

# ***Renal Denervation for milder resistant hypertension : Korean experience***

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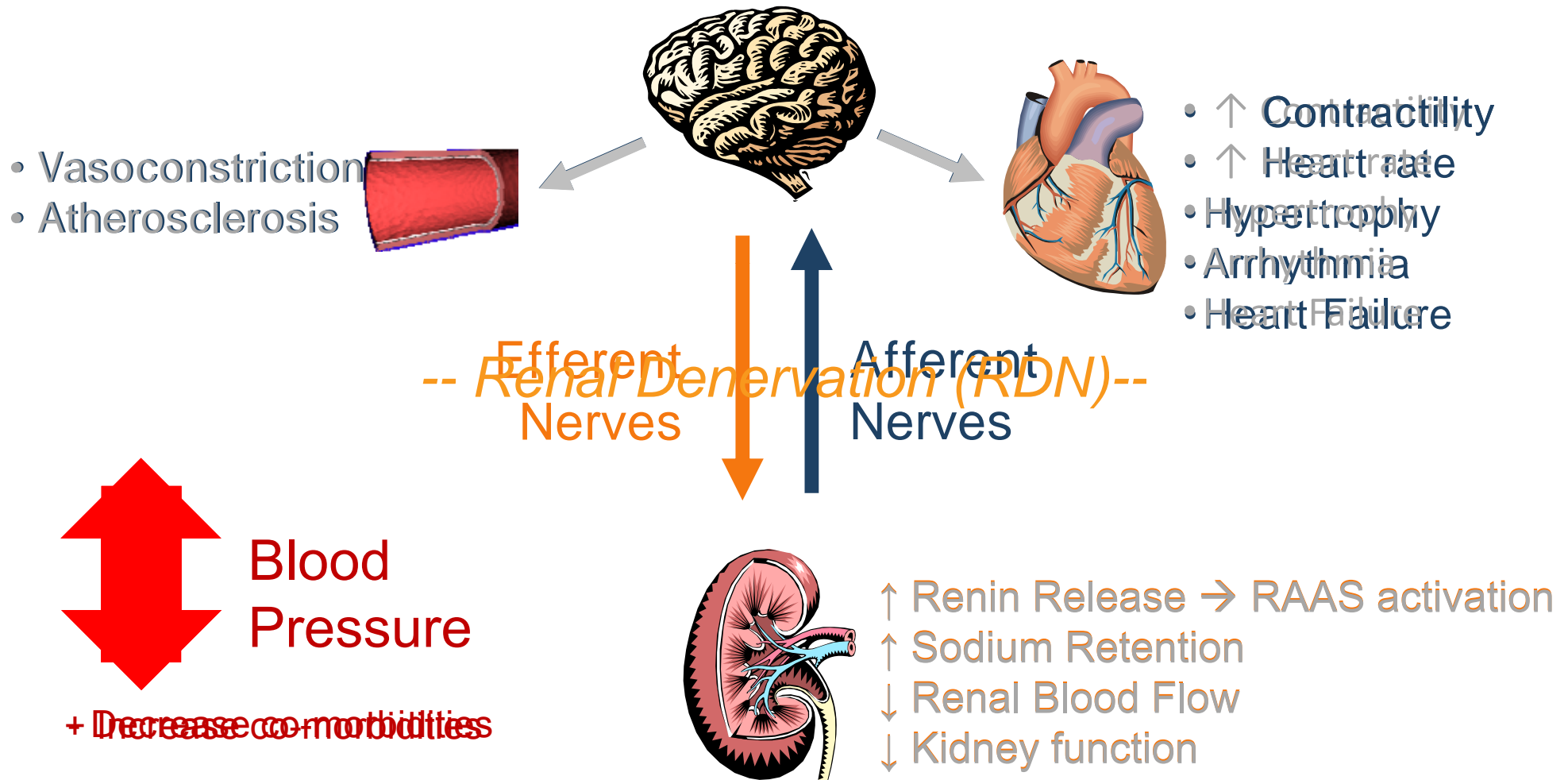


# Contents



- **Concepts of Renal Denervation**
- **Clinical Evidence**
  - **Efficacy of Renal denervation**
  - **Safety of Renal denervation**
- **SMC registry data**

# Renal Sympathetic Nerve Activity: RDN Disrupts Renal Nerves, Lowering SNS Activity



# Micro-anatomy of the renal sympathetic nervous system



## Human postmortem histologic study

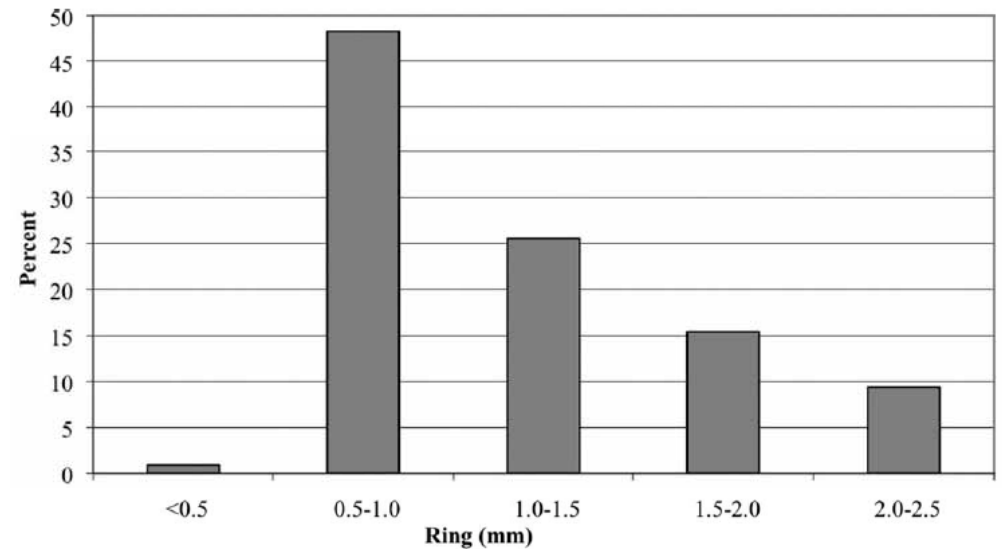
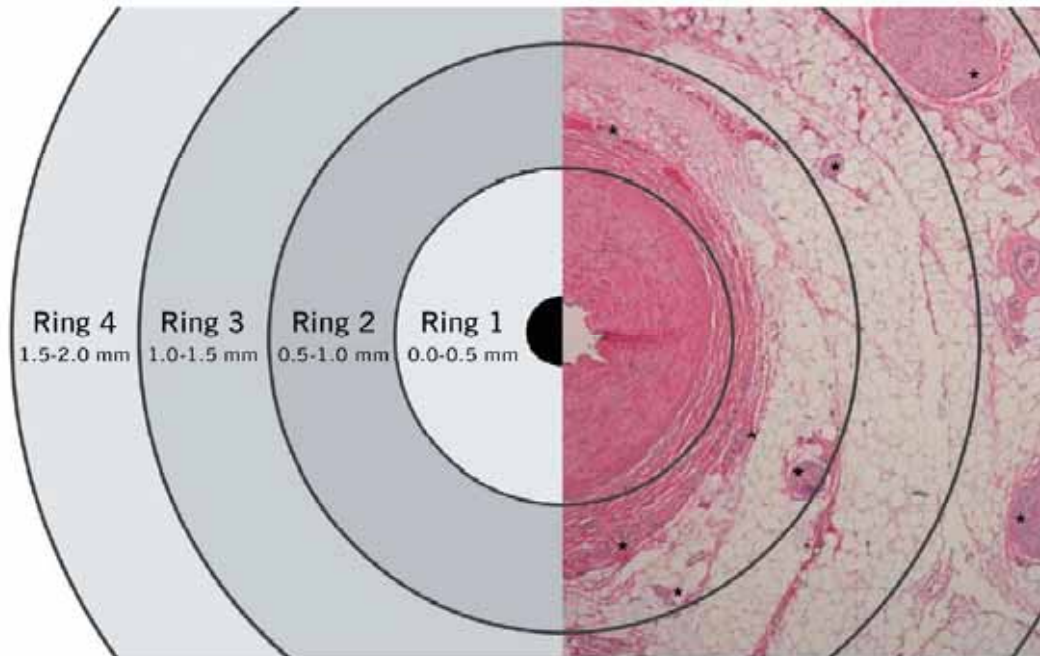


Fig. 2. Percent of total nerves at distance from lumen within each ring.

