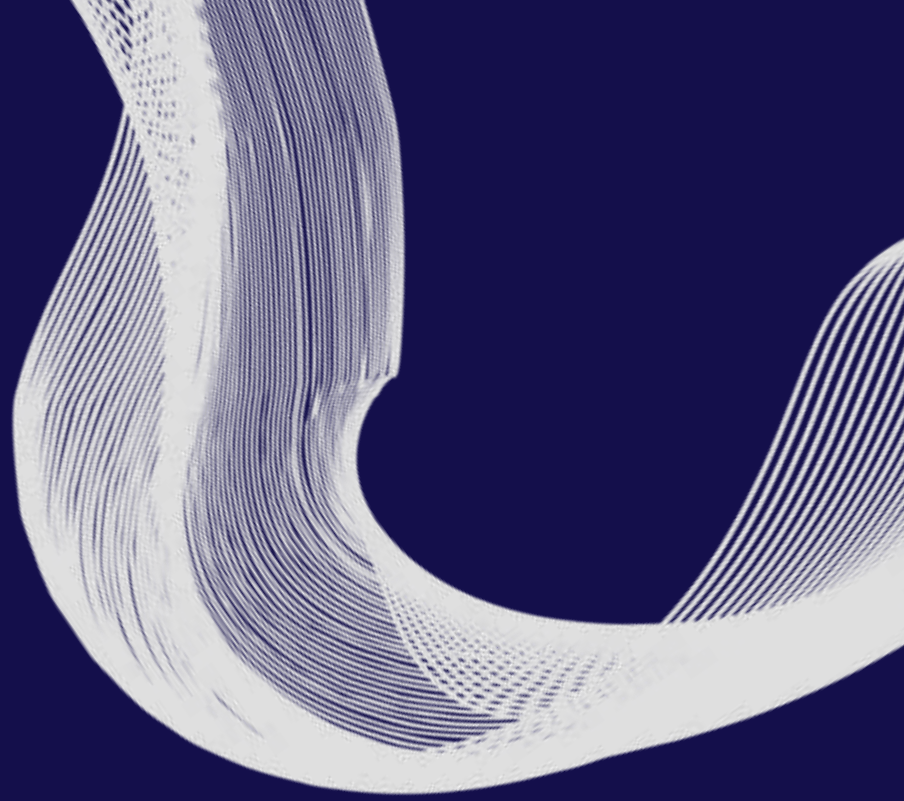


Renal denervation

Evidencia Actual de RDN y Criterios de selección de pacientes.

Dr. Alejandro Ricalde Alcocer
Cardiología Intervencionista
México

Declaración de Conflictos de Interés

Speaker:	Medtronic, Servier, Amgen, Asofarma, Bayer, Boston Scientific, Cordis, MSD, Pfizer, Sanofi, Terumo Medical, Menarini.
Proctor & Advisory Board:	Medtronic, Boston Scientific, Biosensors, Cordis.
Research relationship:	Bayer, MSD, Kardion, Simpson medical, medtronic, Novo Nordisk.

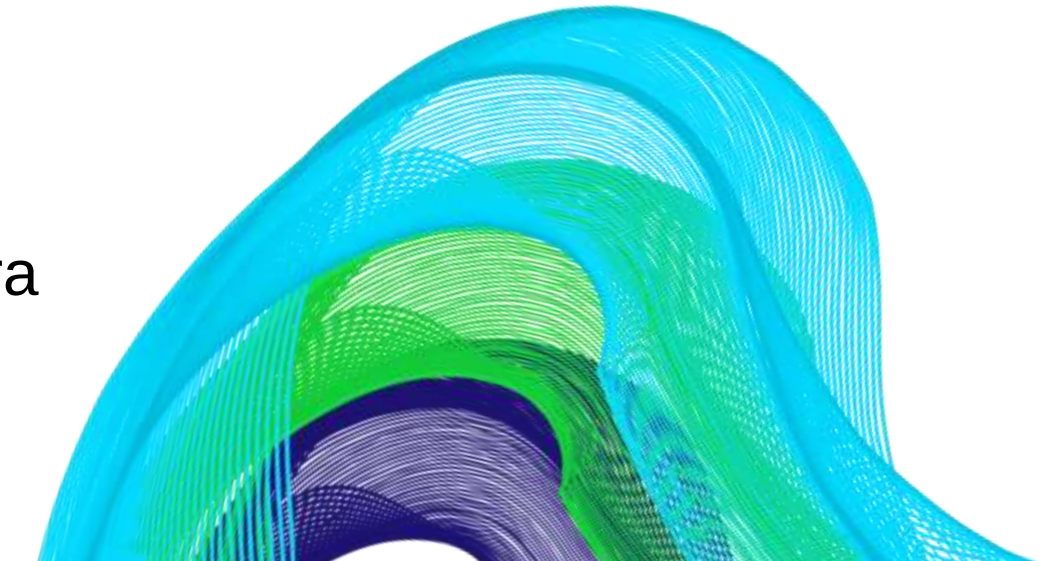
Evidencia Actual de RDN y Criterios de selección de pacientes.

1. Todo lo que si sabemos hoy en DSR…

DSR

2. Lo que está pendiente por saber de la DSR (perspectivas futuras)…

3. Selección del candidato para



RDN Through the years From HTN-1, 2, 3 to Spyral Clinical Trials

Importance of a good Clinical Trial Design, Execution & FU

RDN
1st in Man Case

SYMPLICITY HTN-1[1] &
SYMPLICITY HTN-2[2]

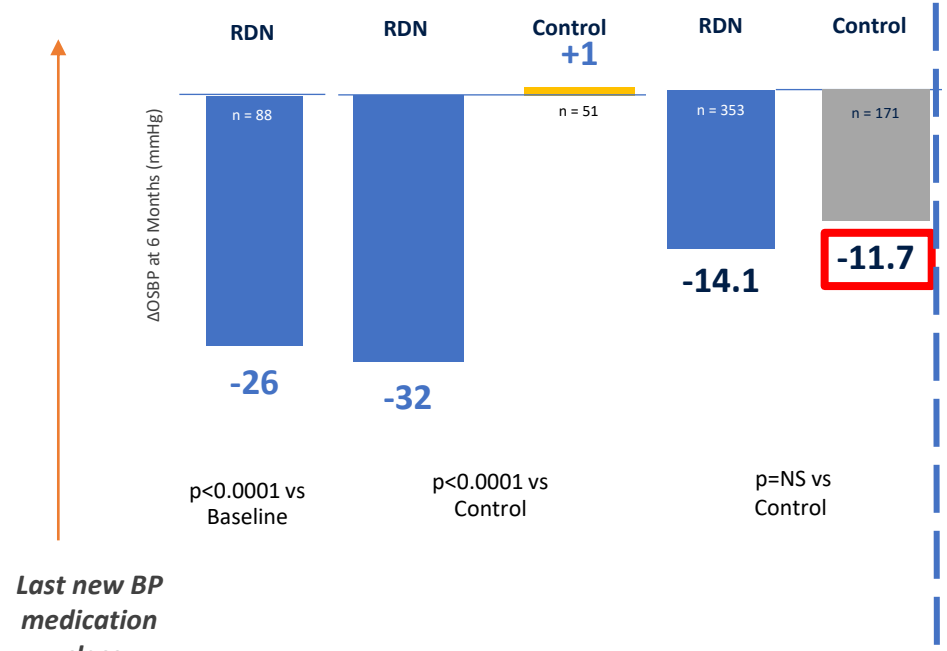
SYMPLICITY HTN-3[3]

Significant SBP reduction in 1st in Man study

Significant SBP red. compared to a medication-only control group

Similar reduction in SBP in both RDN and sham control arms

2007 2009 2010 2014



Last new BP medication class approved by FDA

[1] Krum H, et al. *Lancet*. 2014;383:622–629 [2] SYMPLICITY HTN-2 Investigators. *Lancet*. 2010;376:1903–1909 [3] Bhatt DL, et al. *N Engl J Med*. 2014; 370:1393-1401
[4]. Böhm M, et al. *Lancet*, 2020. [5]. Kandzari DE, et al. Lancet. 2018;391:2346-2355 [6]. Mahfoud. Lancet 2022 Apr 9;399(10333):1401-1410. [7] Bhatt DL, et al. Lancet. September 18, 2022.

RDN Through the years From HTN-1, 2, 3 to Spyral Clinical Trials

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RDN 1st in Man Case

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SYMPLICITY HTN-3[3]

Similar reduction in SBP in both RDN and sham control arms

SPYRAL HTN-ON MED[4]

Significant change in SBP & DBP compared to a sham control group

SPYRAL HTN-OFF MED[5]

Significant change in SBP & DBP compared to a sham control group

SPYRAL HTN-ON MED[6]

Significant change in SBP & DBP compared to a sham control group

SYMPLICITY HTN-3[7]

36 months FU

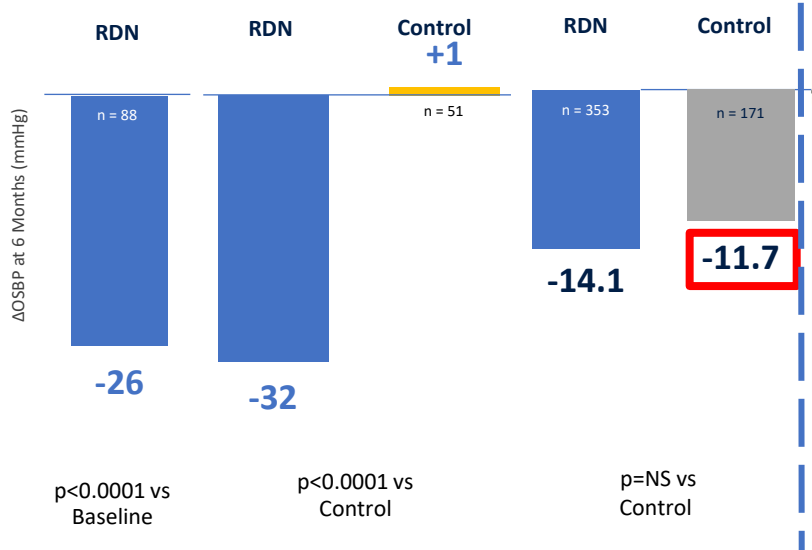
Significant change in SBP & DBP compared to a sham control group

SPYRAL HTN-ON MED[6]

2 Yr FU

Significant vs sham control group

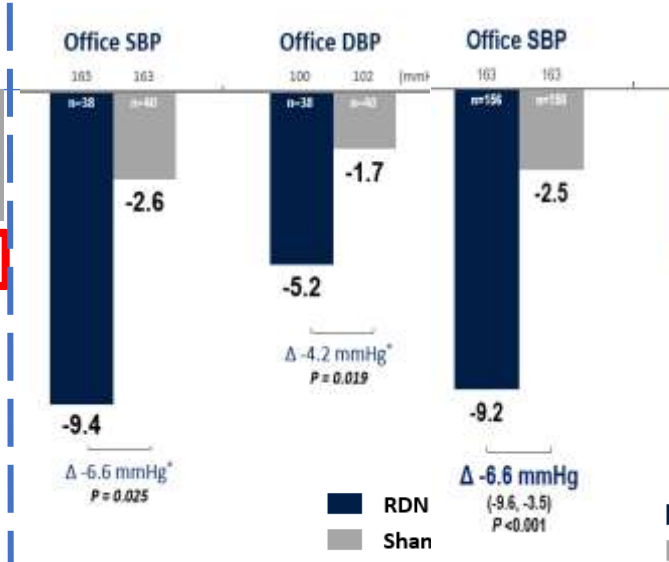
2007 | 2009 | 2010 | 2014 | 2018 | 2020 | 2022 | 2022 | 2024



