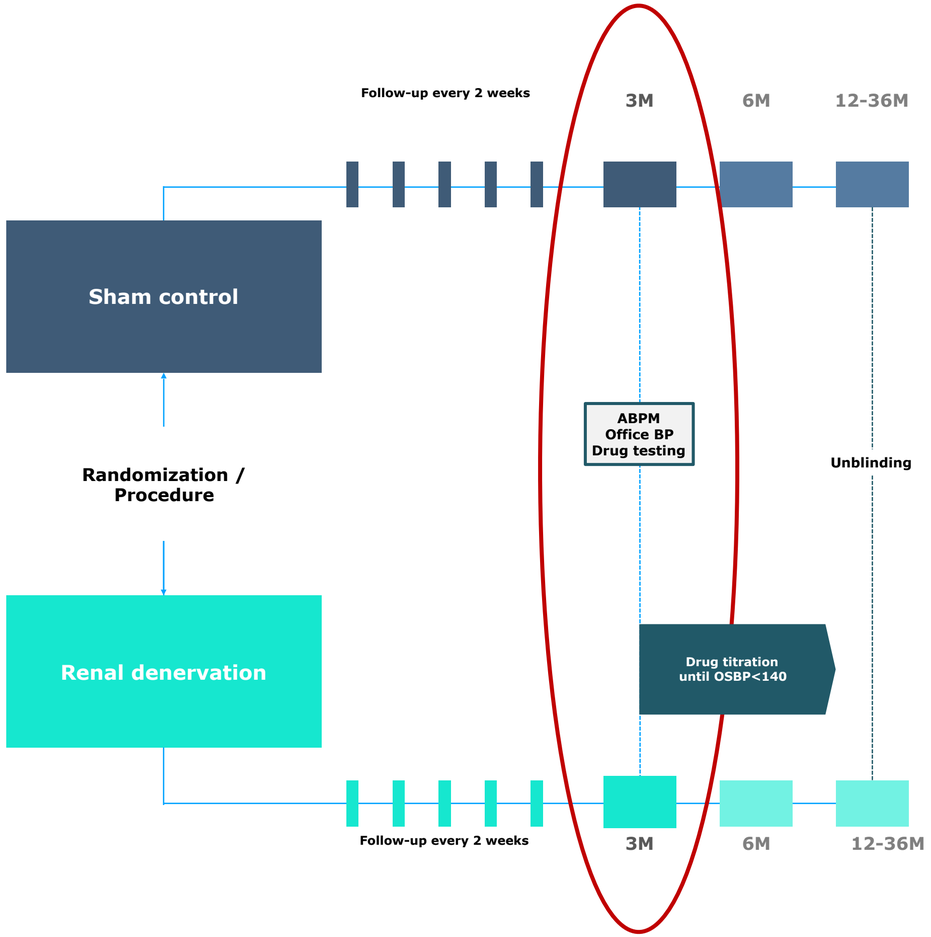


Procedure

European Clinical Consensus Conference for device-based therapies for hypertension 1, Eur Heart J 2015
European Clinical Consensus Conference for device-based therapies for hypertension 2, Eur Heart J 2017

Randomized, sham-controlled, blinded trial, with (ON) or without drugs (OFF)





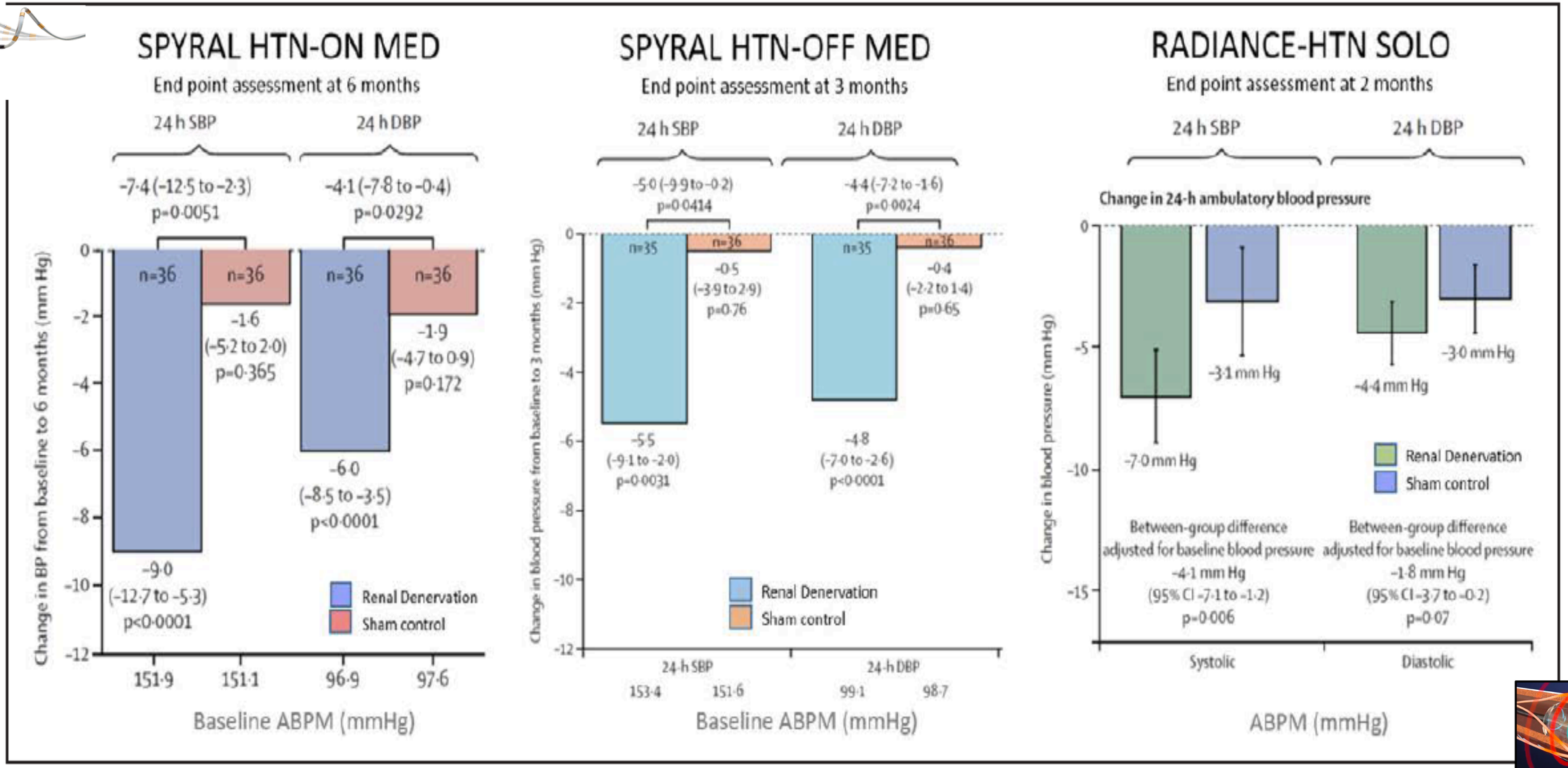
Townsend RR, L

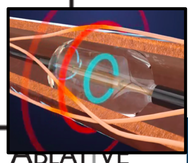
3 techniques

2 types d’essai

1 résultat !

