

CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES
IN VASCULAR SURGERY



JANUARY 23-25 2014

MARRIOTT RIVE GAUCHE & CONFERENCE CENTER PARIS, FRANCE

Renal denervation

How does it work, who should be treated?

www.cacvs.org



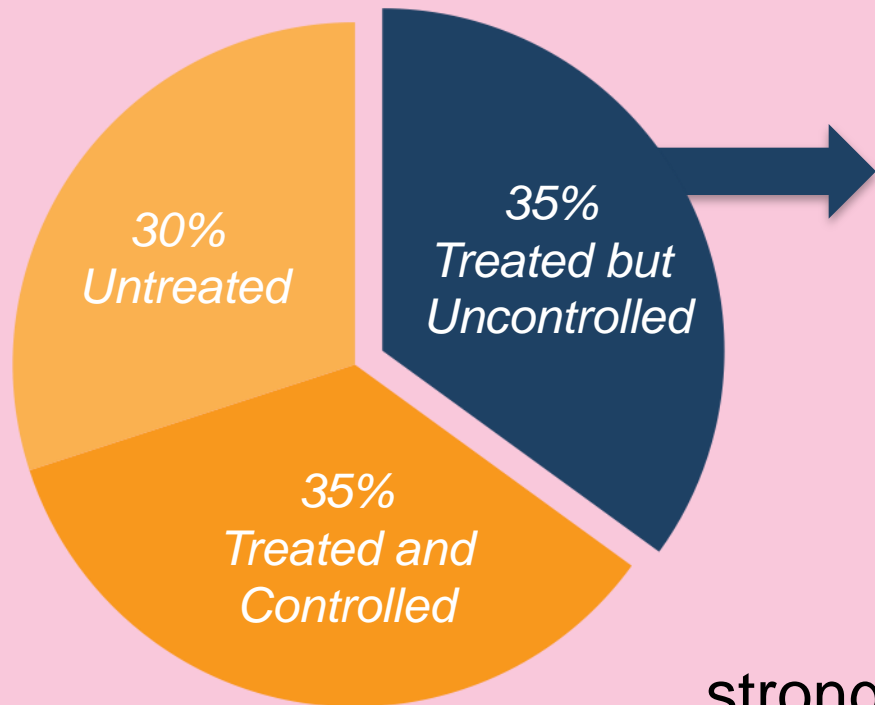
Disclosure

Speaker name:

Iris Baumgartner

- I have the following potential conflicts of interest to report:
 - Consulting
 - Employment in industry
 - Shareholder in a healthcare company
 - Owner of a healthcare company
 - Other(s)
- I do not have any potential conflict of interest

Drugs Work But Not As Well As You Might Think



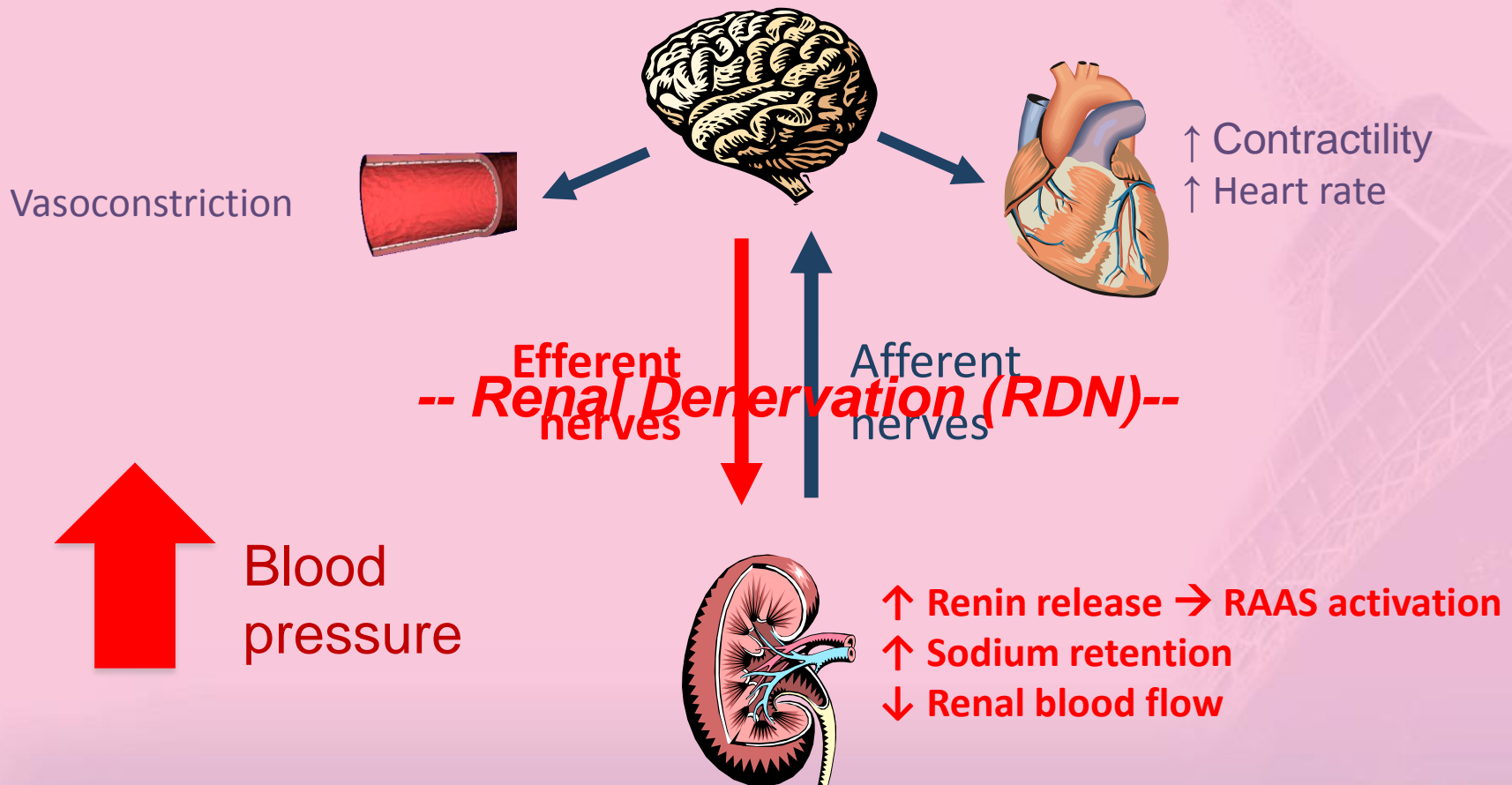
Contributing Factors to Uncontrolled Hypertension:

