YONSEI UNIVERSITY

RADIANCE HTN SOLO Off Trial: ReCor Medical Paradise Technology and Results

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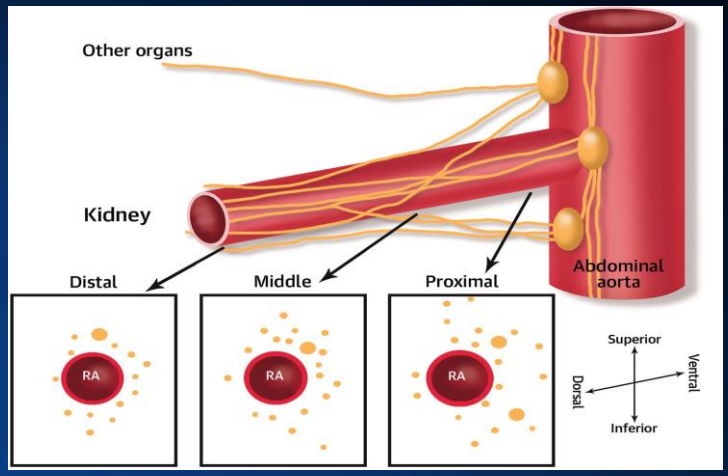
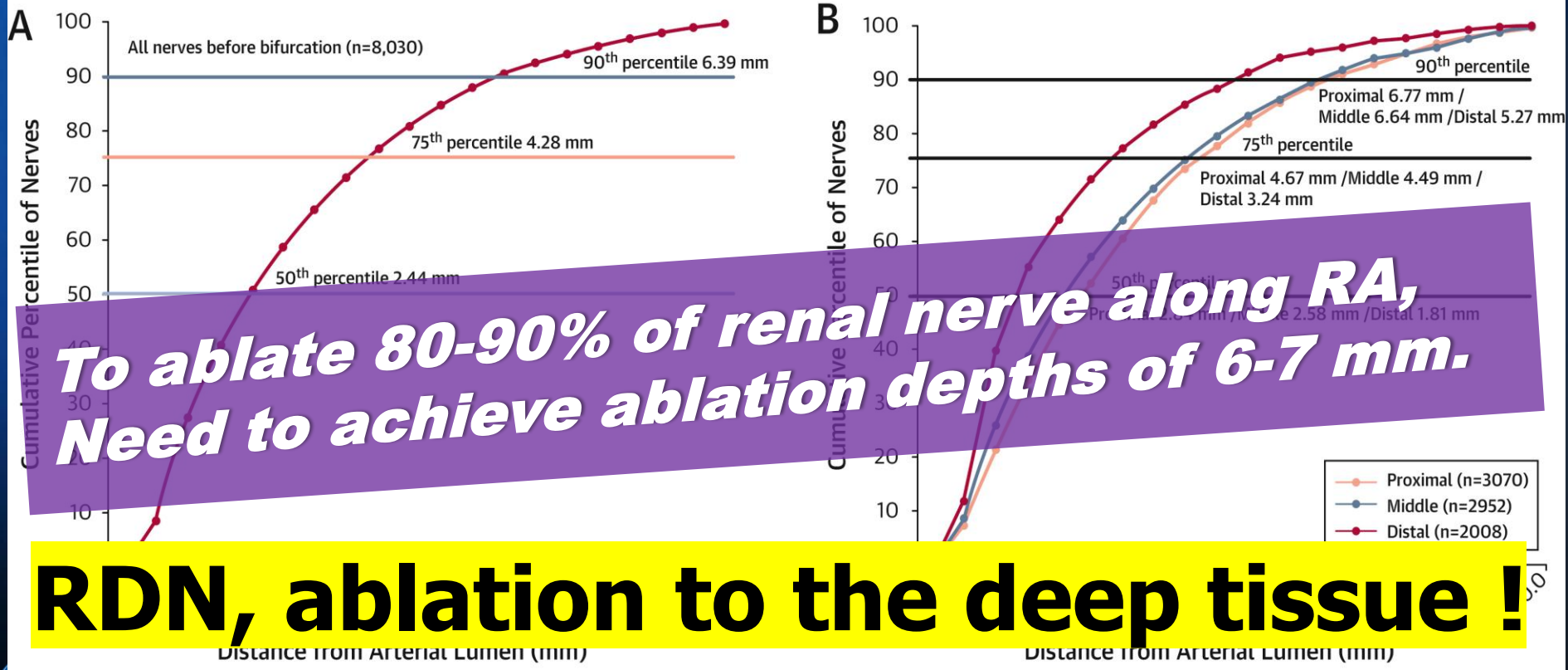
- **Nothing to disclose.**

For the successful RDN for the patients with resistant hypertension, the strategies to overcome technical failures associated with the incomplete denervation are needed.

Understanding of complex peri-renal sympathetic nerves



Cumulative Distribution of Nerves at Distance From Lumen



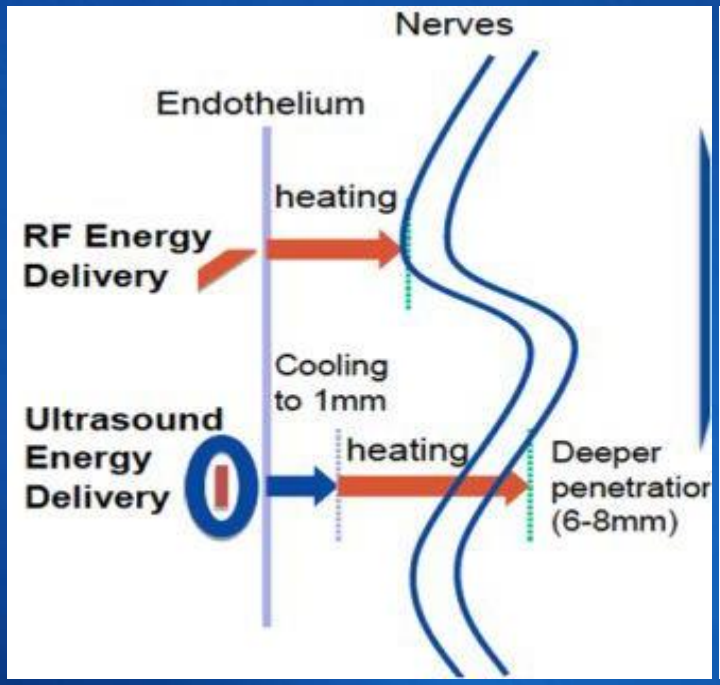
To ablate 80-90% of renal nerve along RA, Need to achieve ablation depths of 6-7 mm.

RDN, ablation to the deep tissue !