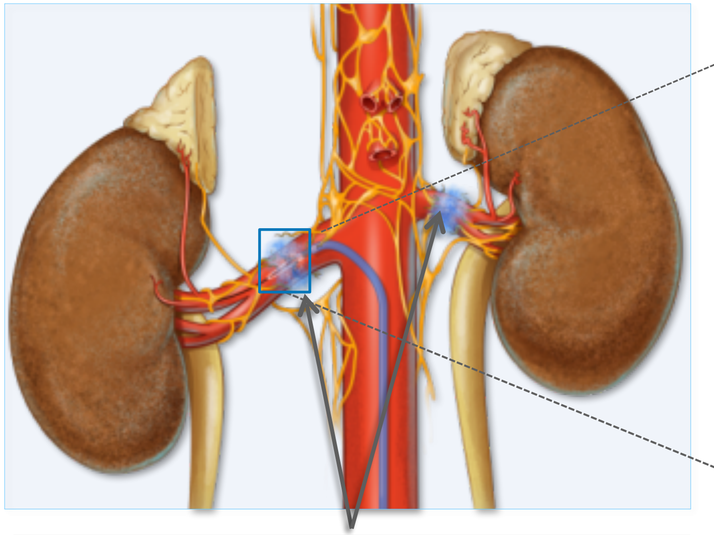
Clinical Trials Results



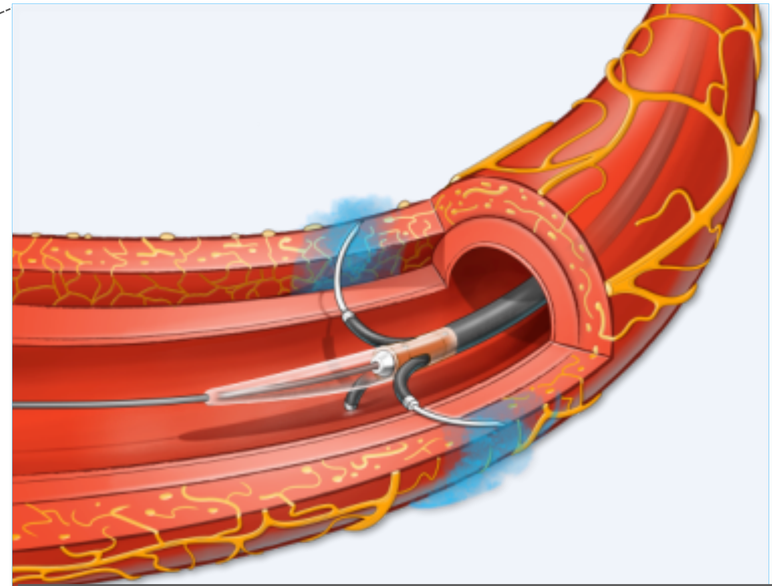


Schlaich et al, Hypertension, 2018

Alcohol-Mediated Denervation via Precise Targeting



Perivascular Sites Where Device Infuses Alcohol



Expanded View of Device Infusing Alcohol

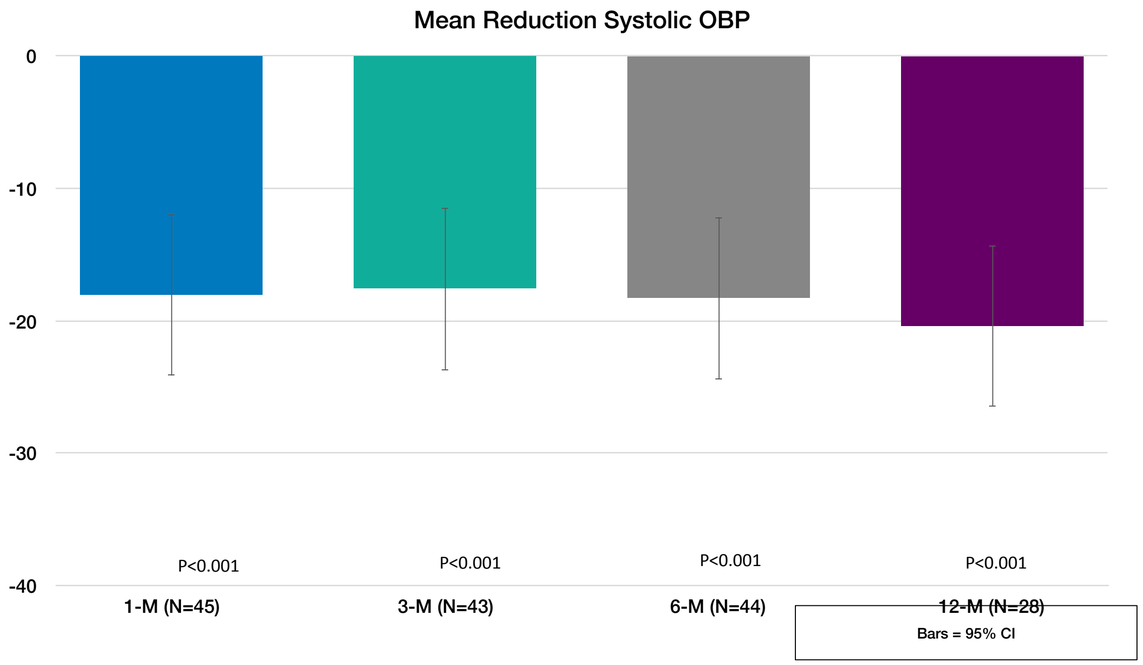
PVRD Chapter 13; RENAL DENERVATION: A New Approach Treatment – Page 107-116;2015

Site-specific delivery of alcohol: Local nerve inactivation

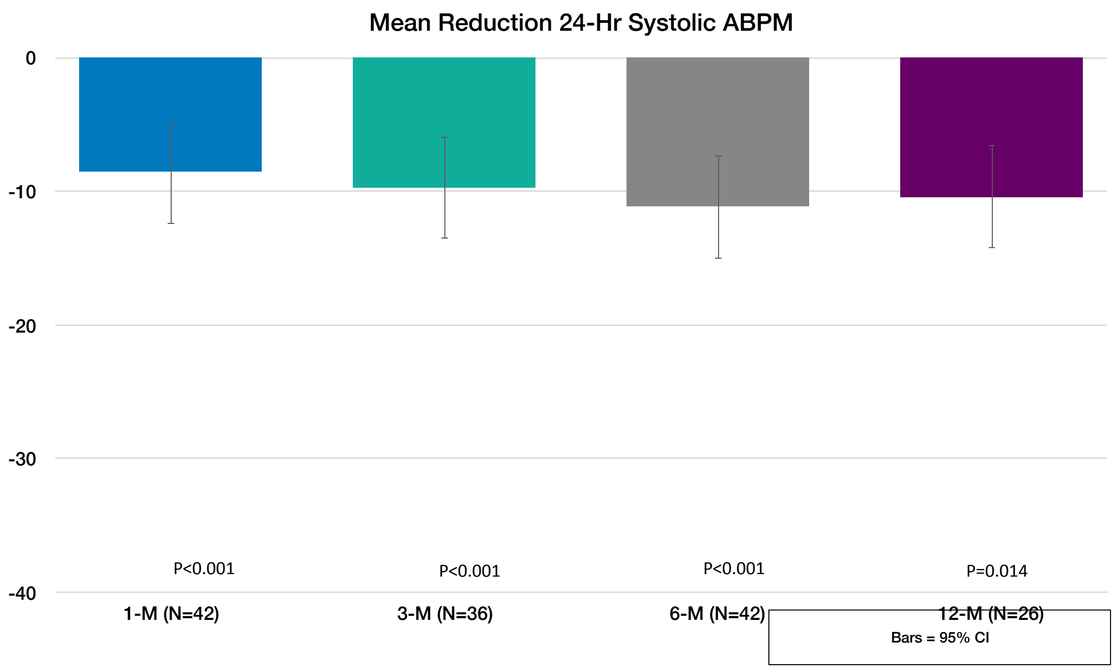
1. Micro-volume (0.3 mL–0.6 mL) infused directly to the perivascular region
2. Extracellular fluid helps spread alcohol circumferentially in the perivascular region
3. Alcohol activity range self-limited through dilution by extracellular fluid

***CAUTION:* "*The Peregrine System Kit is currently being studied to evaluate safety and effectiveness when used in the treatment of patients with uncontrolled hypertension. The Peregrine System Kit is a combination product comprised of the co-packaged CE marked Peregrine System Infusion Catheter and Ablative Solutions dehydrated alcohol, an Investigational Medicinal Product. The use of Ablative Solutions dehydrated alcohol is limited to investigational use in clinical trials*".**

1, 3, 6 and 12 Months Systolic Blood Pressure Reduction*



Baseline OBP: 169 ± 15 mmHg (N=45)



Baseline ABPM: 151 ± 14 mmHg (N=44)

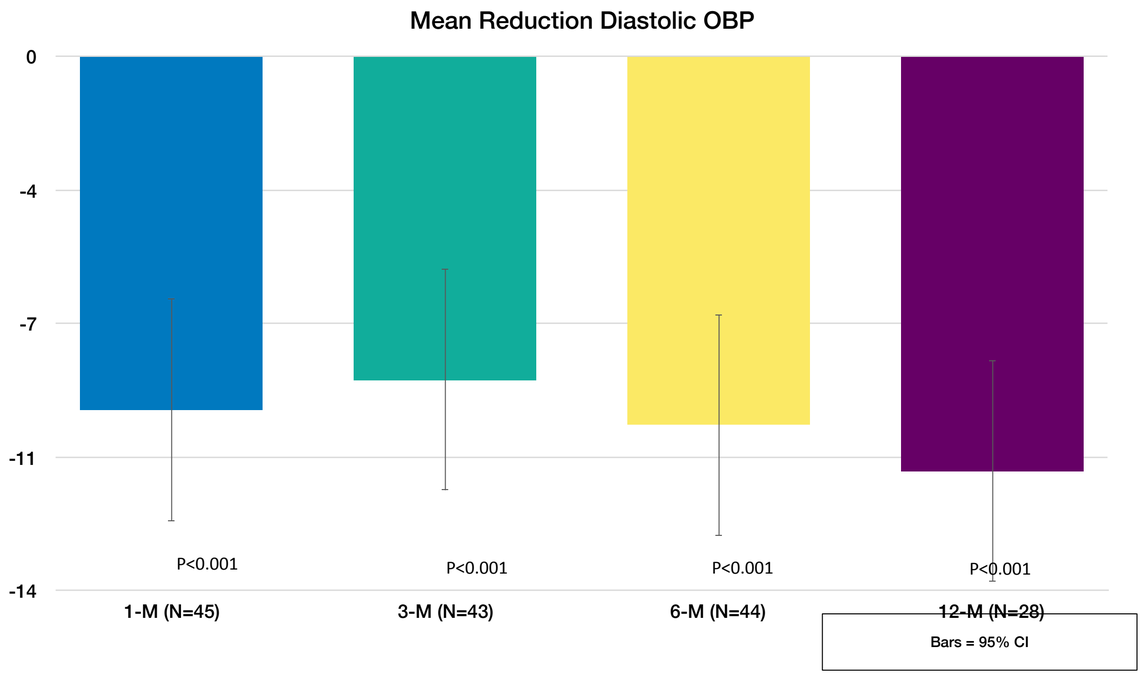
Responders:**	**69%**	**58%**	**61%**	**68%**	**64%**	**67%**	**71%**	**54%**

** 24-hour data from CL; OBP Data: site reported. 12 Month data not yet monitored*

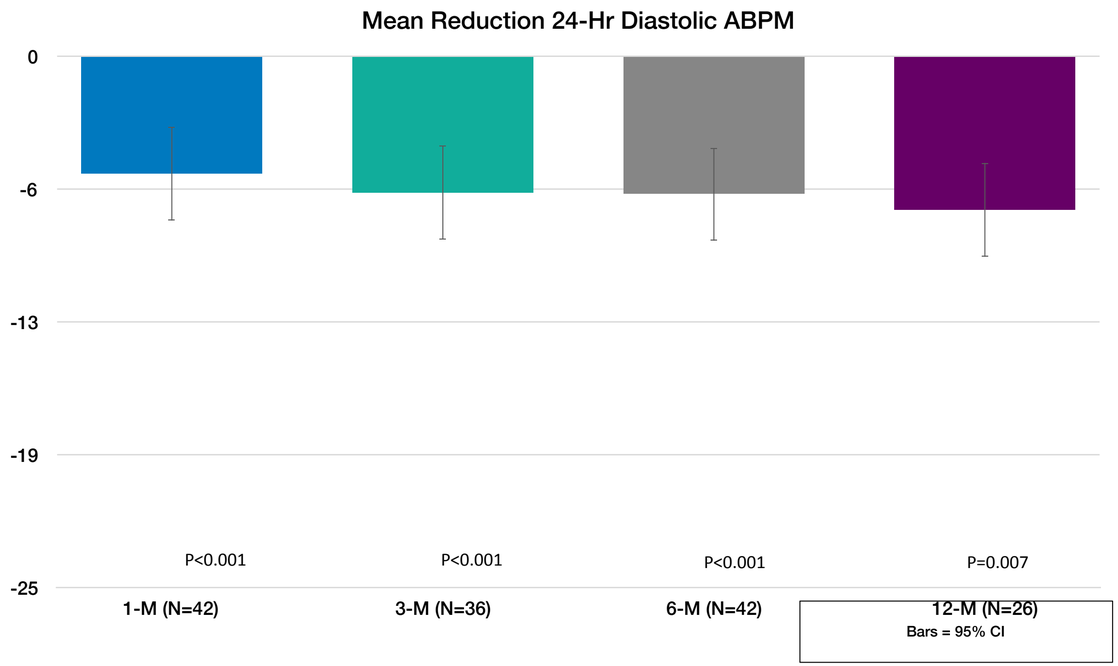
*** Responders are defined as ≥ 10mmHg drop for OBP and ≥ 5mmHg drop for ABPM*