- Physician inertia
- Patient compliance
- Resistant HTN

strong demands for new and safe therapies to control resistant hypertension

Renal Nerve and Sympathetic Activity

Kidney as Origin and Recipient of Central Sympathetic Drive



Physiology Supported by Surgical History

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

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AUGUST 15, 1953

SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Spillhwick, M.D.

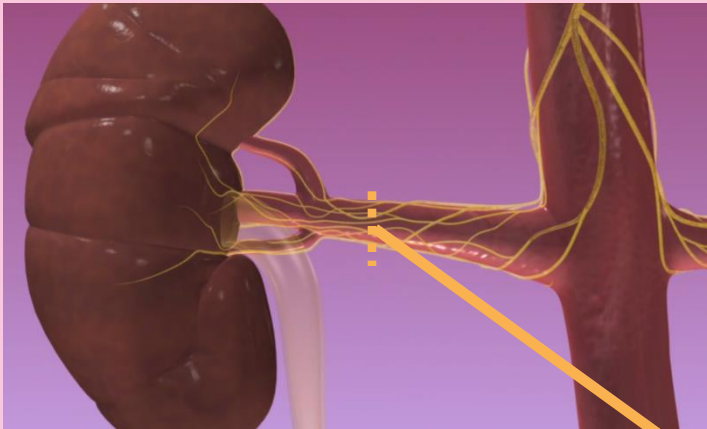
and

Jesse E. Thompson, M.D., Boston

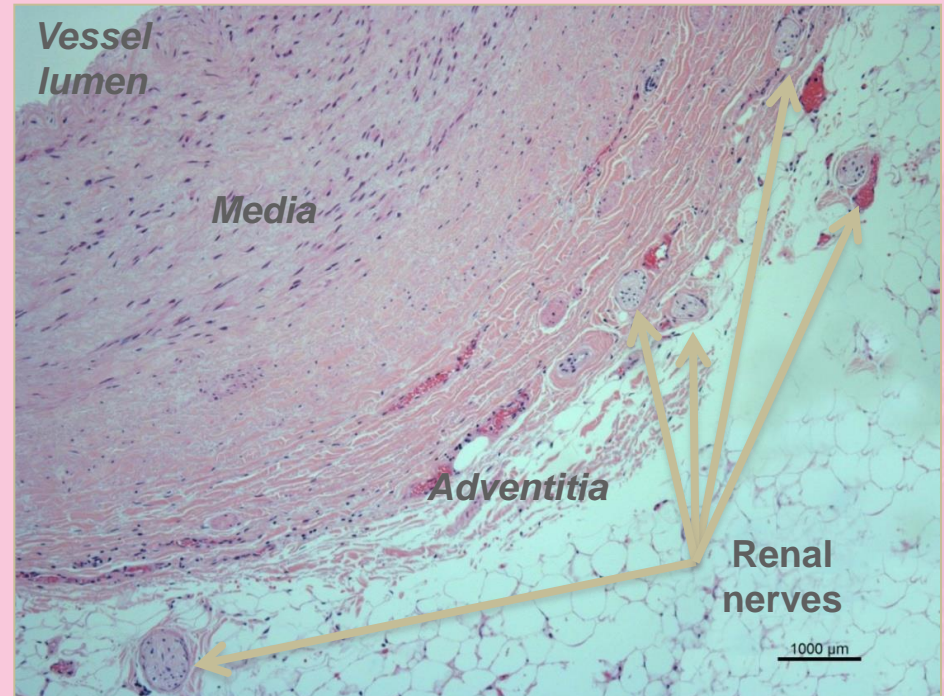
Surgical sympathectomy for blood pressure reduction is an old extremely efficacious therapeutic concept, but...