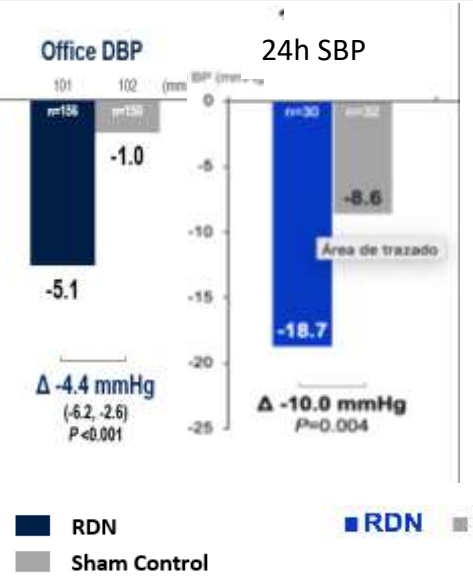
p<0.0001 vs Baseline

p<0.0001 vs Control

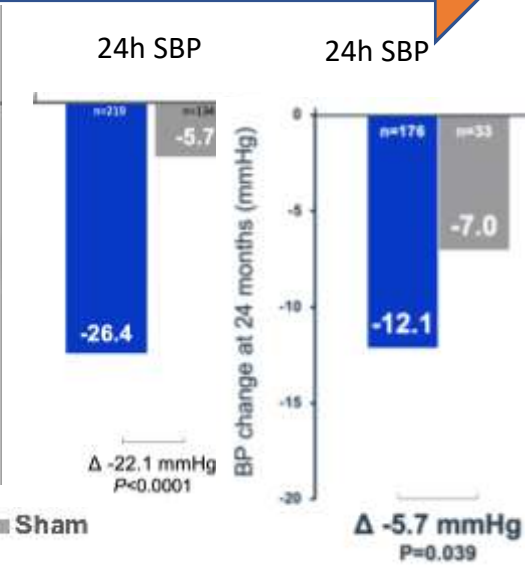
p=NS vs Control



Change from baseline to 6 months



Change from baseline to 3 months



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Renal nerves often bypass the main renal artery and converge on the branches

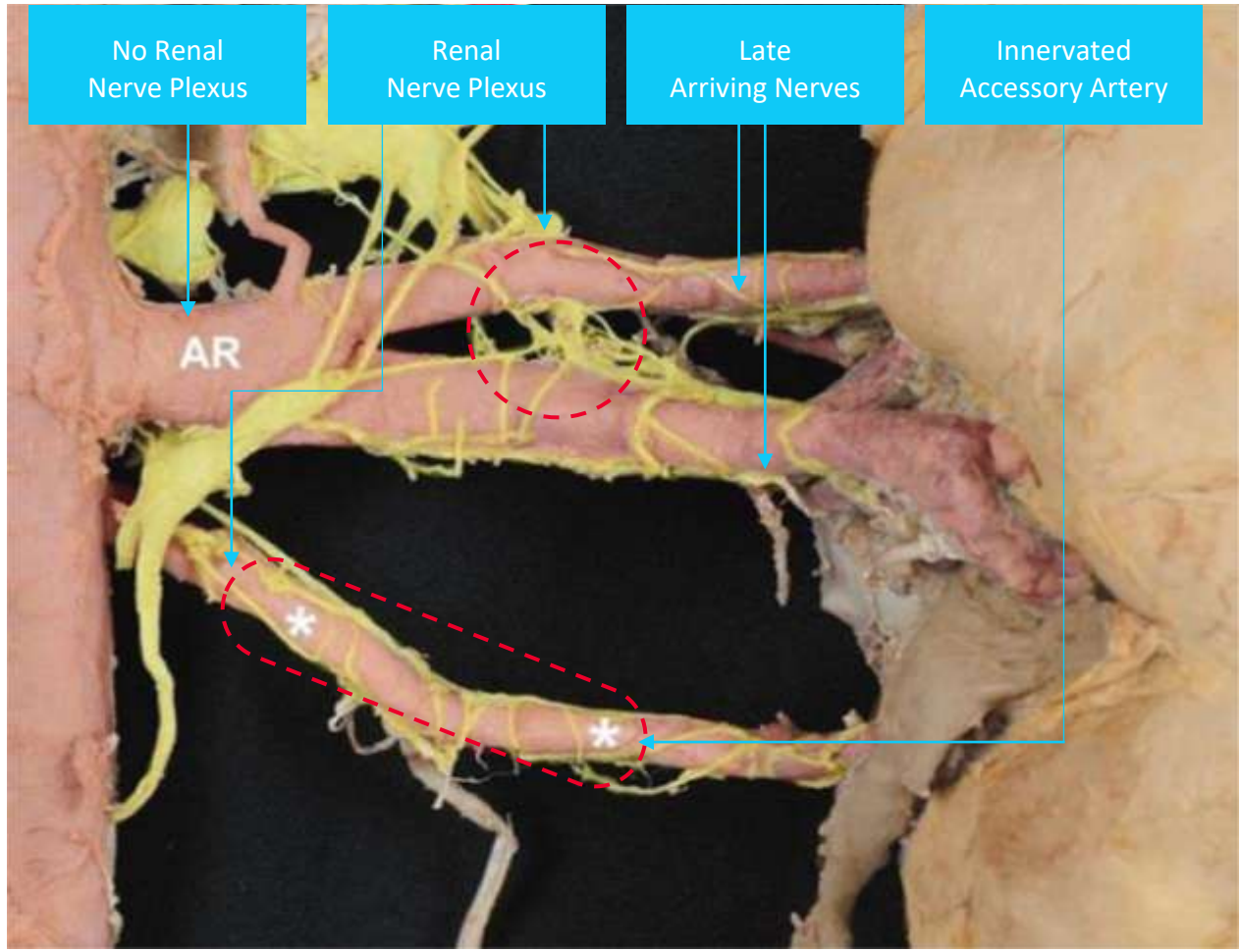
63%

of kidneys had renal nerves that joined distal to the main renal artery bifurcation (late arriving nerves)

>30%

of cadavers had highly innervated accessory arteries

Renal nerve plexus often forms distal to ostium



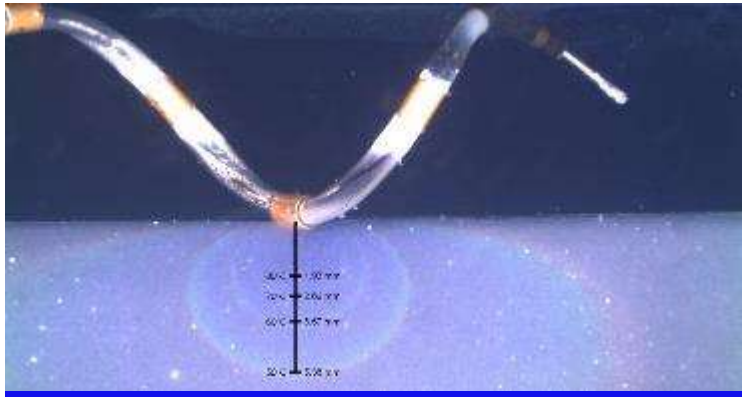
AR: renal artery
*accessory polar renal artery
Touchard et all. Hypertension. 2020.
Mompeo et al. Clin Anat. 2016.

Symplicity Spyral™ Blood Pressure Procedure

Supplies precisely controlled and targeted RF energy to the renal nerves

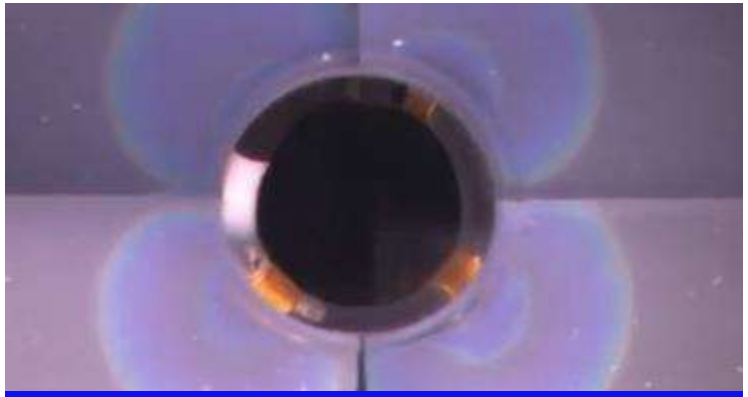
Versatile Design

- One catheter size fits vessels 3-8 mm[1,2]
- Easy-to-use, plug and play design
- Nonocclusive spiral pattern allows continuous renal artery blood flow & protects the vessel wall from thermal damage
- Compatible with commonly applied devices:
  - 0.014” guidewire
  - 6 F guide catheter



Responsive System

- Real-time responsive algorithm automatically adjusts power based on temperature sensor feedback to ensure the safe distribution of energy[1]



Effective Denervation

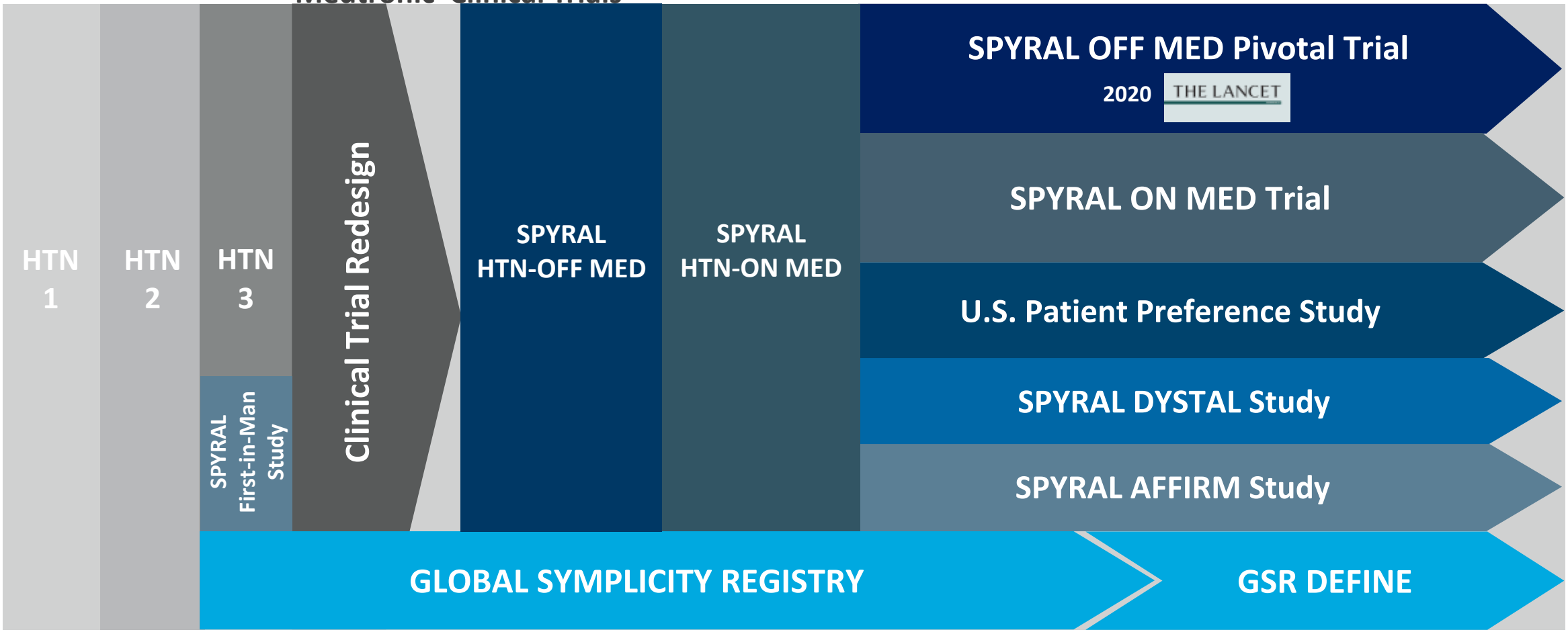
- Multi-electrode design ablates in a longitudinal, helical pattern to maximize the probability of a complete denervation[1,2]

[1]Coates P, Tunev S, Trudel J, et al. Time, temperature, power, and impedance considerations for radiofrequency catheter renal denervation. Cardiovascular Revascularization Medicine, 2022.
[2]Medtronic Symplicity SpyralTM Instructions for Use.