Under review European Heart Journal

1, 3, 6 and 12 Months Diastolic Blood Pressure Reduction*



Baseline DBP: 99 ± 13 mmHg



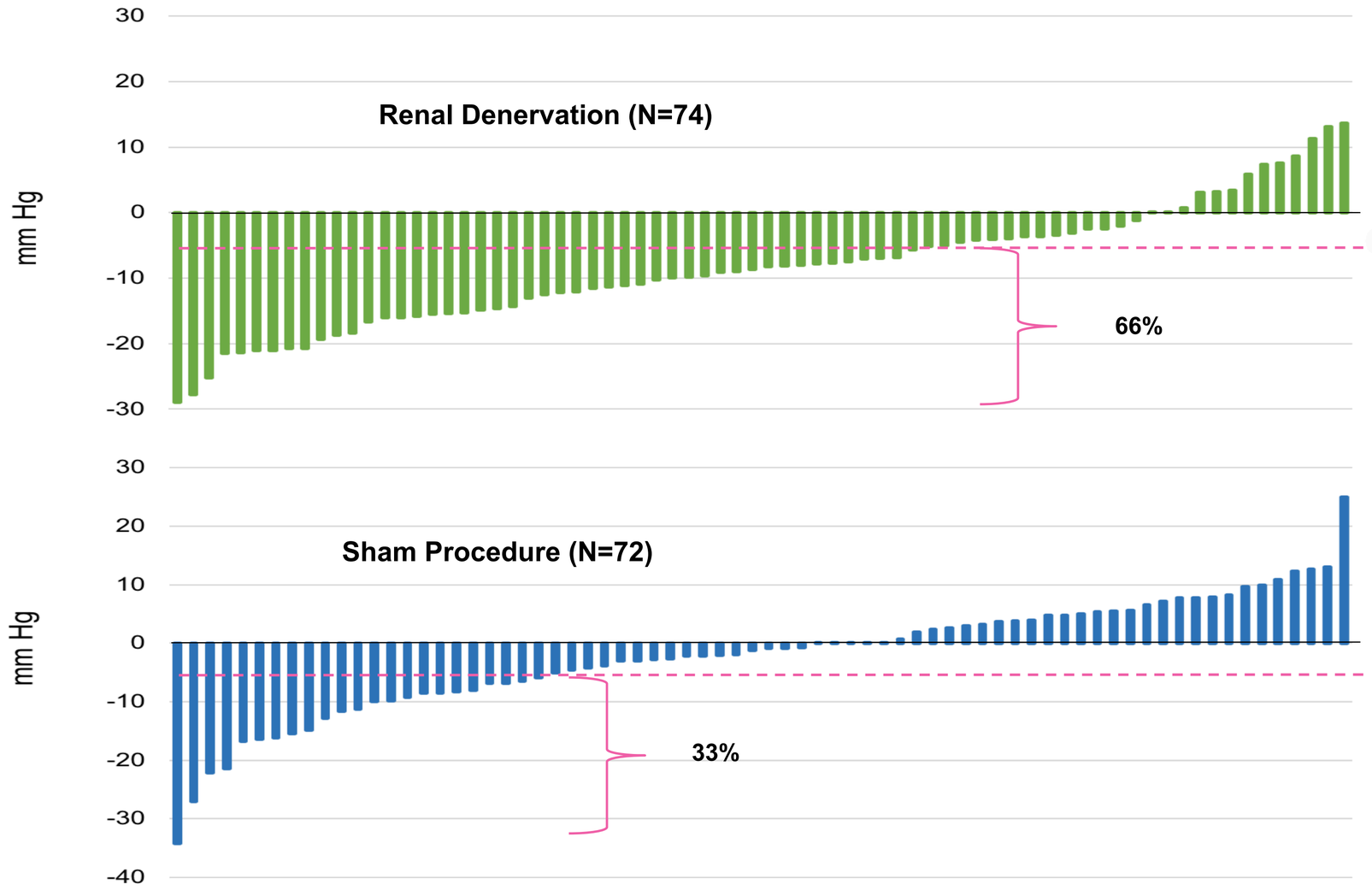
Baseline ABPM: 89 ± 12 mmHg

** 24-hour data from CL; OBP Data: site reported. 12 Month data not yet monitored*

Under review European Heart Journal

Individual Patient Response at 2 Months:

Change in Daytime Ambulatory Systolic BP at 2 Months (ITT Population)



% Patients with
≥ 5 mm Hg Decrease

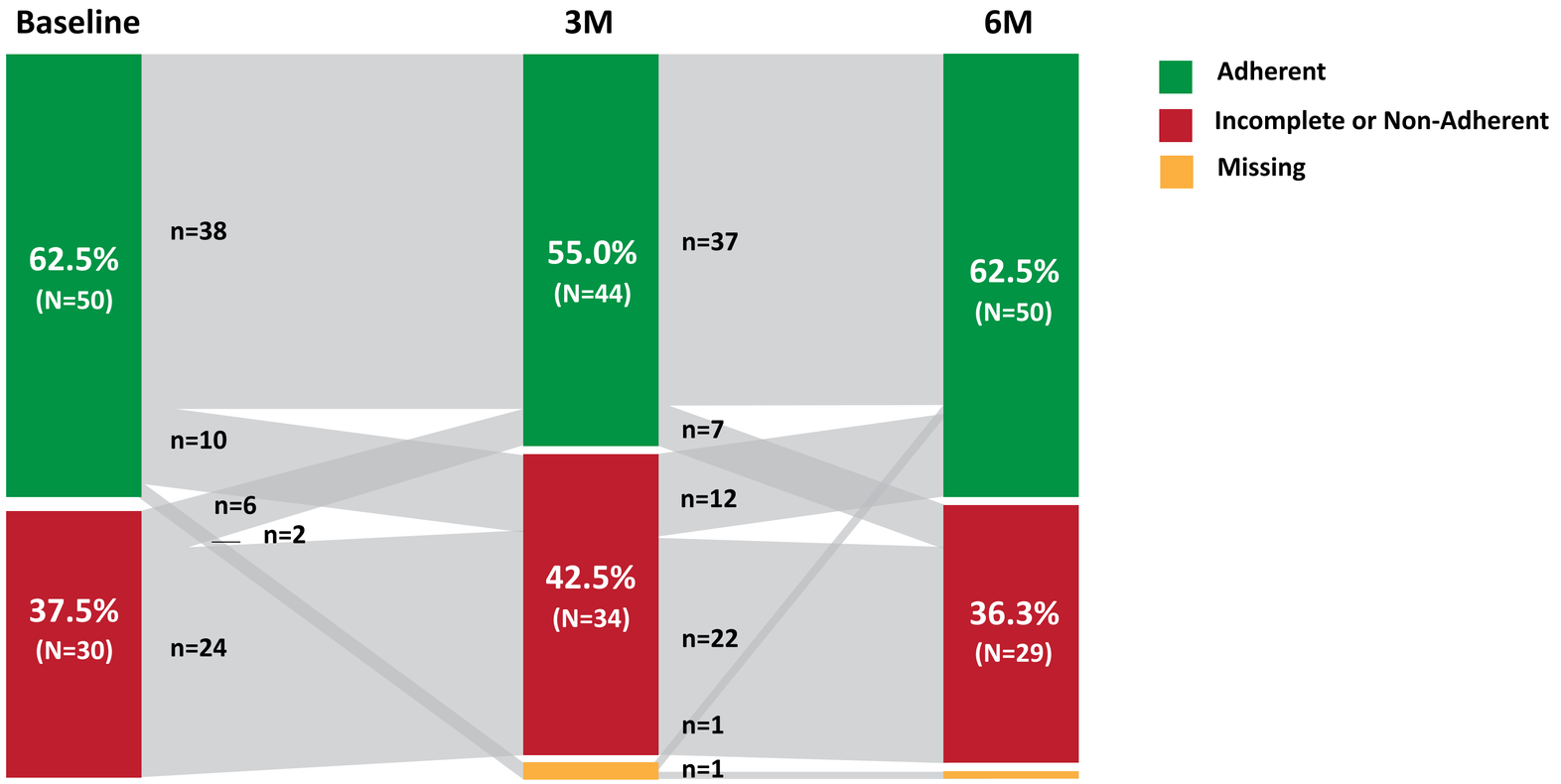
Renal Denervation: 66%
Sham Procedure: 33%