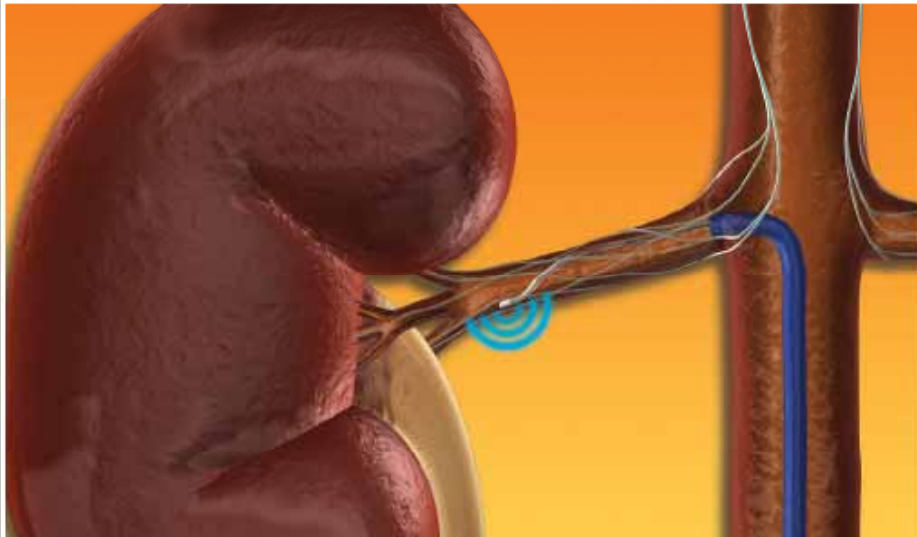
6 patients, 12 renal arteries

Atherton DS et al, Clin Anat. 2011 Oct 4

# RF ablation



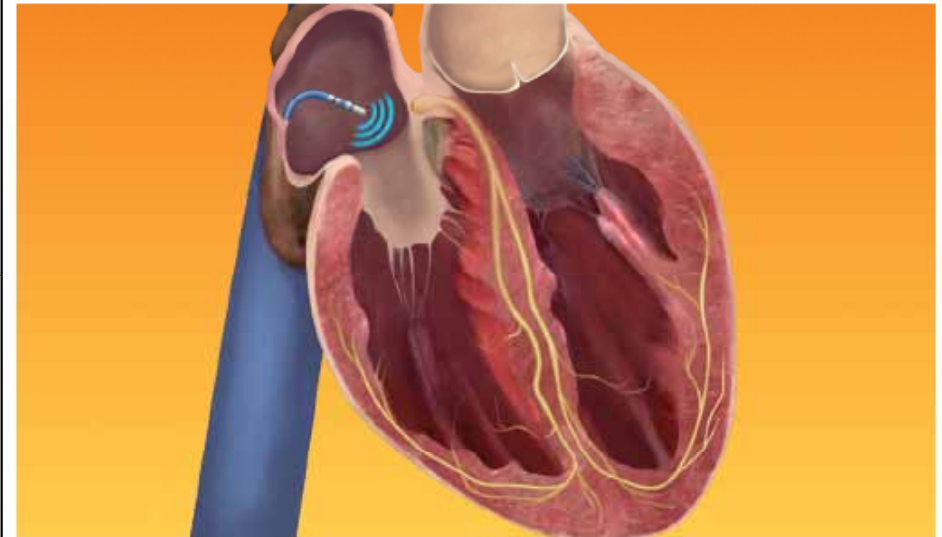
Ablation to Thin Walls of Renal Artery



Vessel wall thickness  
(up to 3 mm)



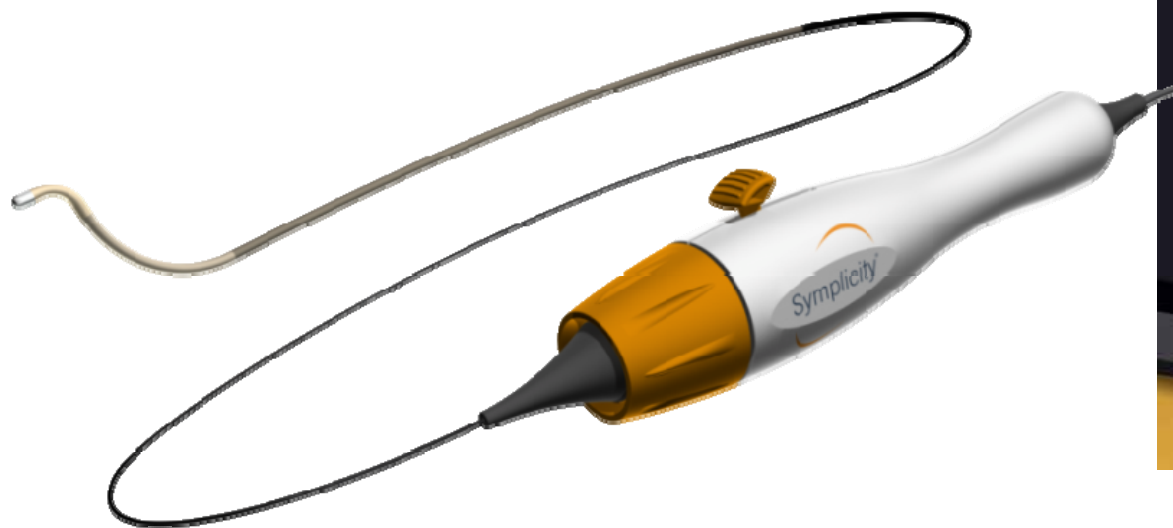
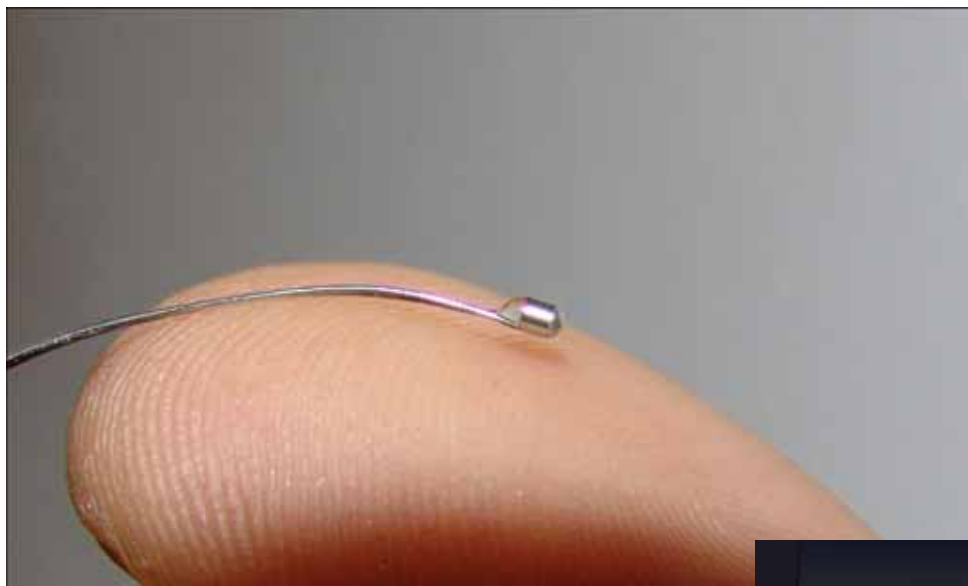
Ablation to Thick Heart Muscle



Muscle wall thickness  
(up to 15 mm)



# Ardian SymPLICity Catheter



# The Symplicity HTN-1 & 2 Trials



## THE LANCET

Volume 373 · Number 9671 · Pages 1223-1310 · April 11-17, 2009

www.thelancet.com

### Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study

Henry Krum, Markus Schlaich, Rob Whitbourn, Paul A Sobotka, Jerzy Sadowski, Krzysztof Bartus, Boguslaw Kapelak, Anthony Walton, Horst Sievert, Suku Thambar, William T Abraham, Murray Esler

*Lancet.* 2009;373:1275-1281

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



*Symplicity HTN-2 Investigators\**

*Lancet.* 2010;376:1903-9

**Circulation**  
JOURNAL OF THE AMERICAN HEART ASSOCIATION



**Renal Sympathetic Denervation for Treatment of Drug-Resistant Hypertension :  
One-Year Results From the Symplicity HTN-2 Randomized, Controlled Trial**  
Murray D. Esler, Henry Krum, Markus Schlaich, Roland E. Schmieder, Michael Böhm and Paul  
A. Sobotka  
for the Symplicity HTN-2 Investigators