Sakakura K et al. JACC. 2014;64:634–643

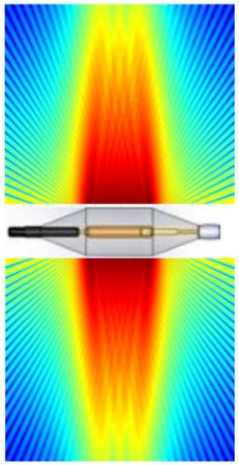
Paradise System

Endovascular Ultrasound Renal Denervation



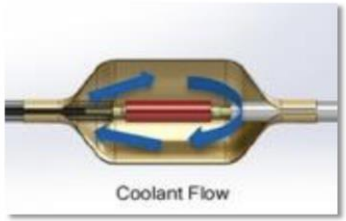
Ultrasonic Heating

Circumferential ablation in the main renal artery



Water Cooling

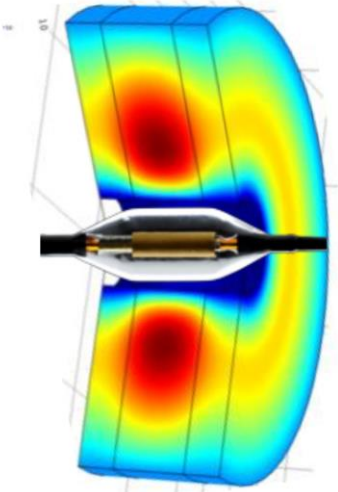
Arterial wall protection by water circulating through balloon



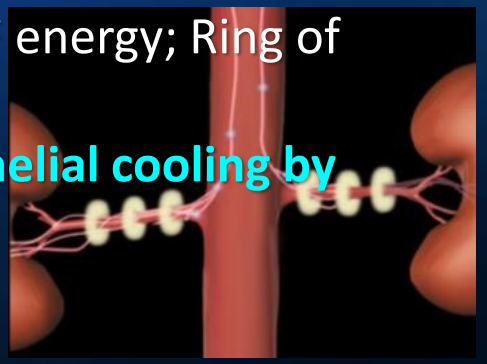
Thermal Profile

Ablation depth of 1-6 mm & length of 5 mm

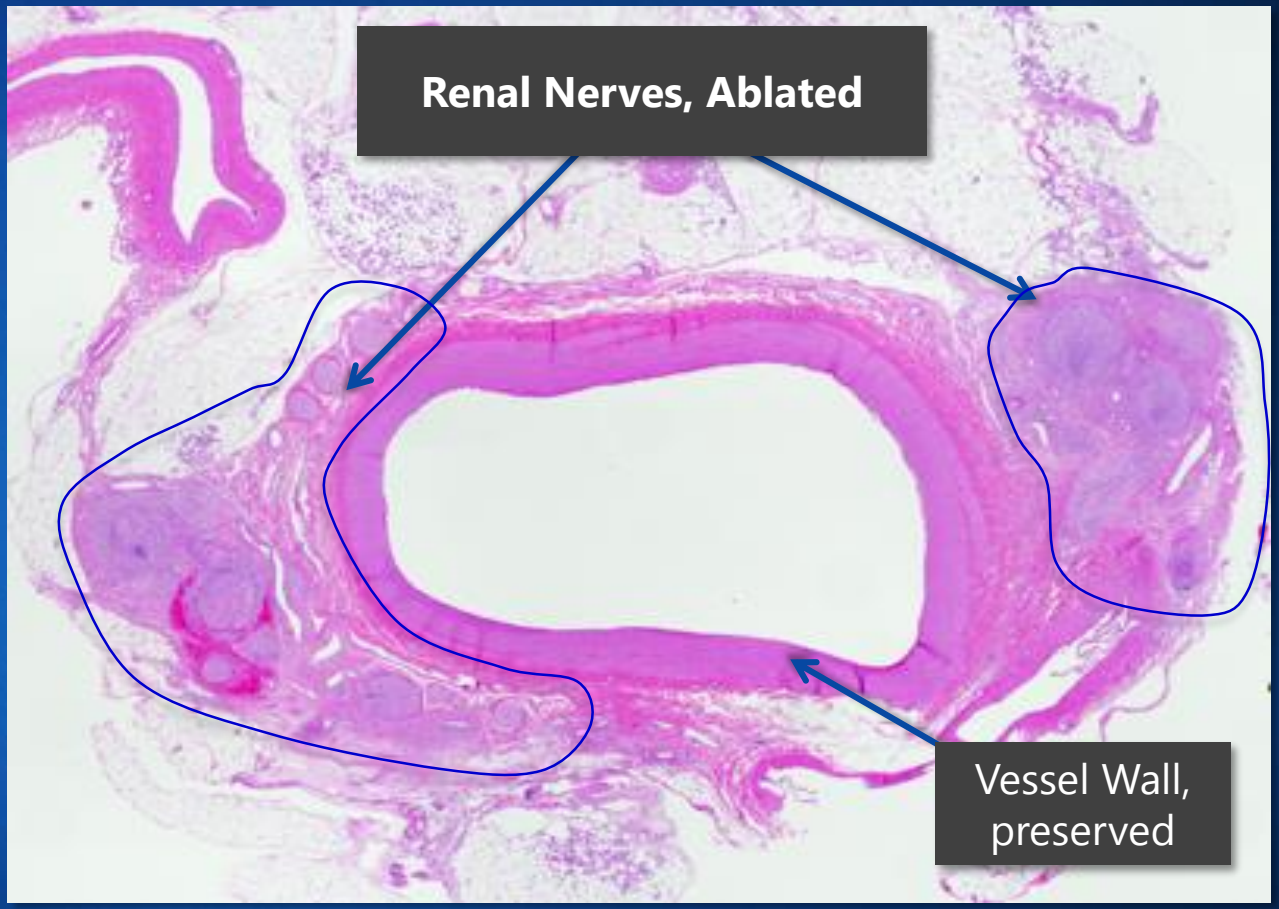
2-3 ablations → 7 seconds each



- **Ultrasound energy delivery, more deeper pentation** than RF energy; Ring of ablative energy (ablation depth of 1-6 mm)
- The thermal injury in intima was inhibited after using **Endothelial cooling by water** circulating through balloon
- 2-3 ablations delivered to each main renal artery