P<0.001

Data presented at euroPCR – RADIANCE SOLO

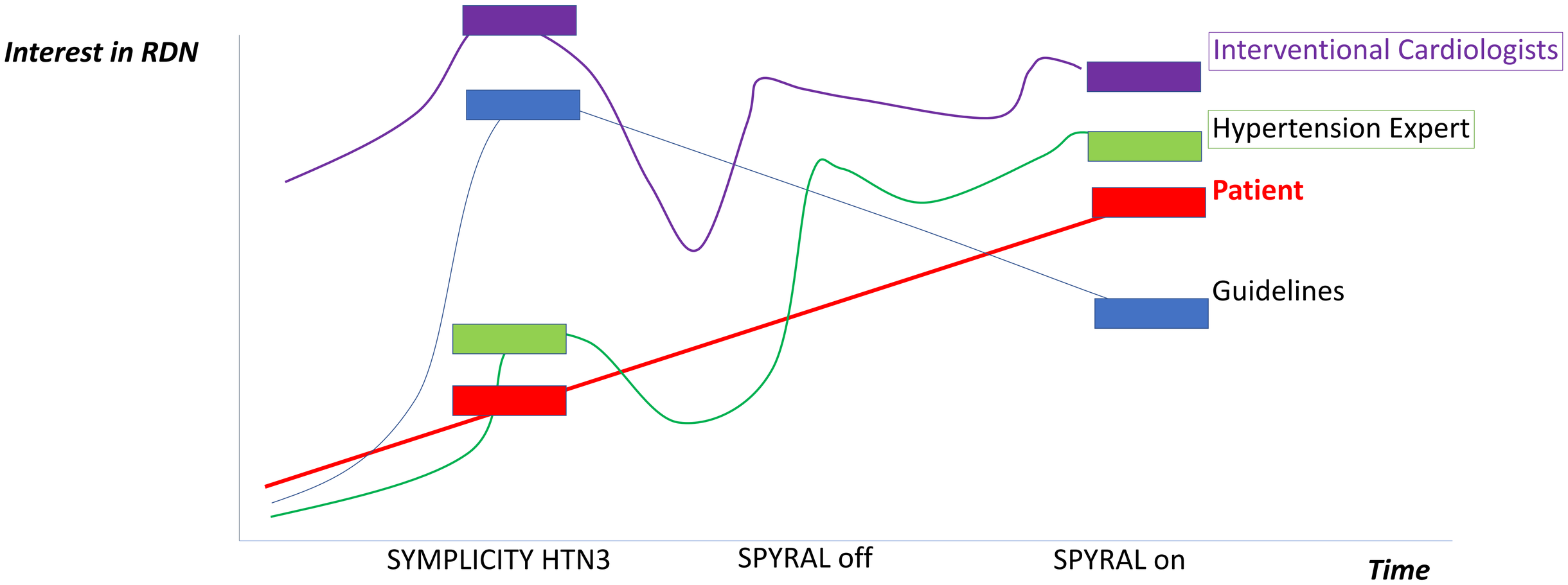
SPYRAL HTN – ON MED

Medication Adherence



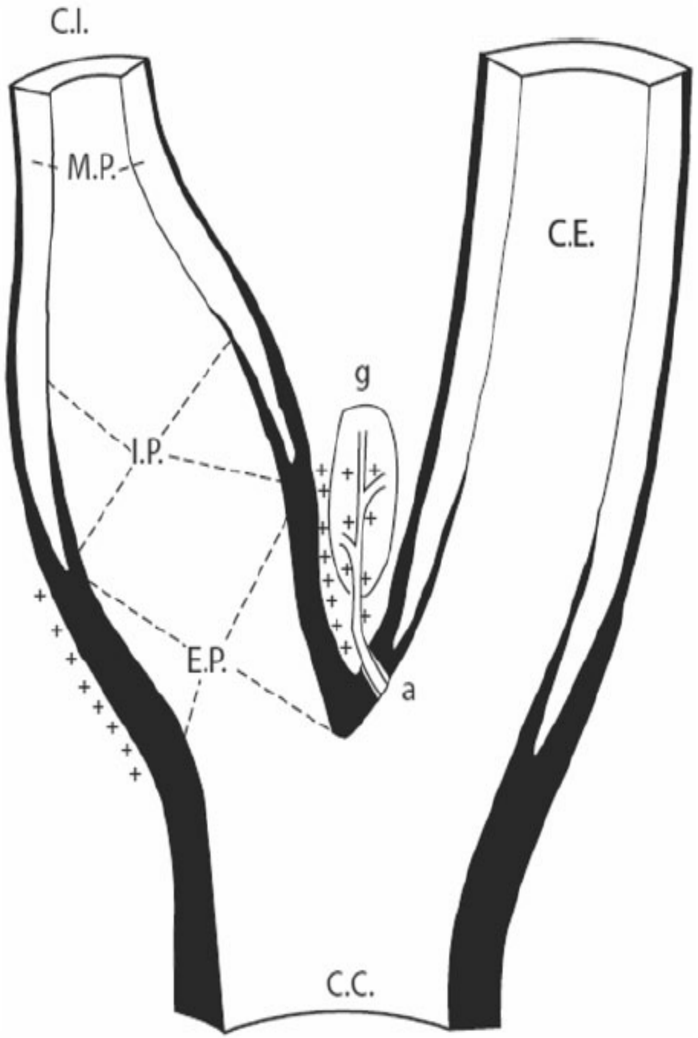
Drug testing of urine and serum by tandem HPLC and mass spectroscopy. Medication adherence defined as detectable levels of all prescribed antihypertensive medications at each follow-up visit and includes cases in which an extra antihypertensive medication was also detected.

