

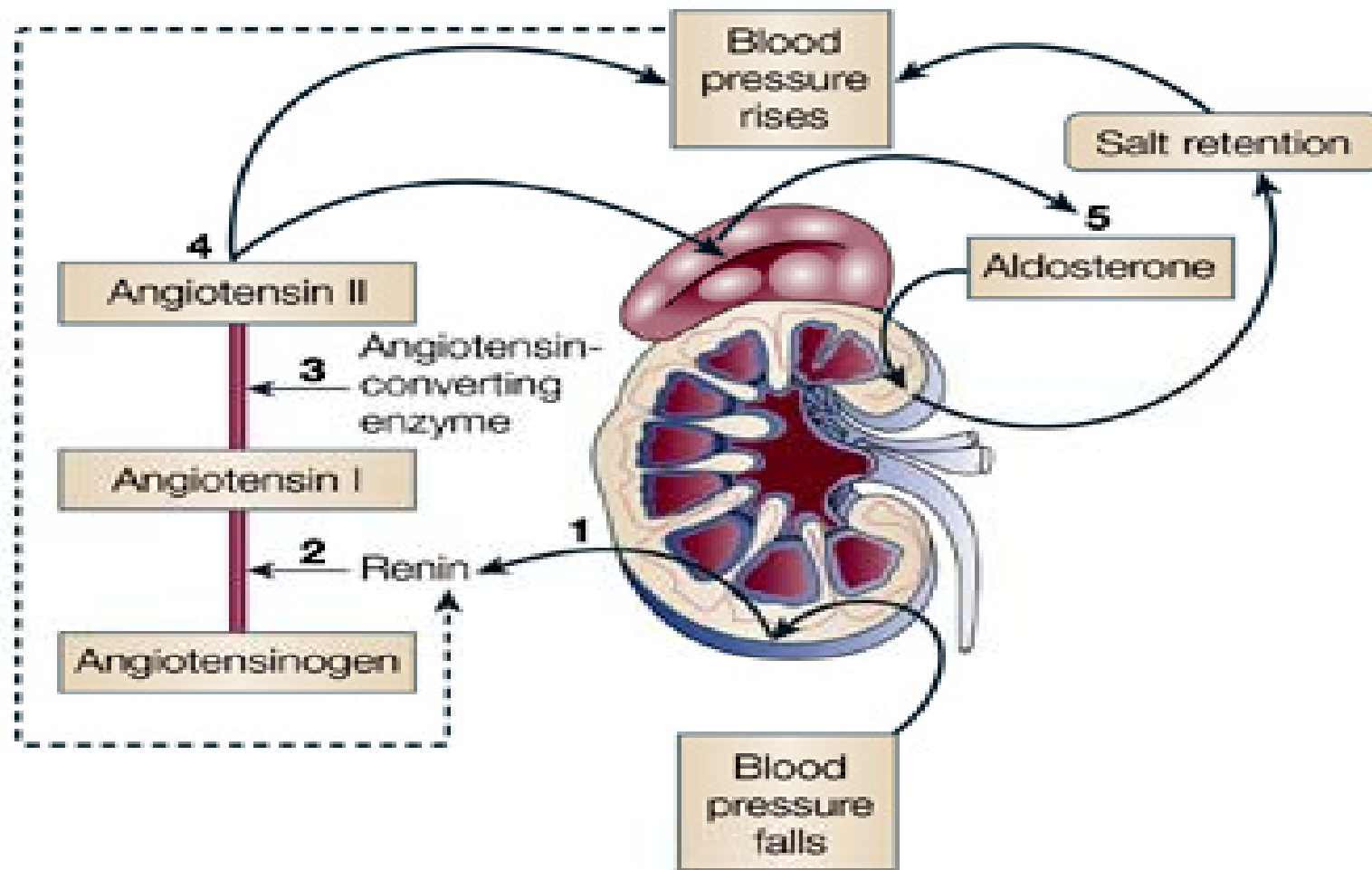
ANGIOPLASTY SUMMIT-TCTAP 2012  
Seoul, Korea, April 24-27, 2012

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Transcatheter Renal Denervation for  
Refractory Hypertension:  
Current Understanding and Future  
Projections

Horst Sievert, Ann-Kathrin Ziegler, Benjamin  
Kaltenbach, Ilona Hofmann, Undine Pittl  
CardioVascular Center Frankfurt,  
Frankfurt, Germany

# The Renin-Angiotensin-System

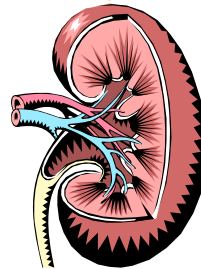


# Renal Sympathetic Efferent Nerves

Kidney as the recipient of central sympathetic signals



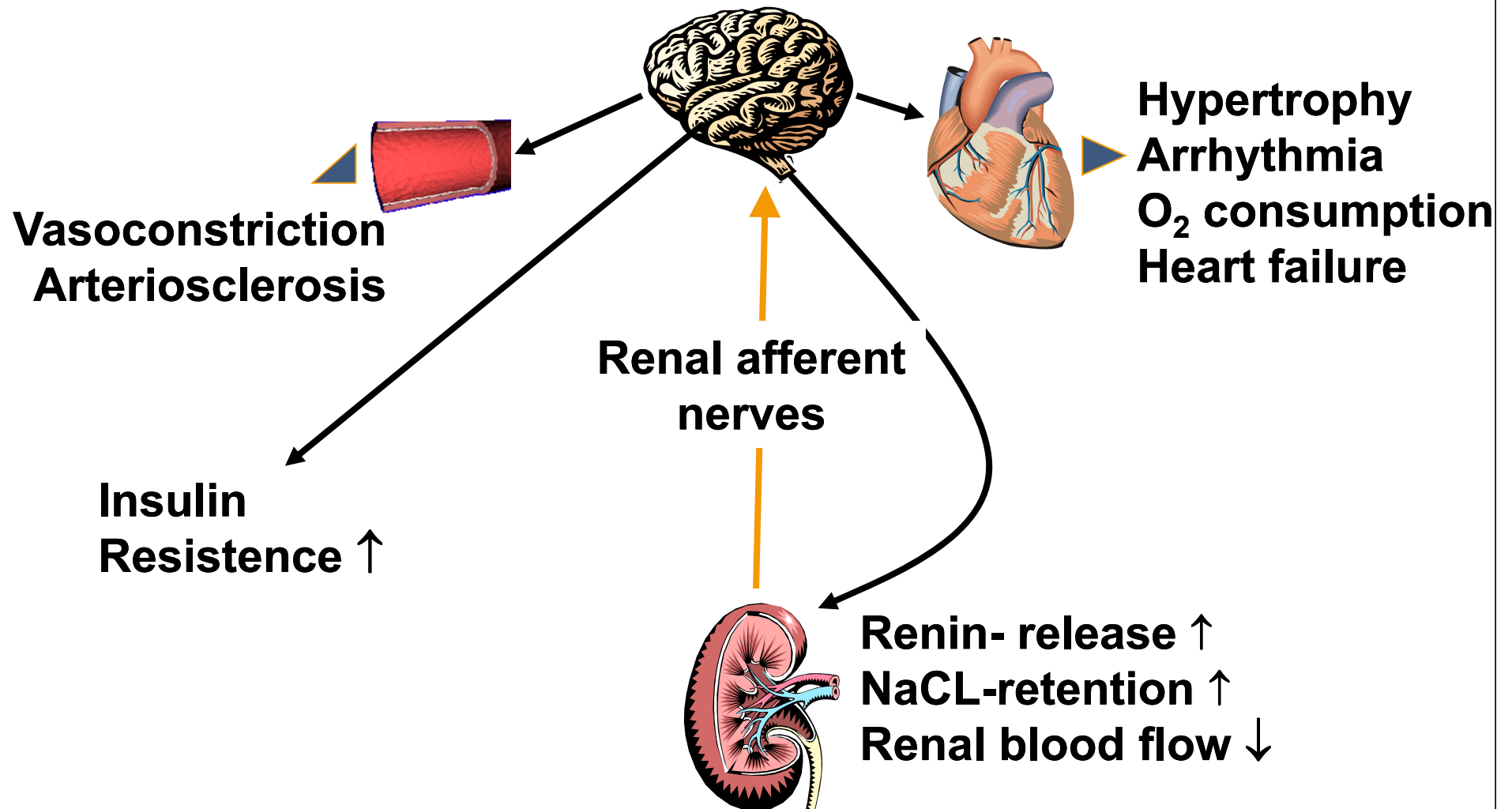
**Renal efferent nerves**



**Renin release ↑**  
**NaCl- retention ↑**  
**Renal blood flow ↓**

# Renal Afferent Nerves

Kidney as the origin of central sympathetic drive



The central sympathetic drive  
is directly influenced by the  
kidneys via afferent renal  
nerves

The interruption of these nerves  
lowers blood pressure and may  
have other beneficial effects