Preclinical Histology

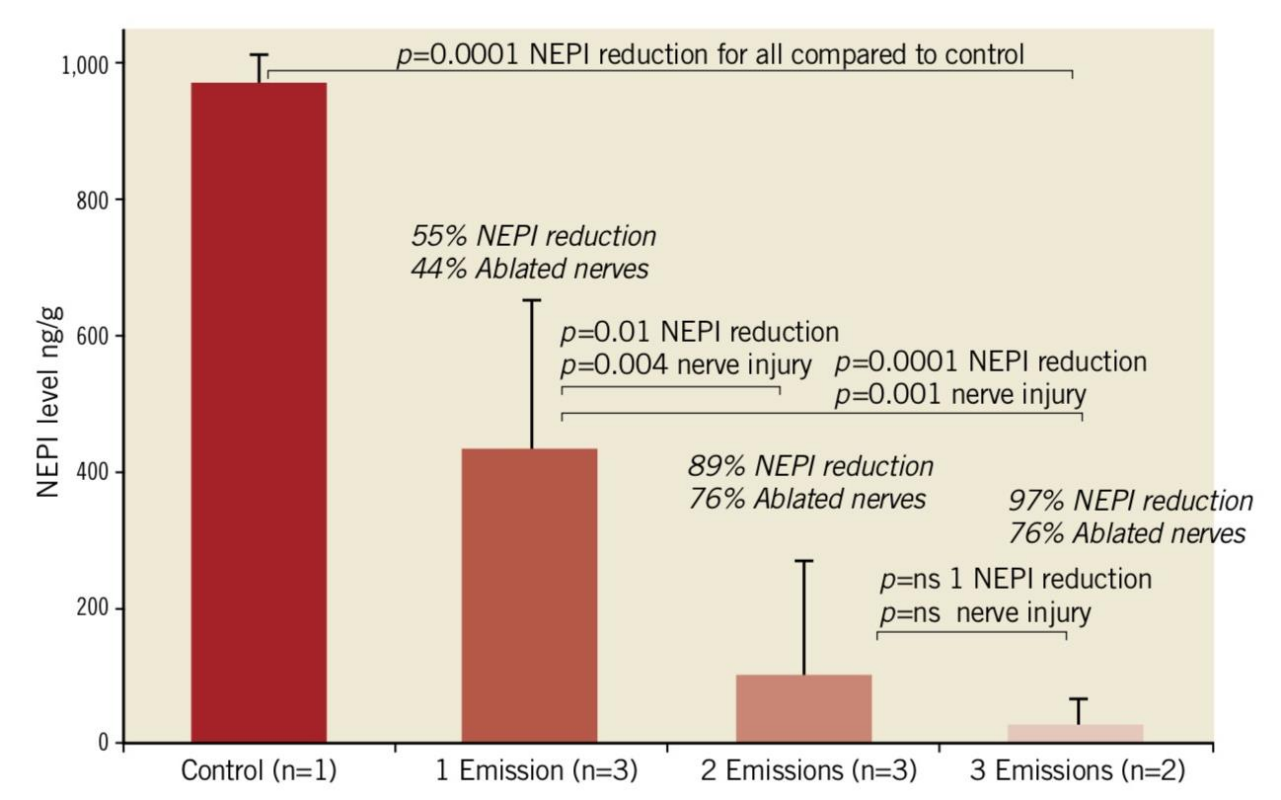


- Renal nerves (even nerves in the deep position) were ablated, yet arterial wall protected from thermal injury.

Renal sympathetic nerve denervation using intraluminal ultrasound within a cooling balloon preserves the arterial wall and reduces sympathetic nerve activity

Atul Pathak[1,2,3,6*], MD, PhD; Leslie Coleman[4], DVM, MS; Austin Roth[4], MS; James Stanley[4], MS; Lynn Bailey[5], DVM, MS; Peter Markham[5]; Sebastian Ewen[7], MD; Charlotte Morel[1,2], PharmD; Fabien Despas[1,2,3], PharmD, PhD; Benjamin Honton[6], MD; Jean Michel Senard[1,2,3], MD, PhD; Jean Fajadet[6], MD; Felix Mahfoud[7], MD, PhD

Porcine Renal Norepinephrine Reduction according to the No of emissions



- **Greater NEPI reduction observed in arteries treated with 2 ~ 3 bilateral ultrasound emissions.**

Pathak et al. EuroIntervention. 2015;11(4):477-84.

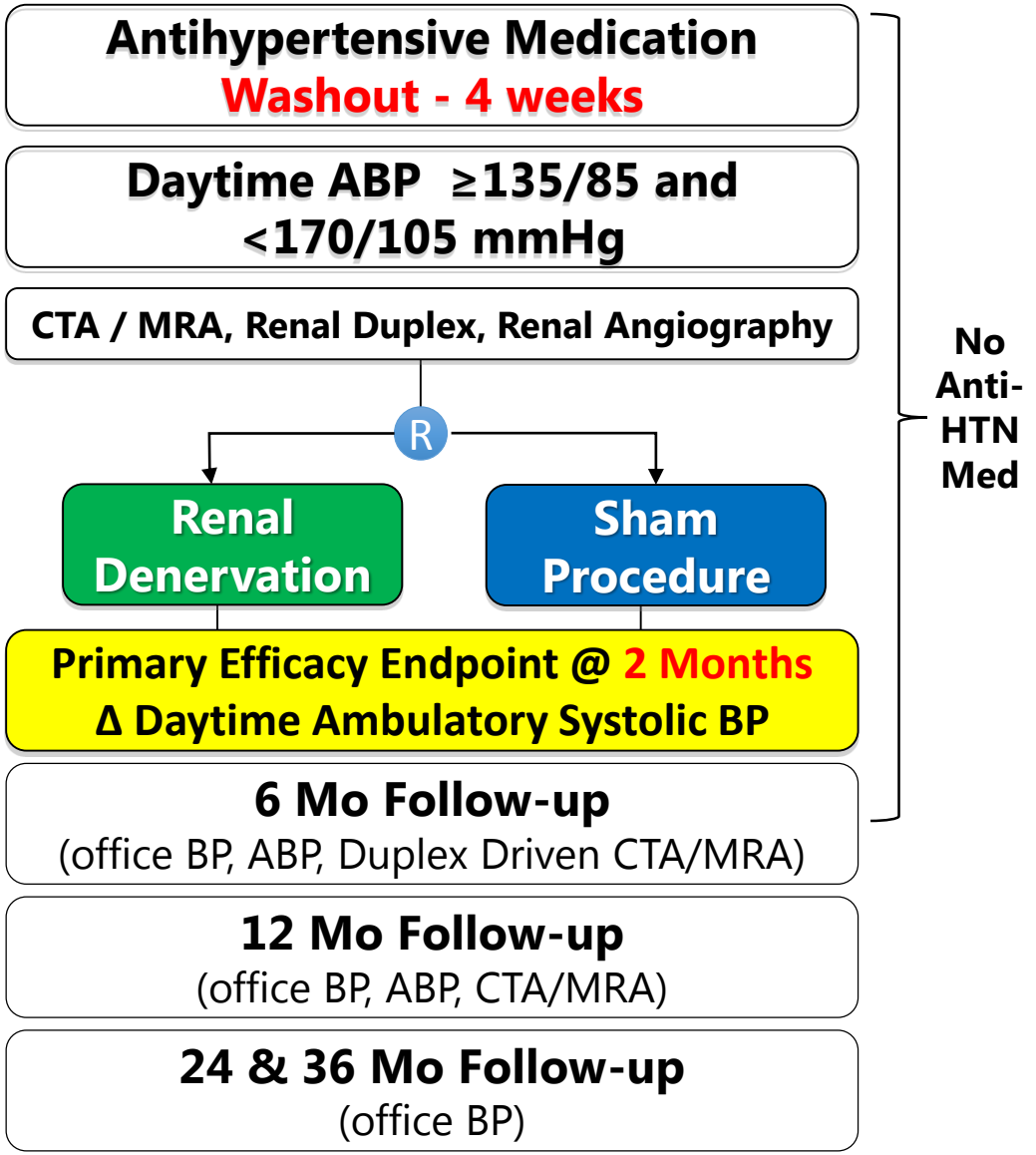
RADIANCE-HTN SOLO study

<Primary Objective>
Evaluate whether RDN with the Paradise System (Ultrasound RDN) can significantly and safely reduce daytime ASBP at 2 mouths compared with a sham procedure

Key Entry Criteria:

- **Hypertension controlled on 1-2 anti-HTN meds or uncontrolled on 0-2 meds**
- **Off-med daytime ABP ≥135/85 & <170/105 mmHg**
- Age18-75years/ No prior CV or CB events
- No Type I or uncontrolled Type II DM
- eGFR ≥40mL/min/m^2
- Eligible renal artery anatomy (bilat Ø 4-8mm, length ≥25mm, and no stenosis ≥30%)

Medications at Screening	**Essential HTN - 0, 1, 2 meds**
Primary Endpoint	**Reduction in mean daytime ambulatory SBP from baseline to 2M**
Sample size	**N=146 (73 vs 73)**
Participating centers	39 center from EU & US