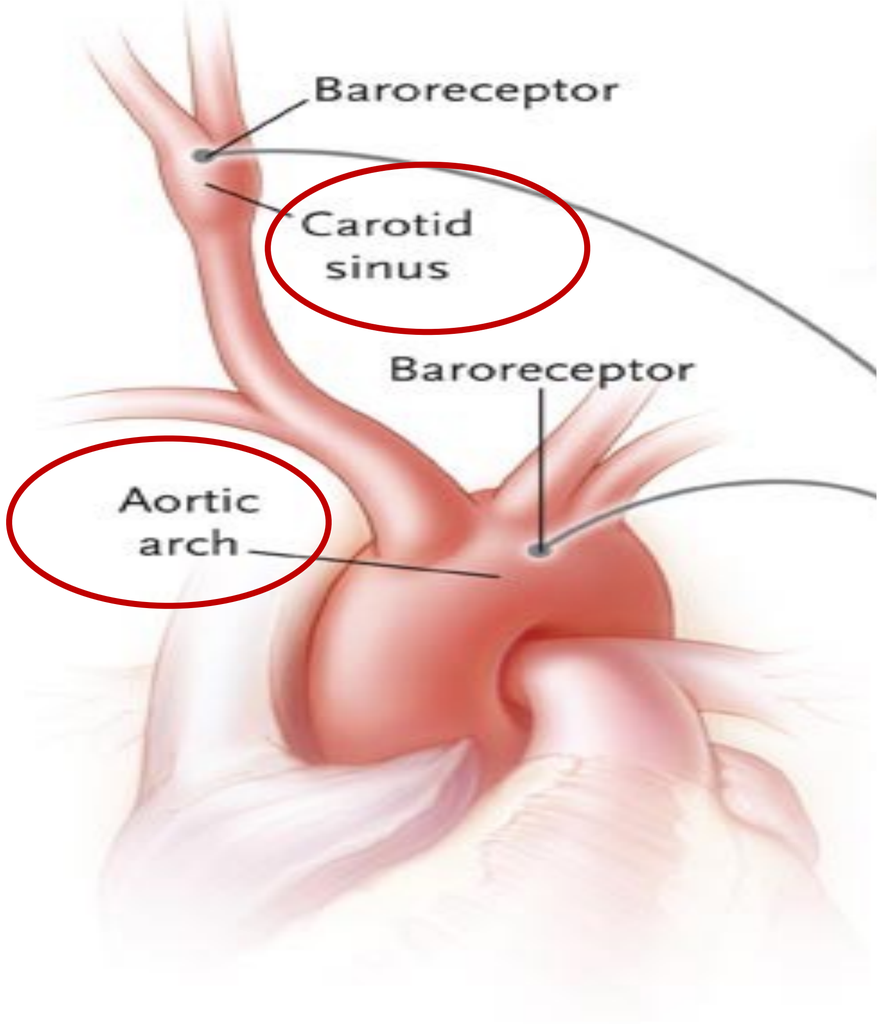
Hope for guidelines Hype for science



Target : the Baroreflex

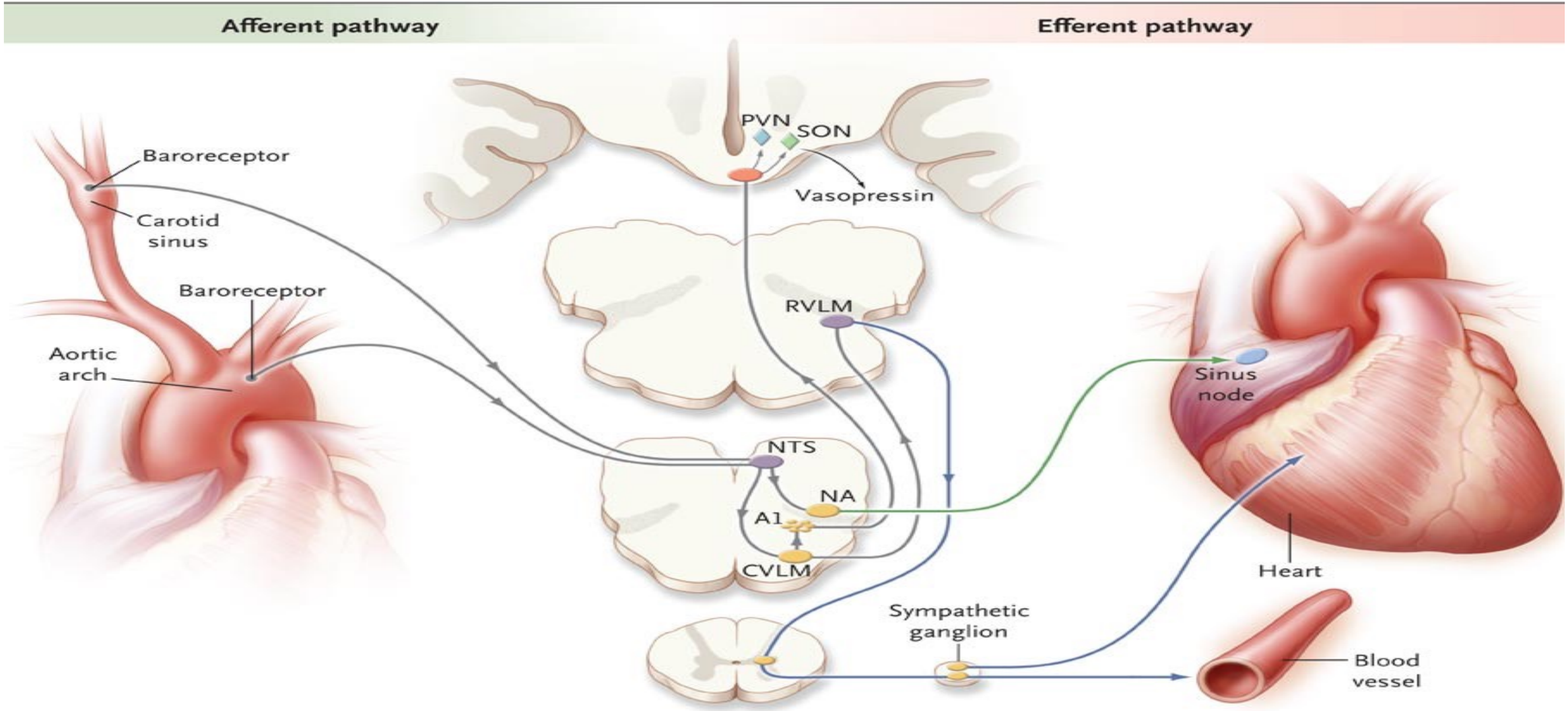
Baroreflex Physiology





Freeman R. N Engl J Med 2008;358:615-624

What happens when BP increases ?

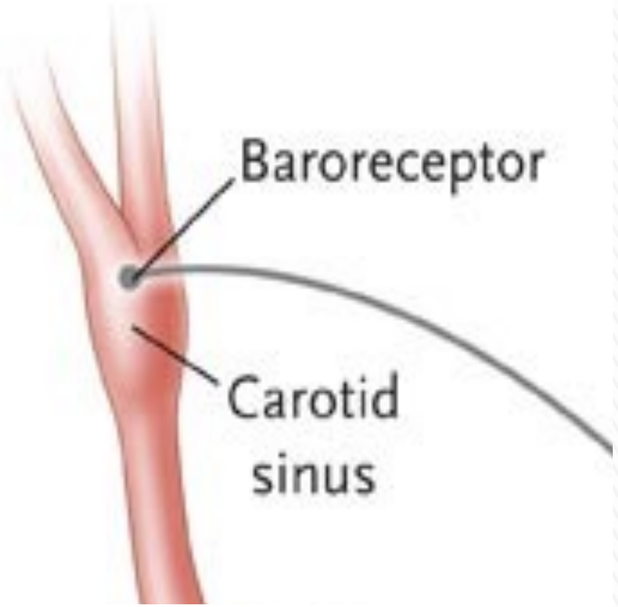


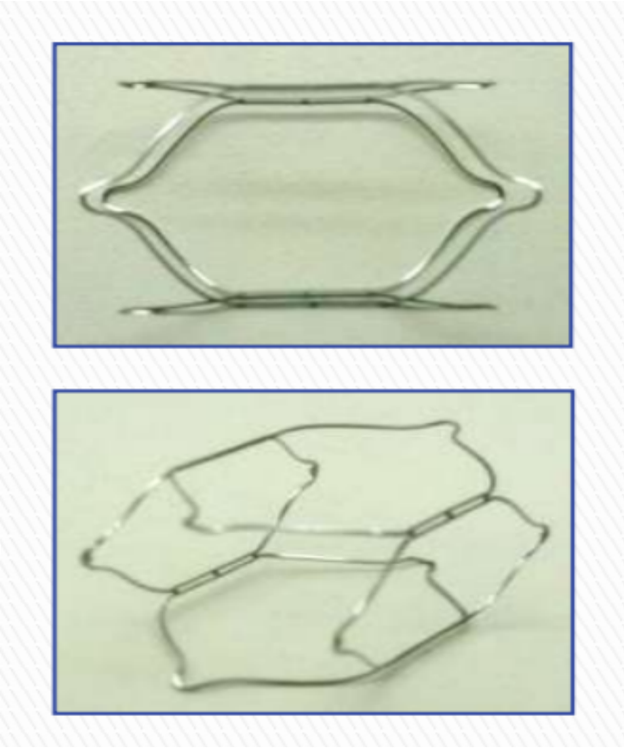
How to play with the Baroreflex ?

- Barostenting

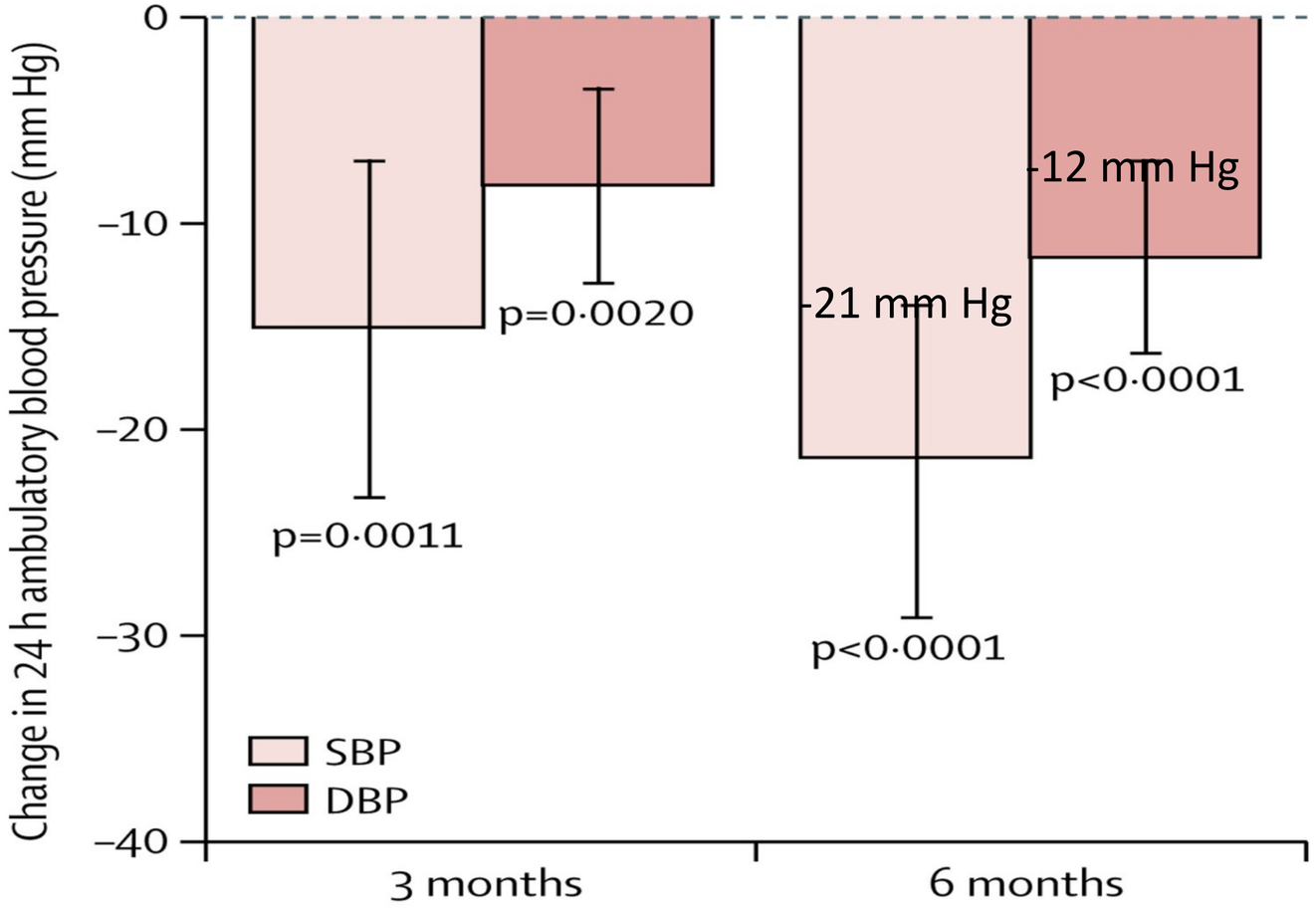
- Baropacing
  - Carotid site
  - Aortic site

Barostenting or Carotid Bulb Modifier: Site of action and Material





ABPM
Baseline 166/100 mm Hg



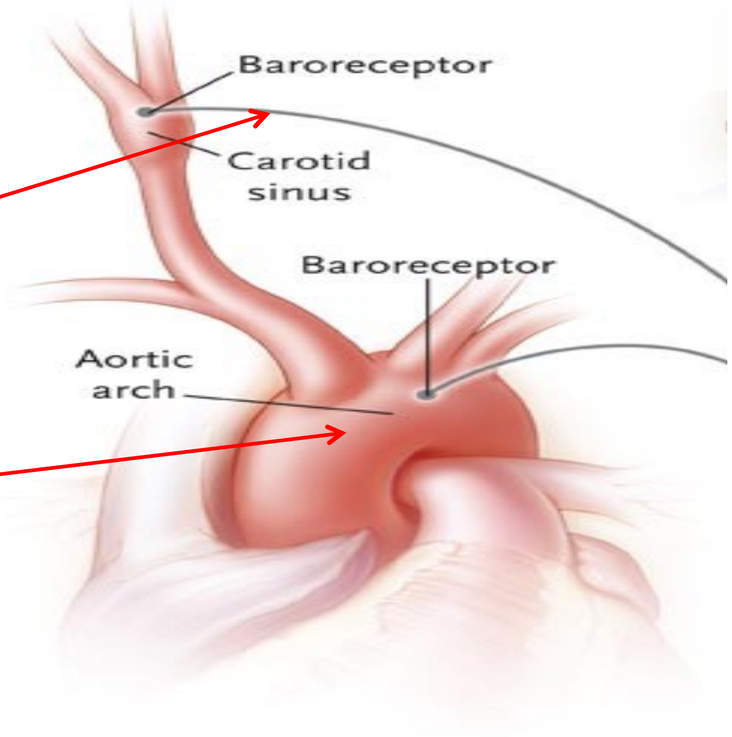
	3 months	6 months
Baseline SBP (mm Hg)	166	166
Baseline DBP (mm Hg)	100	100