# Surgical Precedent of Renal Denervation: Thoracolumbar Sympathectomy

THE EFFECTS OF PROGRESSIVE SYMPATHECTOMY ON  
BLOOD PRESSURE

BRADFORD CANNON

*From the Laboratories of Physiology in the Harvard Medical School*

Received for publication March 24, 1931

THE BRITISH JOURNAL OF SURGERY

1952

SYMPATHECTOMY IN THE TREATMENT OF BENIGN  
AND MALIGNANT HYPERTENSION\*

A REVIEW OF 76 PATIENTS

By C. J. LONGLAND AND W. E. GIBB

## THE JOURNAL of the American Medical Association

*Published Under the Auspices of the Board of Trustees*

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AUGUST 15, 1953

### SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

*Reginald H. Smithwick, M.D.*

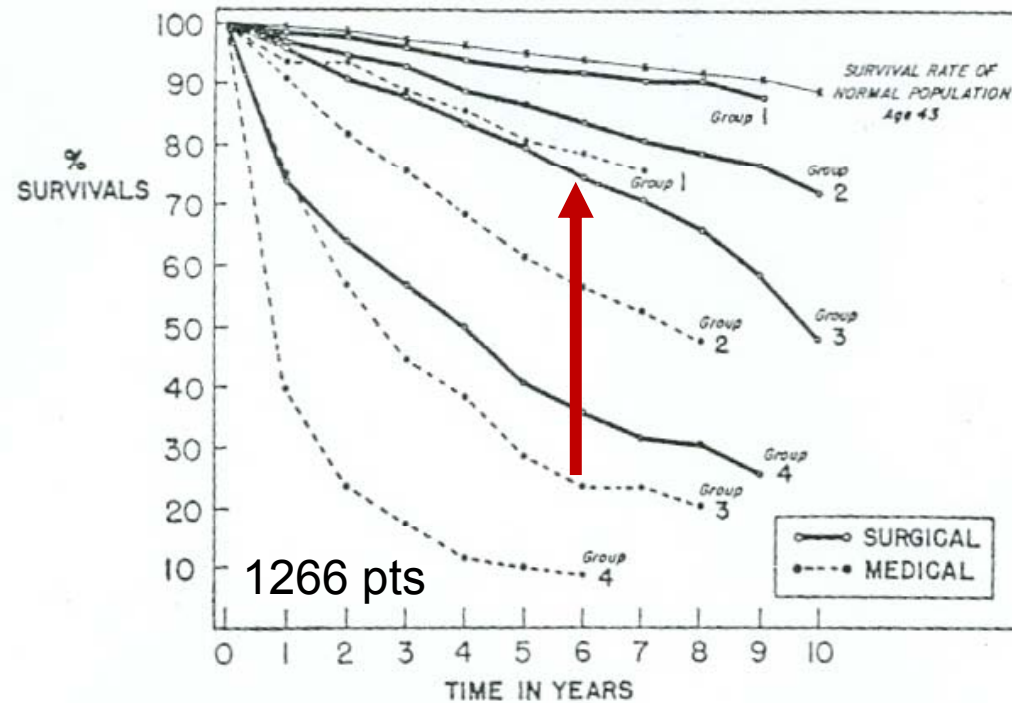
and

*Jesse E. Thompson, M.D., Boston*



Dr. Reginald H. Smithwick

# Sympathectomy in Hypertension: Effects on survival, but side effects and complications



## Denervating lower half of the body produced:

- Mortality benefit
- Inconsistent BP results
- Significant morbidity including orthostatic hypotension, bowel & bladder dysfunction

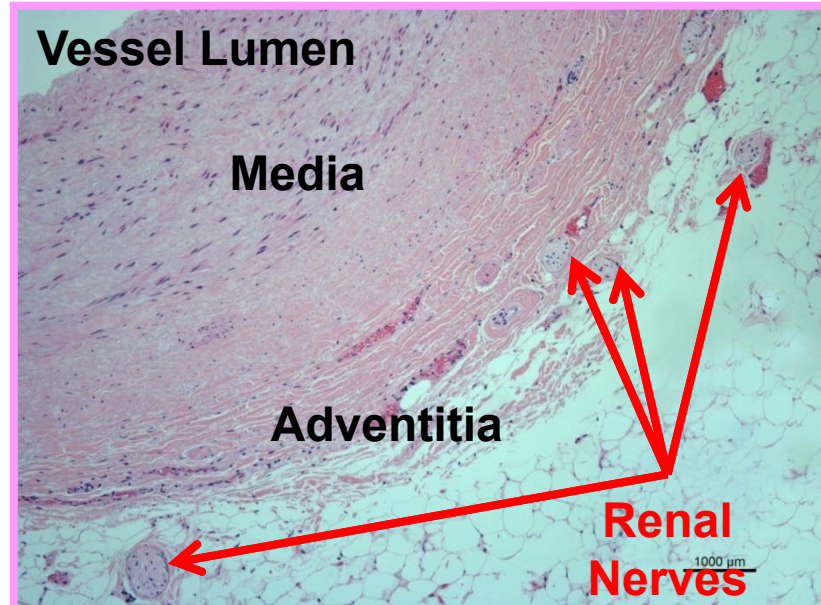
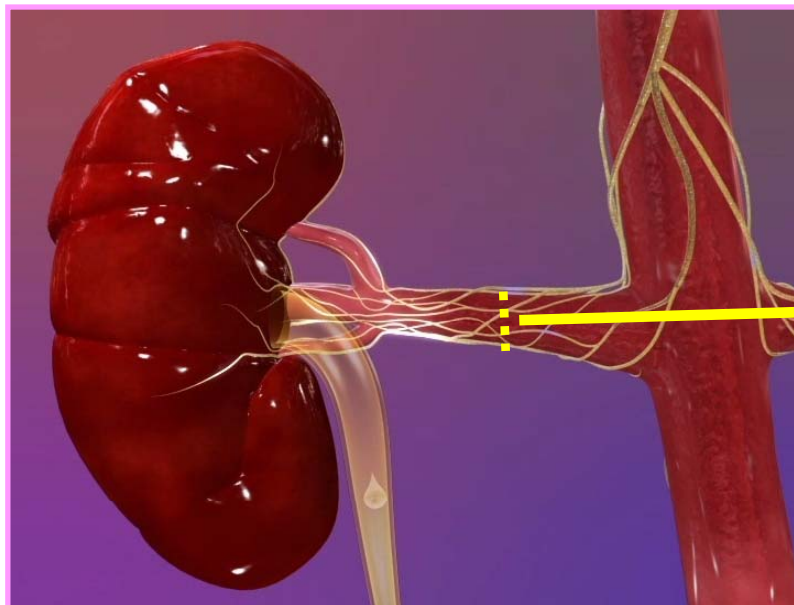
How to do this minimal  
invasively by catheter  
technique?



# The Renal Nerves

---

- Follow the renal artery to the kidney
- Primarily lie within the adventitia



# Generator

- Energy maximum 8 Watt
- It automatically switches off if
  - temperature increases too fast or too slowly
  - temperature is higher than 75 °C
  - Impedance does not decrease sufficiently

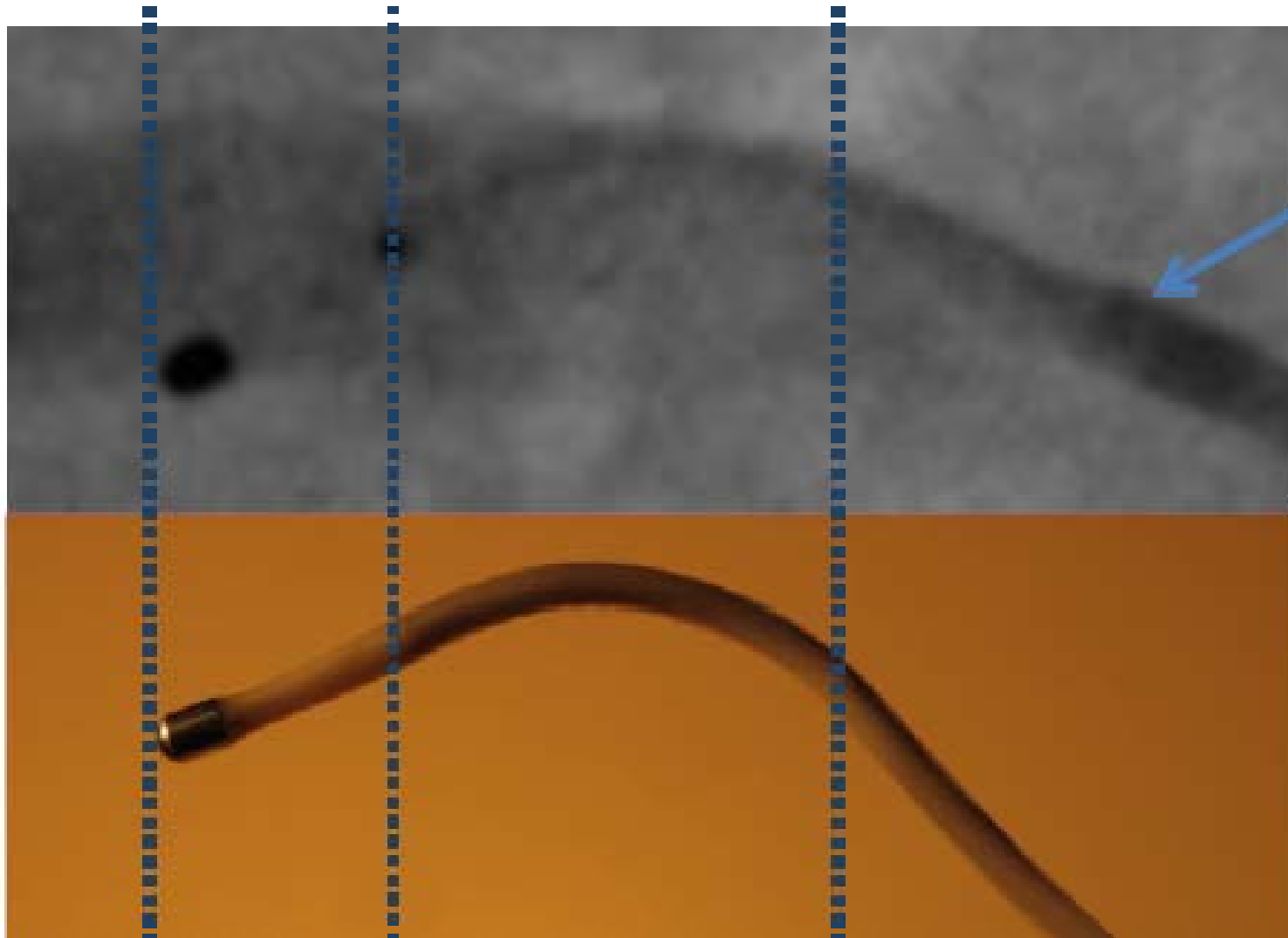


# Simplicity™ Catheter

- Radiofrequency electrode tip
- Handle allows bending of the tip and rotation
- Compatible with a 6 F guiding catheter