SPYRAL HTN Clinical Program

Over 4,000 Patients Studied Across

Medtronic Clinical Trials



SPYRAL HTN Clinical Program

Merits of different evidence sets

>4000 patients in 4 sham-controlled RCT's and real-world evidence

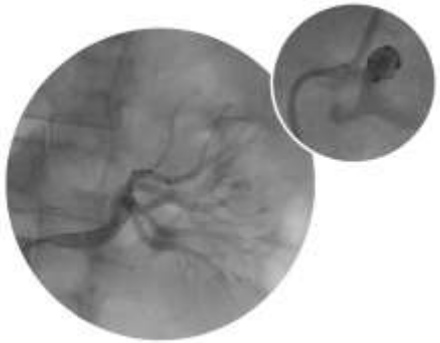
OFF MED trial (N = 331)	**ON MED trial** (N = 337)	**Global SYMPLICITY Registry DEFINE** (N > 3,300)
Scientific evidence of efficacy	Prospective evidence in context of background medication	Large real-world dataset
Sham-controlled RCT	Sham-controlled RCT	Durability outcomes

Safety
Safety evaluated across all studies and populations within the SPYRAL HTN clinical trial program

Medtronic

SPYRAL HTN-ON

Study design



4 sham-controlled RCT's

PILOT Cohort
N=80 patients

Expansion Cohort
N=257 patients

FULL Cohort: N = 337 randomized patients

Screening | **Treatment**

Inclusion criteria:

- Office SBP ≥150 to <180
- Stable on 1, 2, or 3 meds for 6-weeks:
  - Thiazide diuretic
  - Calcium channel blocker
  - ACE/ARB
  - Beta blocker

2 - 4 weeks

Visit 1

- Office SBP
  - SBP ≥150 to <180
  - DBP≥ 90

1 - 2 weeks

Visit 2

- Drug testing
- Office BP
  - SBP ≥150 to <180
  - DBP≥ 90
- 24-hr ABPM+
  - SBP ≥140 to <170

R

2:1[2]

Sham control + medications

1M | 3M+ | 6M+ | 12-36M+

- Office BP

- Office BP
- ABPM[1]
- Drug testing

Renal denervation + medications

Primary endpoint

Screen failure if OSBP ≥180 or DBP <90

Escape criteria met if OSBP ≥180 or investigator discretion

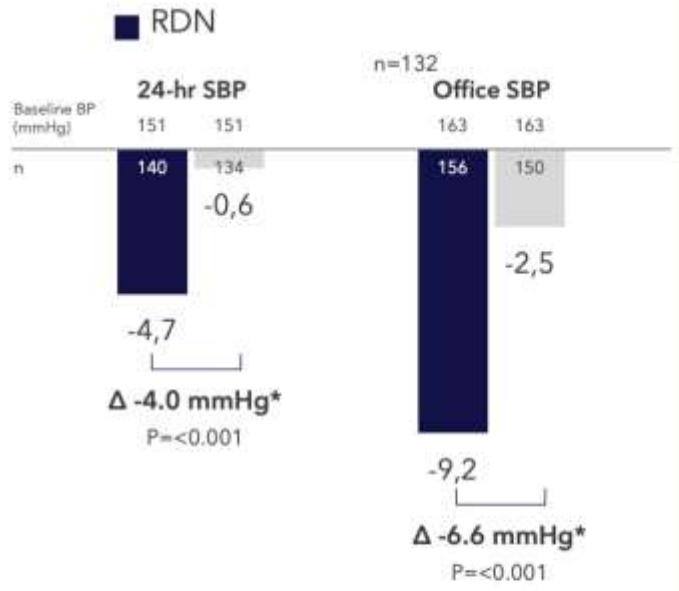
Boehm M, et al. Clin Research in Card, 2020, 109: 289-302, Clintrials.gov Identifier NCT02439775.
[1] All ABPM measurement started after witnessed drug intake.
[2] Pilot cohort 1:1 randomization, Expansion cohort 2:1 after inclusion of first 106 patients.

Medtronic

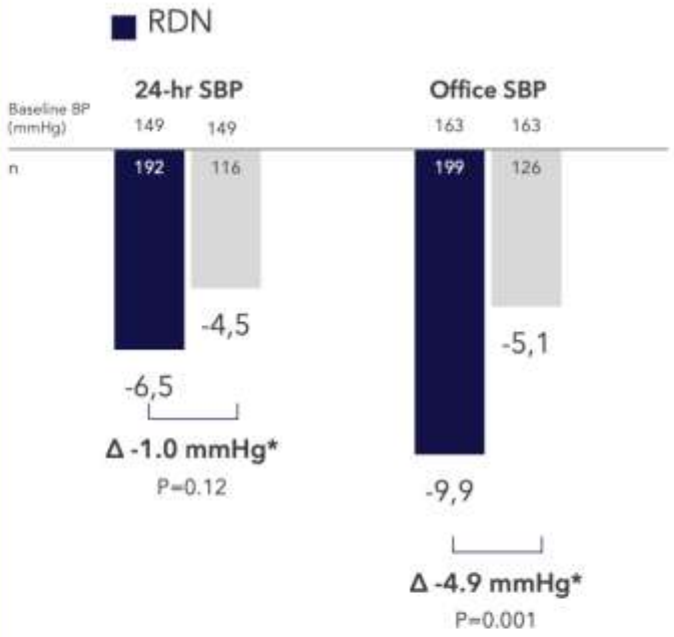
SPYRAL clinical program demonstrated Medtronic RDN efficacy

In sham-controlled RCT's OFF and ON meds and the largest real-world registry

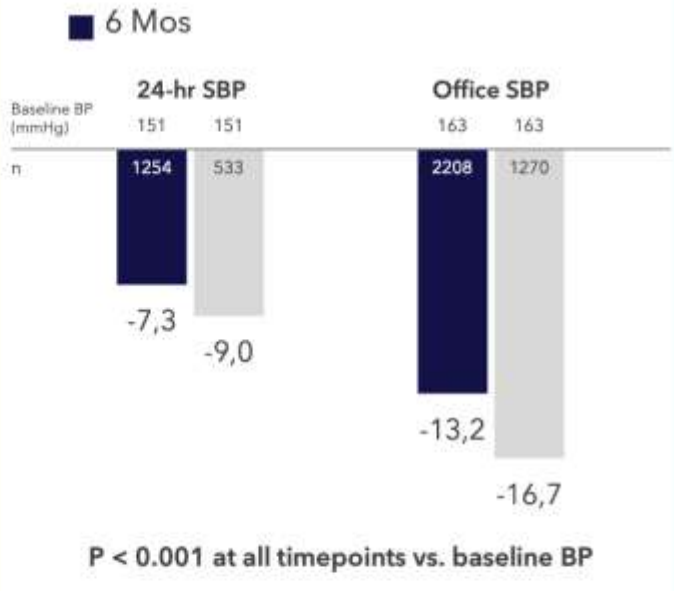
OFF MED Pivotal trial
RDN vs sham at 3 months[1]



ON MED Full Cohort
RDN vs sham at 6 months[2]



GSR DEFINE+
RDN at 6 months and 3 years[3]



[1] Böhm M, et al. Lancet. 2020; 395(10234): 1444-51.

[2] Kandzari D, et al. J Am Coll Cardiol. 2023 Nov 7;82(19):1809-1823

[3] Mahfoud et al. EuroPCR 2022

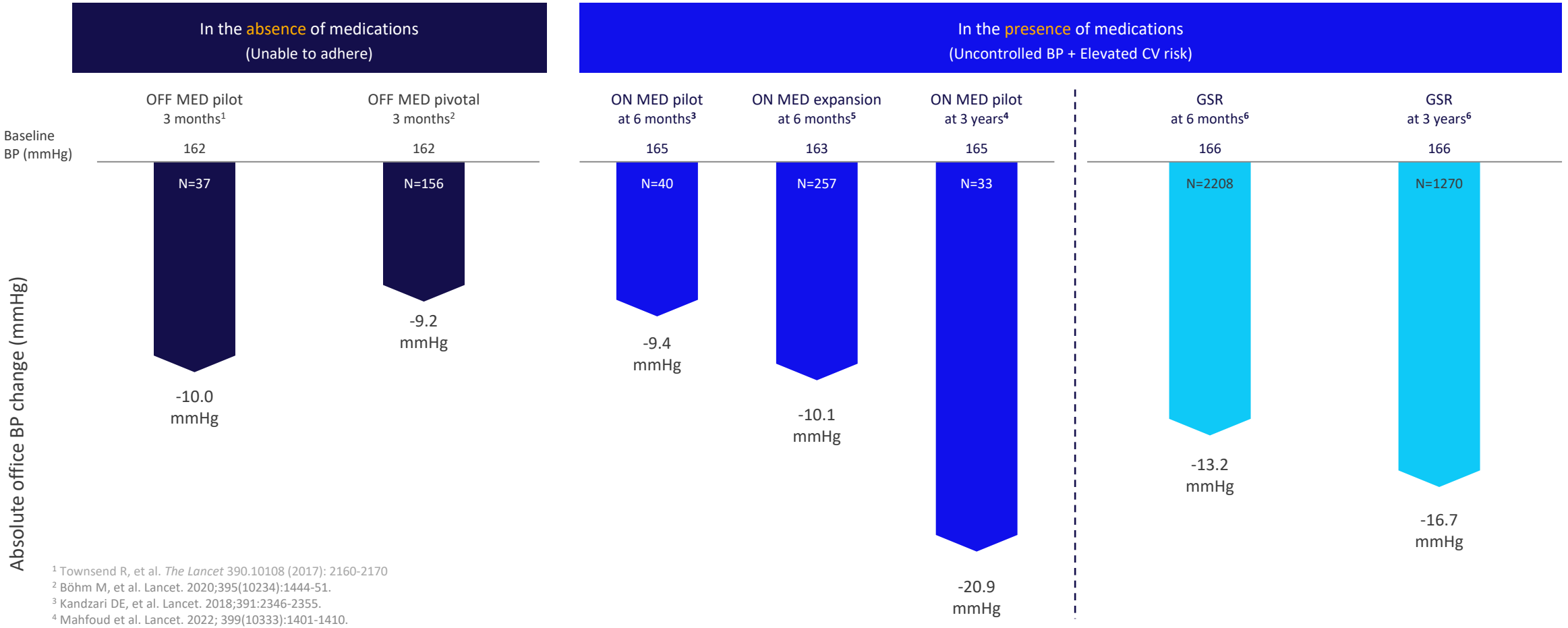
Results from clinical trials is not directly comparable

*ANCOVA adjusted
+ Study was conducted outside of the US ad data includes both Symplicity Flex and Symplicity Spyral catheters

Medtronic

SPYRAL HTN clinical program showed Symplicity™ RF RDN's short and long-term BP reduction efficacy

In sham-controlled RCT's OFF and ON medications and the largest real-world registry

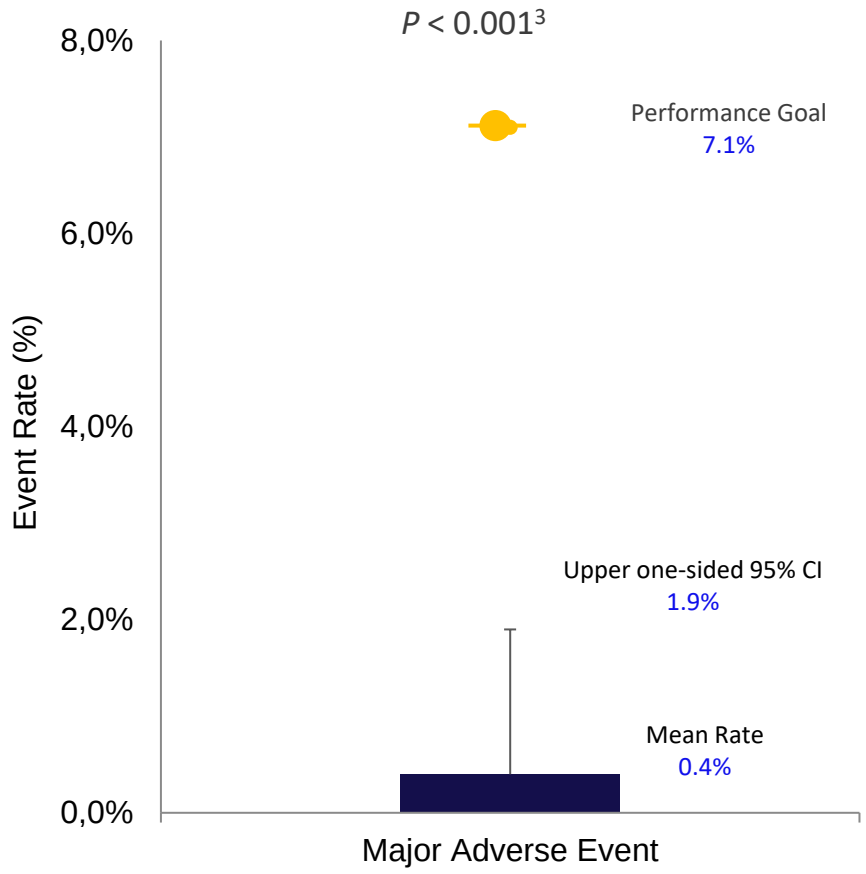


[1] Townsend R, et al. *The Lancet* 390.10108 (2017): 2160-2170
[2] Böhm M, et al. Lancet. 2020;395(10234):1444-51.
[3] Kandzari DE, et al. Lancet. 2018;391:2346-2355.
[4] Mahfoud et al. Lancet. 2022; 399(10333):1401-1410.
[5] Kandzari D, et al. J Am Coll Cardiol. 2023 Nov 7;82(19):1809-18232022.
[6] Mahfoud et al. EuroPCR 2022.
Results from clinical trials is not directly comparable
GSR data is conducted outside of the US and data includes both Symplicity Flex and Symplicity Spyral catheters

Pooled SPYRAL HTN-OFF and ON MED safety endpoint was met

Major adverse events below objective performance goal

Safety Outcomes at 1 Month % (n)	**RDN (N = 253)[1]**
Major Adverse Events	0.4% (1)
All-cause death	0
End Stage Renal Disease	0
Significant embolic event resulting in end-organ damage	0
Renal artery perforation requiring re-intervention	0
Renal artery dissection requiring re-intervention	0
Vascular complications (requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion)	0.4% (1)
Hospitalization for hypertensive crisis/emergency	0
New renal artery stenosis >70%[2]	0



Kandzari D, et al. J Am Coll Cardiol. 2023 Nov 7;82(19):1809-1823.