LauraMauri, Am Heart J 2018;195:115-29

RADIANCE-HTN
SOLO

Subject Flow

803 Patients enrolled

633 Excluded prior to angiography
- 236 Did not meet ABP criteria
- 109 Did not meet renal anatomic criteria on CTA/MRA
- 101 Withdrew consent
- 60 Excluded during washout based on home BP measurement
- 47 Did not meet office BP criteria
- 37 Study complete before patient could be randomized
- 29 Did not meet clinical inclusion criteria
- 14 Did not attend 2nd screening visit

170 Underwent renal angiography

24 Excluded at angiography

146 Randomized

74 Renal Denervation
Intention-to-Treat population
- 74 Available for clinical follow-up
- 73 Completed 2-month ABPM

72 Sham Procedure
Intention-to-Treat population
- 72 Available for clinical follow-up
- 71 Completed 2-month ABPM

10 Excluded
- 2 received anti-HTN meds without meeting escape criteria
- 2 with no renal denervation (both also received anti-HTN meds without meeting escape criteria)
- 1 received anti-HTN med according to escape criteria
- 2 with baseline diastolic ABP lower than entry criteria
- 1 with pre-existing ostial renal artery stenosis
- 1 with unilateral renal denervation
- 1 did not complete ABP measurement

14 Excluded
- 10 received anti-HTN meds without meeting escape criteria
- 3 received anti-HTN med according to escape criteria
- 1 did not complete ABP measurement

64 Included in Per-Protocol population

58 Included in Per-Protocol population

Azizi M, Lancet. 2018 ;391(10137):2335-2345

Baseline Characteristics

Clinical Characteristics	RDN (N=74)	Sham (N=72)
Age (years)	54.4 ± 10.2	53.8 ± 10.0
Female sex (%)	38%	46%
Race (%)		
White	81%	72%
Black	16%	18%
Other	3%	10%
Body mass index (kg/m^2)	29.9 ± 5.9	29.0 ± 5.0
Obstructive sleep apnea (%)	8%	11%
eGFR (ml/min/1.73m^2)	84.7 ± 16.2	83.2 ± 16.1

Baseline Blood Pressures (mm Hg)	RDN (N=74)	Sham (N=72)
Office BP after anti-HTN med washout	154.5/99.7 ± 12.4/7.7	153.6/99.1 ± 15.7/9.4
Daytime ABP after anti-HTN med washout	150.3/93.1 ± 7.8/4.8	150.0/93.5 ± 9.8/5.5
24-hour ABP after anti-HTN med washout	142.6/87.3 ± 8.1/5.0	143.8/88.6 ± 10.4/5.7

Azizi M, Lancet. 2018 ;391(10137):2335-2345

Angiographic and Procedural Characteristics

	RDN (N = 74)	Sham (N = 72)	P Value
Procedure time† (min)	**72·3** (23·3)	38·2 (12·6)	<0·0001
Contrast volume (cm^3)	140·7 (68·8)	78·7 (41·1)	<0·0001
Fluoroscopy time (min)	13·9 (7·0)	4·8 (12·3)	<0·0001
Treatment successfully delivered (minimum 2 emissions bilaterally)	71 (**95·9%**)	NA	-
Total Number of Emissions (n=72)	**5·4** (1·0)	NA	-
Mean Number of Emissions (per vessel)			
Left Renal (n=71)	2·5 (0·5)	NA	-
Right Renal (n=72)	2·8 (0·5)	NA	-
Accessory Renal Arteries (n=9)	1·2 (0·4)	NA	-
Total Emission Time (seconds) (n=72)	37·9 (6·7)	NA	

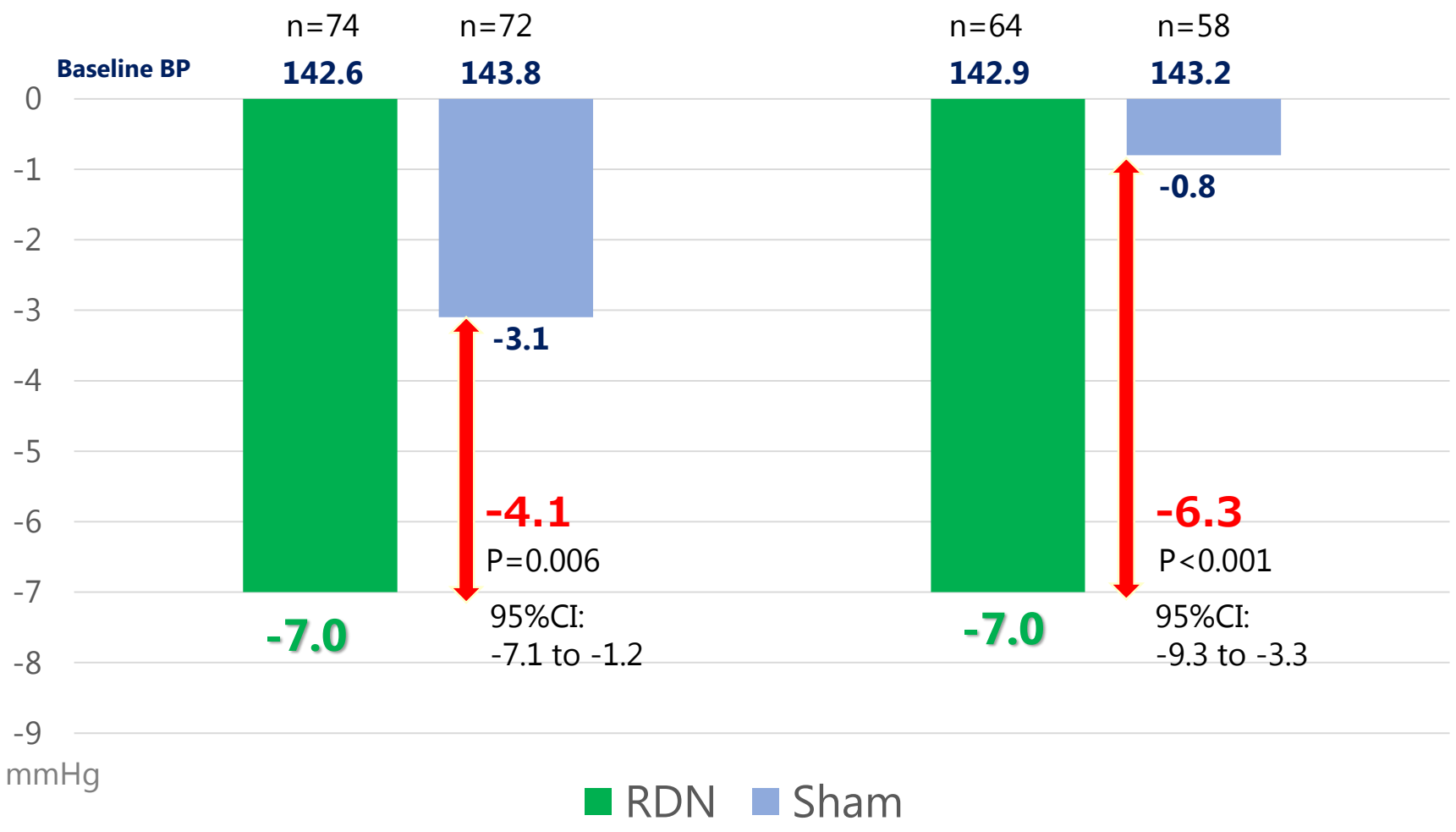
Data displayed as mean (SD) and n (%).