Tip of  
Guiding  
catheter



5mm

12mm

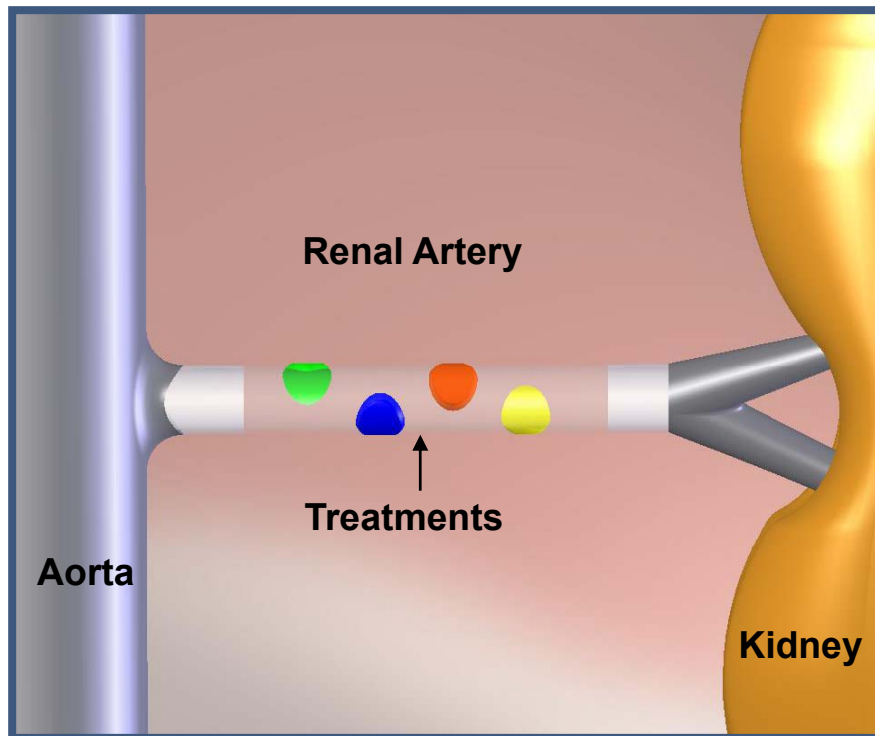
Flexible Tip  
(self-orienting)

Deflectable  
Shaft

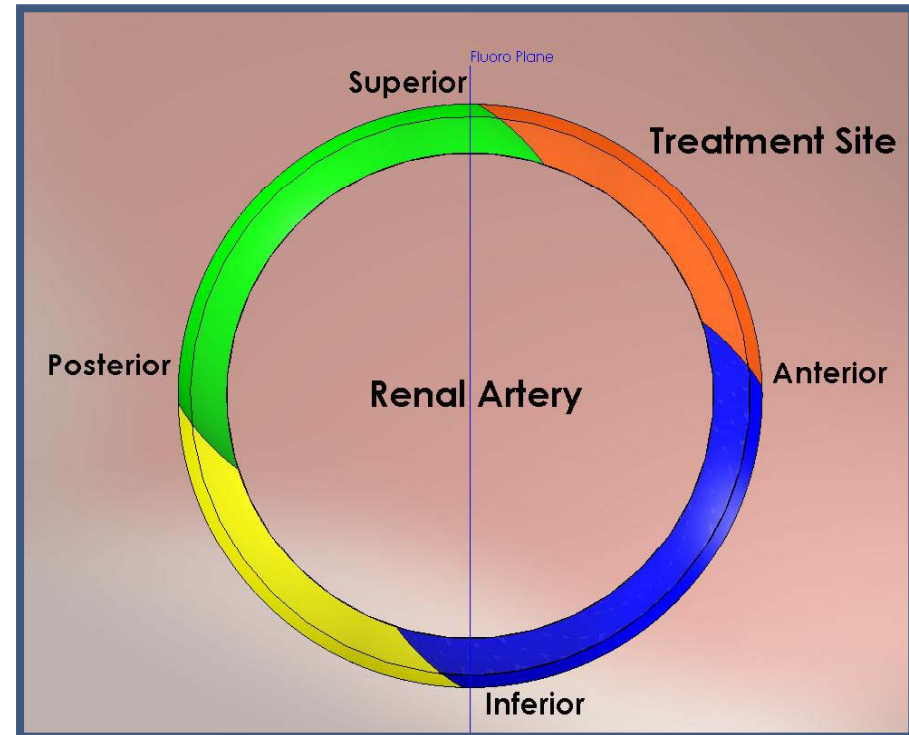
# Procedural details

- Premedication
  - Aspirin 100 mg/day (to be continued for 1 week)
  - 10-20 mg morphin + sedatives
  - 5,000 U heparin
  - Nitro i.a.
- 6 F femoral sheath
- 6 F renal guiding catheter
- Angiography of all renal arteries
- Introduce radiofrequency catheter
- 4-8 ablations, 2 min each

# Treatment Strategy



Focal ablations  
spaced along vessel



Multiple focal ablations  
↑ circumferential coverage

# Example Treatment Locations in a Right Renal Artery

Treatment #1



Treatment #4



Treatment #2



Treatment #5



Treatment #3



Treatment #6





TREND ASIA-PACIFIC  
CSI FOCUS



LIVE  
CASES

# TREND 2012 ASIA-PACIFIC

SEPTEMBER 29, 2012 | HONG KONG



Neuro-Humoral Interventions  
Catheter and Device Based Treatment of Hypertension and Heart Failure  
Transcatheter Renal Denervation

[www.csi-trend.org](http://www.csi-trend.org)

TREND Frankfurt, Germany, Frankfurt, March 1-2. 2013



**Where is the evidence?**

Symplicity HTN-1 Trial  
single arm  
with extended cohort

Symplicity HTN-2 Trial  
randomized

Symplicity HTN-3 Trial  
randomized, sham control  
ongoing

# Symlicity HTN-2

## THE LANCET

Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symlicity HTN-2 Trial): a randomised controlled trial

SymlicityHTN-2 Investigators\*

*Lancet.* 2010;376:1903-1909

- **Study design:** randomized, controlled, clinical trial
- **Patients:** 106 patients randomized 1:1 to treatment with renal denervation vs. control
- **Clinical Sites:** 24 centers in Europe, Australia, & New Zealand

# Symplicity HTN-2 Trial

## **Inclusion Criteria:**

- Office SBP  $\geq$  160 mmHg  
( $\geq$  150 mmHg with type II diabetes mellitus)
- 3+ more anti-HTN medications
- Age 18-85 years

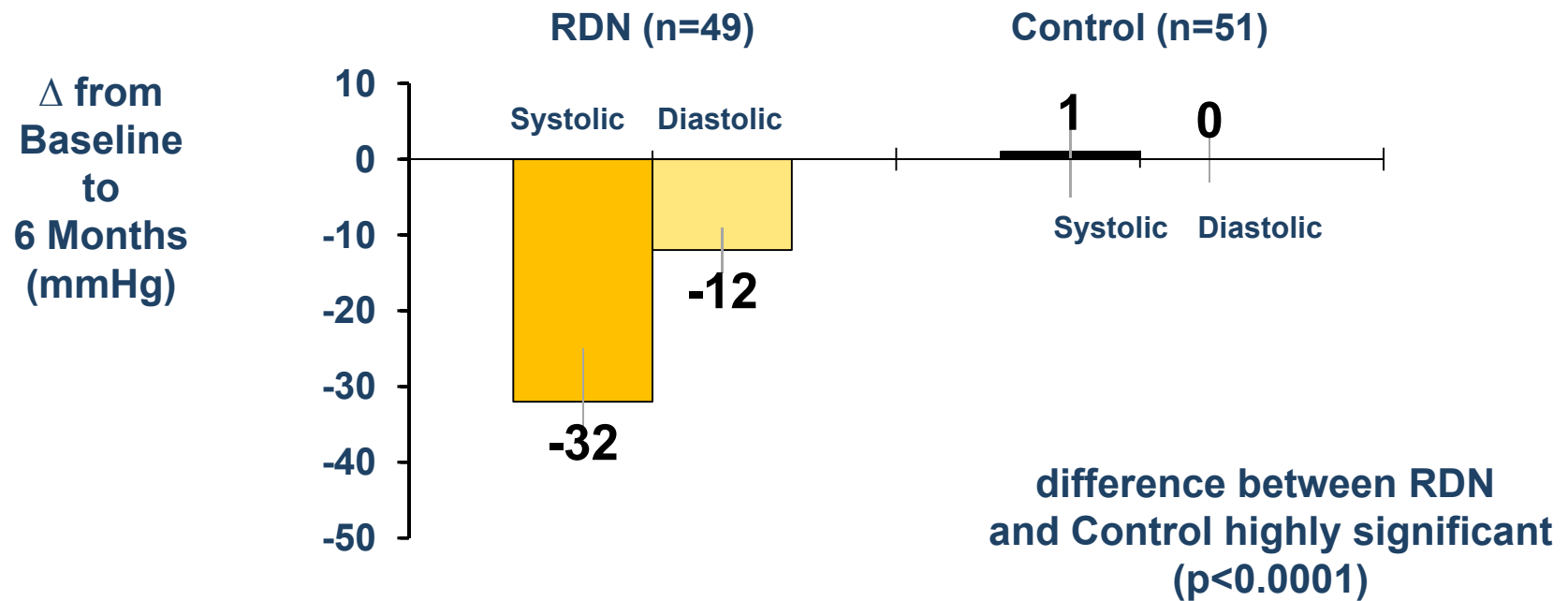
## **Exclusion Criteria:**

- Significant renal artery abnormalities or prior renal artery intervention
- eGFR  $<$  45 mL/min/1.73m<sup>2</sup> (MDRD formula)
- Type 1 diabetes mellitus
- Contraindication to MRI
- Stenotic valvular heart disease for which reduction of BP would be hazardous
- MI, unstable angina, or CVA in the prior 6 months