Spieri ng et al. Lancet . Volume 390, No. 10113, p2655–2661, 16 December 2017

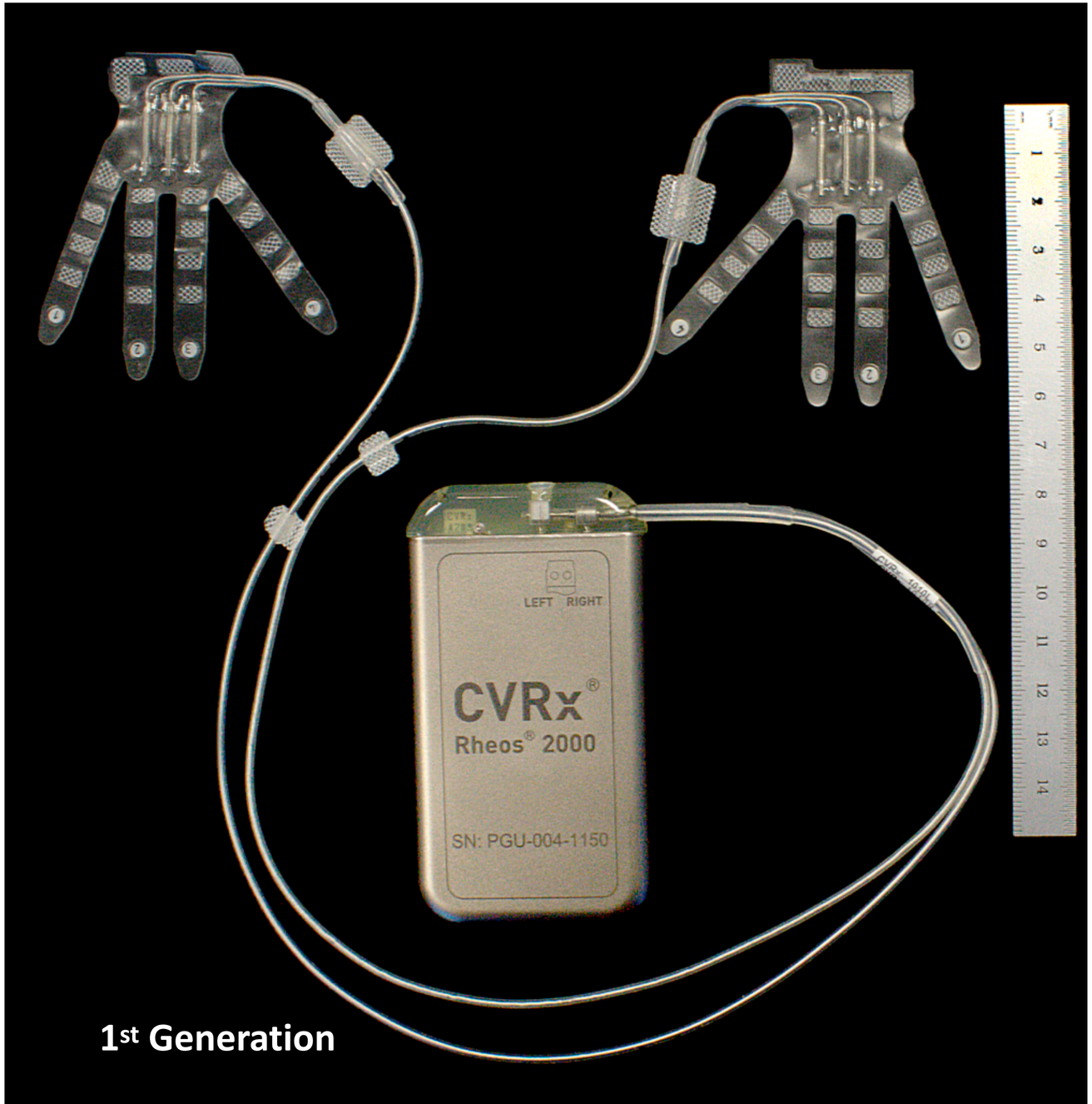
How to play with the Baroreflex ?
Site of action

- Barostenting

- Baropacing
  - Carotid site
    - Extravascular stimulation
  - Aortic site
    - Intravascular stimulation



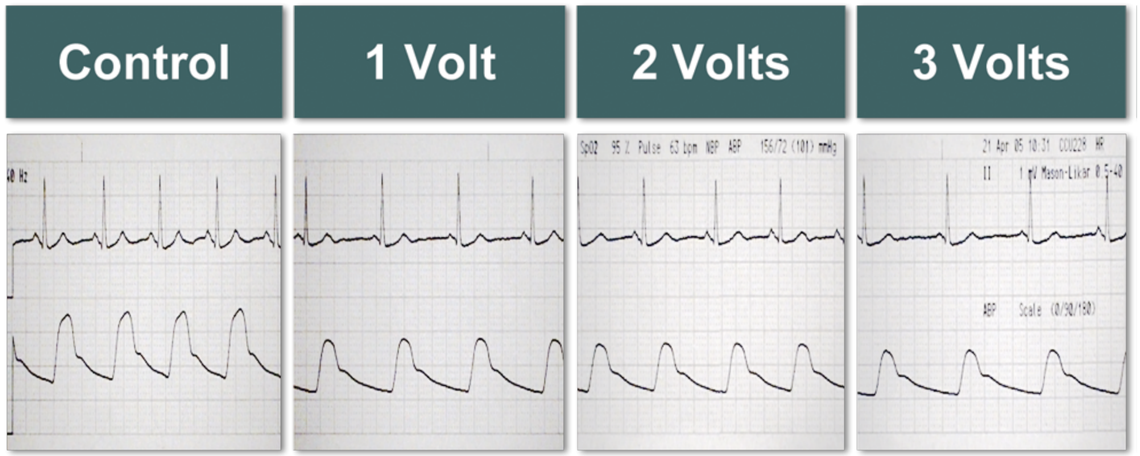
Rheos™



Acute Effects of Baroreflex Activation

- BRASS :
  - proof of the concept study,
  - dose dependent BP reduction.

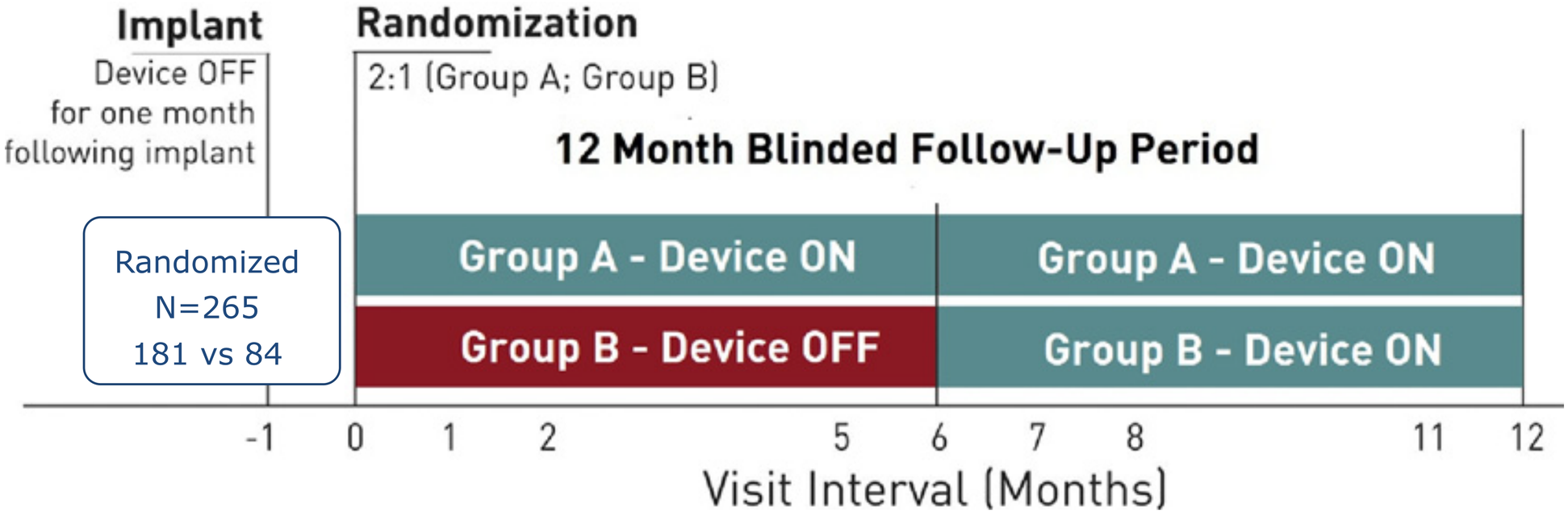
63 yo female, 1 day after device implant



	Control	1 Volt	2 Volts	3 Volts
Heart Rate bpm	71	56	58	50
Blood Pressure mmHg	210 / 96	168 / 73	156 / 72	144 / 66

~ 4 min

Rheos Trial



J Am Coll Cardiol. 2011; 58:765-73

Efficacy and safety

5 pre-specified co-primary endpoints

1. Acute efficacy
   NS
2. Sustained efficacy on BP control
   Significant
3. Procedural safety
   Comparable to AICD or Pacemaker procedure
4. BAT safety
   Early treatment reduces complication.
5. Device safety
   Higher rate of complication +++++

Summary of Adverse Events

Procedural	68 (25.5)
Surgical complication	13 (4.8)
Nerve injury with residual deficit	13 (4.8)
Transient nerve injury	12 (4.4)
Respiratory complication	7 (2.6)
Wound complication	7 (2.6)
BAT	
Hypertensive crisis (Group A)	9 (5.0)
Hypertensive crisis (Group B)	7 (8.3)
Device	34 (12.8)
Hypertension-related stroke	6 (2.3)