† Procedure time was defined as the time from arterial sheath placement to sheath removal.

Azizi M, Lancet. 2018 ;391(10137):2335-2345

RADIANCE-HTN
SOLO

Change in 24-h systolic ABP at 2mo



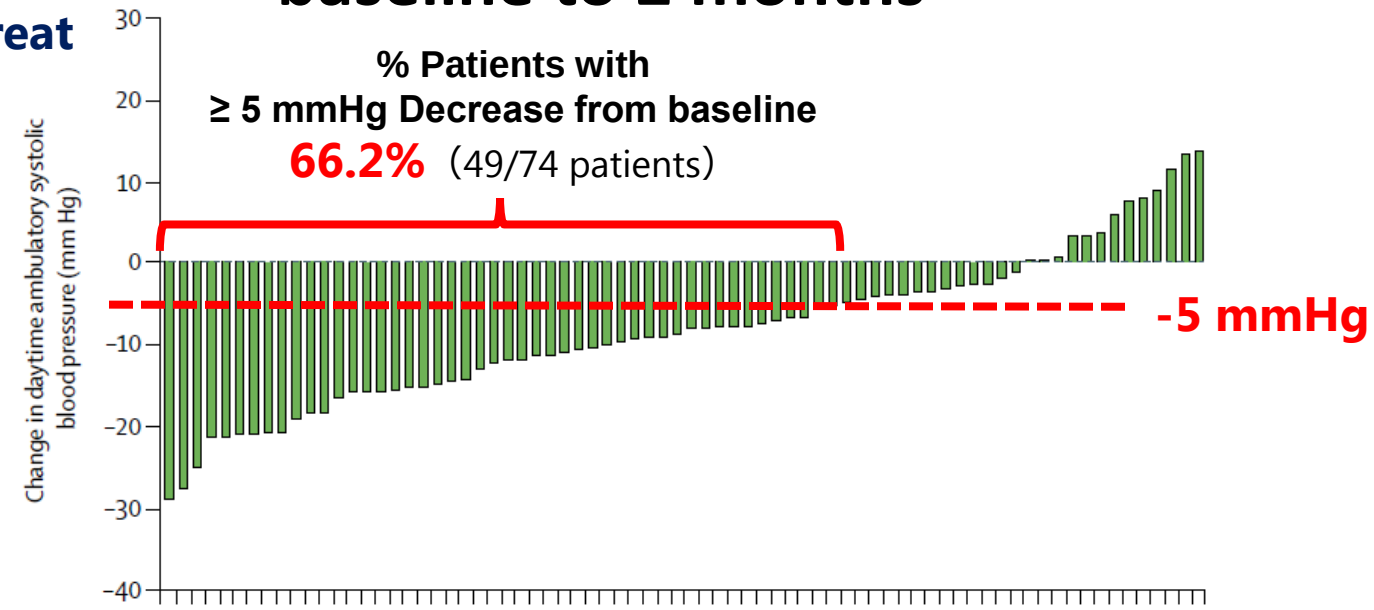
ITT: Intention-to-Treat
PP: Per-Protocol

Azizi M, Lancet. 2018 ;391(10137):2335-2345

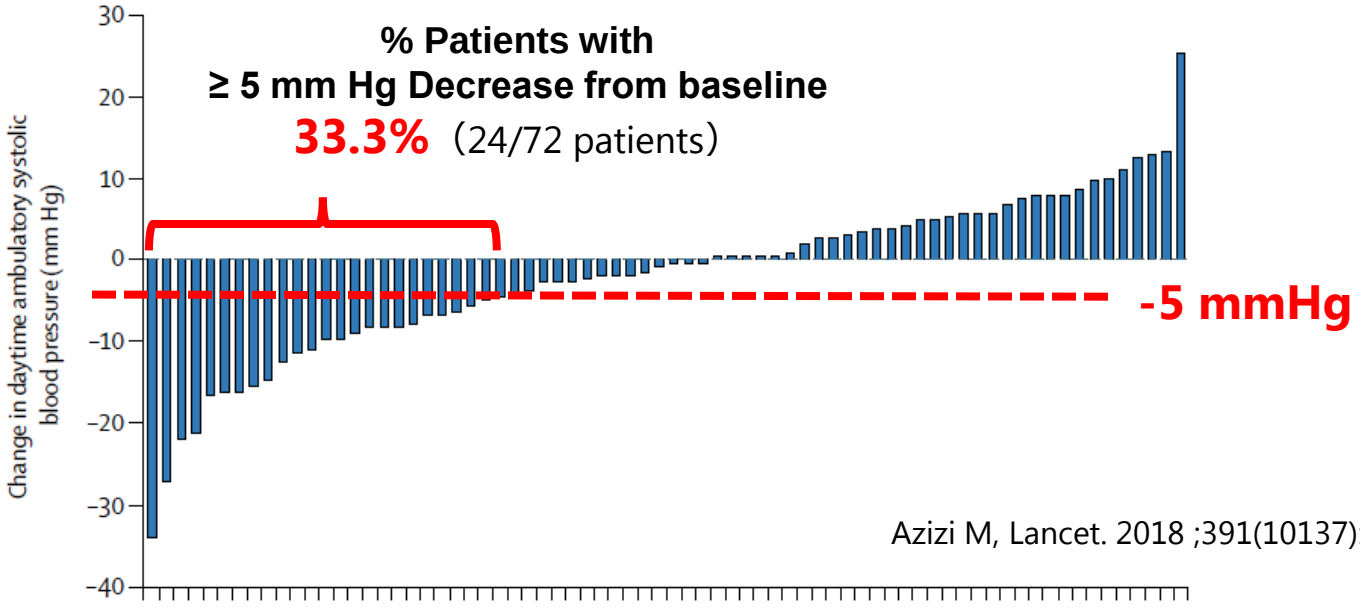
Individual Patient changes in Daytime Systolic ABP from baseline to 2 months