# Safety

- No serious device or procedure related adverse events (n=52)
- No change in renal function
- No severe hypotension or orthostasis
- Minor adverse events (all unrelated to RF)
  - 1 femoral artery pseudoaneurysm → manual compression
  - 1 post-procedural drop in BP resulting in a reduction in medication
  - 1 urinary tract infection
  - 1 prolonged hospitalization for evaluation of paraesthesias
  - 1 back pain treated with pain medications & resolved after one month
- 6-month renal imaging (n=43)
  - No vascular abnormality at any RF treatment site
  - 1 MRA indicates possible progression of a pre-existing stenosis unrelated to RF treatment (no further therapy)

# Primary Endpoint: 6-Month Office BP

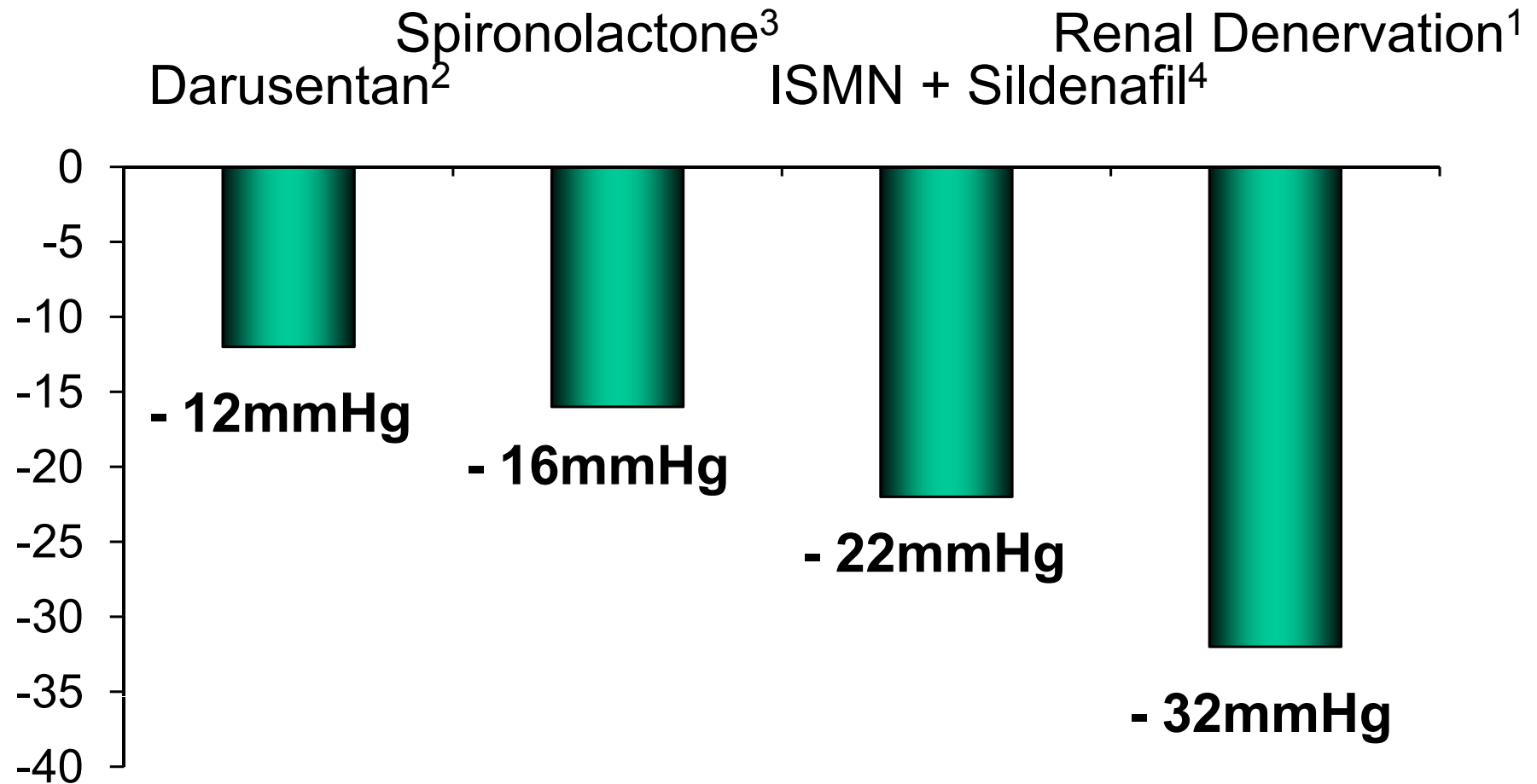


- 84% of RDN patients had  $\geq 10$  mmHg reduction in SBP
- Only 10% of RDN patients had no reduction in SBP

How does this compare  
to medical treatment?

# Randomized Trials in Resistant Hypertension

## Mean Reduction in Systolic BP



<sup>1</sup>Lancet. 2010

<sup>2</sup>Curr Hypertens Rep. 2008 Dec;10(6):429-31.

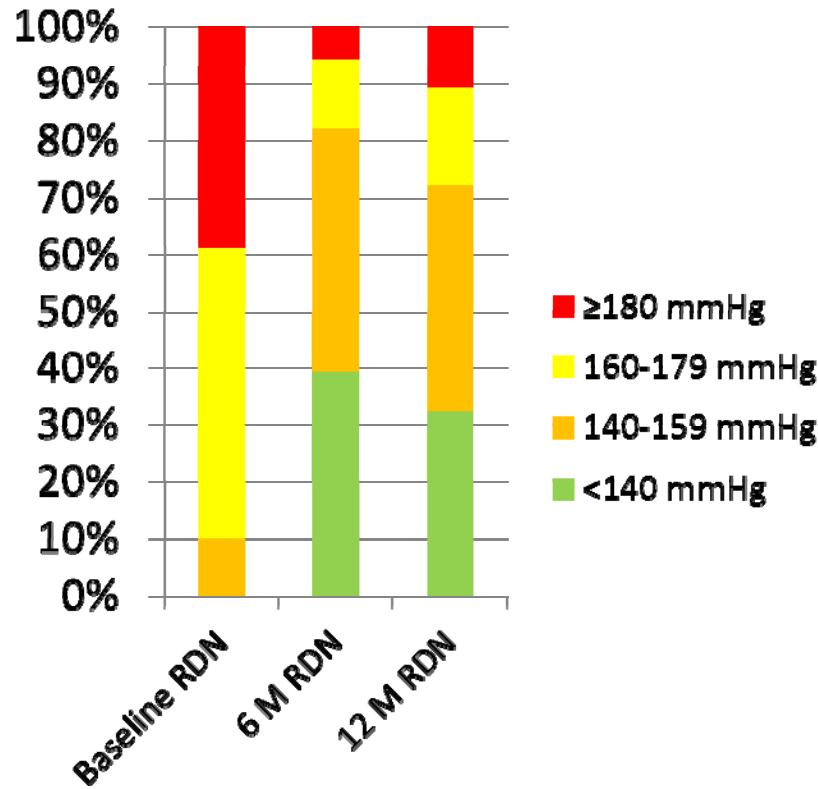
<sup>3</sup>Hypertension. 2010 Jan;55(1):147-52

<sup>4</sup>Hypertension. 2010 Jul;56(1):22-3.