J Am Coll Cardiol. 2011; 58:765-73

From First to Second Generation Device

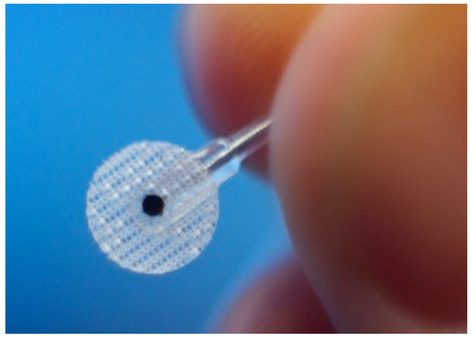
1 side

1 electrode

1 inch incision

1 hour procedure

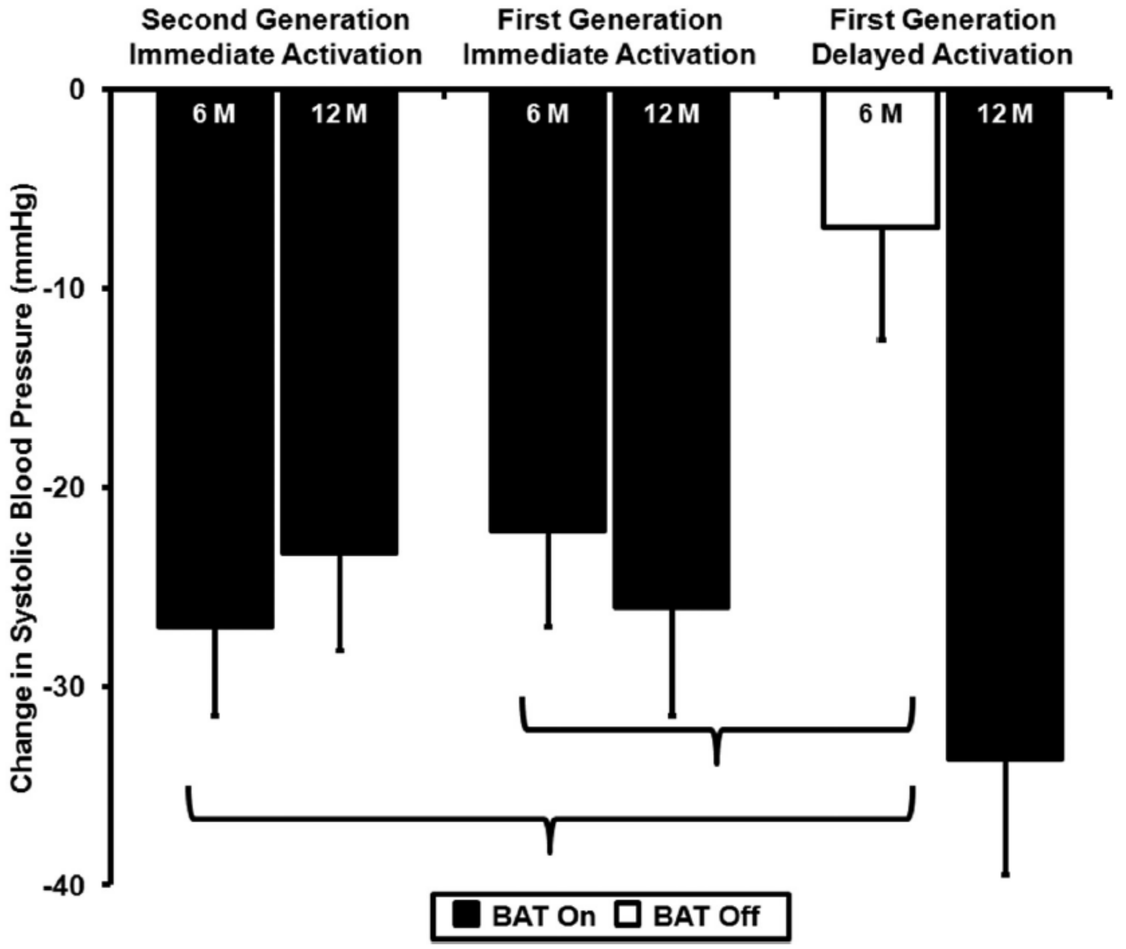
1 hospital day



Research Article

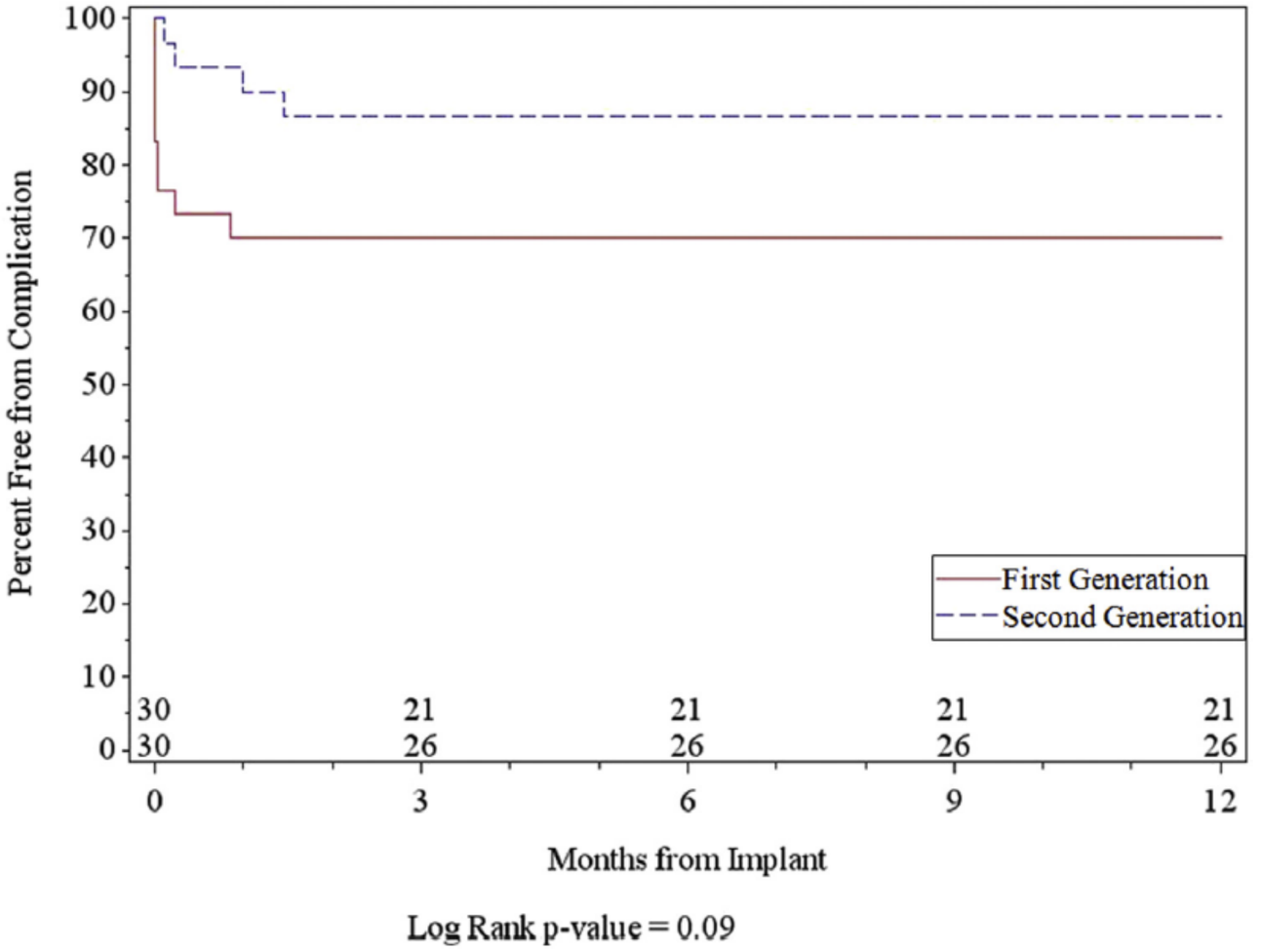
An exploratory propensity score matched comparison of second-generation and first-generation baroreflex activation therapy systems

Rolf Wachter, MD[a,*], Marcel Halbach, MD[b], George L. Bakris, MD[c],



Journal of the American Society of Hypertension 11(2) (2017) 81–91

Safety of the 2nd Generation Device



Journal of the American Society of Hypertension 11(2) (2017) 81–91

JACC: HEART FAILURE VOL. 3, NO. 6, 2015
JUNE 2015:487–96

Baroreflex Activation Therapy for the Treatment of Heart Failure With a Reduced Ejection Fraction

ABSTRACT

OBJECTIVES The objective of this clinical trial was to assess t

BACKGROUND Increased sympathetic and decreased parasym
toms and disease progression. Baroreflex activation therapy (BA
outflow and increased parasympathetic activity.

METHODS Patients with New York Heart Association (NYHA)
chronic stable guideline-directed medical therapy (GDMT) wer
Europe. They were randomly assigned to receive ongoing GD
(treatment group) for 6 months. The primary safety end poi
neurological and cardiovascular events. The primary efficacy
quality-of-life score, and 6-minute hall walk distance.

RESULTS One hundred forty-six patients were randomize
neurological and cardiovascular event-free rate was 97.2%
BAT, compared with control group patients, experienced in
1.5 ± 13.2 m; $p = 0.004$), quality-of-life score ($-17.4 \pm 2.$
class ranking ($p = 0.002$ for change in distribution). BAT
($p = 0.02$) and was associated with a trend toward fewe

CONCLUSIONS BAT is safe and improves functional status, quality of
uretic peptide, and possibly the burden of heart failure hospitalizations in patients with GDMT-treated
III HF. (Barostim Neo System in the Treatment of Heart Failure; NCT01471860; Barostim HOPE4HF [Hope for Heart Failure]
Study; NCT01720160) (J Am Coll Cardiol HF 2015;3:487–96) © 2015 by the American College of Cardiology Foundation.