Intention-to-Treat

RDN

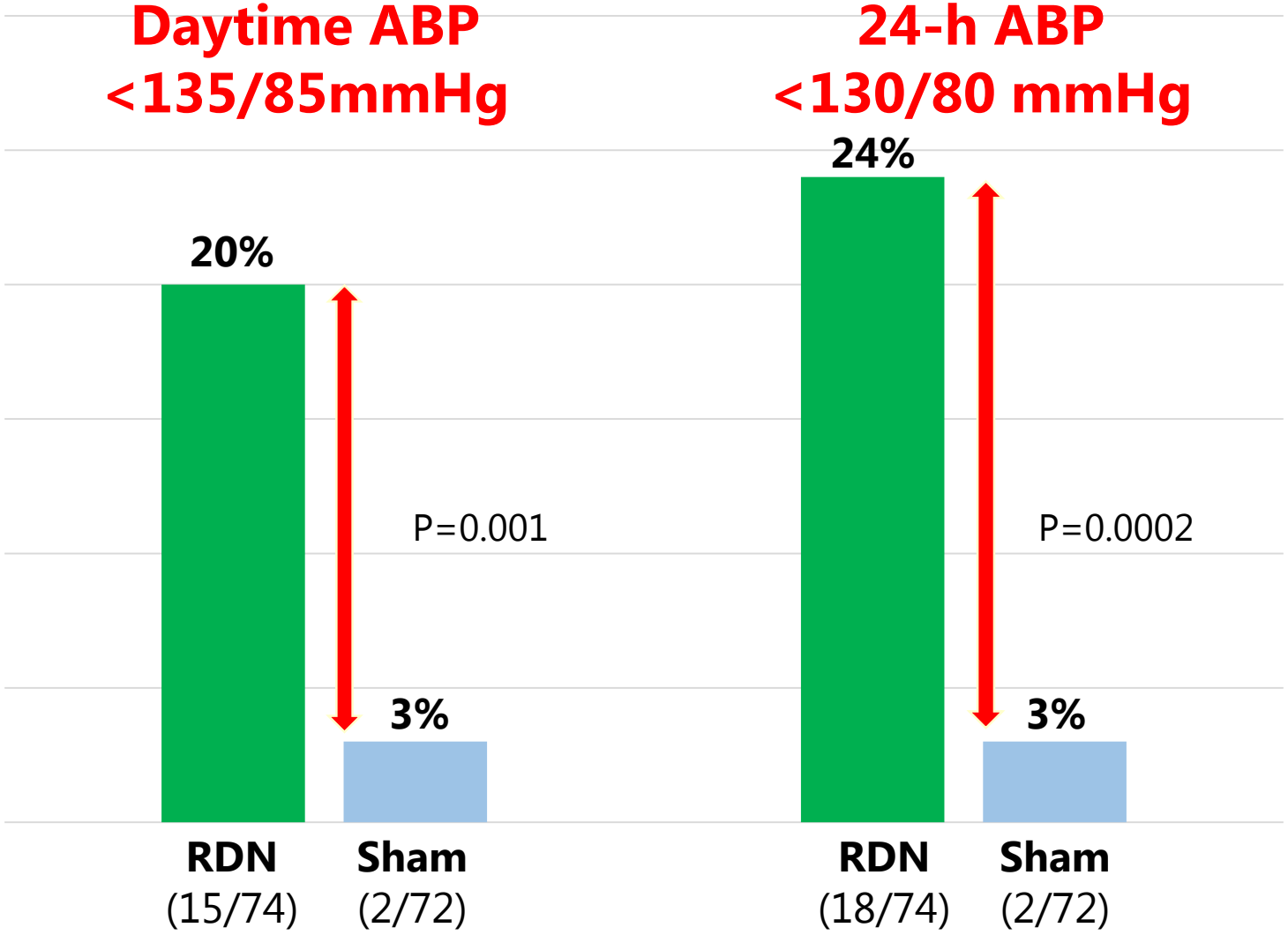


Sham



Azizi M, Lancet. 2018 ;391(10137):2335-2345

Subjects achieving controlled BP in the absence of anti-THN



Azizi M, Lancet. 2018 ;391(10137):2335-2345

Safety Events at 1 mo

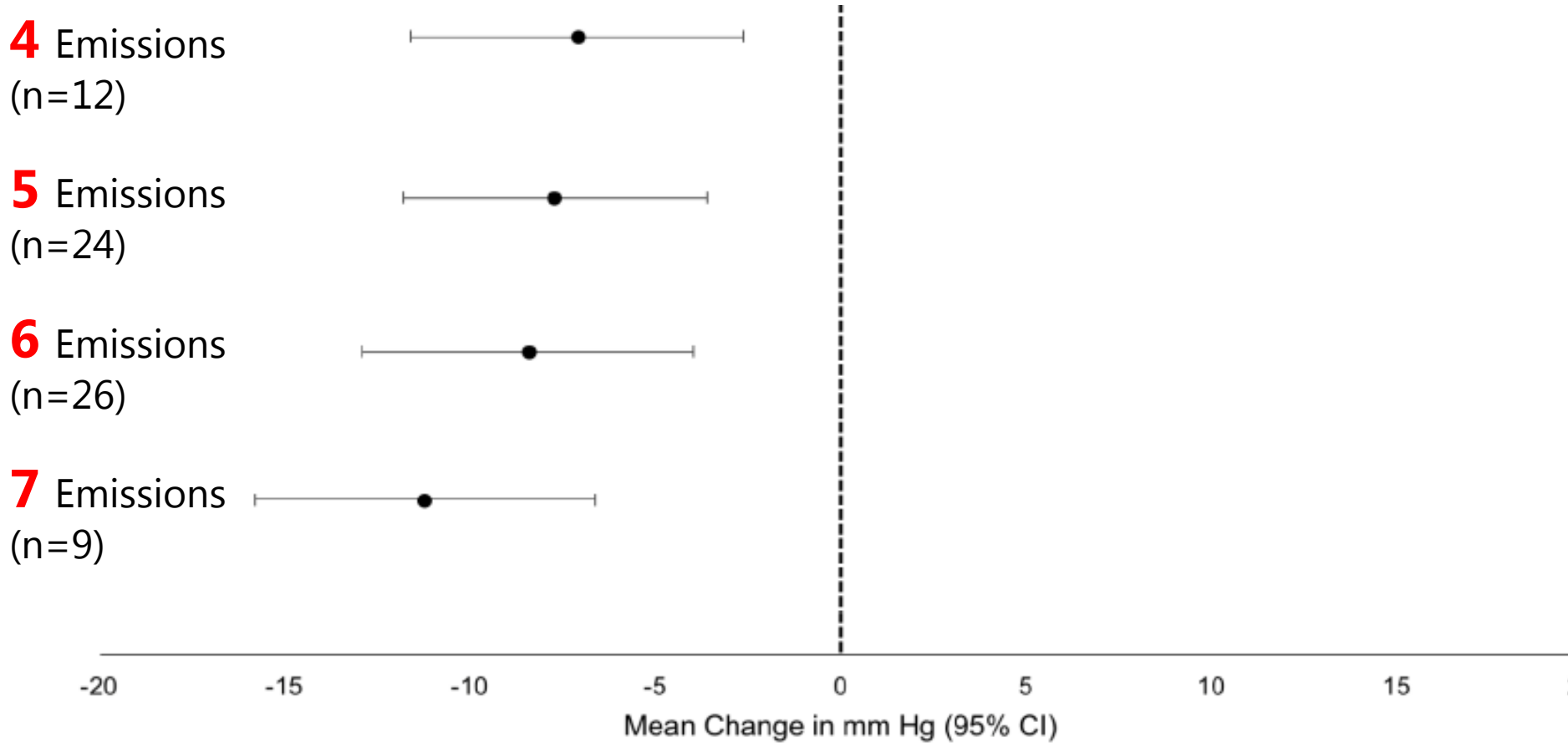
Event	RDN (N = 74)	Sham (N = 72)
Major adverse event (%)	0%	0%
Death within 30 days	0%	0%
Acute renal failure within 30 days	0%	0%
Embolic event resulting in end-organ damage within 30 days	0%	0%
Renal artery or other vascular complication requiring intervention within 30 days	0%	0%
Hypertensive crisis within 30 days	0%	0%
New renal artery stenosis of more than 70% within 6 months[†]	0%	0%

- **No major adverse events were reported in either group.**

[†] Non-invasive renal imaging was performed in 71 denervation patients and 68 sham patients at 2 months. At the time of the report, 43 patients in the denervation group and 41 patients in the control group had 6-month follow-up imaging. There have been no patients with new renal artery stenosis through 6 months.