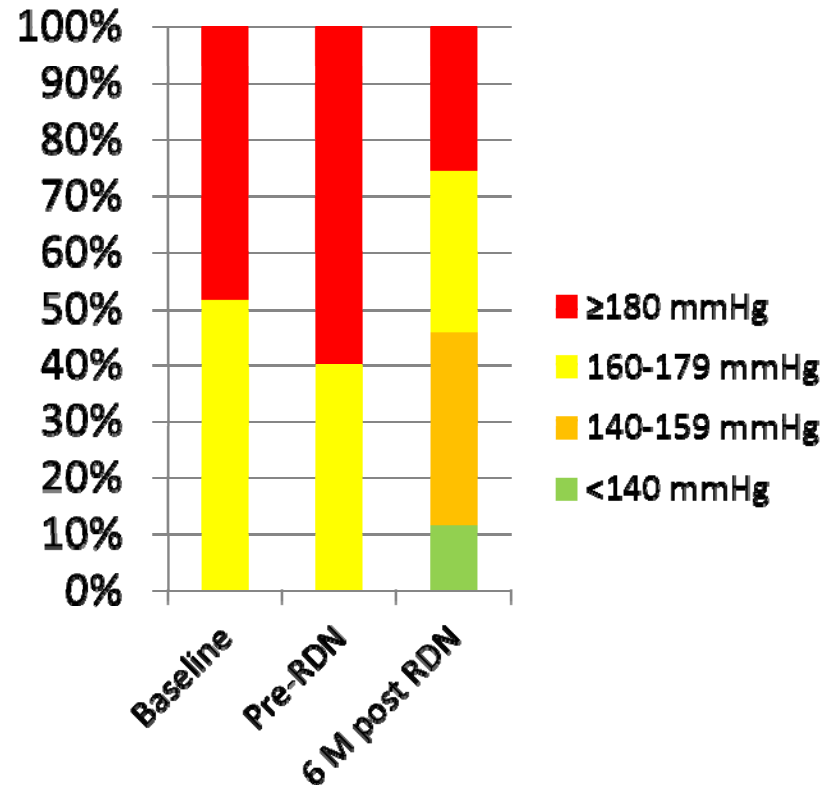


# Symplicity HTN-2 Trial – Distribution of Office SBP Post-RDN

## Treated with RDN



## Crossover group Treated after 6 M follow up



# Subgroup analyses

- Age
- Gender
- Diabetes

—————→ no differences

**Any late complications?**

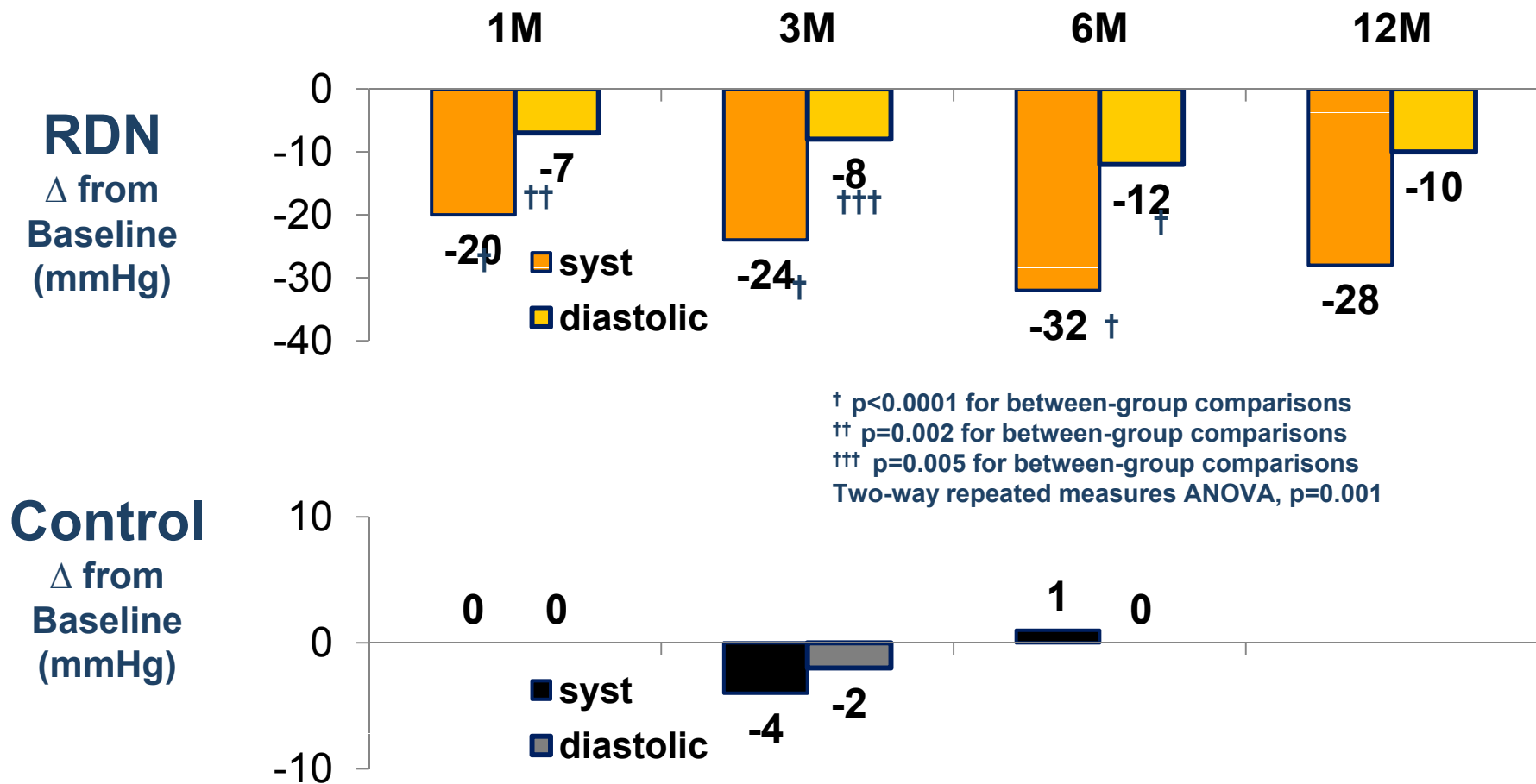
# HTN-1: Chronic Safety Out to 3 Years

- One progression of a pre-existing stenosis unrelated to RF treatment (stented without further sequelae)
- One new moderate stenosis which was not hemodynamically relevant and no treatment
- 3 deaths within the follow-up period; all unrelated to the device or therapy
- No hypotensive events that required hospitalization
- There were no observed changes in mean electrolytes or eGFR

What is the time course of the effect?