- significant morbidity
- medical therapy improved significantly & obsoleted surgical need

Renal Anatomy Allows a Catheter-based Approach



- Arise from T10-L2
- Follow the renal artery to the kidney
- Primarily lie within the adventitia*
- Renal arteries are a location where renal efferent and afferent nerves travel together



novel, minimally invasive, device-based therapy, specifically targeting and ablating the renal artery

Safe, Superior and Sustained Results Specific to the Symplicity™ RDN System



The catheter is introduced through the femoral artery and is threaded through the renal artery near each kidney.

Once in place, the tip of the catheter delivers low-power RF energy to several locations to disable the sympathetic nerves throughout the artery.

Companies are pursuing technologies with alternative approaches for RND

RF based: Enlighten Renal Denervation System; V² bipolar balloon catheter; OneShot Balloon catheter.





Ultrasound based: PARADISE™; TIVUS system

Alternative approaches: Beta-Cath™; Vincristine; Guanetidine

Little has been published on preclinical and clinical experience with these new devices

Symlicity RDN Global Clinical Program

ENROLLMENT COMPLETE OR IN FOLLOW-UP

Symlicity HTN-1		Series of nonrandomised pilot studies	N = 153
Symlicity HTN-2		Randomised, controlled study	N = 106
SYMPPLICITY HTN-3		Randomised, controlled study	N = 530
SYMPPLICITY SPYRAL FIM		Feasibility study	N = 50

3 yr

NOW ENROLLING OR BEING PLANNED

Global SYMPPLICITY Registry		Prospective registry	N = 5000
SYMPPLICITY-HF		Feasibility study	N = 40
SYMPPLICITY HTN-Japan		Randomised, controlled study	N = 100
SYMPPLICITY HTN-4		Randomised, controlled study	N = 580
SYMPPLICITY HTN-India		Single-arm study	Planned

Enroll

Enroll

Enroll

Plan

Plan

Symplicity HTN-1: Non-Randomised Studies

First-in-Man Cohort:

- 45 patients, EU, Australia
- Nonrandomised
- First patient enrolled: June 2007
- 12-month initial report in *The Lancet*, 2009