*Circulation* 2012;126:2976

# Inclusion and exclusion criteria



- **Key inclusion criteria**

- Office blood pressure  $\geq 160$  mmHg ( $\geq 150$  mmHg for diabetics) despite  $\geq 3$  anti-hypertensive medications
- eGFR (MDRD)  $\geq 45$  mL/min/1.73m<sup>2</sup>

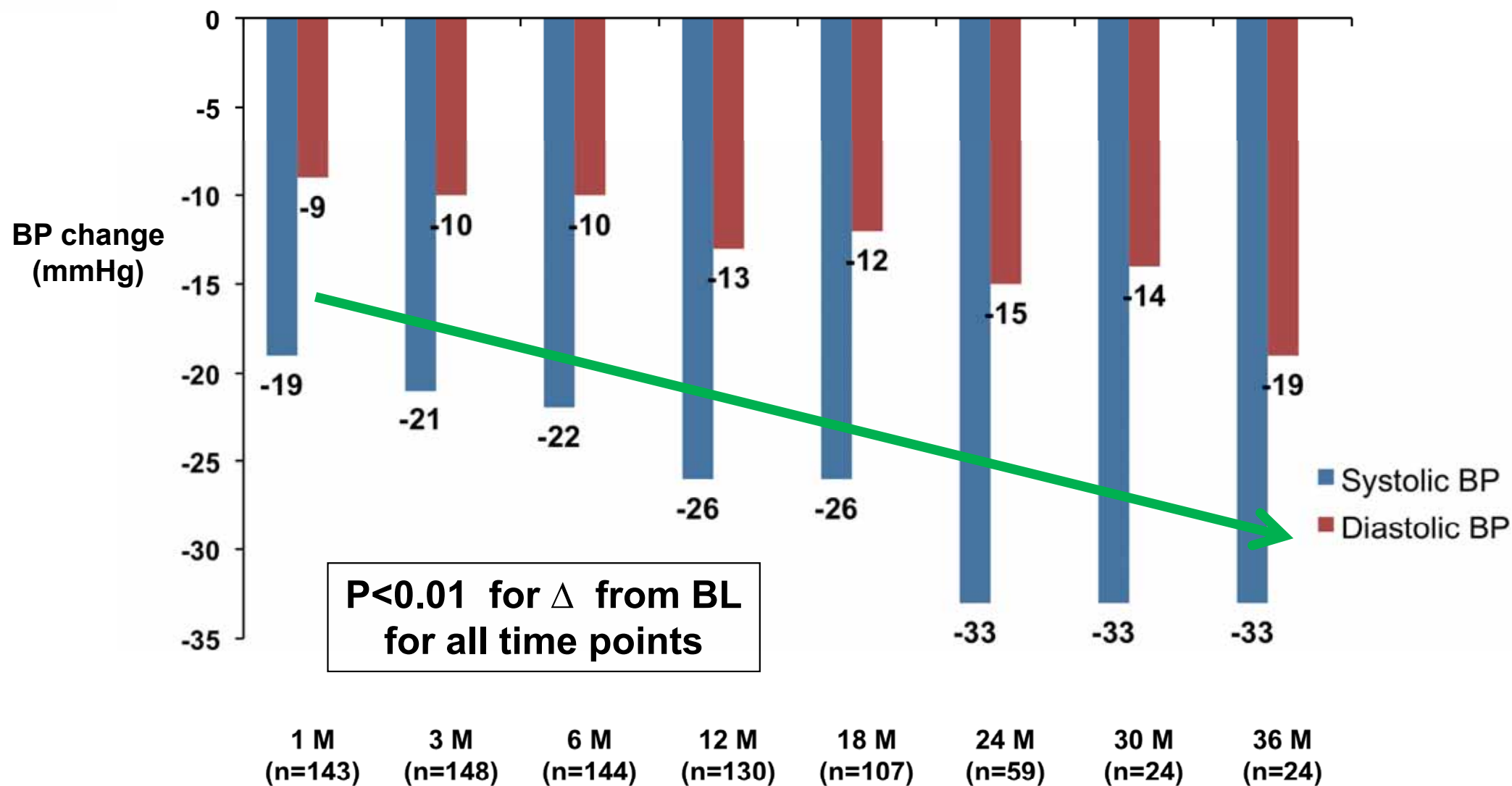
- **Key exclusion criteria**

- known secondary cause of hypertension
- Type I diabetes mellitus
- renovascular abnormalities: significant renal artery stenosis, prior renal stenting or angioplasty, dual renal arteries



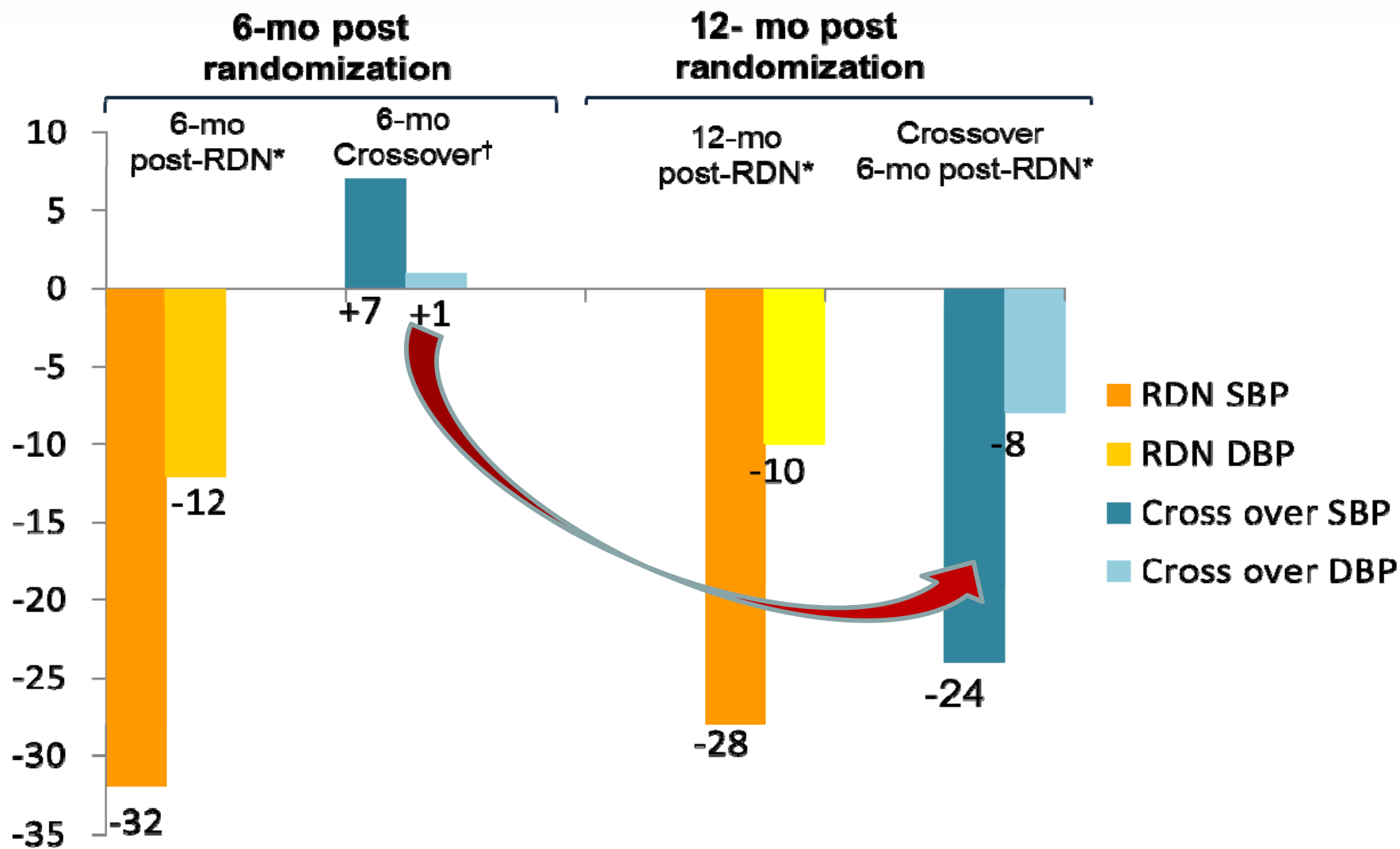
# The Symplicity HTN-1 Trial

## 36 month F/U data



# The Symplicity HTN-2 Trial

## 12 month F/U data





# The Symplicity HTN-1 & 2 Trial



- Procedure complication rate 3% (4/153 pts)
  - Renal artery dissection : 1
  - Pseudoaneurysm/hematoma : 3
- Short-term renal angiography (n=20)
  - no stenosis
- 6 months imaging study (MRA, CTA, Duplex)(n=81)
  - no stenosis
- Renal function
  - no class IV CKD, no dialysis required
  - no Cr double
- Death : 2 patients (MI, Sudden cardiac death)