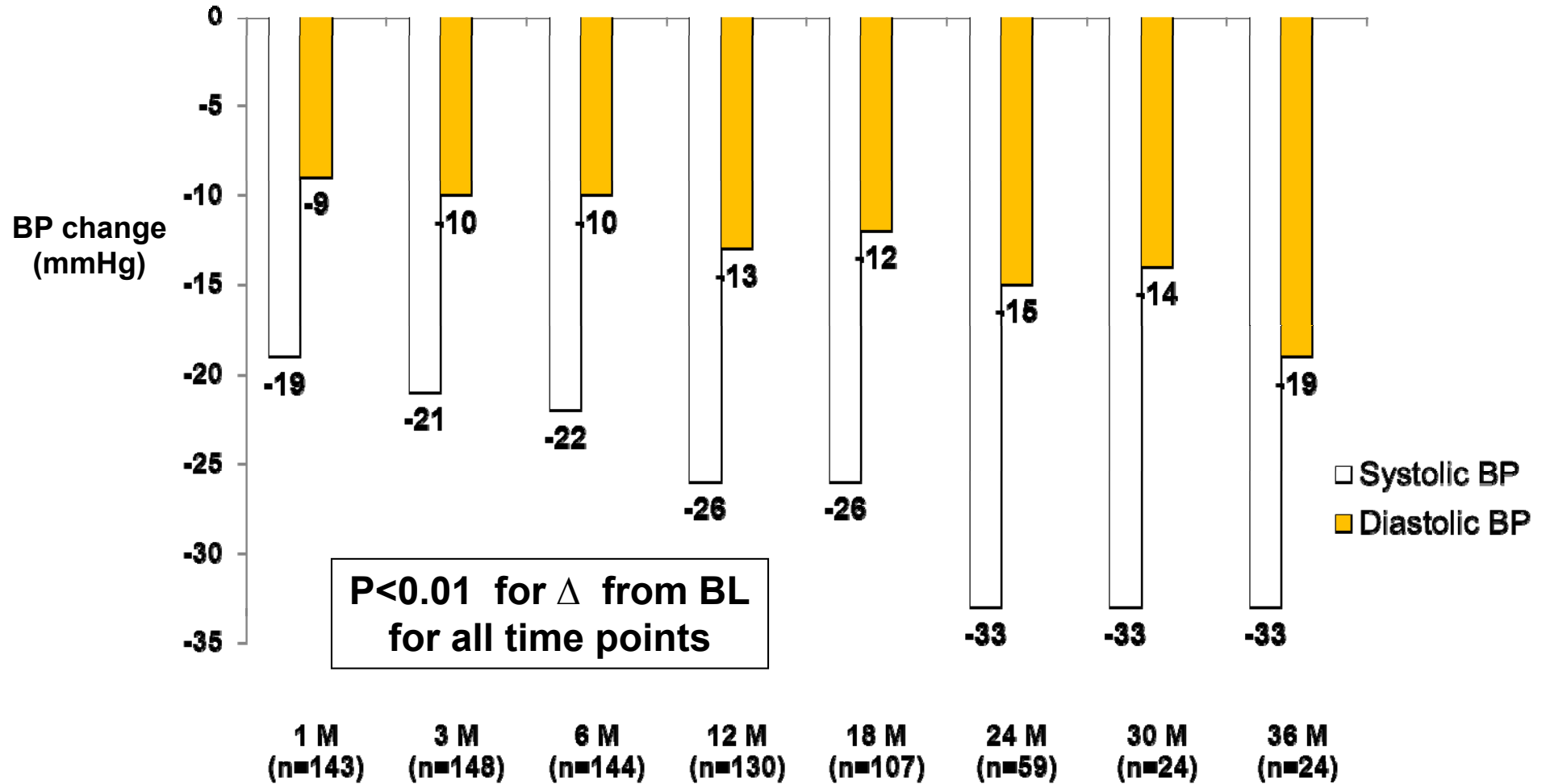
# Symplicity HTN-2

## Time Course of Office BP Change



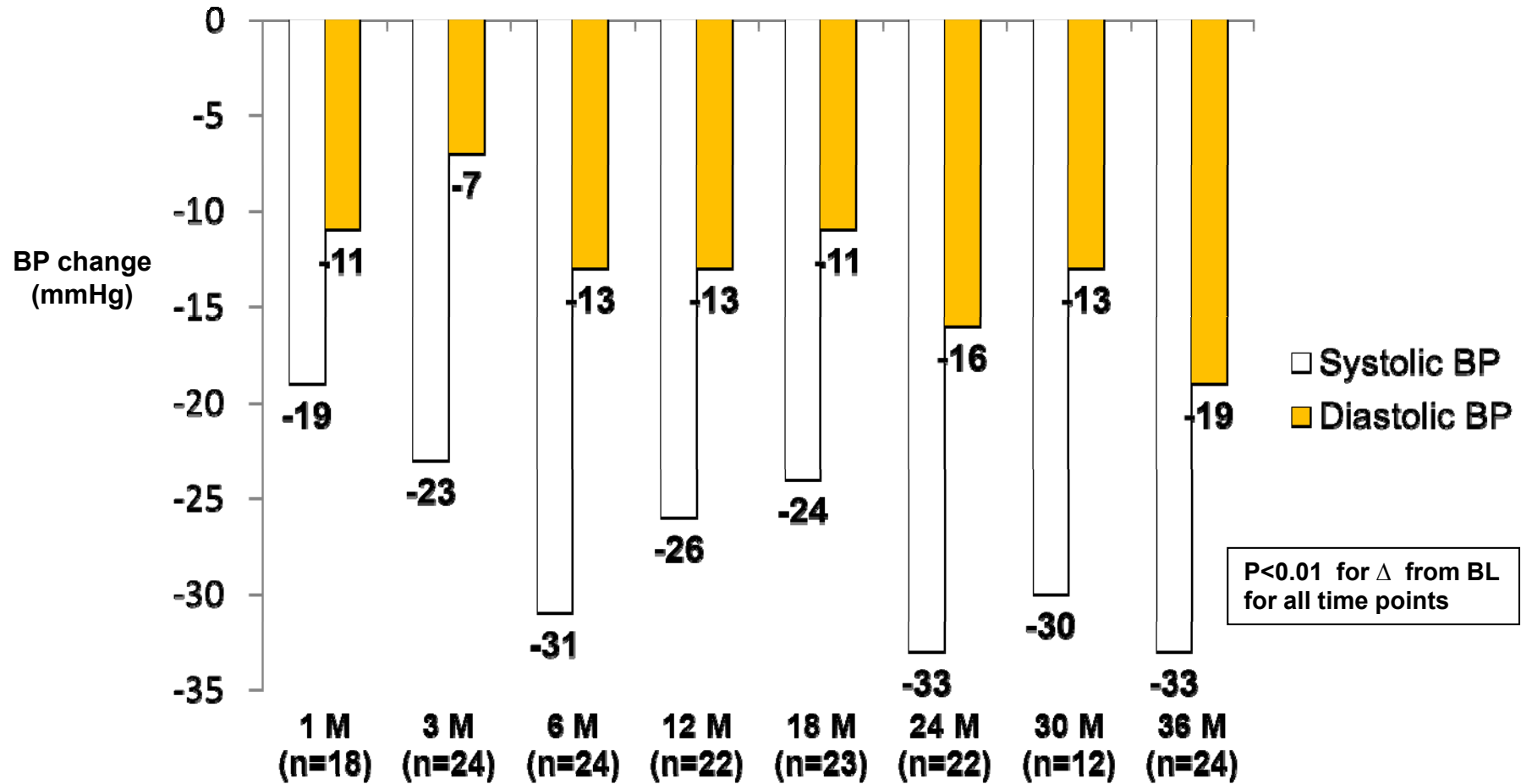
# Symplicity HTN-1

## Significant, Sustained BP Reduction through 3 yrs



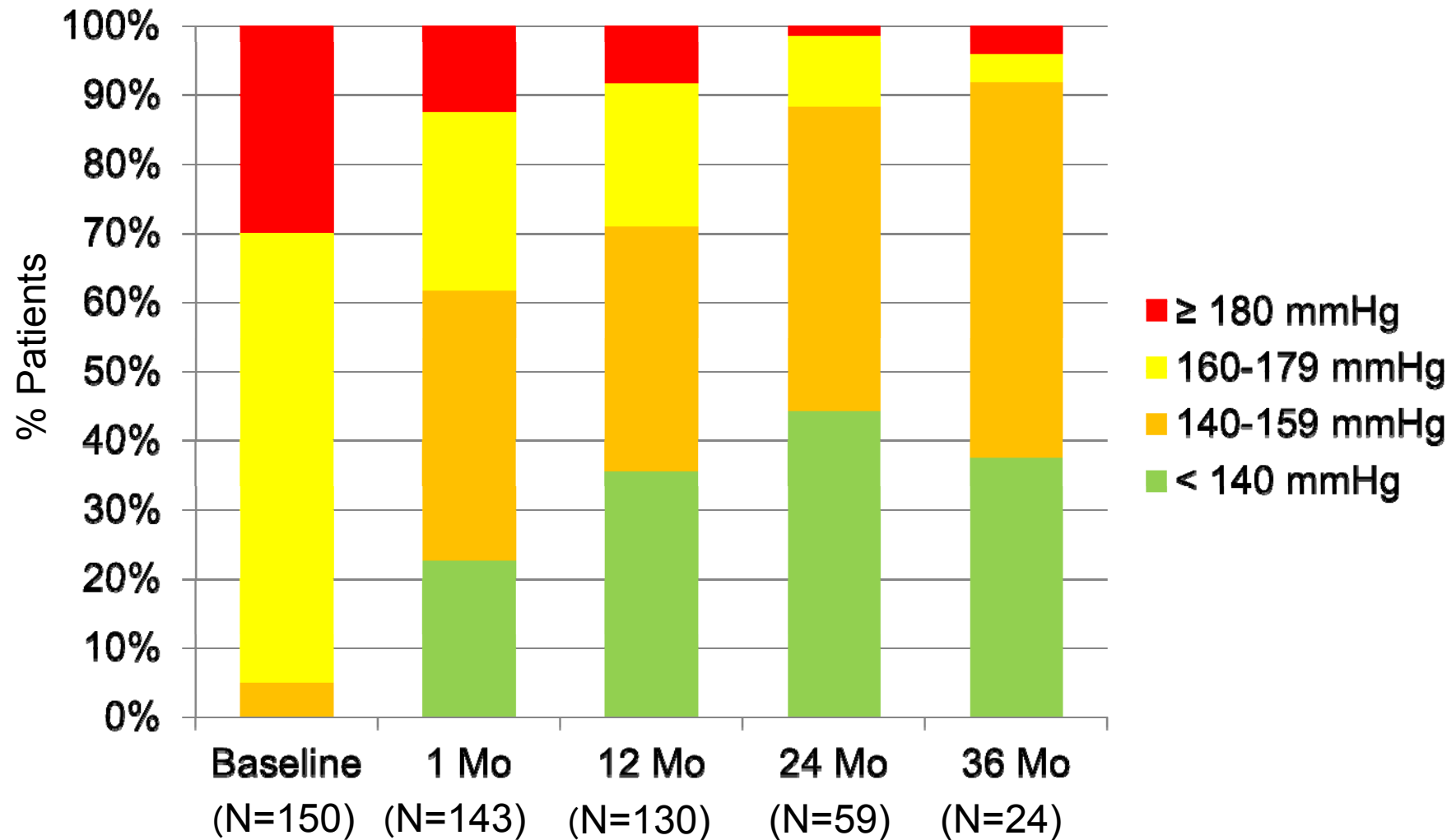
# Symplicity HTN-1

## Change in Office Blood Pressure for 24 Pts with 3 yrs