Symplicity HTN-1 Patients Reflect Treatment-Resistant Population

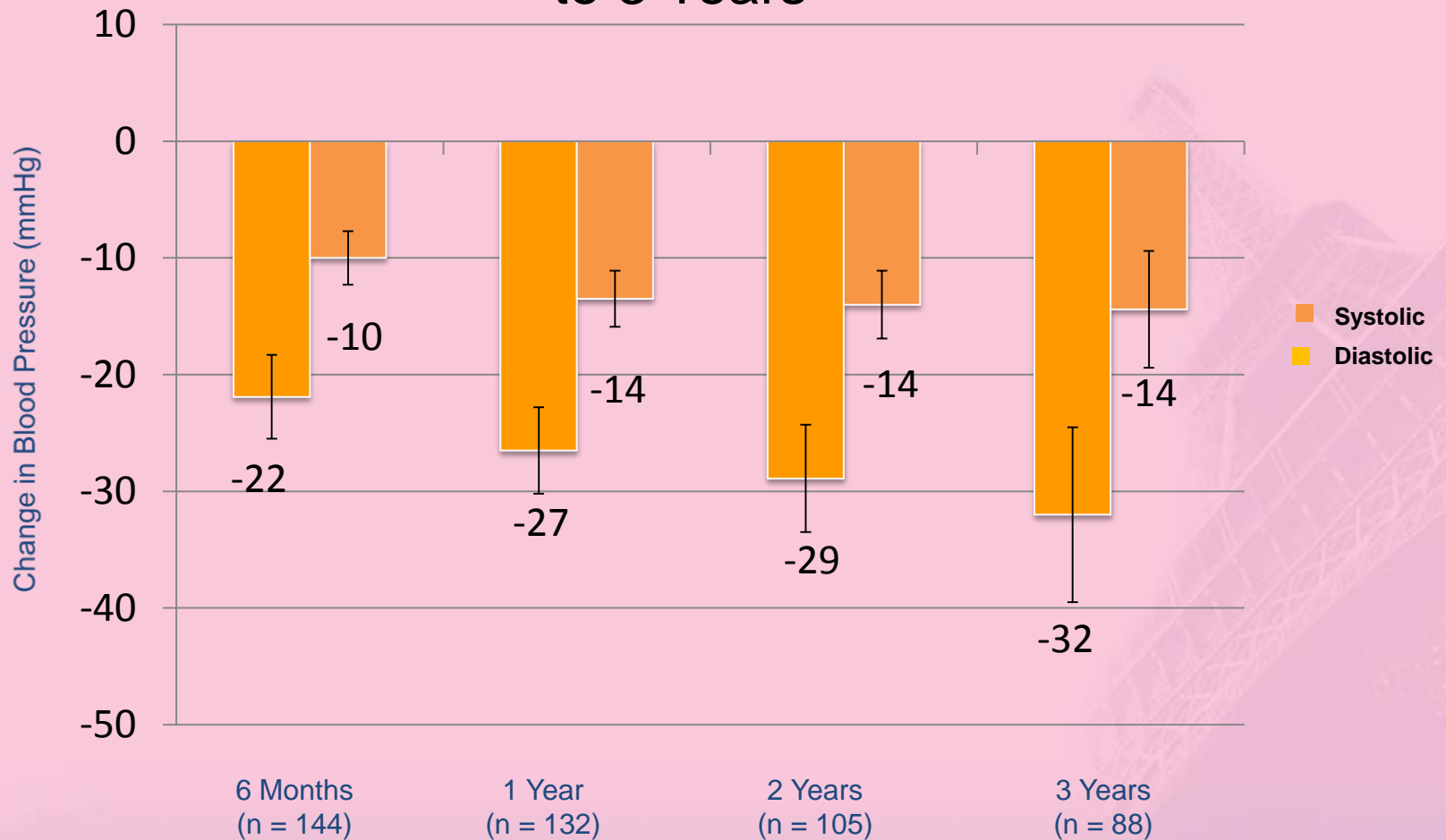
Expanded Cohort*

- 153 patients, EU, Australia, USA
- Nonrandomised
- 36-month follow-up

Key Inclusion Criteria

- Office SBP ≥ 160 mmHg
- Stable drug regimen of 3+ more antihypertension medications
- eGFR ≥ 45 mL/min/1.73m²

Symplivity HTN-1: Significant, Sustained BP Reduction to 3 Years



$p < 0.01$ for Δ from baseline for all time points.

Data is reported only on the patients available at each time point.

Symplicity HTN-2: Randomized Controlled Trial

	RDN (n = 52)	Control (n = 54)	p-Value
Baseline systolic BP (mmHg)	178 ± 18	178 ± 16	0.97
Baseline diastolic BP (mmHg)	97 ± 16	98 ± 17	0.80
# antihypertension meds	5.2 ± 1.5	5.3 ± 1.8	0.75
Age	58 ± 12	58 ± 12	0.97
Gender (female)	35%	50%	0.12
Race (caucasian)	98%	96%	>0.99
BMI (kg/m ²)	31 ± 5	31 ± 5	0.77
Type 2 diabetes	40%	28%	0.22
Coronary artery disease	19%	7%	0.09
Hypercholesterolemia	52%	52%	>0.99
eGFR (MDRD, ml/min/1.73m ²)	77 ± 19	86 ± 20	0.013
Serum creatinine (mg/dL)	1.0 ± 0.3	0.9 ± 0.2	0.003

Symplicity HTN-2 Patients Reflect Treatment-Resistant Population

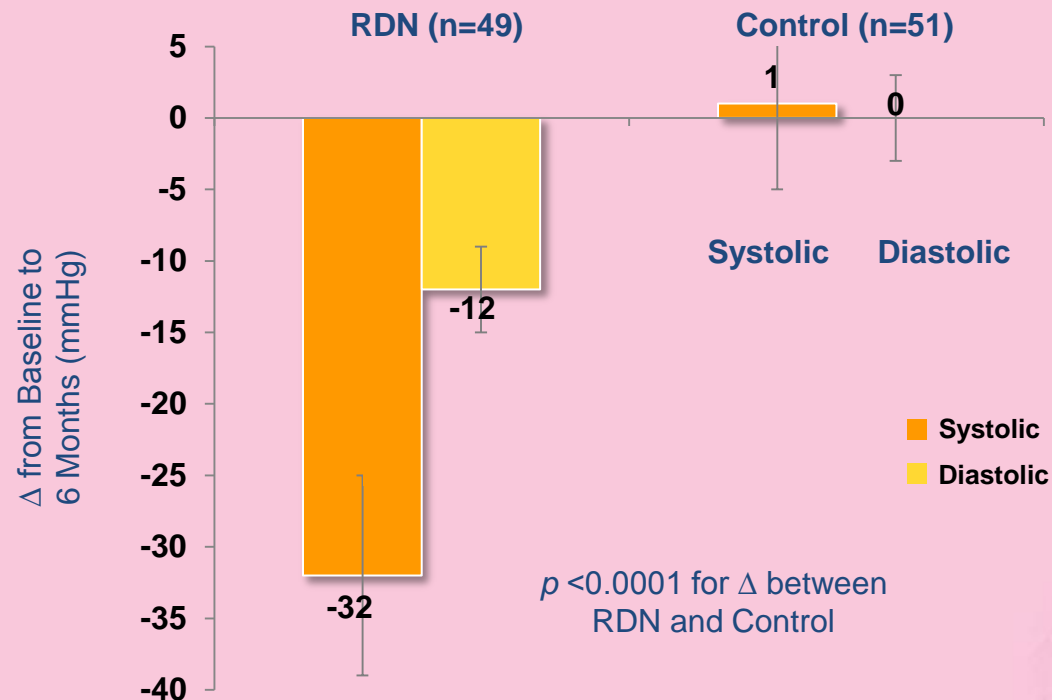
*n = 42 for RDN and n = 43 for Control. Wilcoxon rank-sum test for two independent samples used for between-group comparisons of UACR.