[1] All subjects treated with RDN (including Crossovers) in OFF MED and ON MED trials.

[2] Major Adverse Events are measured at 1 month, except renal artery stenosis which is evaluated at 6 months by duplex ultrasound, and confirmed by angiogram.

[3] P value based on a one-sided exact binomial test.

GSR DEFINE: Expanding GSR to 5000 patients

Prospective, global, open-label, observational study with data monitoring

Real world patients with uncontrolled HTN:

Treated with RDN per local IFU

No blood pressure thresholds

RDN with Symplicity Spyral™ RDN system

N = 2000 Patients

New enrollment cohort

GSR cohort: **N ≤ 700 patients**

Spyral treated patients to enroll for additional 24 months of follow up

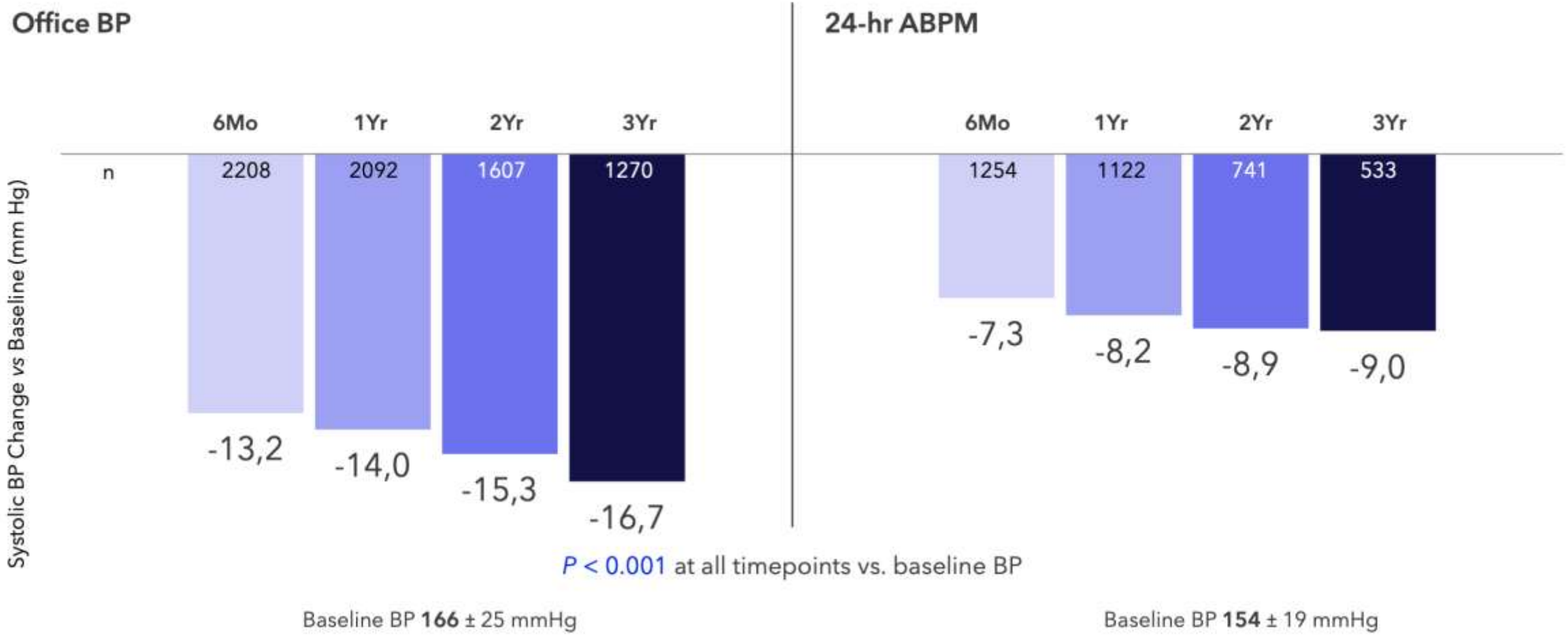
Study objective:	Document real-world acute and long-term safety, effectiveness and durability (up to 5 years) of Symplicity RDN system
Efficacy objective:	Efficacy outcomes: acute and long-term office and 24-hr blood pressure changes
Safety objectives:	Safety outcomes, including mortality, end-stage renal disease, stroke events

GSR data is conducted outside of the US and data includes both Symplicity Flex and Symplicity Spyral catheters

Medtronic

Significant SBP reductions over 3 Years in real-world setting

GSR DEFINE



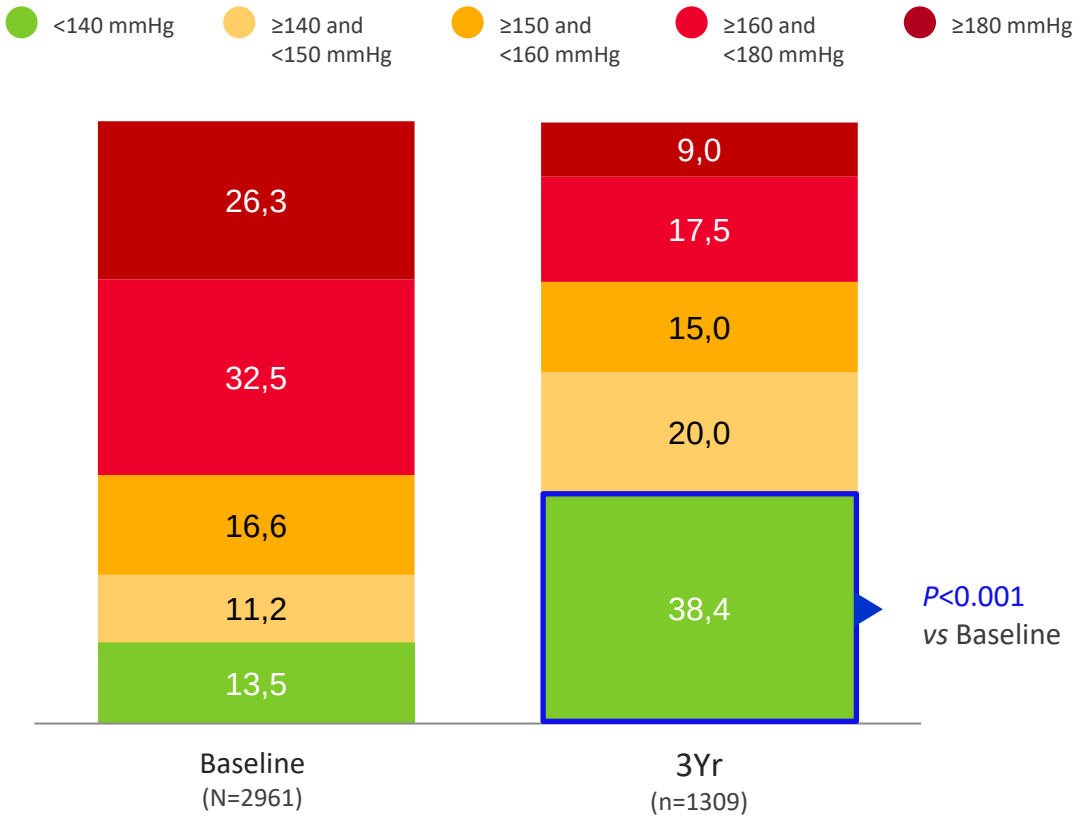
Mahfoud et al. EuroPCR 2022. Blood Pressure and MACE reductions after Renal Denervation: 3-year GSR Results
Note: patient numbers reflect those who had completed follow-up at the time of analysis.
GSR data is conducted outside of the US ad data includes both Symplicity Flex and Symplicity Spyral catheters

Medtronic

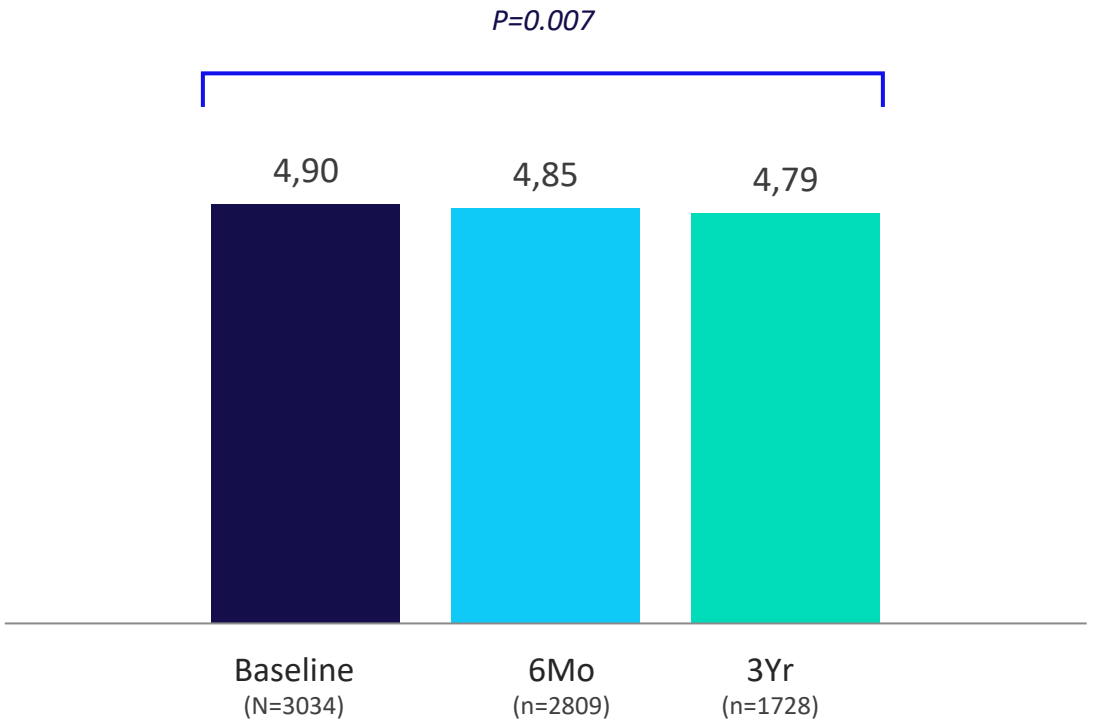
Symplicity™ RF RDN decreased BP without increasing medications in GSR DEFINE

Three-fold increase in % of patients with BP <140 mmHg over 3 years

Office Systolic BP Distribution
(% Patients)