Hypertension 2011;57:911-17

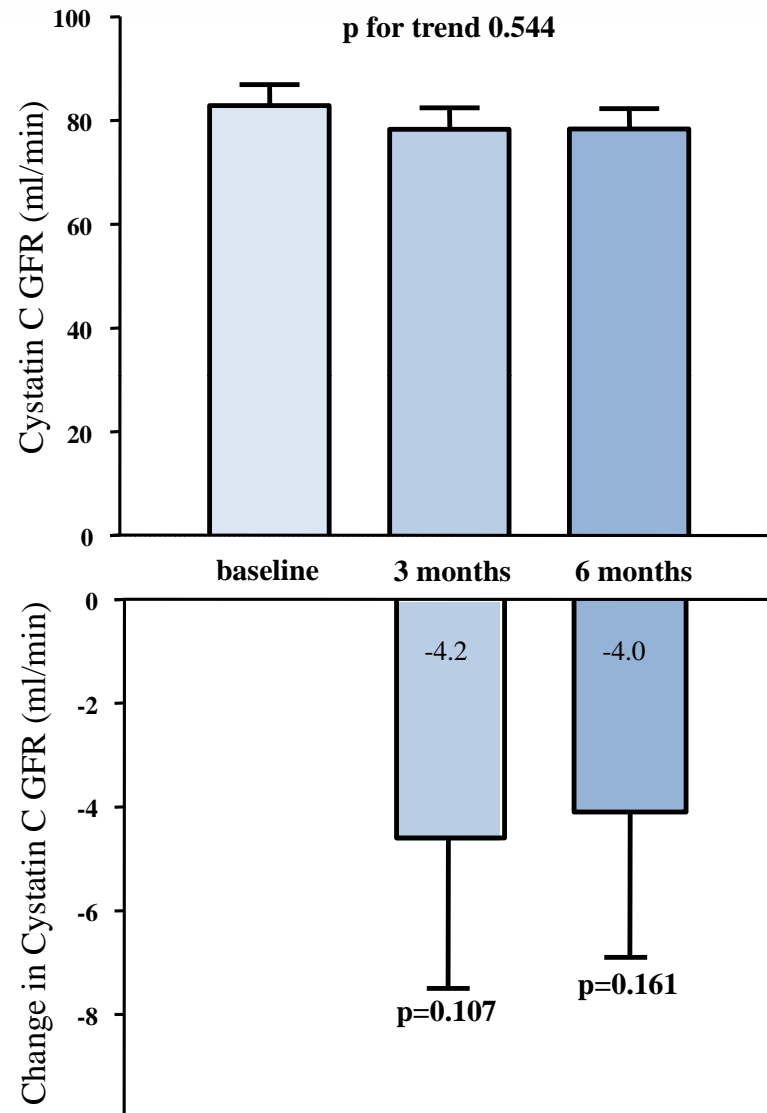
	Renal denervation group		Control group		Difference in mean change (95% CI)	p value
	Patients (n)	Mean change (SD)	Patients (n)	Mean change (SD)		
eGFR* (mL/min per 1.73 m <sup>2</sup> )	49	0.2 (11)	51	0.9 (12)	-0.7 (-5.4 to 3.9)	0.76
Serum creatinine (μmol/L)	49	0.2 (17.6)	51	-1.1 (10.3)	1.3 (-4.5 to 7.0)	0.67
Cystatin C (mg/L)	37	0.1 (0.2)	40	0.0 (0.1)	0.0 (0.0 to 0.1)	0.31

eGFR=estimated glomerular filtration rate. \*Calculated on the basis of Modification of Diet in Renal Disease Study criteria.<sup>12</sup>

**Table 2:** Baseline, change from baseline to 6 months, and difference in change in measured concentrations of eGFR, serum creatinine, and cystatin C for renal denervation and control groups

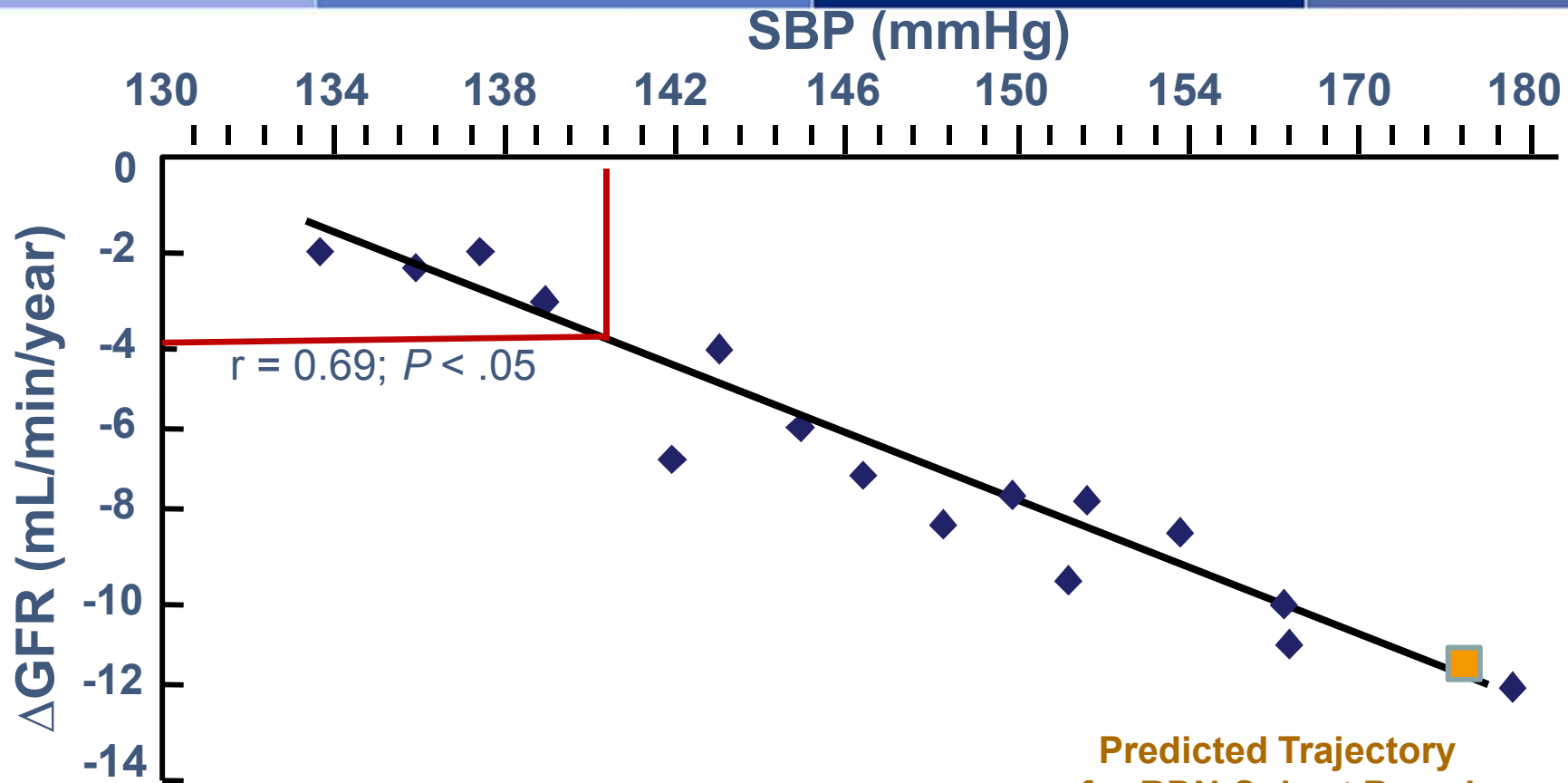
# Renal Hemodynamics and Renal Function After Catheter-Based Renal Sympathetic Denervation in Patients With Resistant Hypertension

Felix Mahfoud, Bodo Cremers, Julia Janker, Britta Link, Oliver Vonend, Christian Ukena, Dominik Linz, Roland Schmieder, Lars Christian Rump, Ingrid Kindermann, Paul Andrew Sobotka, Henry Krum, Bruno Scheller, Markus Schlaich, Ulrich Laufs and Michael Böhm