*n = 39 for RDN and n = 42 for Control

*Symplicity HTN-2 Investigators. *The Lancet*. 2010.

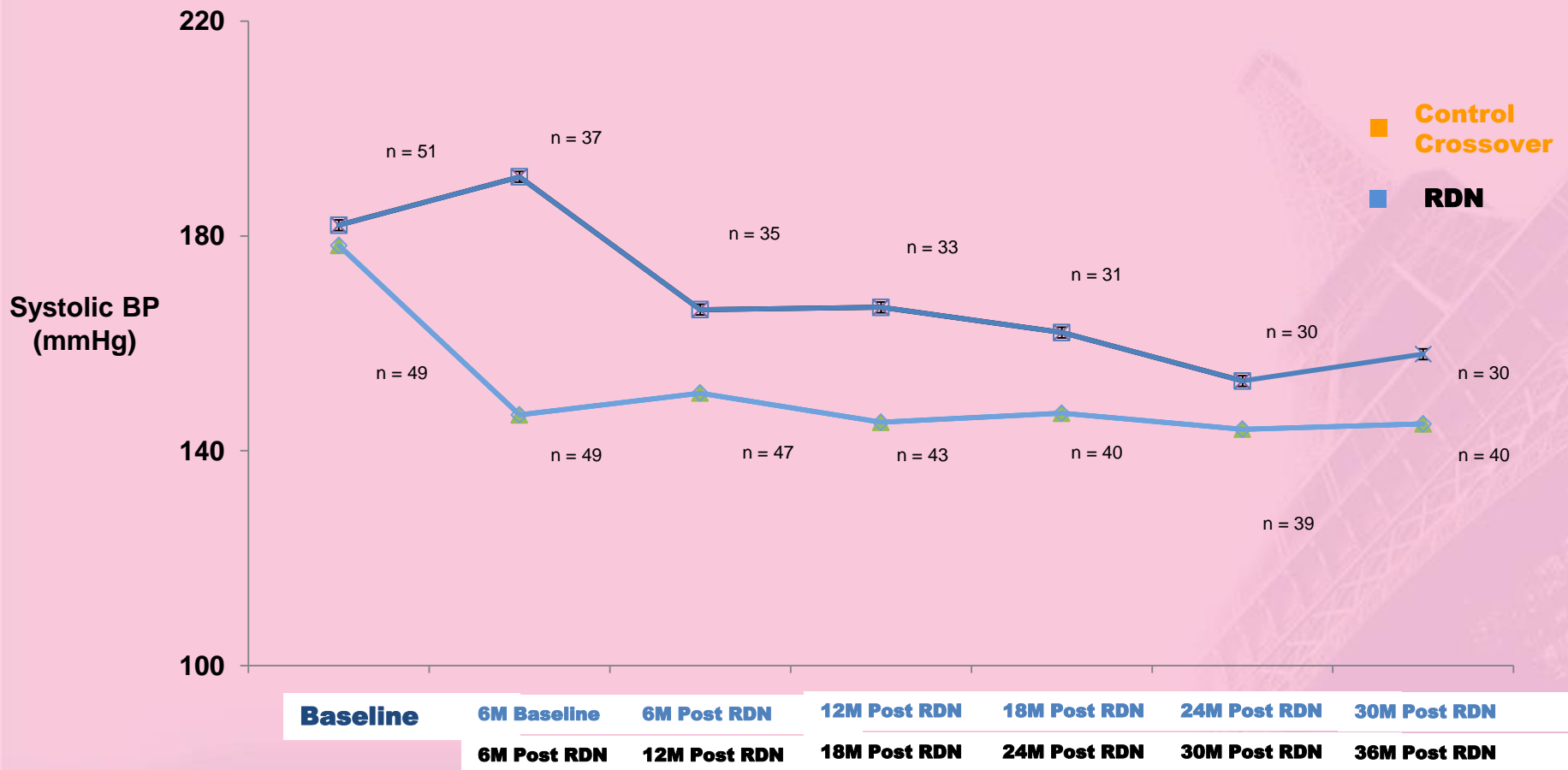
Symplicity HTN-2: Significant Reductions in BP RDN Superior to Medical Management at 6M