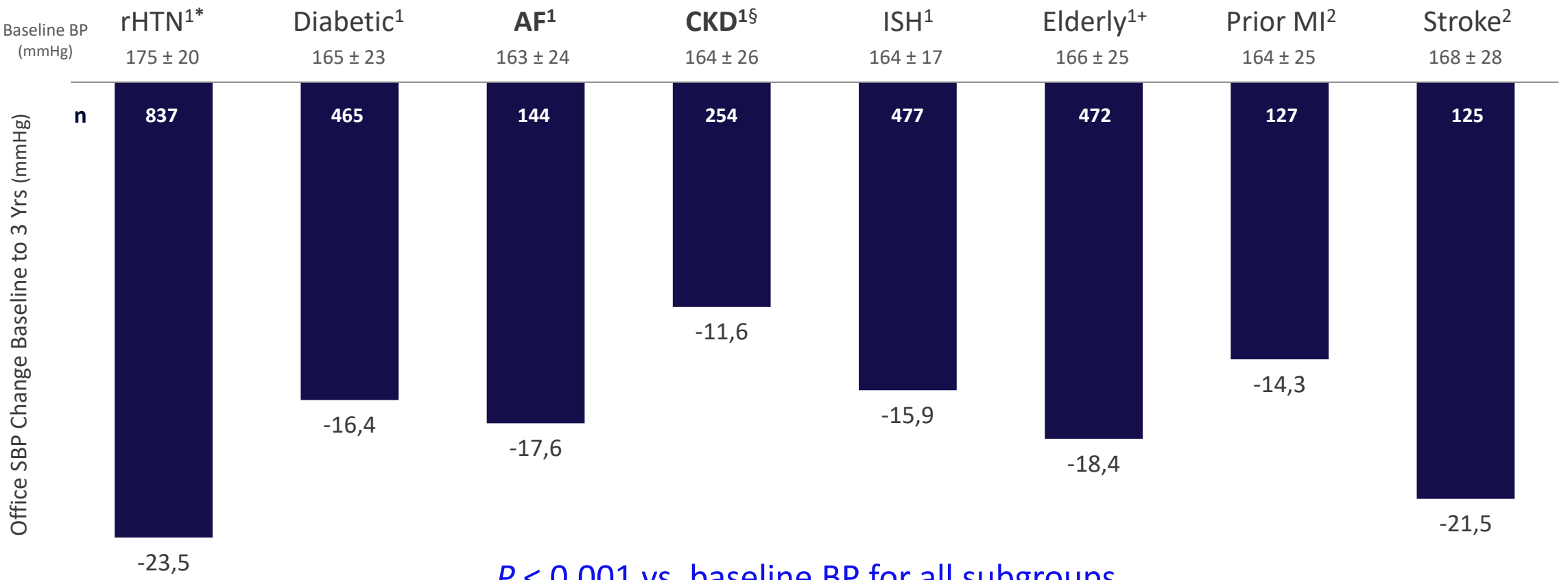
Number of Medications
(mean)



GSR data is combined Symplicity Flex and Symplicity Spyral.
Mahfoud F, et al. PCR 2022. Blood Pressure and MACE reductions after Renal Denervation: 3-year GSR Results
GSR data is conducted outside of the US ad data includes both Symplicity Flex and Symplicity Spyral catheters

RDN reduced BP in a variety of patient subgroups

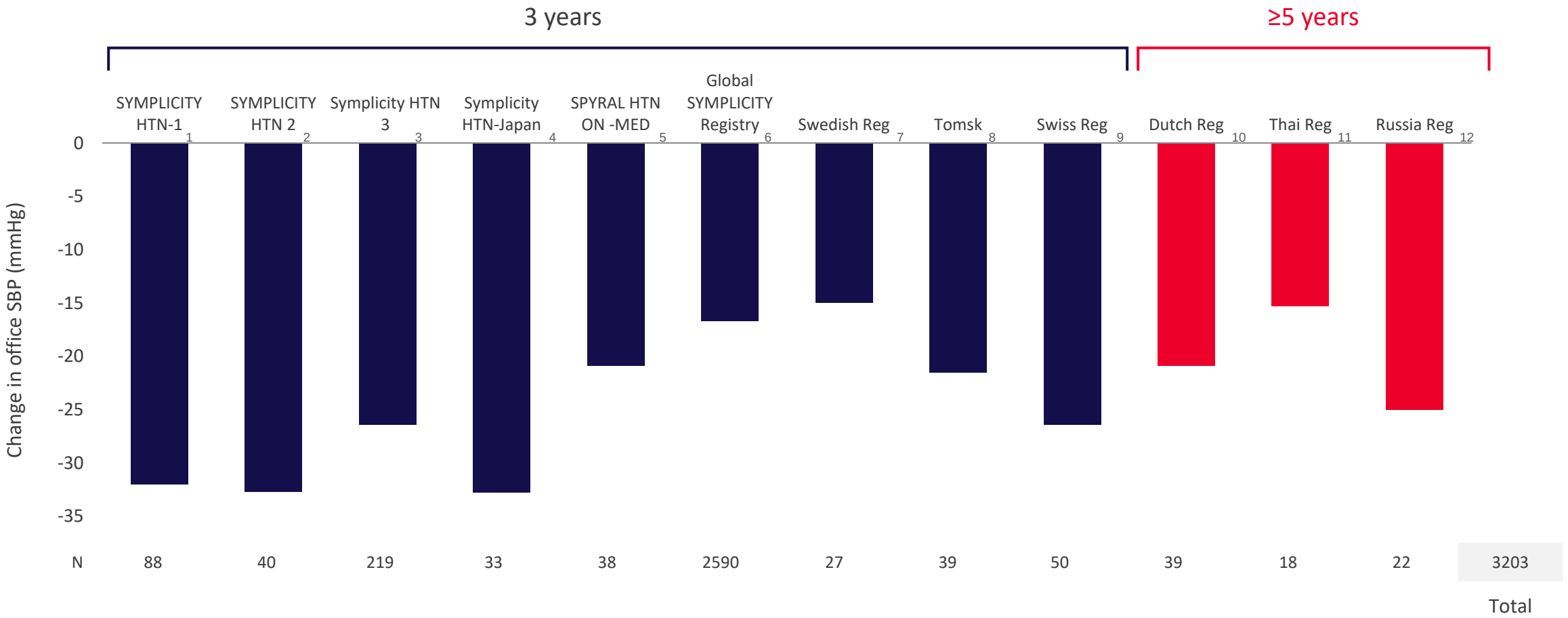
Office SBP reductions at 3 years in GSR DEFINE



P < 0.001 vs. baseline BP for all subgroups

[1] Mahfoud F, et al. *J Am Coll Cardiol*. 2020;75:2879-2888.
[2] Mahfoud F, et al. ESH 2022.
* Resistant hypertension defined as OSBP>150 mmHg, ≥3 anti-hypertensive medications
§ CKD defined as eGFR <60ml/min/1.73m^2.
+ Elderly defined as ≥ 65 years old
GSR data is conducted outside of the US and data includes both Symplicity Flex and Symplicity Spyral catheters

Multiple clinical trials and registries have demonstrated sustained BP reduction to 3 years and beyond following Symplicity™ RF renal denervation



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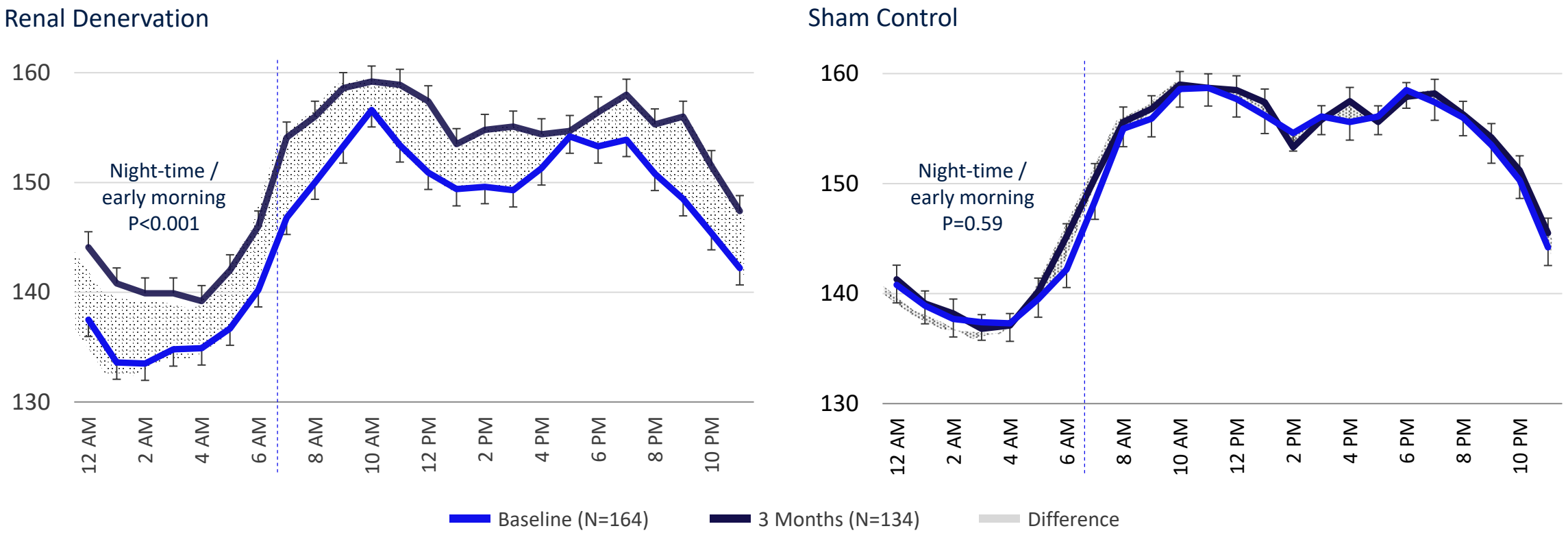
[1] Krum H, et al. *Lancet* 2014; 383:622-9. [2] European Heart Journal.2014; 35:1752–1759. [3] Bhatt et al, Lancet. 2022;400(10361):1405-1416. doi:10.1016/S0140-6736(22)01787-1 [4] Kario K, et al. *Circ J* 2019; 83: 622 – 629. [5] Mahfoud et al. ACC 2022. [6] Mahfoud, et al. EuroPCR 2022. [7] Volz S, et al. *Hypertension* 2018, 36:151–158. [8] Heliyon, et al.2022; 8:e08747. [9] Naduvathumuriyli et al, *J Clin Hypertens* 2020;00:1-11. [10] Zeljen, et al. Clin Res Card. 2022. [11] Hypertension Research 2022. [12] Arterial Hypertension.2021;27:318–332.
GSR data is conducted outside of the US and data includes both Symplicity Flex and Symplicity Spyral catheters

Symplicity™ RF RDN demonstrated “always on” effect on 24-hr BP lowering[1]

24-Hr systolic blood pressure: OFF MED Pivotal

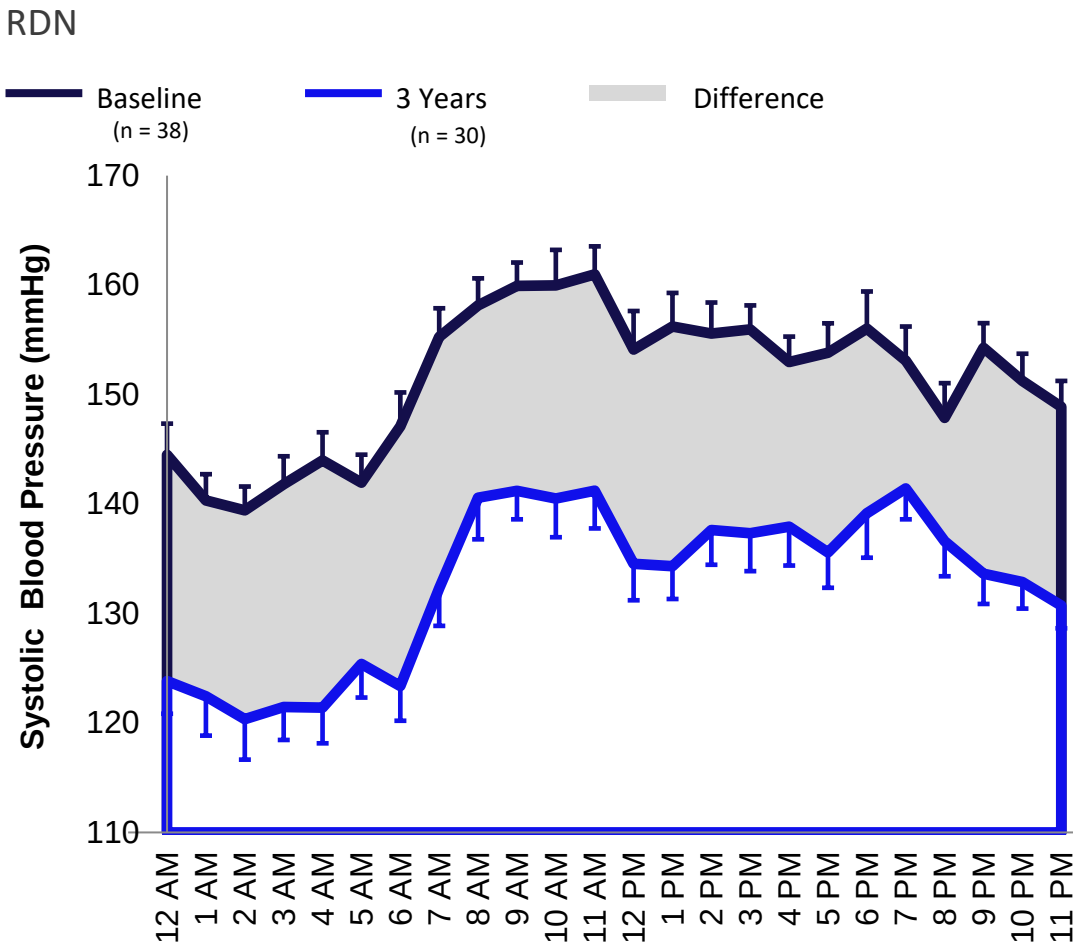


The nighttime / early morning period is associated with increased risk for stroke and cardiovascular events[2,3]

[1] Böhm M, et al. *Lancet*. 2020;395:1444-51. [2] Amodeo C, *Blood Pressure Monit*, 2014. [3] Boggia J, *Lancet*, 2007.