N=100 patients

# Renoprotection ?



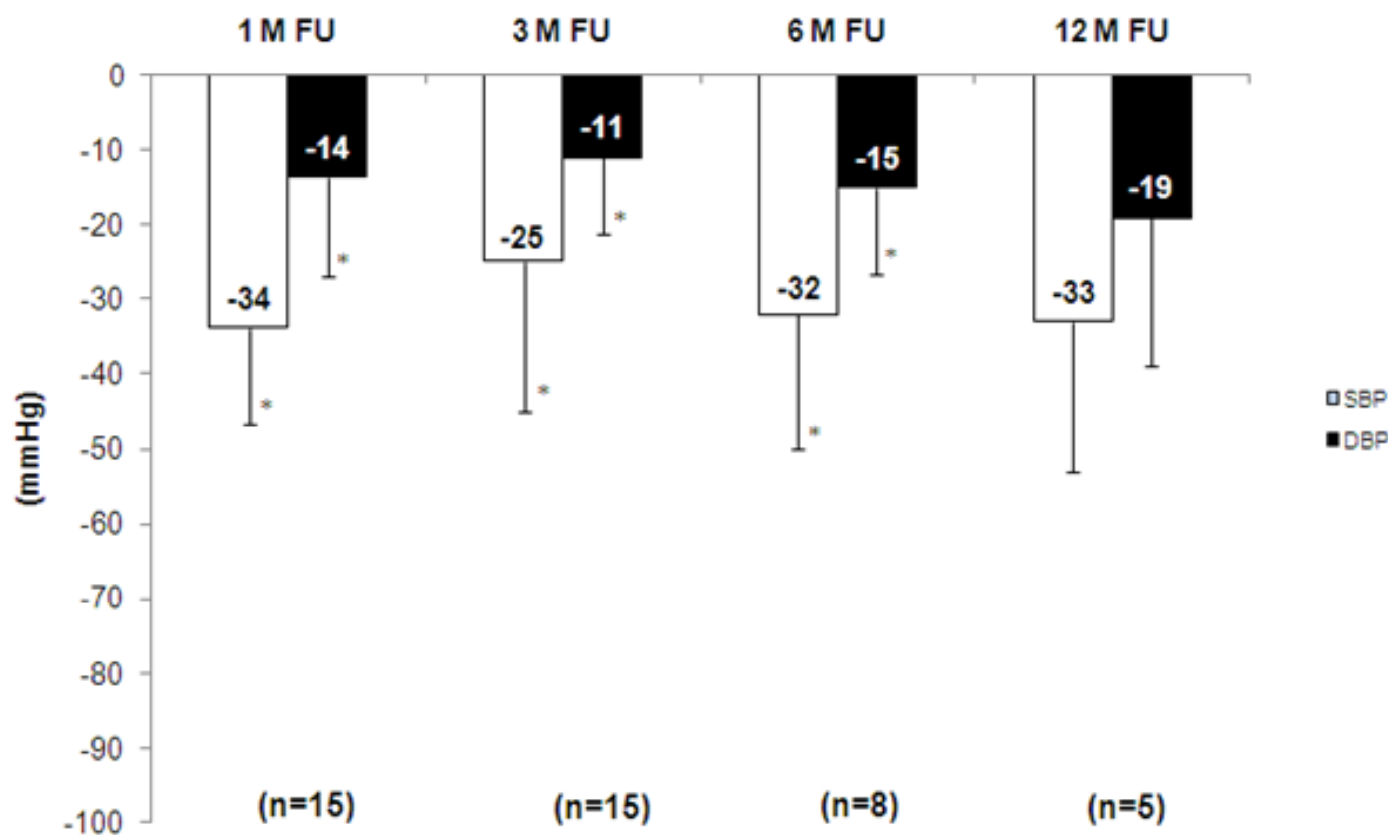
Parving HH, et al. Br Med J. 1989.  
Viberti GC, et al. JAMA. 1993.  
Klahr S, et al. N Eng J Med. 1994.  
Hebert L, et al. Kidney Int. 1994.  
Lebovitz H, et al. Kidney Int. 1994.

Moschio G, et al. N Engl J Med. 1996.  
Bakris GL, et al. Kidney Int. 1996.  
Bakris GL. Hypertension. 1997.  
The GISEN Group. Lancet. 1997.

# Renal Denervation in Moderate to Severe CKD

Dagmara Hering,<sup>\*†</sup> Felix Mahfoud,<sup>‡</sup> Antony S. Walton,<sup>§</sup> Henry Krum,<sup>§</sup> Gavin W. Lambert,<sup>\*</sup> Elisabeth A. Lambert,<sup>\*</sup> Paul A. Sobotka,<sup>||¶</sup> Michael Böhm,<sup>‡</sup> Bodo Cremers,<sup>‡</sup> Murray D. Esler,<sup>\*§</sup> and Markus P. Schlaich<sup>\*§</sup>

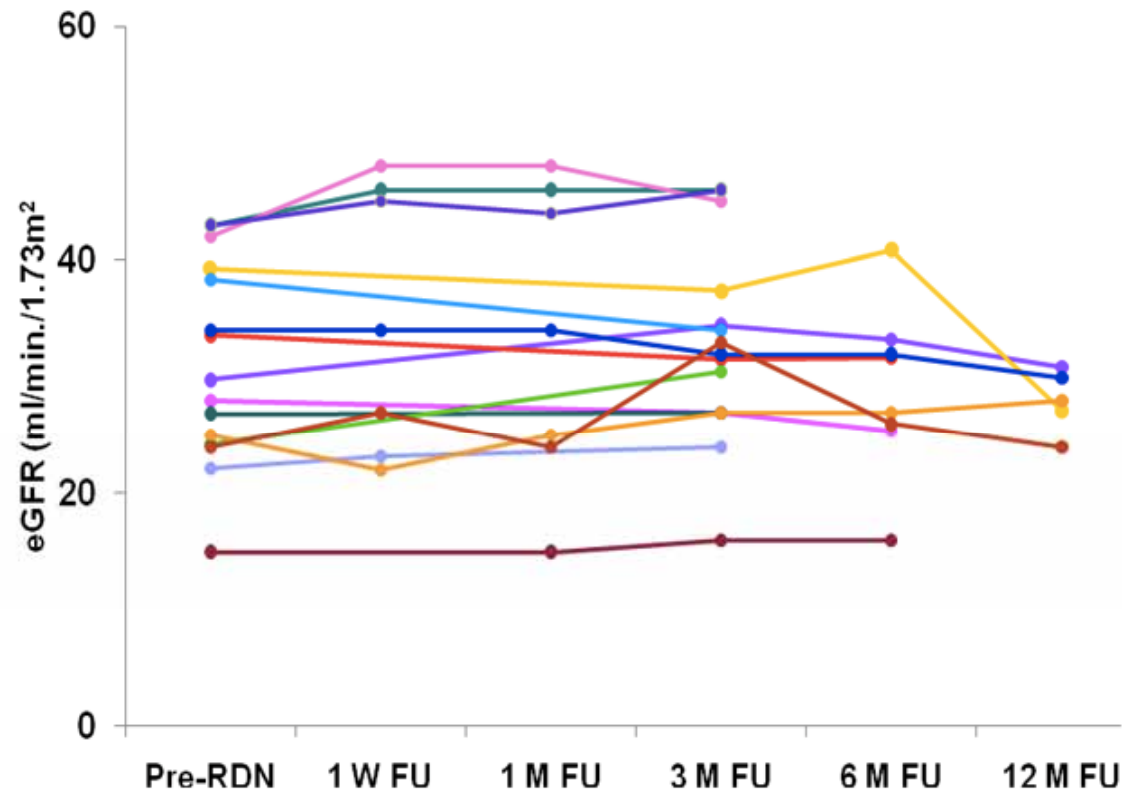
- **baseline BP 174 ± 22 / 91 ± 16 mmHg**
- **5.6 ± 1.3 antihypertensive drugs**
- **Mean GFR : 31ml/min/1.73m<sup>2</sup>**



# RDN in CKD 3-4 – a pilot study



- 15 patients with CKD 3-4
  - Baseline: mean GFR  $31.2 \pm 8.9$  ml/min/1.73 m<sup>2</sup>