Primary Endpoint (6M post Randomisation)



>80% of RDN patients had ≥ 10 mmHg reduction in SBP

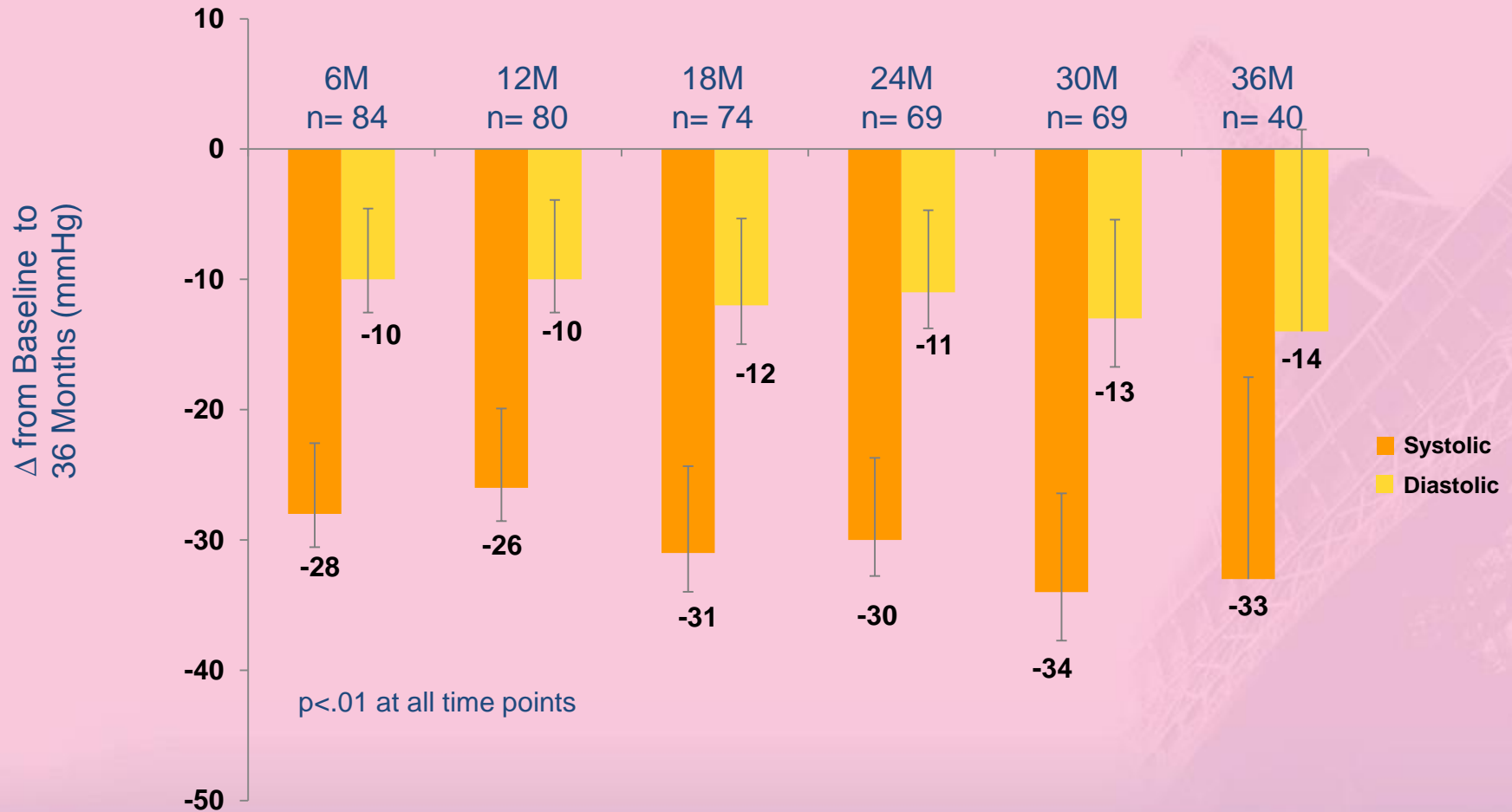
Symplivcity HTN-2: Control Group Showed BP Reduction from RDN After Crossover*



*Only patients in the treatment group reached the 36 month follow up visit
 Expanded results presented at the Transcatheter Cardiovascular Therapies annual meeting 2013