Symplicity^{TM} RF RDN demonstrated an “always on” effect on 24-hr BP lowering at 3 years

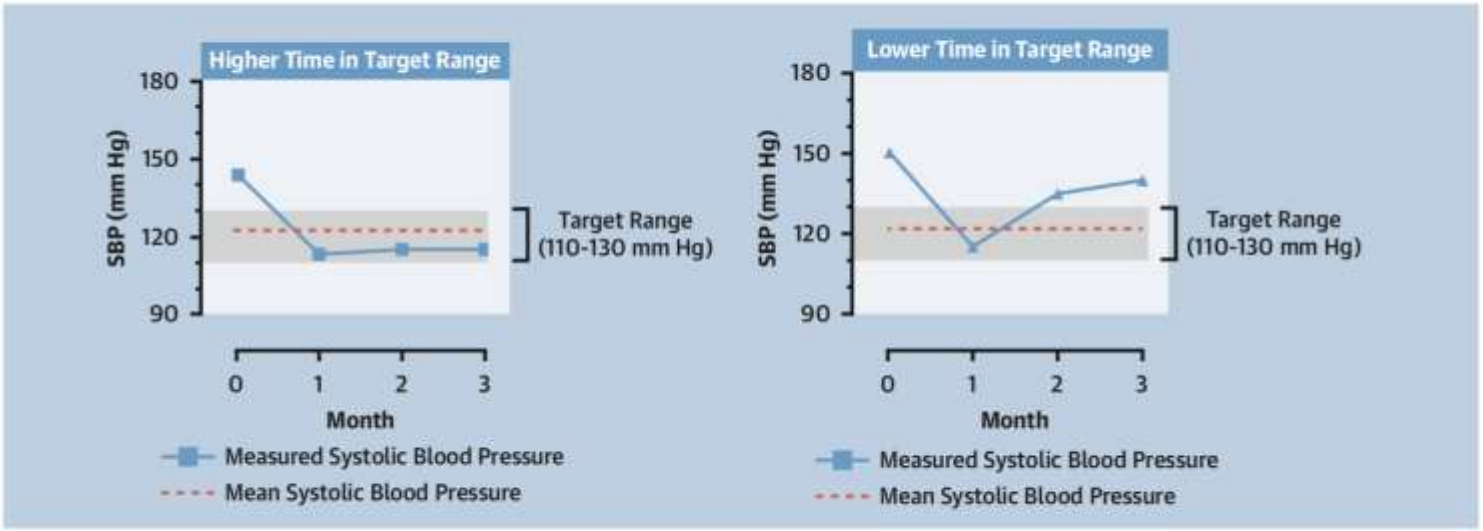
Baseline and 3 Years: SPYRAL HTN-ON MED Pilot

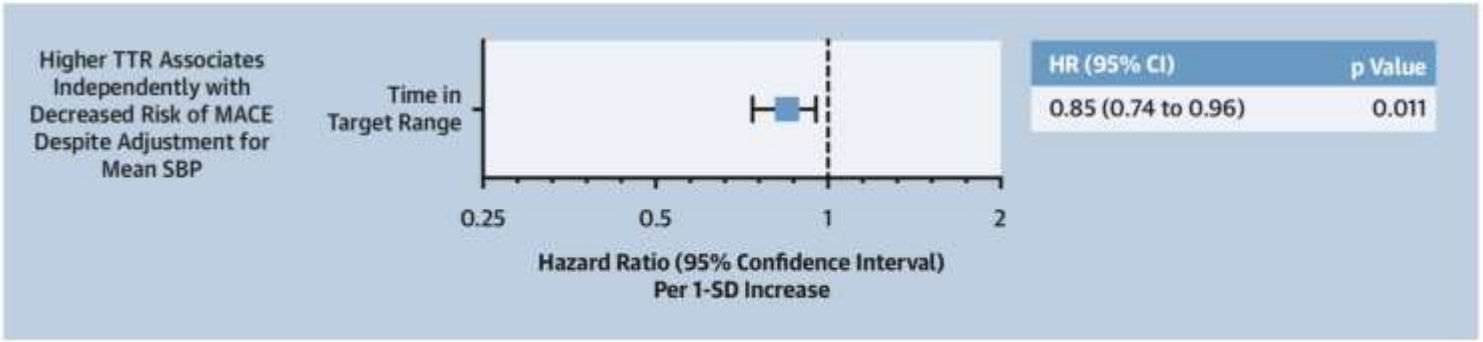


Mahfoud et al. *Lancet*. 2022;399(10333):1401-1410.

TTR increased to nearly 35% over 3 years in real-world setting

CENTRAL ILLUSTRATION **Systolic Blood Pressure Time in Target Range as an Independent Predictor of Cardiovascular Outcomes**





Fatani, N. et al. J Am Coll Cardiol. 2021;77(10):1290-9.

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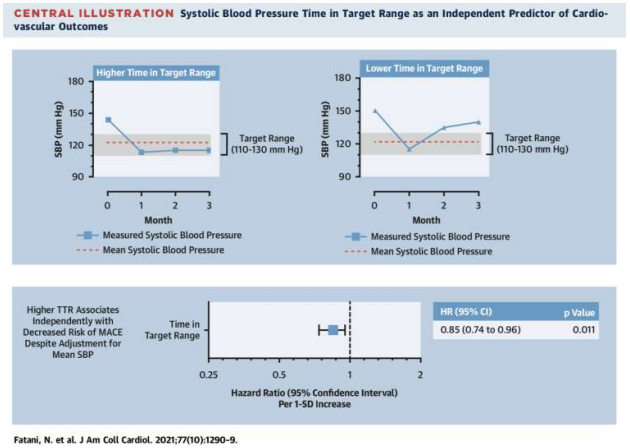
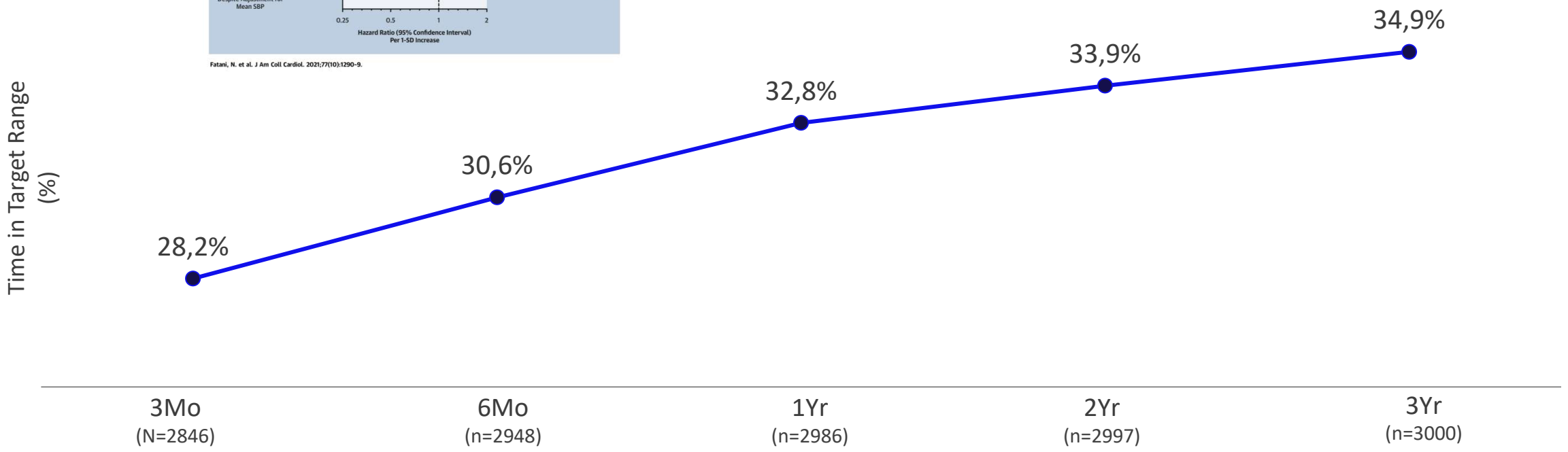


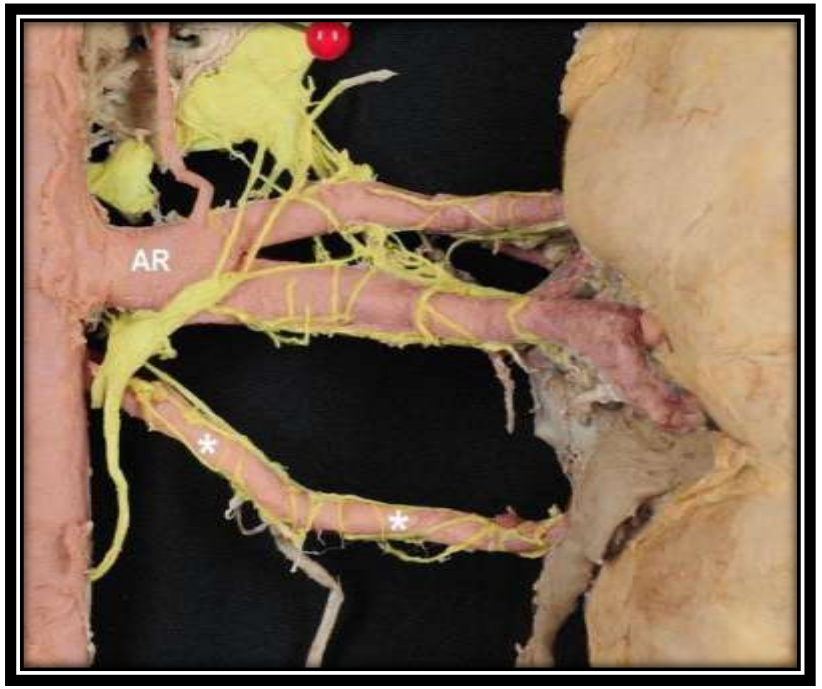
GSR-DEFINE



Every 10% increase in TTR at 6 months resulted in a 16% decrease in MACE

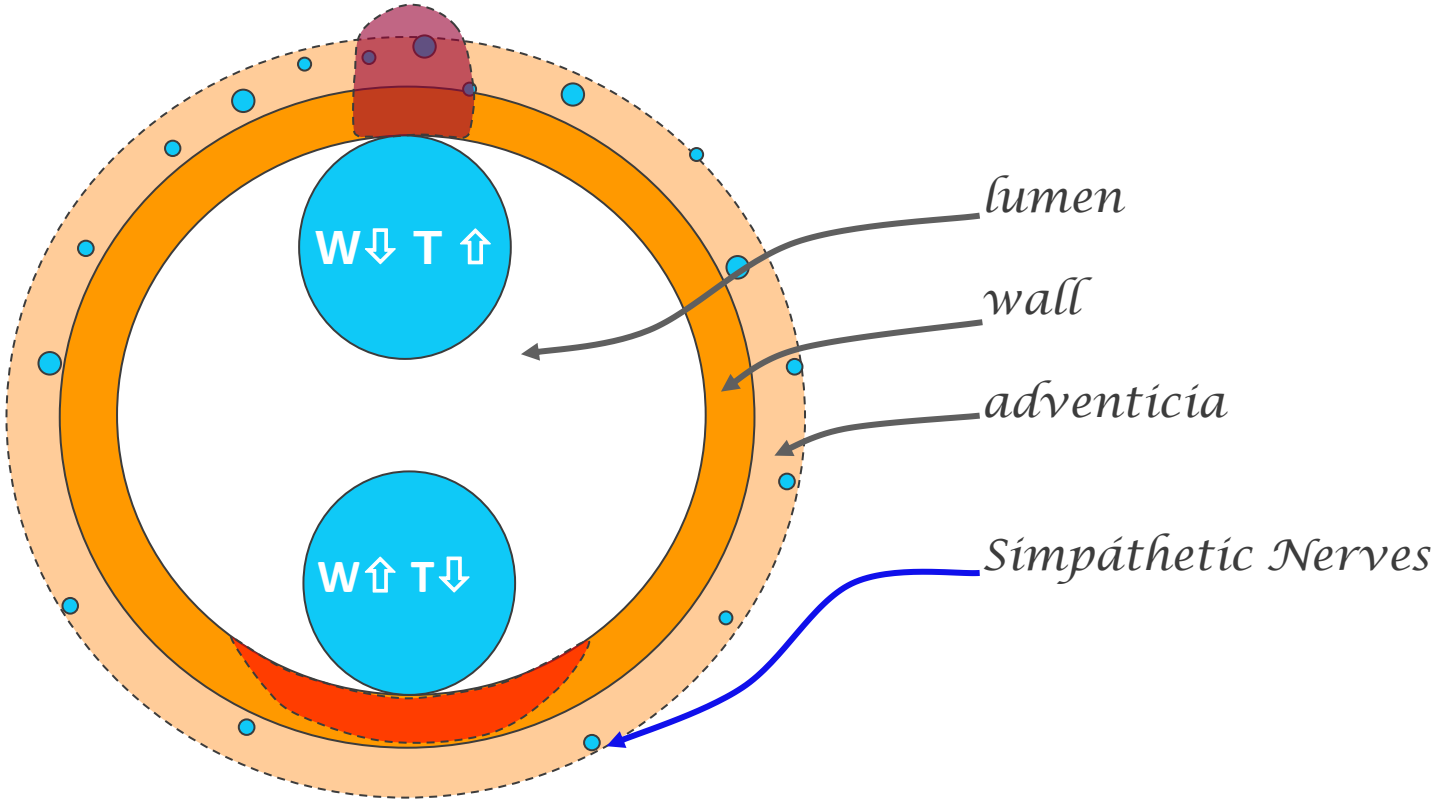
Mahfoud et al. Blood Pressure and MACE Reductions After Renal Denervation: 3 Year GSR Results. EuroPCR 2022.
TTR calculated as target SBP range OSBP≤140 mmHg and/or ASBP≤130 mmHg.