Follow-up



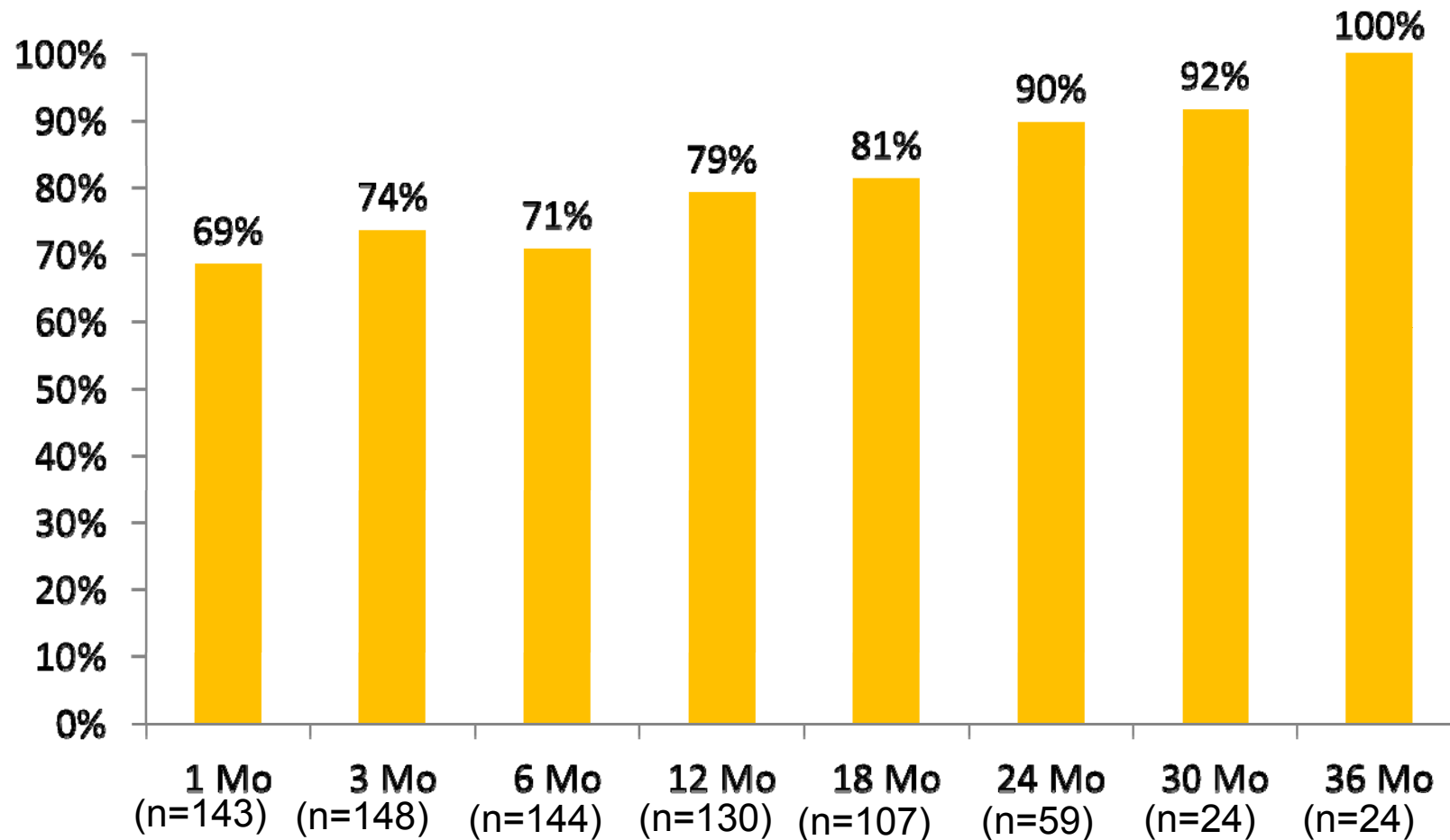


# Distribution of SBP Change at BL, 1, 12, 24, and 36 Months



# Percentage Responders Over Time

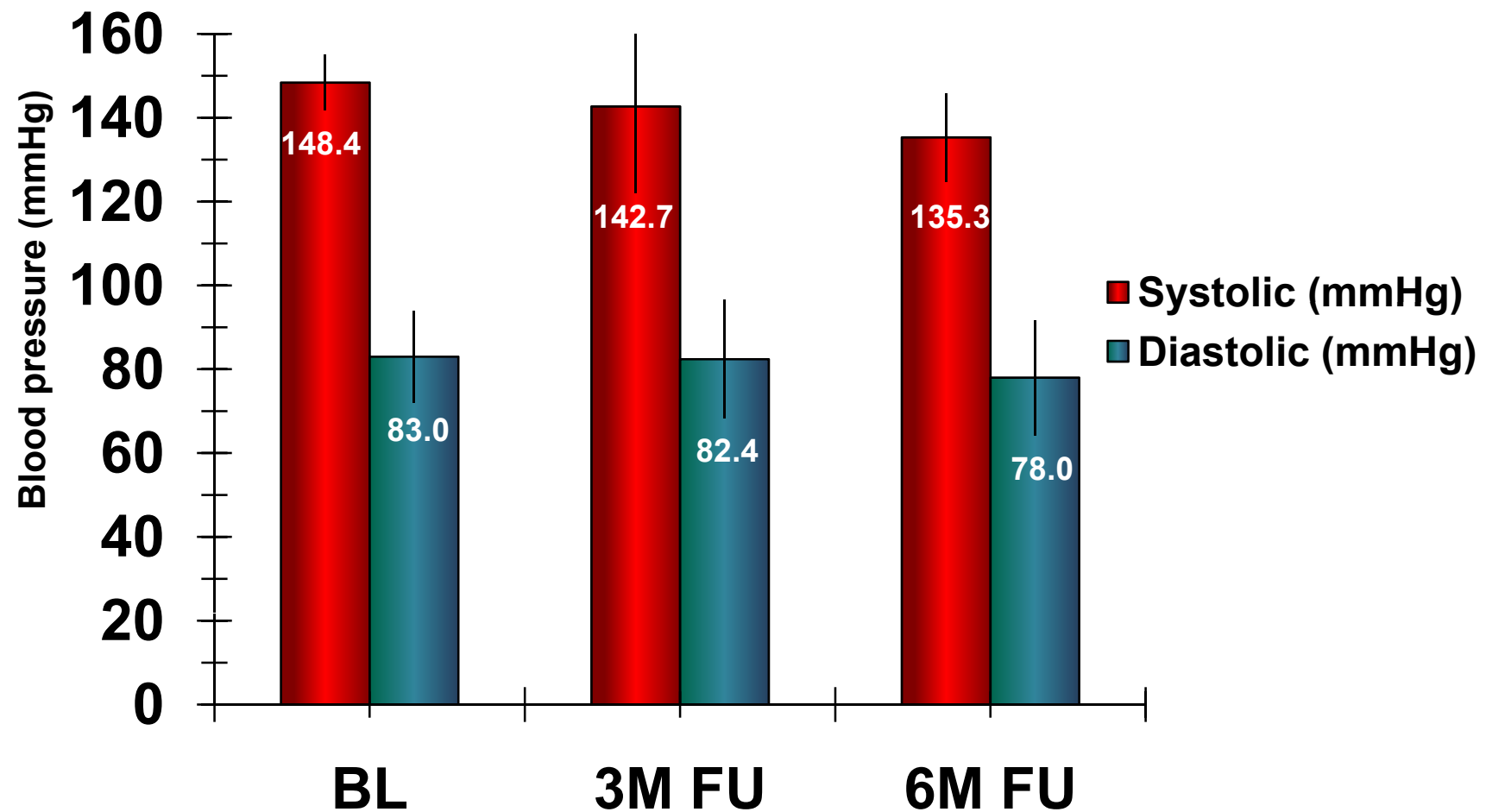
Responder was defined as an office SBP reduction  $\geq 10$  mmHg



.... and the future?

Does it work in less  
severe resistant  
hypertension?