Symplicity HTN-2: BP Reductions Sustained to 3 Years

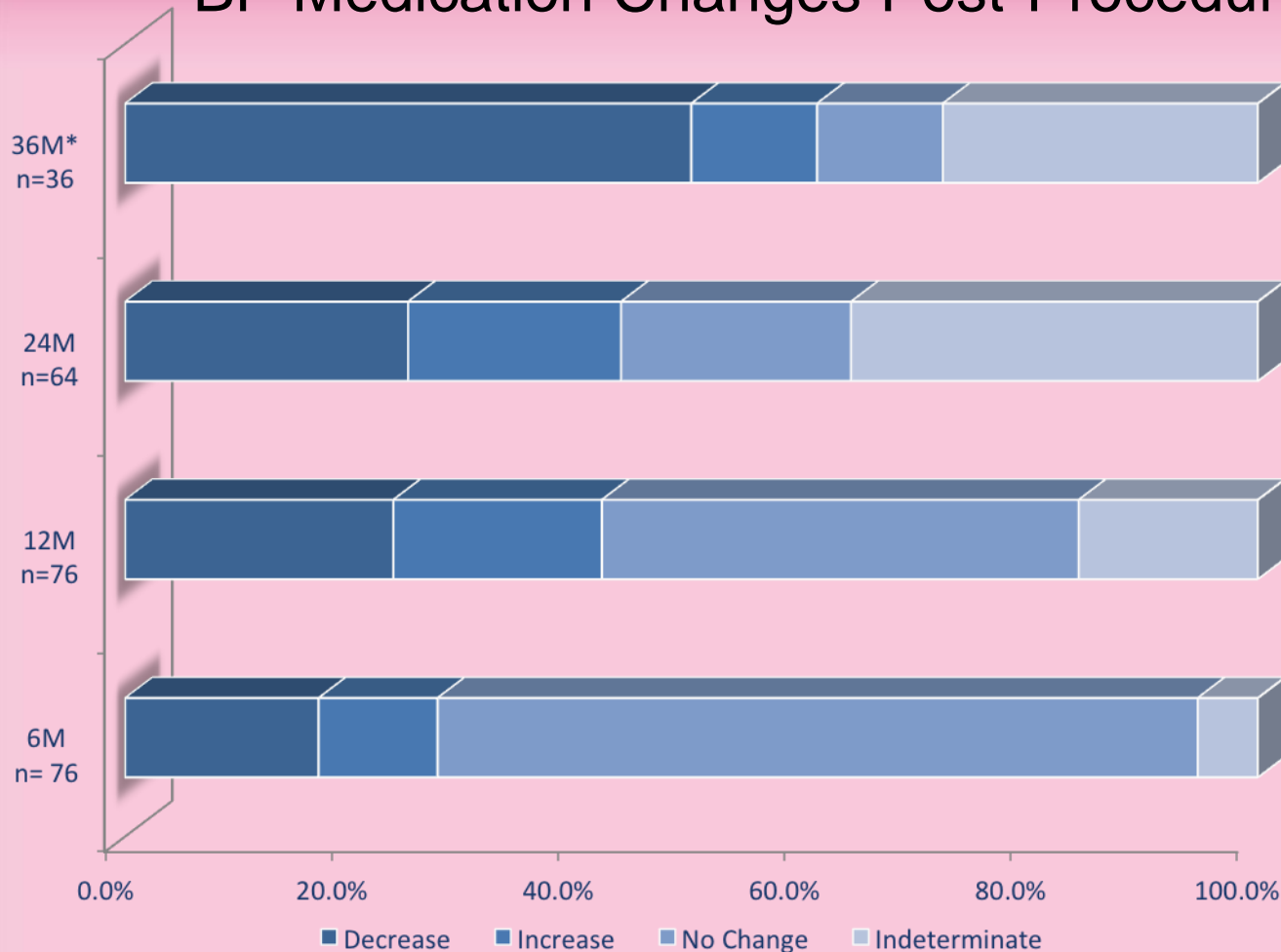
Sustained Reductions in the Pooled (RDN and Crossover) Group*



*Only patients in the RDN group reached the 36 month follow up visit

Expanded results presented at the Transcatheter Cardiovascular Therapies annual meeting 2013

BP Medication Changes Post-Procedure



Data Lock	SBP Change (mmHg, Pooled)	AVG # Meds
6M	-28	5.0
12M	-26	5.0
24M	-31	4.8
36M*	-33	4.6

Increase: if any or both meds and/or dose increase

Decrease: if any or both meds and/or dose decrease.

Indeterminate: All other combinations

Physicians were encouraged to maintain medications and dosages up to the 6-month primary endpoint.

*Only patients in the RDN group reached the 36 month follow up visit

Expanded results presented at the Transcatheter Cardiovascular Therapies annual meeting 2013.