CONCEPTS of RF RDN



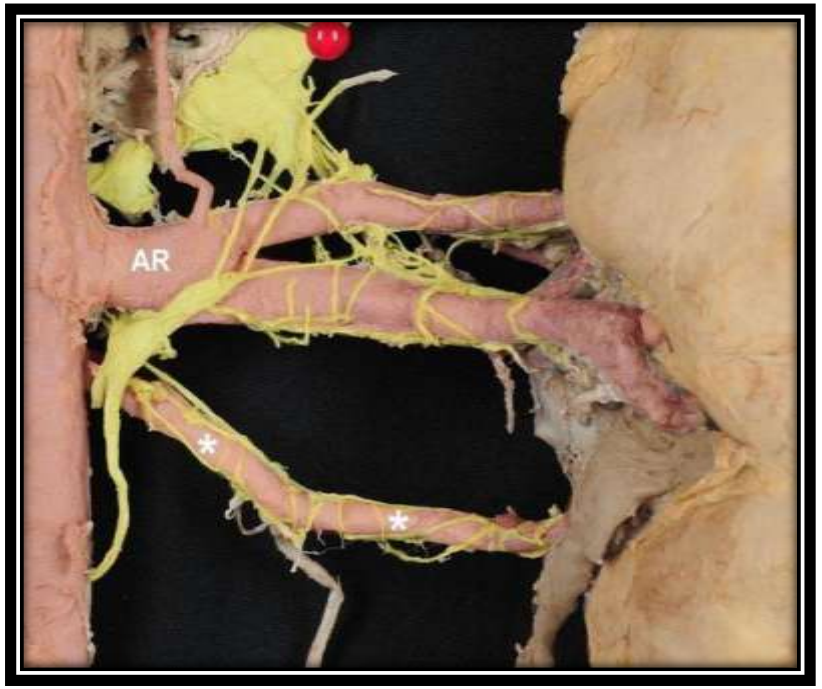
- 8 Watts
- 2 minute
- Temperature Control ….
- Impedance Monitorization