EUROPEAN SOCIETY OF CARDIOLOGY

European Journal of Heart Failure (2015)
doi:10.1002/ejhf.299

Baroreflex activation therapy for the treatment of heart failure with a reduced ejection fraction: safety and efficacy in patients with and without cardiac resynchronization therapy

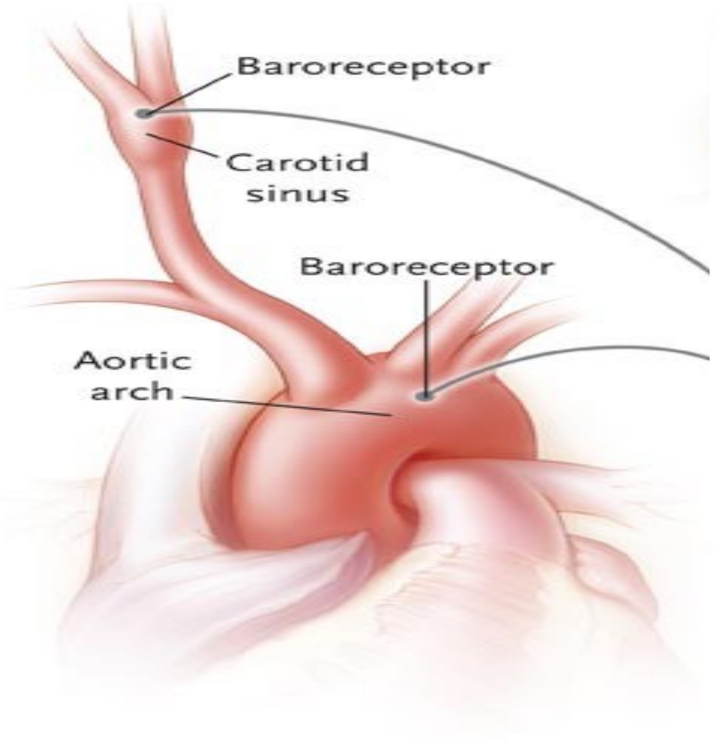
Michael R. Zile[1]*, William T. Abraham[2], Fred A. Weaver[3], Christian Butter[4], Anique Ducharme[5], Marcel Halbach[6], Didier Klug[7], Eric G. Lovett[8], Jochen Müller-Ehmsen[9], Jill E. Schafer[10], Michele Senni[11], Vijay Swarup[12], Rolf Wachter[13], and William C. Little[14]

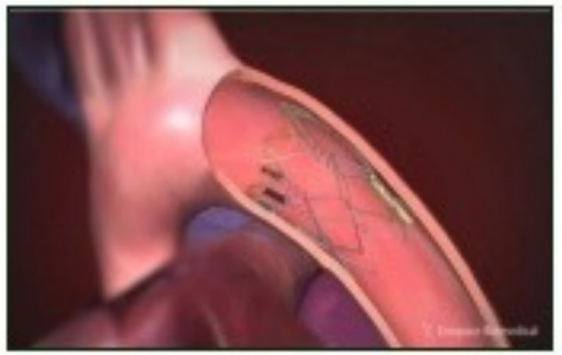
[1]Division of Cardiology, Department of Medicine, Medical University of South Carolina, 114 Doughty Street, Thurmond/Gazes, 323, Charleston, SC 29425, USA and Ralph H. Johnson Department of Veterans Affairs Medical Center, Charleston, SC, USA; [2]Division of Cardiovascular Medicine, The Ohio State University, Columbus, OH, USA; [3]Division of Vascular Surgery and Endovascular Therapy, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; [4]Department of Cardiology, Immanuel Heart Center Bernau—Medical School Brandenburg, Bernau, Germany; [5]Montreal Heart Institute, University of Montréal, Montreal, Quebec, Canada; [6]Department of Internal Medicine III, University Hospital of Cologne, Cologne, Germany; [7]Department of Cardiology A, University Hospital, Lille, France; [8]Department of Research, CVRx, Inc., Minneapolis, MN, USA; [9]Department of Medicine, Asklepios Klinik Altona, Hamburg, Germany; [10]Department of Statistics, NAMSA, Inc., Minneapolis, MN, USA; [11]Cardiovascular Department, Ospedale Papa Giovanni XXIII, Bergamo, Italy; [12]Department of Electrophysiology, Arizona Heart Hospital, Phoenix, AZ, USA; [13]Clinic for Cardiology and Pneumology, University Medicine Göttingen and German Cardiovascular Research Center (DZHK), Göttingen, Germany; and [14]Division of Cardiology, University of Mississippi Medical Center, Jackson, MS, USA

Received 23 April 2015; revised 13 May 2015; accepted 14 May 2015

How to play with the Baroreflex ?
Site of action

- Aortic site
  - Intravascular stimulation

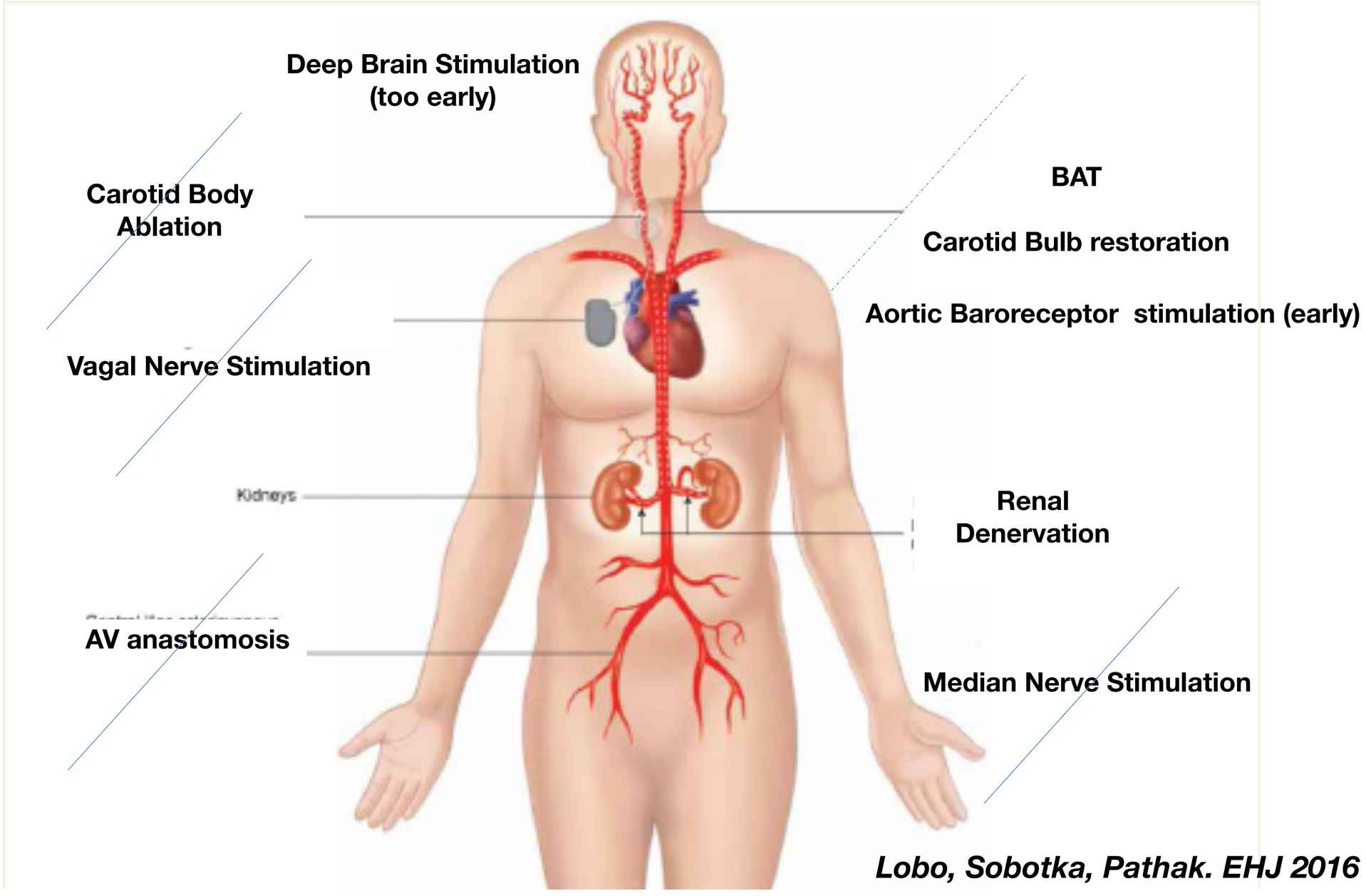




Aortic Baroreceptor

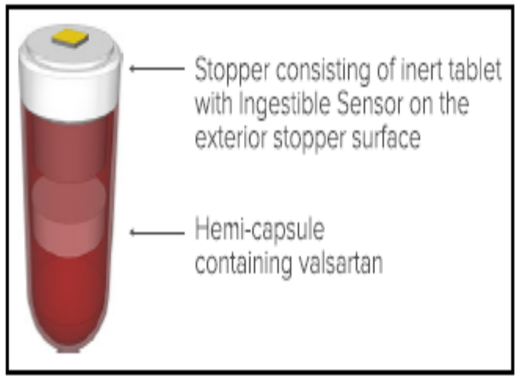
- Enopace Neurostimulator
- Scaffold with electrodes
- Driven wirelessly via handheld or subcutaneous device
- Aim to improve cardiac efficiency

Future of Devices for HTN



Lobo, Sobotka, Pathak. EHJ 2016

La révolution est en marche



Adhesive Patch
Up to 7-day wear during all activities
Confirms ingestion of Ingestible Sensor

Mobile Device
Encrypted data relayed to secure server

Patient

-Easy BP measurement
Centered approach
-Algorithm
-Network

Provider Report
Report contains:

Pattern & Regularity of medicines use
Blood Pressure
Circadian patter of rest & activity
Daily step count

Secure Servers

Provider

-Data Management

Demain ?

- Denervation renale plus tot, malade moins sévère
- Dispositif de plus en plus physiologique
- Gestion moderne de la mesure à l’analyse des données, du phenotypage à l’intervention