# SMC registry



- To investigate the efficacy and safety of RDN in patients with milder resistant hypertension
- **Key inclusion criteria**
  - Office blood pressure  **$\geq 140$  mmHg** despite  $\geq 3$  anti-hypertensive medications
  - eGFR (MDRD)  $\geq 45$  mL/min/1.73m<sup>2</sup>
- **Key exclusion criteria**
  - known secondary cause of hypertension
  - Type I diabetes mellitus
  - renovascular abnormalities: significant renal artery stenosis, prior renal stenting or angioplasty

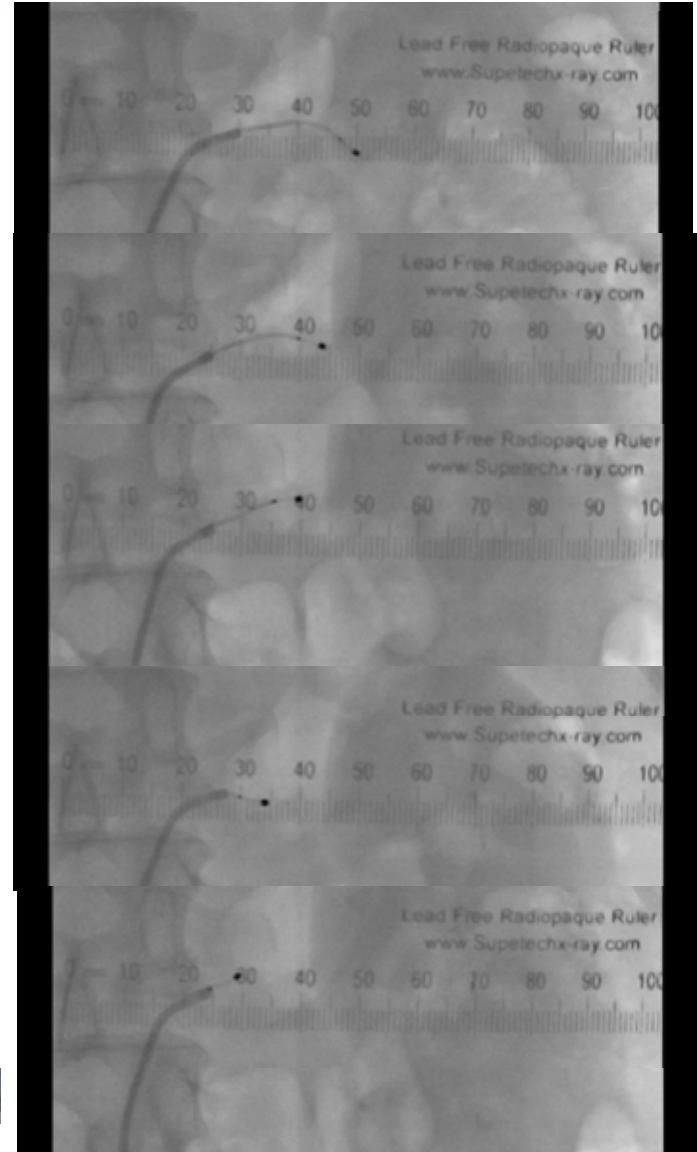
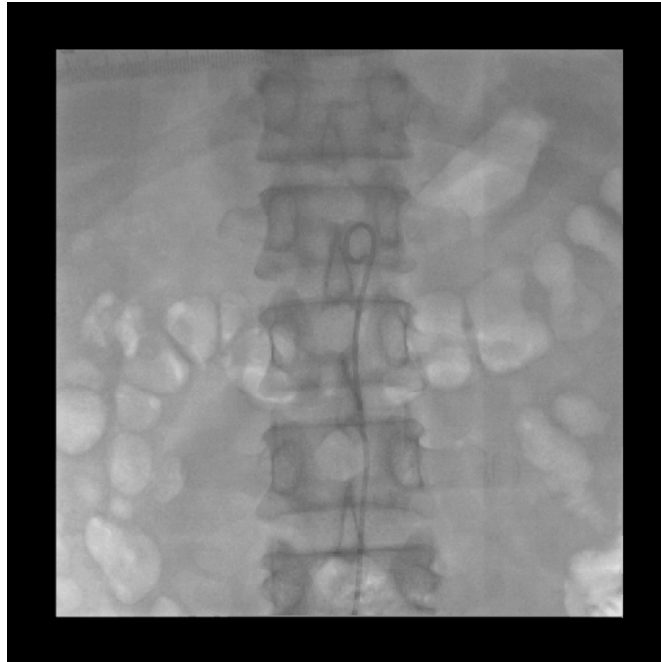
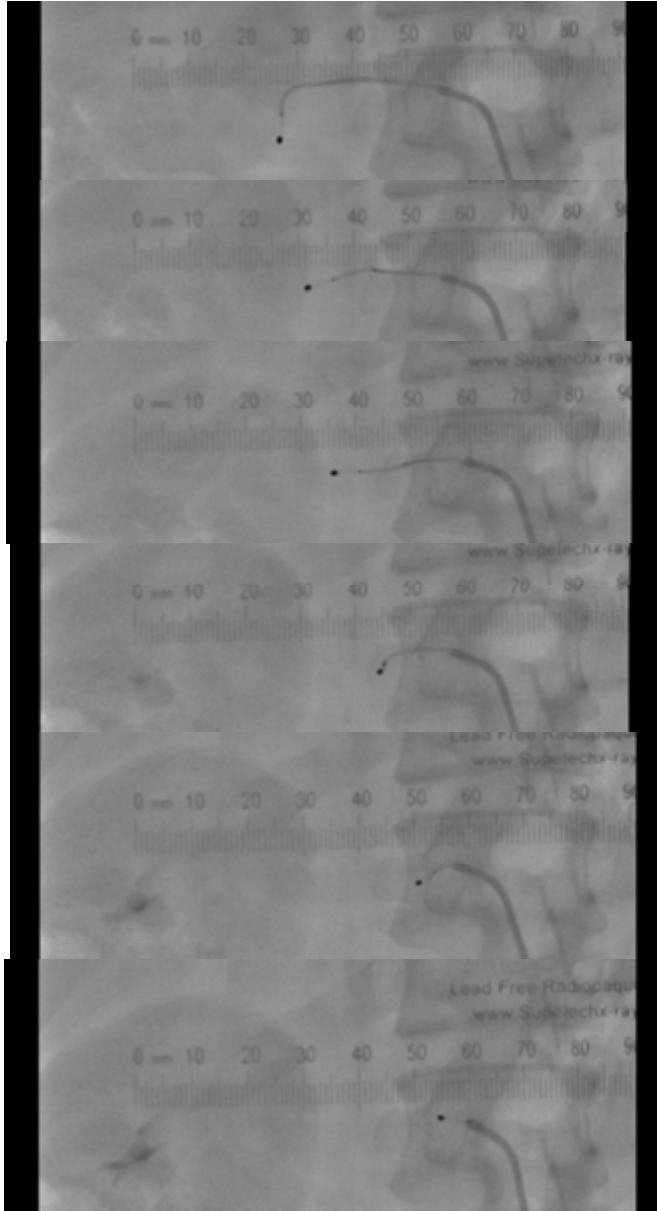
# Case



- **M/45**
- **Office BP : 170/115 mmHg HR: 88/min**
- **171cm, 94 kg, policeman**
- **Hypertension for 5 year**
- **Medication Chart**

<b>Office BP</b>	<b>170/115mmHg</b>
Felodipine	5 mg
Carvedilol	50mg
Valsartan	320mg
Hydrochlorothizide	12.5mg

# Case : Renal denervation



# Blood Pressure F/U



**Weight gain : 5 kg**

<b>Months</b>	<b>Initial (3/12/12)</b>	<b>1</b>	<b>6</b>	<b>9</b>	<b>12 (4/1/13)</b>
<b>BP mmHg</b>	<b>170/115</b>	<b>144/90</b>	<b>130/85</b>	<b>110/75</b>	<b>105/70</b>