Azizi M, Lancet. 2018 ;391(10137):2335-2345

Influence of Total Number of Emissions on Daytime Systolic ABP from Baseline to 2 Mo



P value for linear trend 0·33.

CI: Confidence interval

Azizi M, Lancet. 2018 ;391(10137):2335-2345

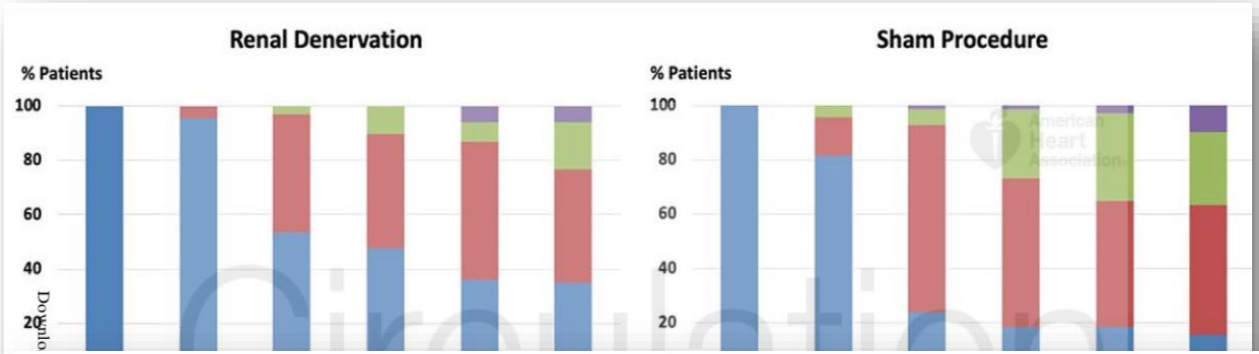
Conclusion of RADIANCE-HTN SOLO

In patients with combined systolic–diastolic primary hypertension who were not receiving antihypertensive medications, RDN with endovascular ultrasound safely reduced ambulatory, home, and office BP by more than a sham procedure at 2 months.

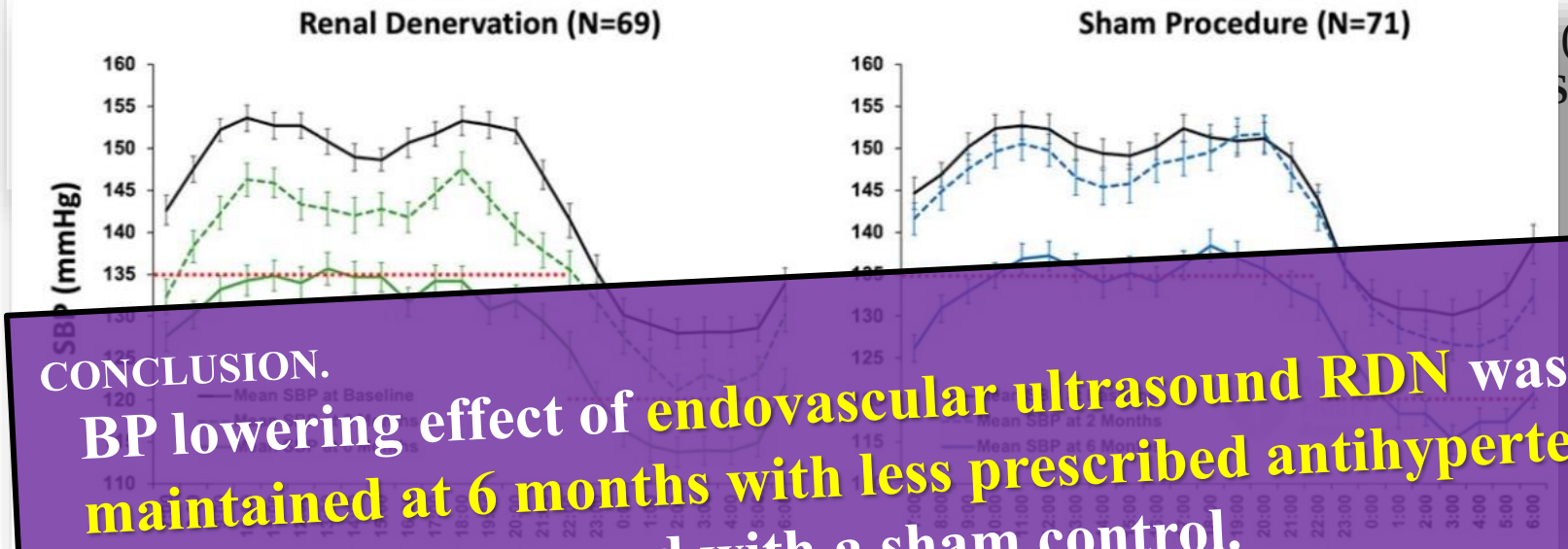
Azizi M, Lancet. 2018 ;391(10137):2335-2345

Six-Months Results of RADIANCE-HTN SOLO

- Between 2 and 5 months, if monthly measured home BP was ≥135/85 mmHg, a standardized stepped-care antihypertensive treatment (SSAHT) was recommended; amlodipine/ ACE-I-ARB/ Hydrochlorothiazide.



SSAHT@ 6 months, 65.2% in the RDN group vs. 84.5% in the sham group (p=0.008)
Average No. of antihypertensive medications, 0.9±0.9 (RDN group) vs. (p=0.010)
SSAHT in RDN



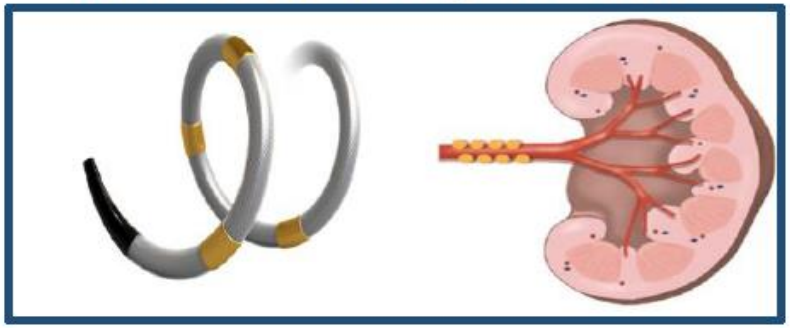
CONCLUSION.
BP lowering effect of endovascular ultrasound RDN was maintained at 6 months with less prescribed antihypertensive medications compared with a sham control.

- Reduced 6M daytime ambulatory SBP to a greater extent than sham (-18.1±12.2 vs. -15.6±13.2 mmHg, p=0.024).

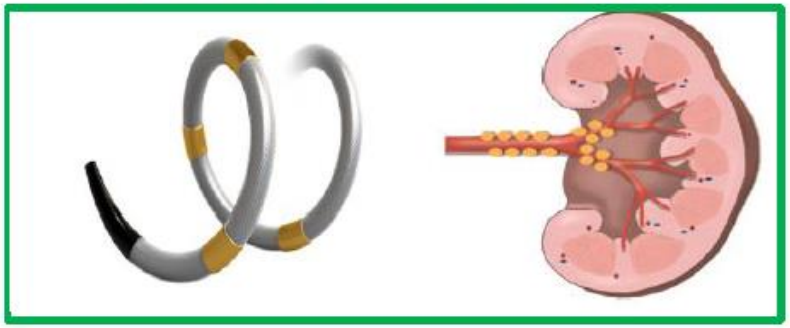
Azizi M, et al. Circulation. 2019 Mar 17.