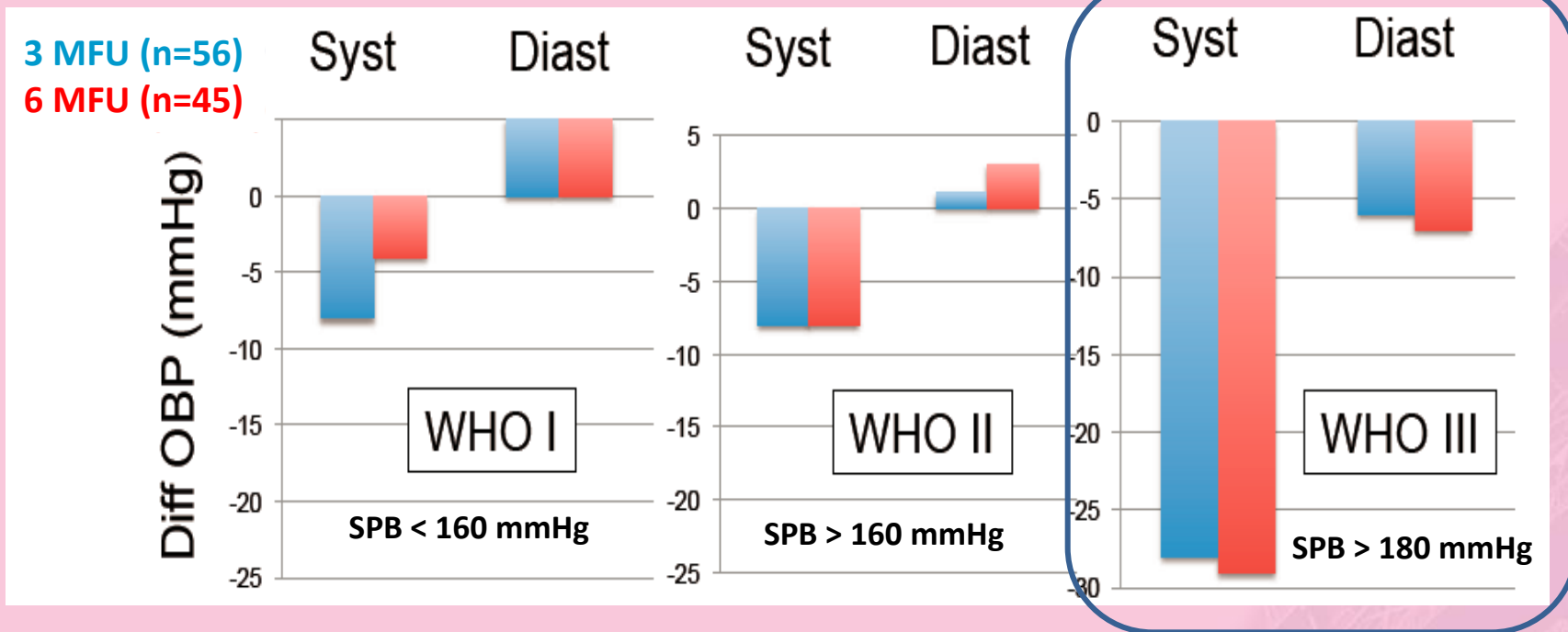
Impressive Procedural Safety Profile in Over 1,000 Patients

	%	n/N
Renal artery re-intervention	0.09%	1/1162
Renal artery re-intervention due to dissection	0.09%	1/1162
Vascular complication at access site	0.34%	4/1162
Vascular complication at access site, pseudoaneurysm	0.34%	4/1162
Vascular complication at access site, hematoma	0.09%	1/1162

Conclusions

- Transcatheter renal sympathetic denervation is safe
- It is simple to be performed
- Significant reductions in blood pressure were achieved in patients with multi-drug resistant hypertension
- Effect has been sustained through at least 36 months
- No significant decline in renal function

Leipzig Registry – Results Office Blood Pressure



(mmHg)	n=16	n=16	n=9	n=6	n=31	n=23
OBP ↓	68% (11)	56% (9)	67% (6)	50% (3)	90% (28)	87%(20)
↓ >10	44% (7)	38% (6)	44% (4)	50% (3)	70% (22)	73%(17)
OBP ↑	31% (5)	46% (7)	33 % (3)	30% (2)	10% (3)	13% (3)

Press Release

- SYMPLICITY HTN-3, the Medtronic U.S. pivotal trial in RND for treatment-resistant hypertension, failed to meet its primary efficacy endpoint. The DSMB concluded that there were no safety concerns.
- Medtronic will form a panel of independent advisors of physicians and researchers to help guide its decisions regarding the future of the Symplicity Trial Program and physician and patient access to the Simplicity technology in countries with regulatory approvals.
- Today Medtronic cannot disclose any details until they have a full picture and analyzed all the findings. The 6-months trial results will be presented around mid-March and published at the same time.