Medication

Felodipine 5mg  
Carvedilol 50mg  
Valsartan 320mg  
Hydrothiazide 12.5mg

dizziness

160mg ↓

# Total SMC RDN (n=36)



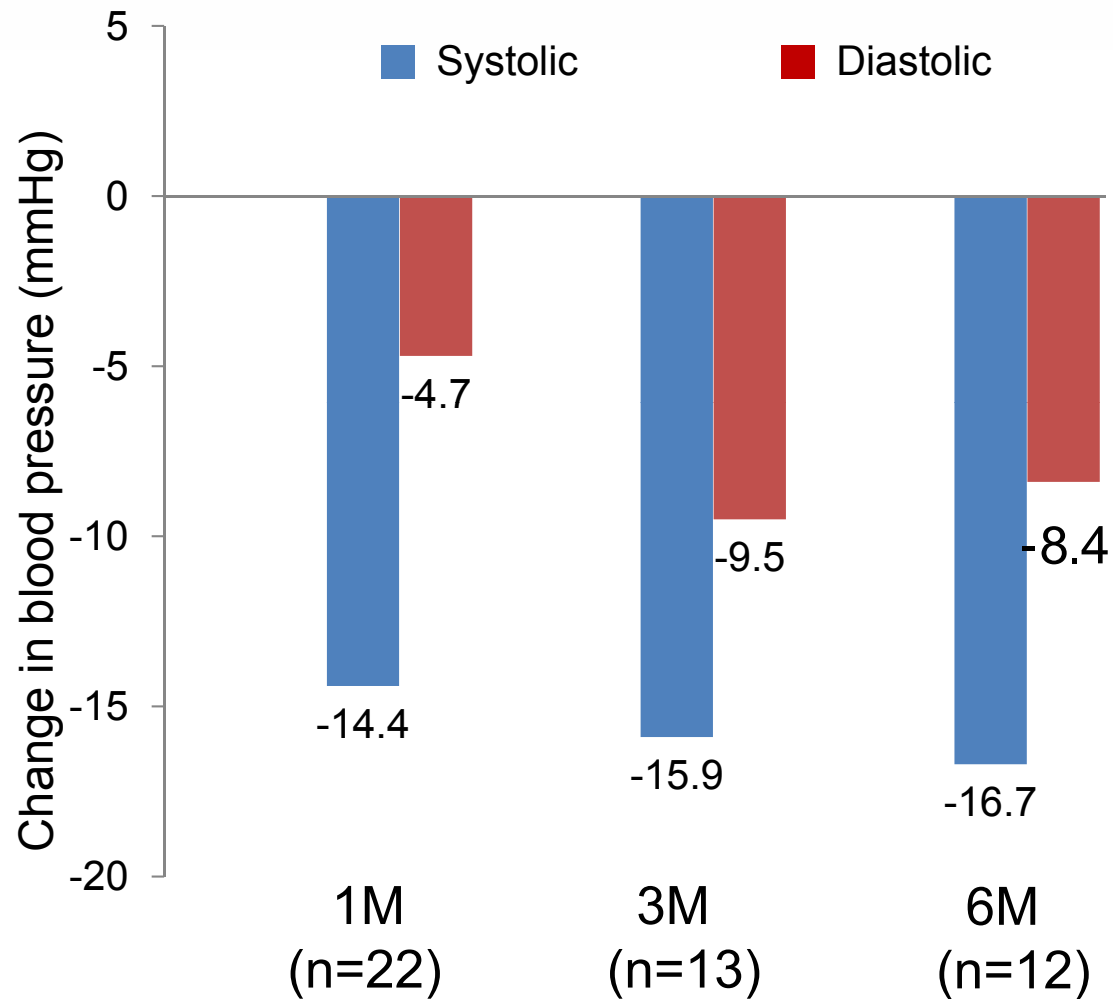
<b>Demographics</b>	Age (years)	52.6 ± 13
	Gender (% female)	20.0%
<b>Co-morbidities</b>	Diabetes Mellitus II (%)	25.7%
	CAD (%)	19.2%
	Hyperlipidemia (%)	54.3%
	eGFR (mL/min/1.73m <sup>2</sup> )	78.1 ± 16.7
<b>Blood Pressure</b>	<b>Baseline BP (mmHg)</b>	<b>164/101 ± 19/19</b>
	<b>Number of anti-HTN meds (mean)</b>	<b>4.0 ± 1.3</b>
	ACE/ARB (%)	94.3%
	Beta-blocker (%)	74.3%
	Calcium channel blocker (%)	77.1%
	Vasodilator (%)	2.9%
	Diuretic (%)	77.1%
	Spironolactone (%)	14.3%
Alpha-blocker(%)	2.9%	

# SMC registry (n=27)



<b>Demographics</b>	Age (years)	51 ± 13
	Gender (% female)	15.4%
<b>Co-morbidities</b>	Diabetes Mellitus II (%)	11.5%
	CAD (%)	23.8%
	Hyperlipidemia (%)	42.3%
	eGFR (mL/min/1.73m <sup>2</sup> )	77.3 ± 16.4
<b>Blood Pressure</b>	<b>Baseline BP (mmHg)</b>	<b>166/104 ± 18/21</b>
	<b>Number of anti-HTN meds (mean)</b>	<b>3.5 ± 0.6</b>
	ACE/ARB (%)	92.3%
	Beta-blocker (%)	69.2%
	Calcium channel blocker (%)	84.6%
	Vasodilator (%)	3.8%
	Diuretic (%)	84.6%
	Spirolactone (%)	11.5%
	Alpha-blocker(%)	3.8%

# Office BP change (n=27)



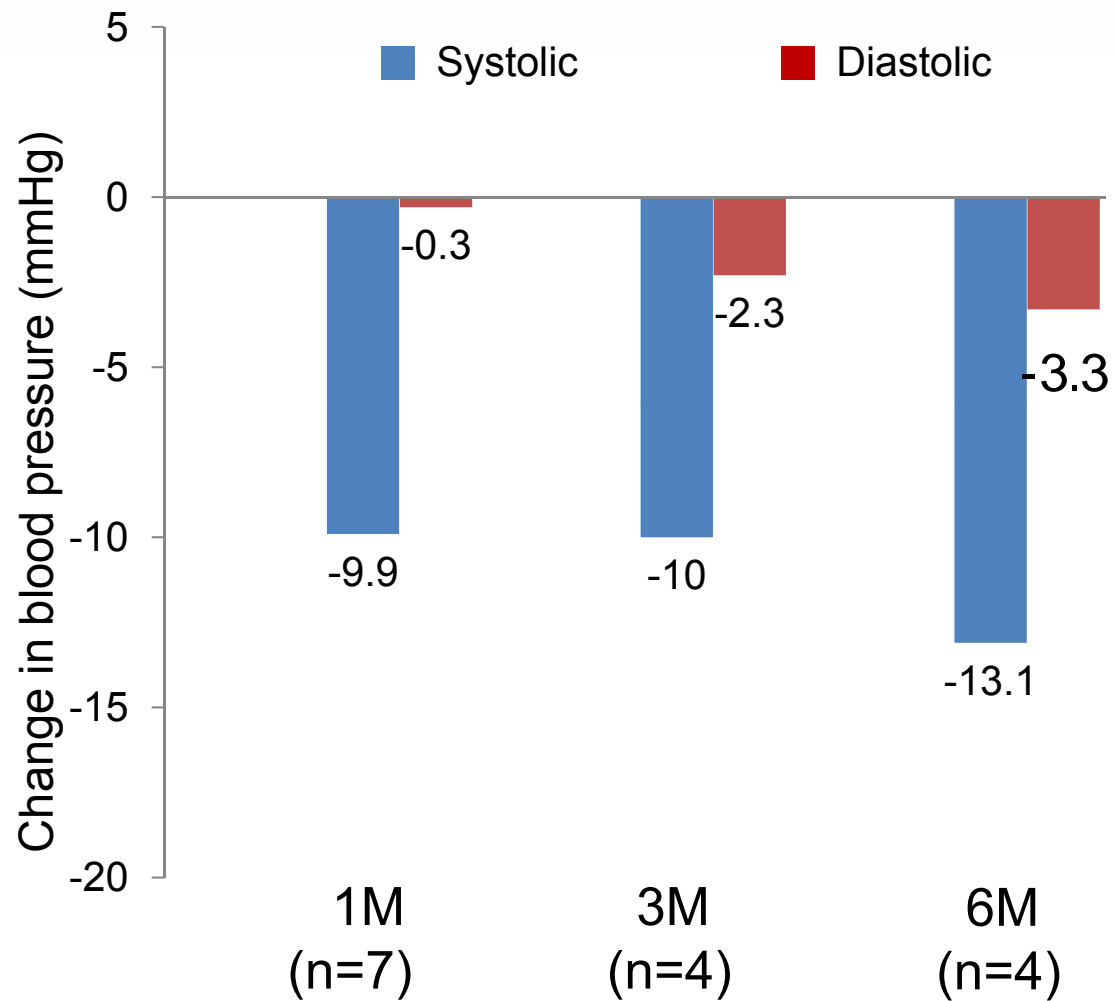
**1 Month Non-responder : 5/22(22.7%)**  
**: defined as a SBP reduction of < 10mmHg**