# Renal Denervation in Borderline Hypertension - Mean Office BP

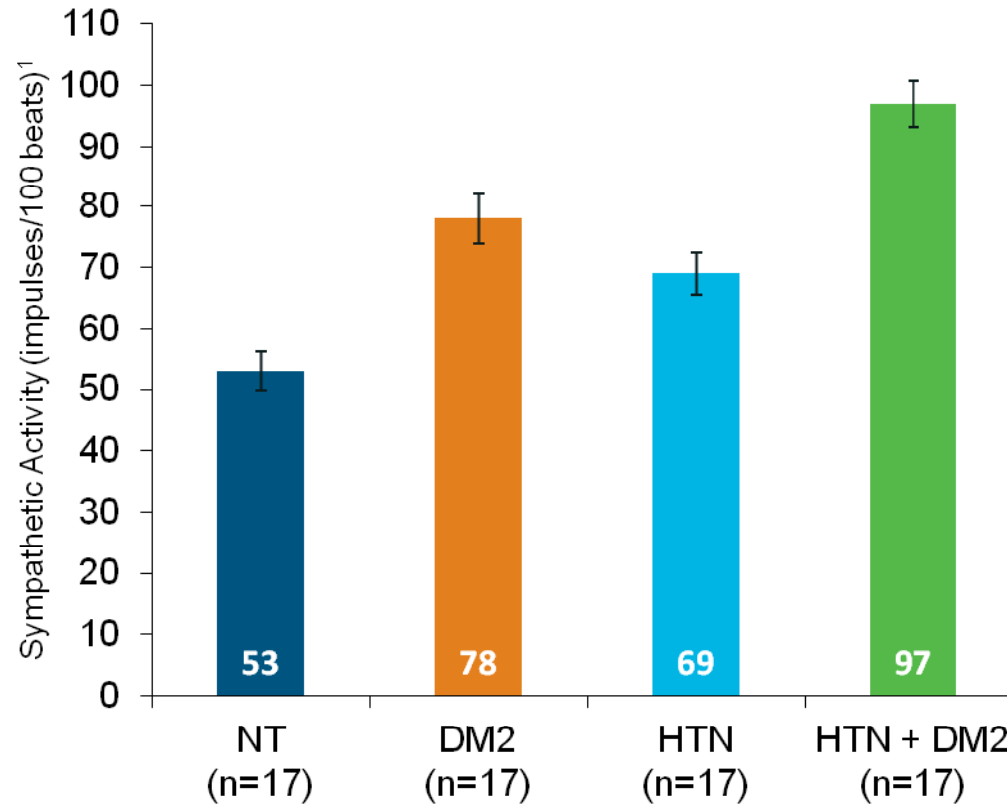


# Other potential indications

- Sleep apnea syndrom
- Heart failure
- Ventricular arrhythmias
- Diabetes

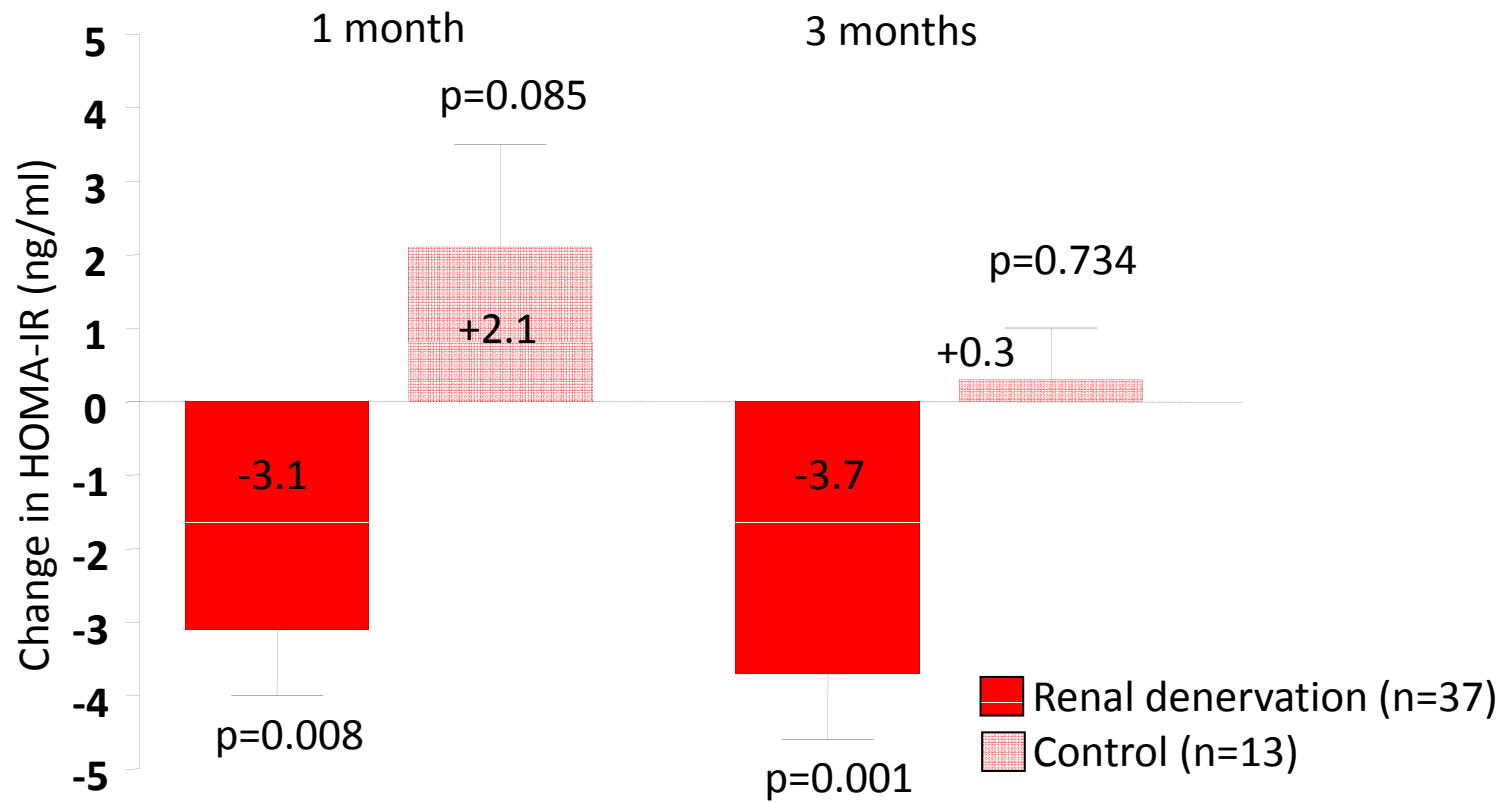
# Impact of Type 2 Diabetes Mellitus on Sympathetic Neural Mechanisms in Hypertension

Robert J. Huggett, MB, BS; Eleanor M. Scott, BM, BS, MD; Stephen G. Gilbey, BA, MD;  
John B. Stoker, BSc, MB, ChB; Alan F. Mackintosh, MA, MD; David A.S.G. Mary, MB, ChB, PhD



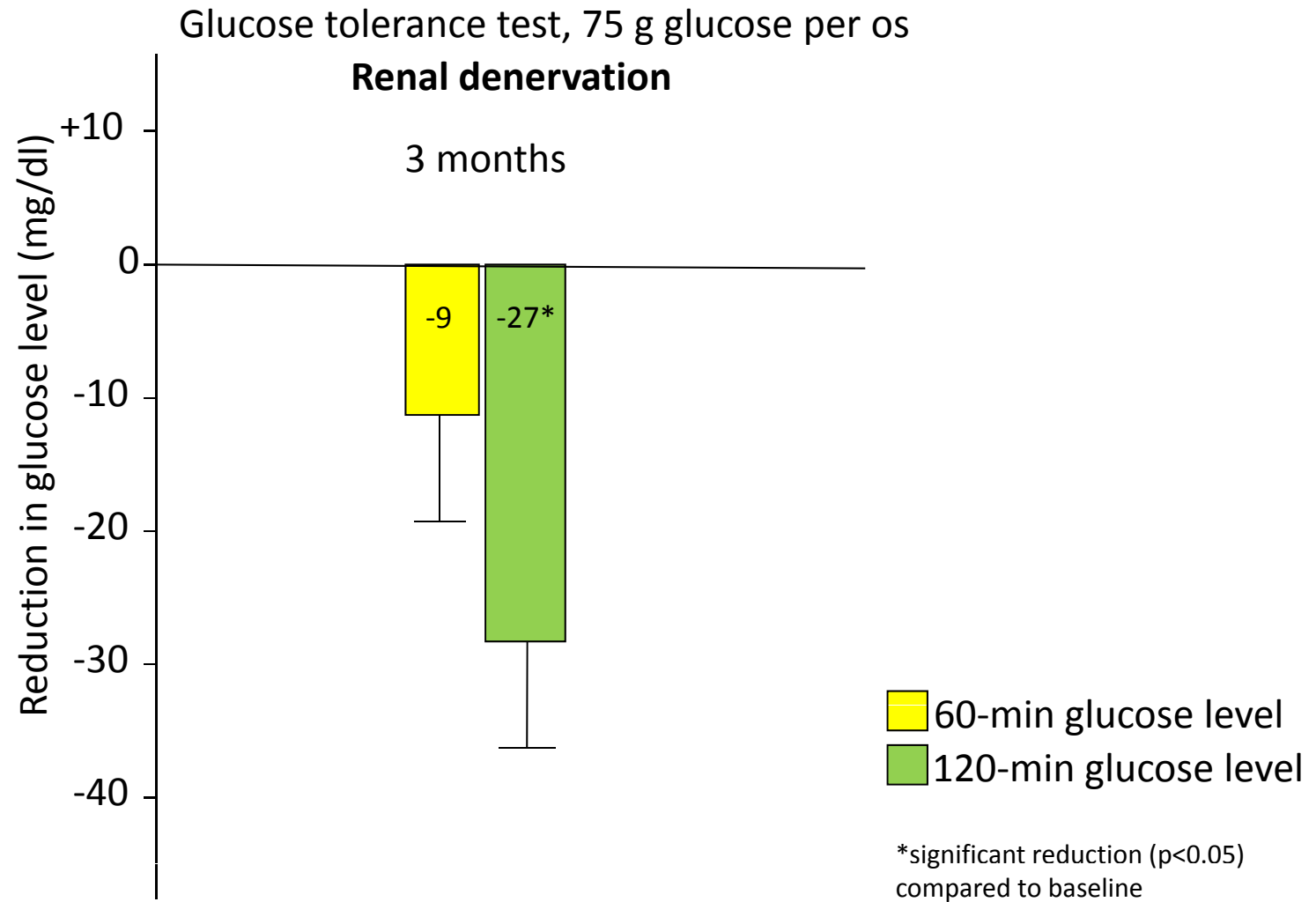
NT: normo tensive controls; DM: diabetes; HTN: hypertension; HTN+DM: hypertension+diabetes

# RD improves insulin sensitivity



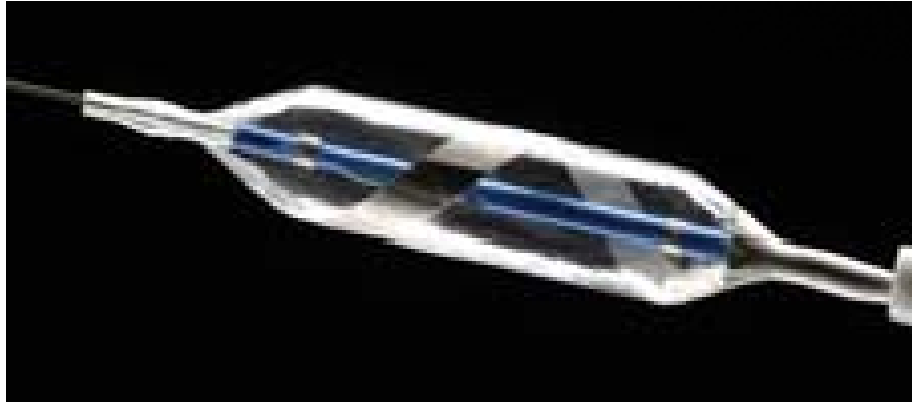


# RD improves glucose tolerance



# New Devices for Renal Denervation

# Balloons with radiofrequency



Maya Medical



Vessix Vascular

# Other radiofrequency techniques

- St. Jude Medical
- Cordis
- ....

# Balloon with needle



Mercator  
Medsystems

## Bullfrog<sup>®</sup> Micro-Infusion Catheter

- Low pressure balloon (2 atm)
- Deploys micro-needle into the adventitia
- Allows drug delivery to renal sympathetic nerve sheath
  - Guanethidine
- Catheters available for >2 mm arteries

# Ultrasound

- Recor Medical
- CardioSonic
- Sound Interventions
- Kona

# Radiation

- Best Medical International

# Take Home Messages

- Trans-catheter Renal Denervation results in significant reductions in BP
- With the Ardian-Medtronic system, no major complications occurred
- TRenD is beneficial for patients with treatment-resistant essential hypertension
- The effect is sustained up to 3 years
- It may also be beneficial in patients with diabetes, heart failure and other diseases
- New devices are on the horizon