A Three-Arm Randomized Trial of Different Renal Denervation Devices and Techniques in Patients with Resistant Hypertension (RADIOSOUND-HTN)

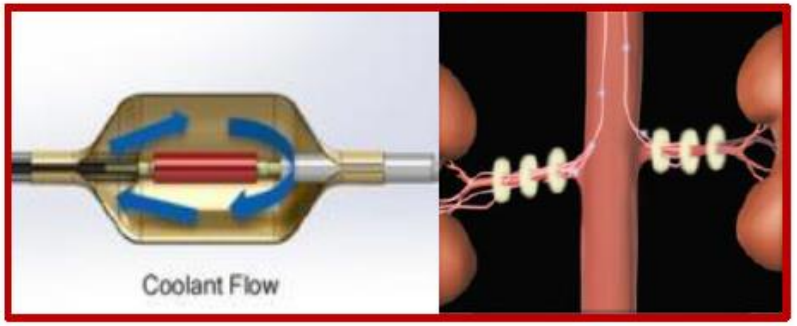
1: Radiofrequency
main renal artery ablation



2: Radiofrequency
main and branch renal artery ablation



3: Ultrasound
main renal artery ablation

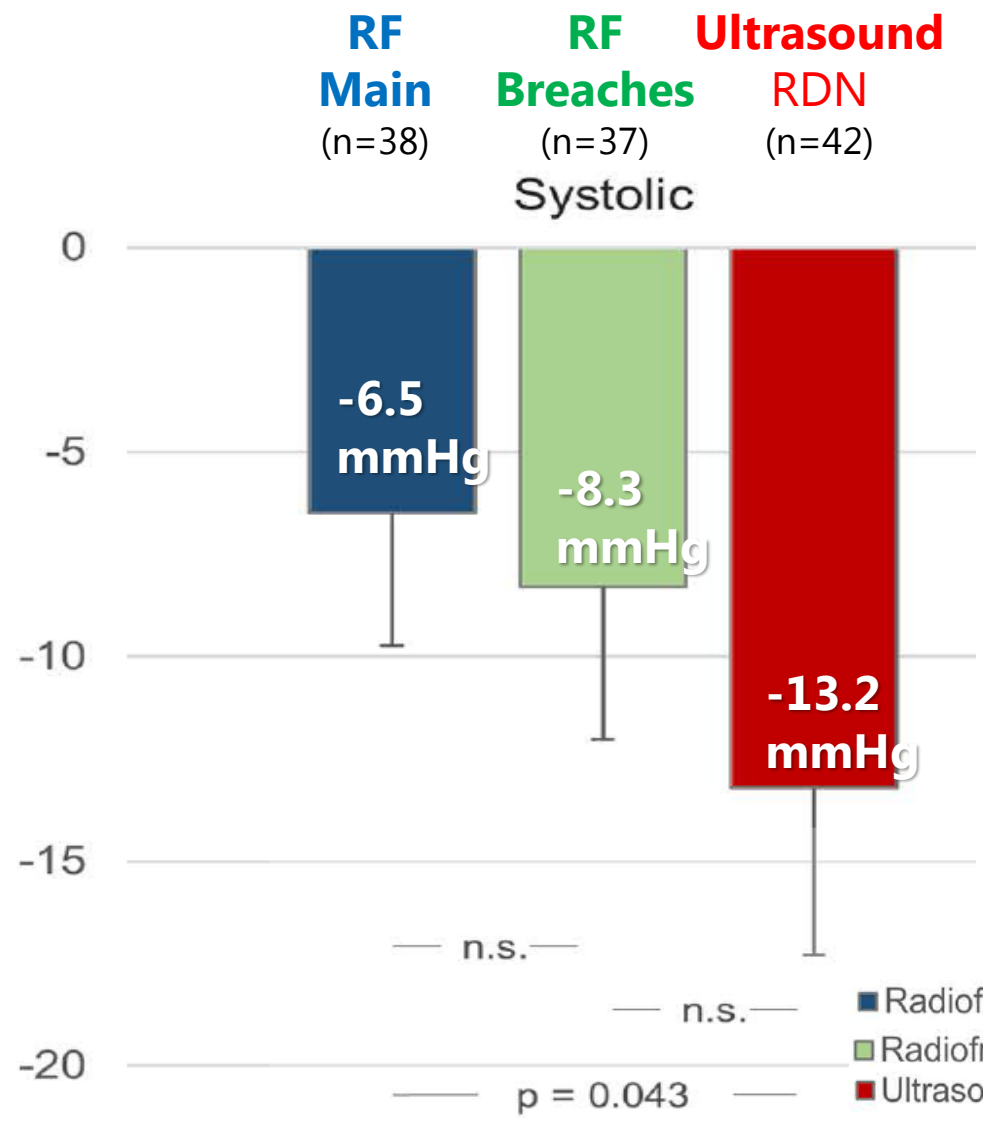


- **Primary end point; Change in systolic daytime ambulatory BP at 3 months.**

Fengler K, et al. Circulation. 2019;139:590-600.

A Three-Arm Randomized Trial of Different Renal Denervation Devices and Techniques in Patients with Resistant Hypertension (RADIOSOUND-HTN)

Change in systolic Daytime ABP @3mo



Between group difference
RF main artery vs. ultrasound
-6.7 mm Hg
(98.3% CI, -13.2 to -0.2; P=0.043)

BP reduction was **not found to be significantly different between the ultrasound and side branch ablation groups.**

CONCLUSIONS: Endovascular ultrasound–based RDN was found to be superior to radiofrequency ablation of the main renal arteries only, whereas **a combined approach of radiofrequency ablation of the main arteries, accessories, and side branches was not.**

Fengler K, et al. Circulation. 2019;139:590-600.

Ultrasound-RDN: Study

	REQUIRE	RADIANCE-HTN
Medications at screening	Resistant HTN on ≥3 meds	Resistant HTN on ≥3 meds
Medication post consent	Standard of Care	Single-pill, fixed-dose, triple-drug combination
Seated office BP (mmHg)	≥150/90	≥140/90
Ambulatory BP (mmHg)	24-h BP ≥140 systolic	Daytime ≥135/85
Primary Endpoint	Reduction in the mean 24-h systolic ABP from baseline to 3 mo	Reduction in the mean daytime systolic ABP from baseline to 2 mo
Sample size	140	146
Follow-up	1 y	3 y
Location	Japan, Korea	US, EU

LauraMauri, Am Heart J 2018;195:115-29

Take-home Message

doi:10.1093/eurheartj/ehy718

Renal artery sympathetic denervation: Back on track!

Sharp ASP, et al. Eur Heart J. 2018 Dec 7;39(46):4056-4057.

- ✓ RADIANCE-HTN SOLO trial demonstrated that endovascular ultrasound-based RDN effectively lowered BP in patients with mild to moderate hypertension who were randomized and followed for 2 months off medications (greater reduction in daytime ambulatory systolic BP.
- ✓ The BP lowering effect of endovascular ultrasound RDN was maintained at 6 months with less prescribed antihypertensive medications compared with a sham control.
- ✓ Await the results of long-term follow-up, ongoing clinical trial, and further comparison among different treatment strategies (REQUIRE study for resistant hypertension)


Thank you for your attention