# SMC data for mild hypertension (n=9)

<b>Demographics</b>	Age (years)	53.1 ± 14
	Gender (% female)	11.1%
<b>Co-morbidities</b>	Diabetes Mellitus II (%)	22.2%
	CAD (%)	22.2%
	Hyperlipidemia (%)	66.7%
	eGFR (mL/min/1.73m <sup>2</sup> )	84.6 ± 23.3
<b>Blood Pressure</b>	<b>Baseline BP (mmHg)</b>	<b>154/94 ± 5/11</b>
	<b>Number of anti-HTN meds (mean)</b>	<b>3.7 ± 1.3</b>
	ACE/ARB (%)	88.9%
	Beta-blocker (%)	66.7%
	Calcium channel blocker (%)	88.9%
	Vasodilator (%)	11.1%
	Diuretic (%)	88.9%
	Spironolactone (%)	11.1%
Alpha-blocker(%)	11.1%	



# SMC data for mild hypertension (n=9)



# Safety profile – data from SMC

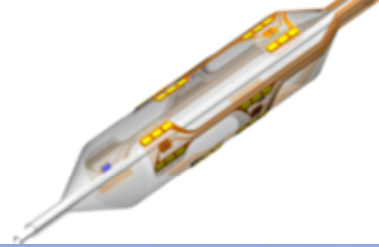


- **procedure related complications (n=36)**
  - No access site complications
  - No renal artery complications including dissection
  - 3 spasm
  - 1 junctional bradycardia
- **Long term complications**
  - No renal artery stenosis at 6 month duplex (n= 18)
  - No renal dysfunction at 6 months lab (n= 19 )

# Take Home Message



- **Renal denervation is an effective and safe treatment modality for resistant hypertension**
- **Renal denervation may be a safe and effective treatment for patients with milder resistant hypertension**



**Thank you  
for your attention**



## CORRESPONDENCE

## Research Correspondence

### Secondary rise in blood pressure after renal denervation

Oliver Vonend, Gerald Antoch, Lars Christian Rump, Dirk Blondin

Lancet 2012; 380: 778

University Düsseldorf, Medical Faculty, Department of Nephrology (O Vonend MD, Prof L C Rump MD), and Department of Diagnostic and Interventional Radiology (Prof G Antoch MD, D Blondin MD), Heinrich-Heine-University Düsseldorf, Medical Faculty, Düsseldorf, Germany

Correspondence to: Prof Lars Christian Rump, Moorenstr. 5, 40225 Düsseldorf, Germany christian.rump@med.uni-duesseldorf.de

In July, 2011, a 58-year-old man with type II diabetes and hypertension resistant to treatment was referred to our hospital for renal denervation. He had had hypertension for 30 years and had been in minor stroke implanted. His blood pressure was 170/90 mm Hg. He was treated with amlodipine and lisinopril. His hypertension was confirmed by ambulatory blood pressure measurement. He was treated with Aldosterone antagonist. He had no renal artery stenosis on both sides

on both sides. His medication was not changed. In February, 2012, blood pressure had increased to 180/102 mm Hg. Serum creatinine was stable, but renin

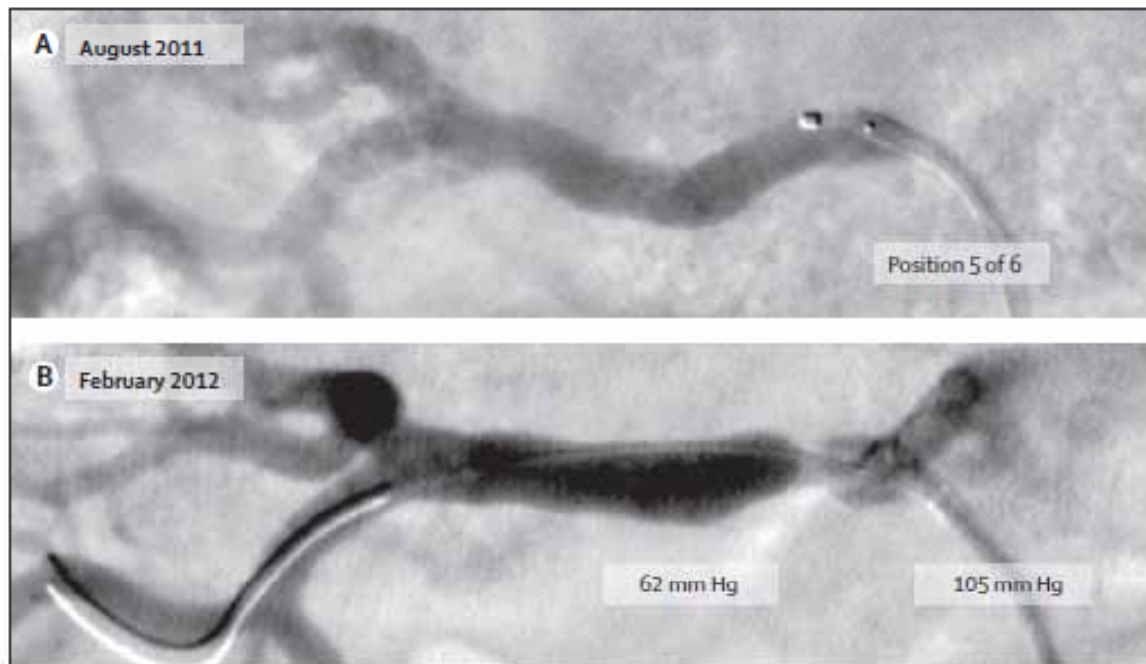
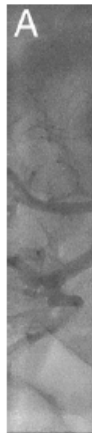


Figure: Digital subtraction angiography showing (August, 2011) renal denervation at a superior position (position 5 of 6) near the ostium; and (February, 2012) ostial stenosis and blood pressure gradient across the stenosis.

5 months f/u

# For mild hypertension ?

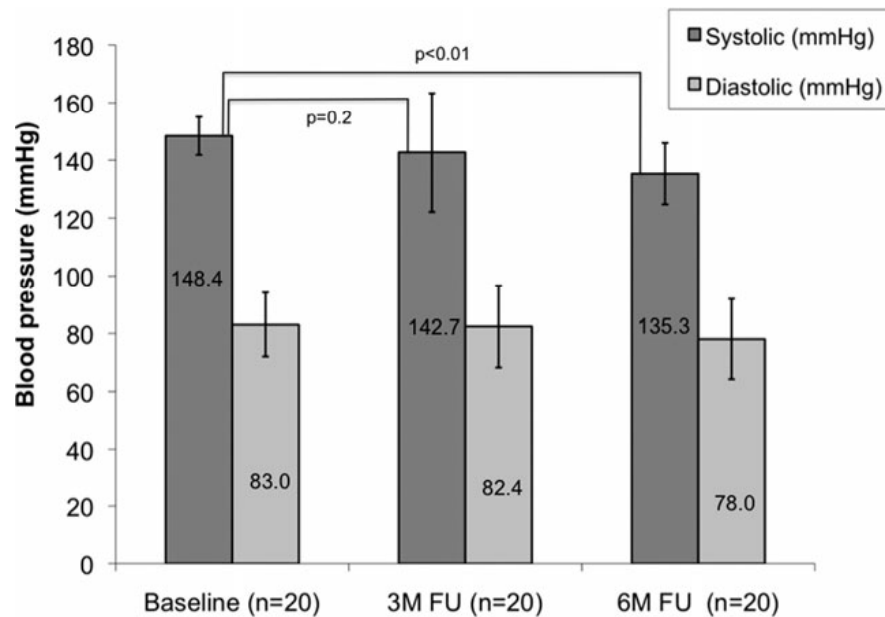


## Original Studies

### Renal Sympathetic Denervation as Second-Line Therapy in Mild Resistant Hypertension: A Pilot Study

N=20 patients  
Baseline systolic BP 148.8 mmHg  
diastolic BP 83.0 mmHg  
No of medications : 5.4

Benjamin Kaltenbach,<sup>1</sup> Jennifer Franke,<sup>1</sup> MD, Stefan C. Bertog,<sup>1,2</sup> MD, FACC, FSCAI,  
Daniel H. Steinberg,<sup>3</sup> MD, Ilona Hofmann,<sup>1</sup> MD, and Horst Sievert,<sup>1\*</sup> MD, FACC, FSCAI, FESC



6 months F/U : **-13.1 mmHg**