ABLATON TECHNIQUE & ITS DIFFERENCE TO CARDIAC ARRYTHMIAS ABLATION



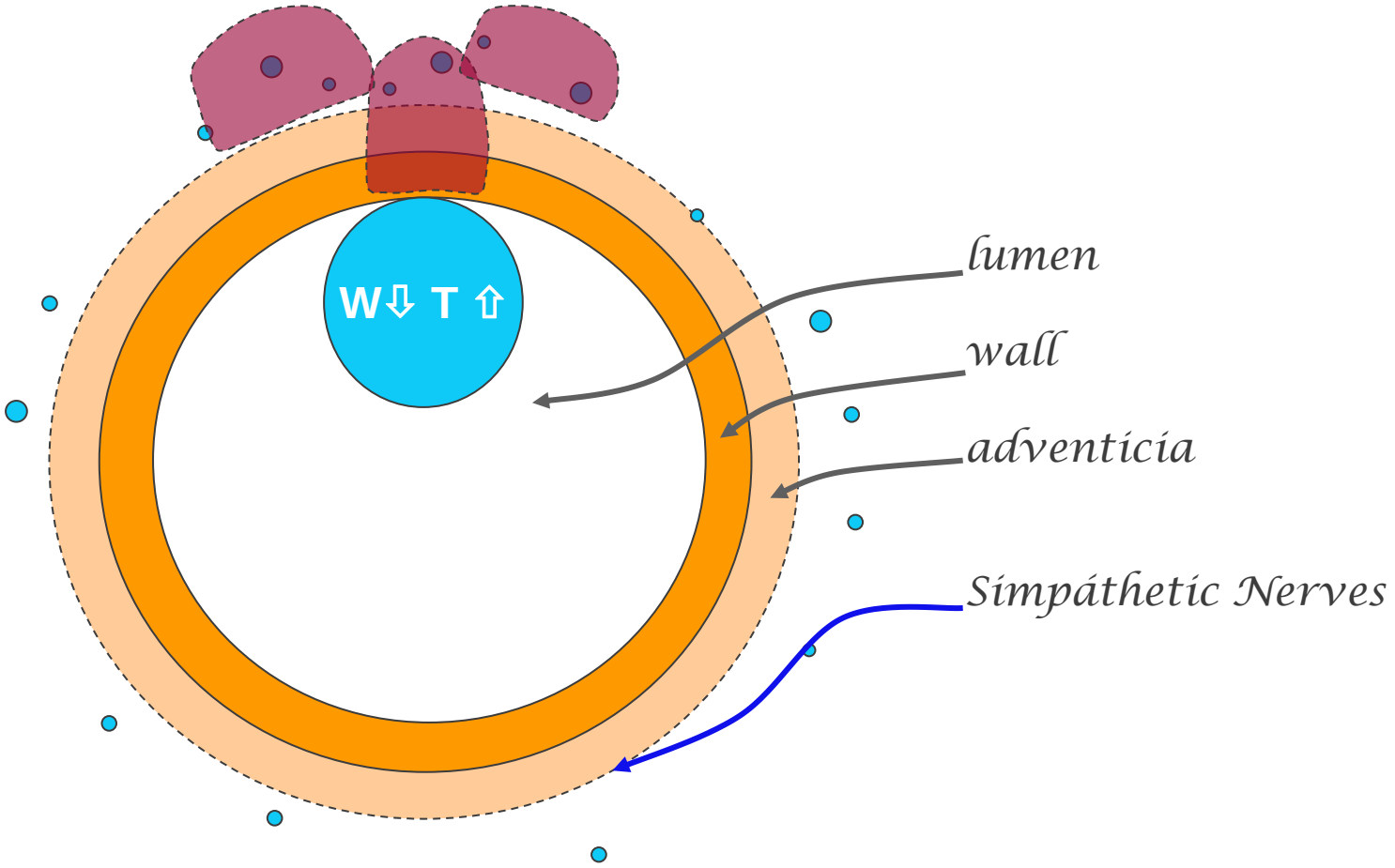
Medtronic

CONCEPTS of RF RDN



- 8 Watts
- 1 minute
- Temperature Control ….
- Impedance Monitorization

ABLATON TECHNIQUE & ITS DIFFERENCE TO CARDIAC ARRYTHMIAS ABLATION



Medtronic

Unrecoverable sympathetic nerve activity after RF RDN

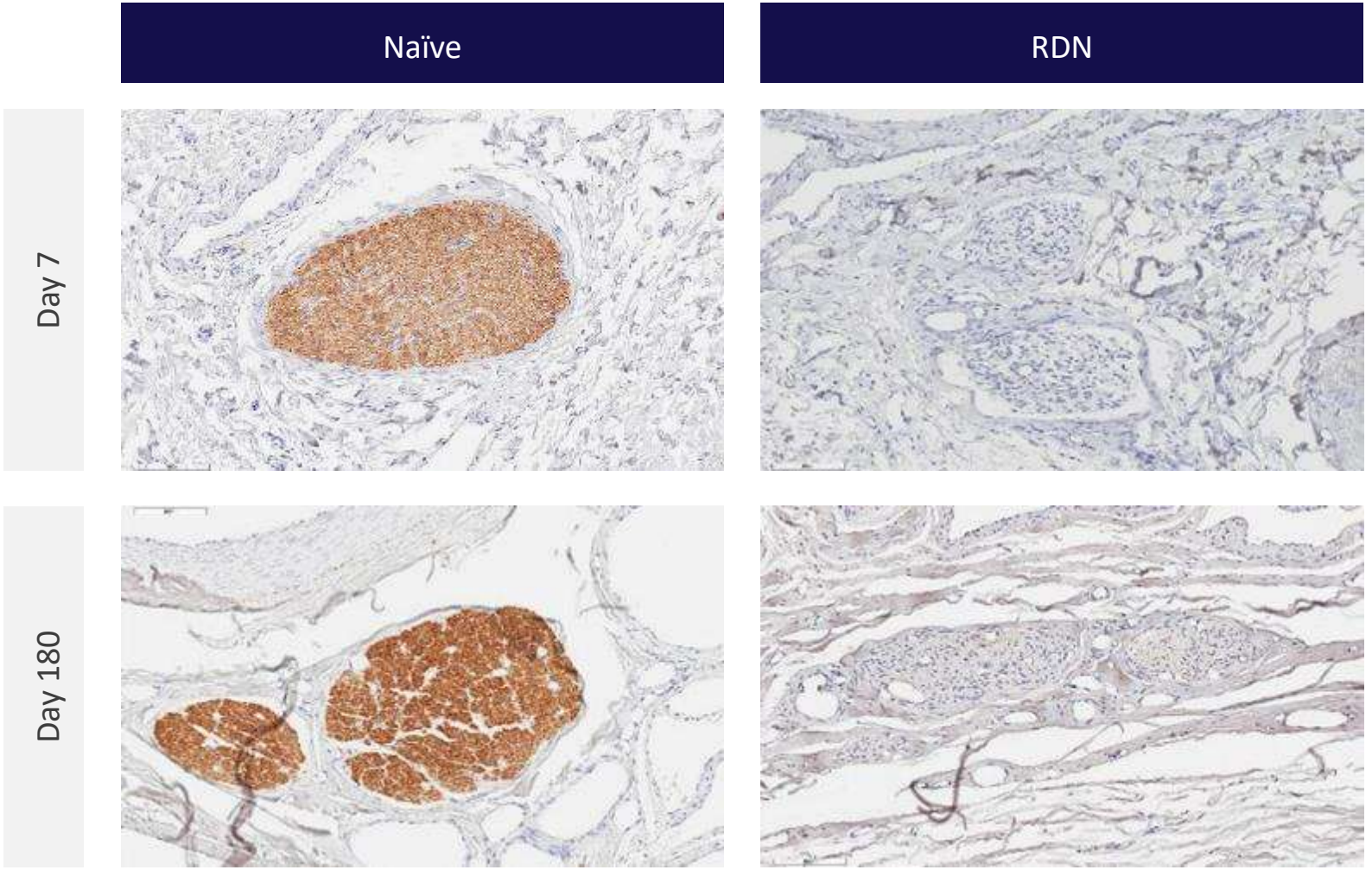
Permanent axonal destruction

and sustained reductions

in renal norepinephrine

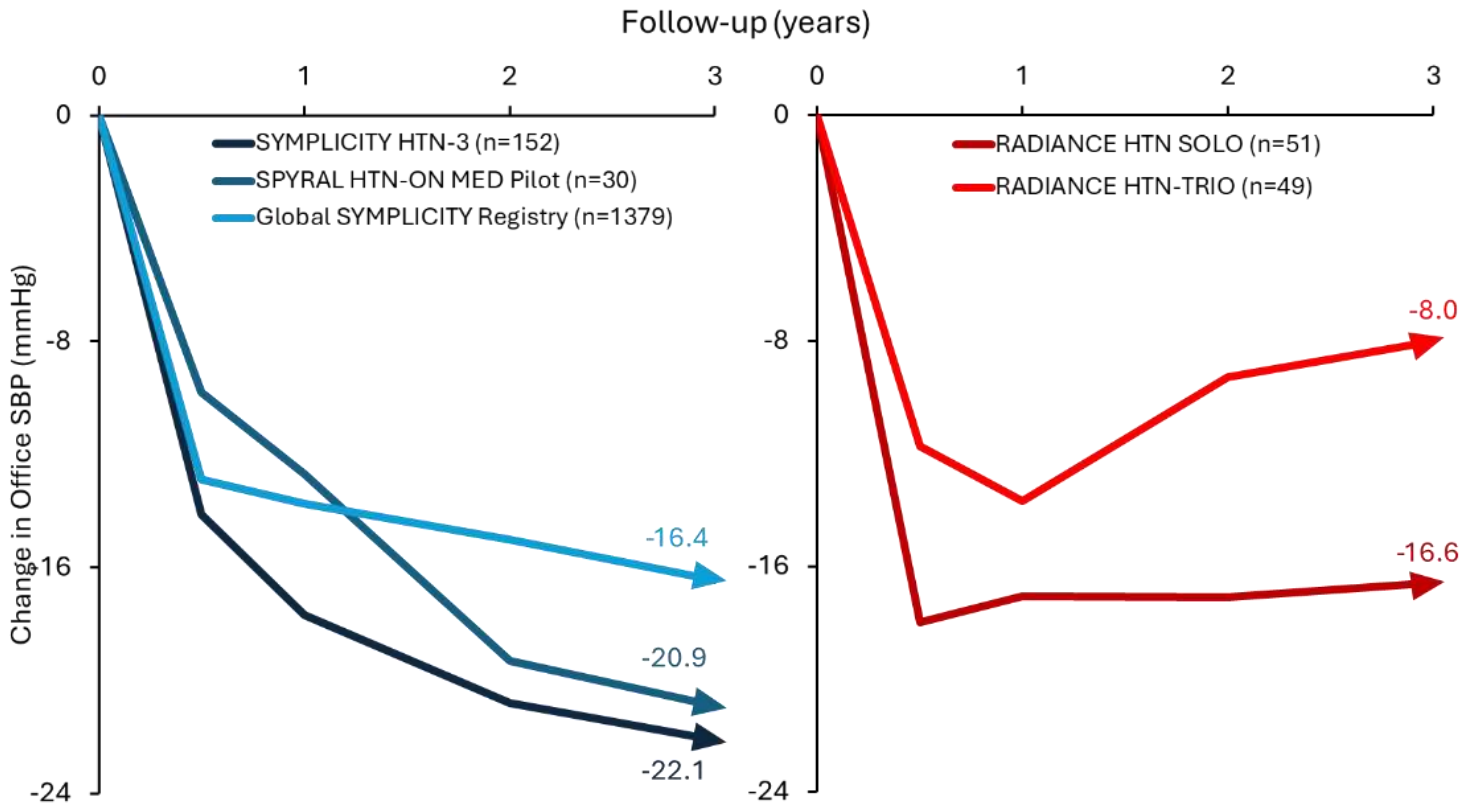
Renal Nerve Viability Assessment

Brown staining (TH) indicates viable axons. Lack of staining to 180 days demonstrates sustained axonal destruction.

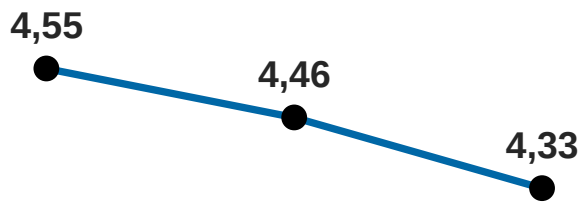


Sharp et al, TCT 2021
Mahfoud et all J Am Coll Cardiol. 2021;77(23):2909-2919. doi:10.1016/j.jacc.2021.04.044

Patients information and follow-up



Number of Medication Classes (mean)



***p*<0.001 at 3 years *vs* Baseline**

Baseline	6Mo	3Yr
(N=2836)	(n=2688)	(n=1659)

2018

European Society of Cardiology

European Society of Hypertension

2019

Taiwan Society of Cardiology

Israeli Society of Hypertension

2020

Italian Society of Arterial Hypertension (SIIA)

European Clinical Consensus Conference

Asia Consortium (ARDeC)

Russian Medical Society of Arterial Hypertension

Brazil Society of Cardiology

2021

European Society of Hypertension

South African HTN Society
SA Society of CV Intervention

International Society of Hypertension

Spanish Society of HTN
Spanish Society of Cardiology

Society for Cardiovascular Angiography & Intervention / National Kidney Foundation

2022

Malaysian Renal Nerve Denervation Working Group (My RDN)

Danish Society of Cardiology †

Taiwan Society of Cardiology †

Netherlands Expert Consortium

2023

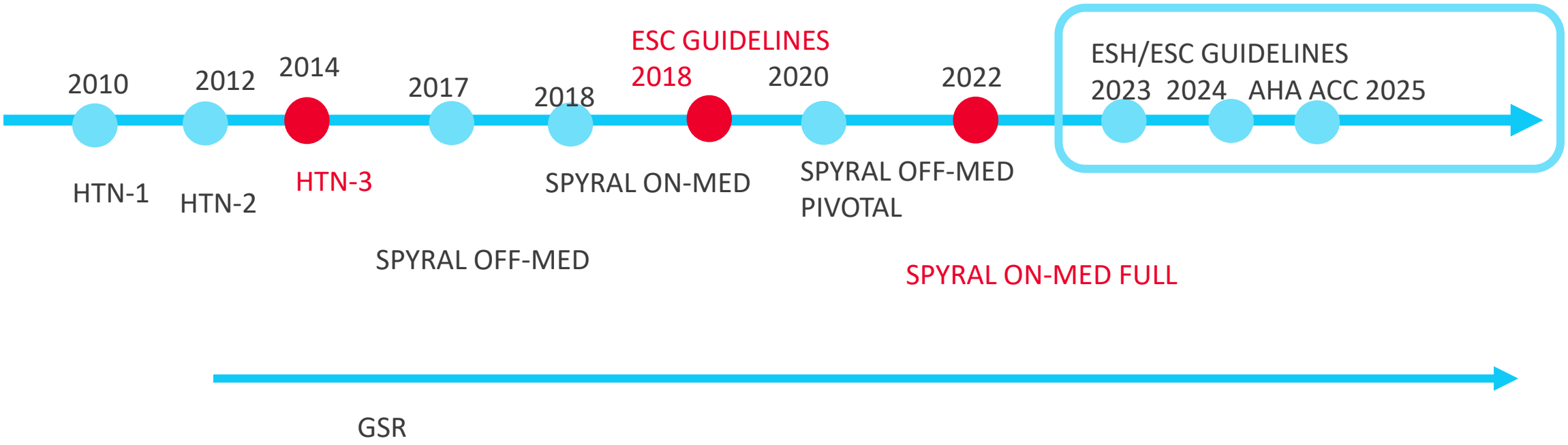
European Society of Cardiology
European Association of Percutaneous CV Interventions
Consensus Statement

Thai Hypertension Society

European Society of Hypertension (ESH)

ESH Guidelines† for Management of Hypertension

Current guidelines indication based on clinical evidence for RDN therapy



European Society of Hypertension (ESH) 2023 Guidelines

Recommend Renal Denervation as a Class II

Recommendations and statements	Class of recommendation	Level of evidence
• RDN can be considered as a treatment option in patients with an eGFR >40 ml/min/1.73m^2 who have **uncontrolled BP** despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	II	B
• RDN can be considered as an **additional treatment option (adjunct)** in patients with **resistant hypertension** if eGFR is >40 ml/min/1.73m^2		
• Selection of patients to whom RDN is offered should be done **in a shared decision-making** process after objectives and complete patient's information	I	C
• Renal denervation should be performed in **experienced centers to guarantee appropriate selection of eligible patients** and completeness of the denervation procedure		

ESH Guidelines Publication Link

Mancia G. et al. Journal of Hypertension 2023, 41:000–000 DOI:10.1097/HJH.0000000000003480

Revised recommendations (14)

2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation)					
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	**III**	**B**	To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	**IIb**	**B**

Revised recommendations (14)

2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation)					
Use of dev… …pies is not recomm… …e treatme… …unless in the conte… …ies and RCTs, u… …egarding their saf… …comes available.	III	B	To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite a three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment	IIb	B

IIb – May be considered

B- Single RCT or Large non randomized studies

2024 ESC Guidelines for the management of elevated blood pressure and hypertension
(European Heart Journal; 2024 – doi: 10.1093/eurheartj/ehae178)

ACC/AHA GUIDELINES

2025

Recommendations for Resistant Hypertension and Renal Denervation

2b	B-R	4. In carefully selected patients with systolic and diastolic hypertension (office SBP 140-180 mm Hg and DBP ≥90 mm Hg) and eGFR ≥40 mL/min/1.73 m^2 who have resistant hypertension despite optimal treatment, or intolerable side effects to additional antihypertensive drug therapy, renal denervation (RDN) may be reasonable as an adjunct treatment to BP medications and lifestyle modification to reduce BP.[12-14]

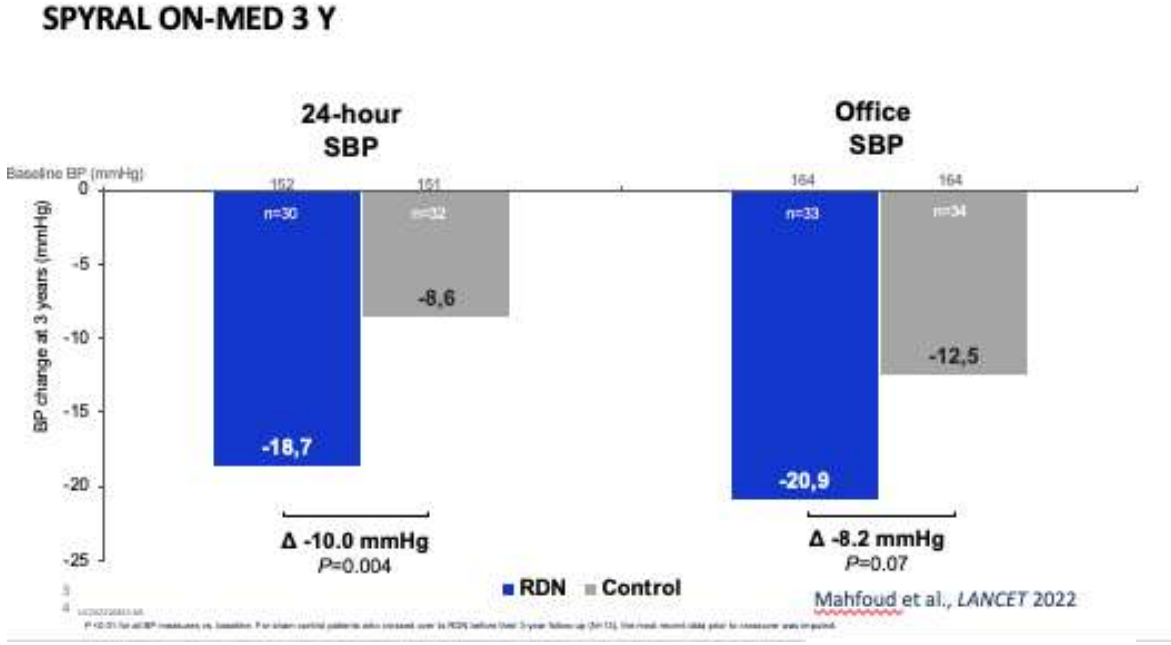
Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults JACC 25

ESC 2024 / AHA ACC 2025

Recommendations for RDN

1. Performed in a medium-to-high volume center.
   Once / Twice a week (50 to 100 /y). IIb - B

2. May be considered for RHTN pts with uncontrolled BP despite a 3 BP drug combination (+ thiazide), as na adjunct treatment. IIb - B



FEITOSA ADM, MOTA-GOMES MA, PASSARELLI O Jr., BARROSO WS, MIRANDA RD, BARBOSA ECD, BRANDÃO AA, NADRUZ W Jr. Pharmacological treatment of hypertension: from the golden trio to the octet. Arq Bras Cardiol. 2020.

ACC/AHA GUIDELINES

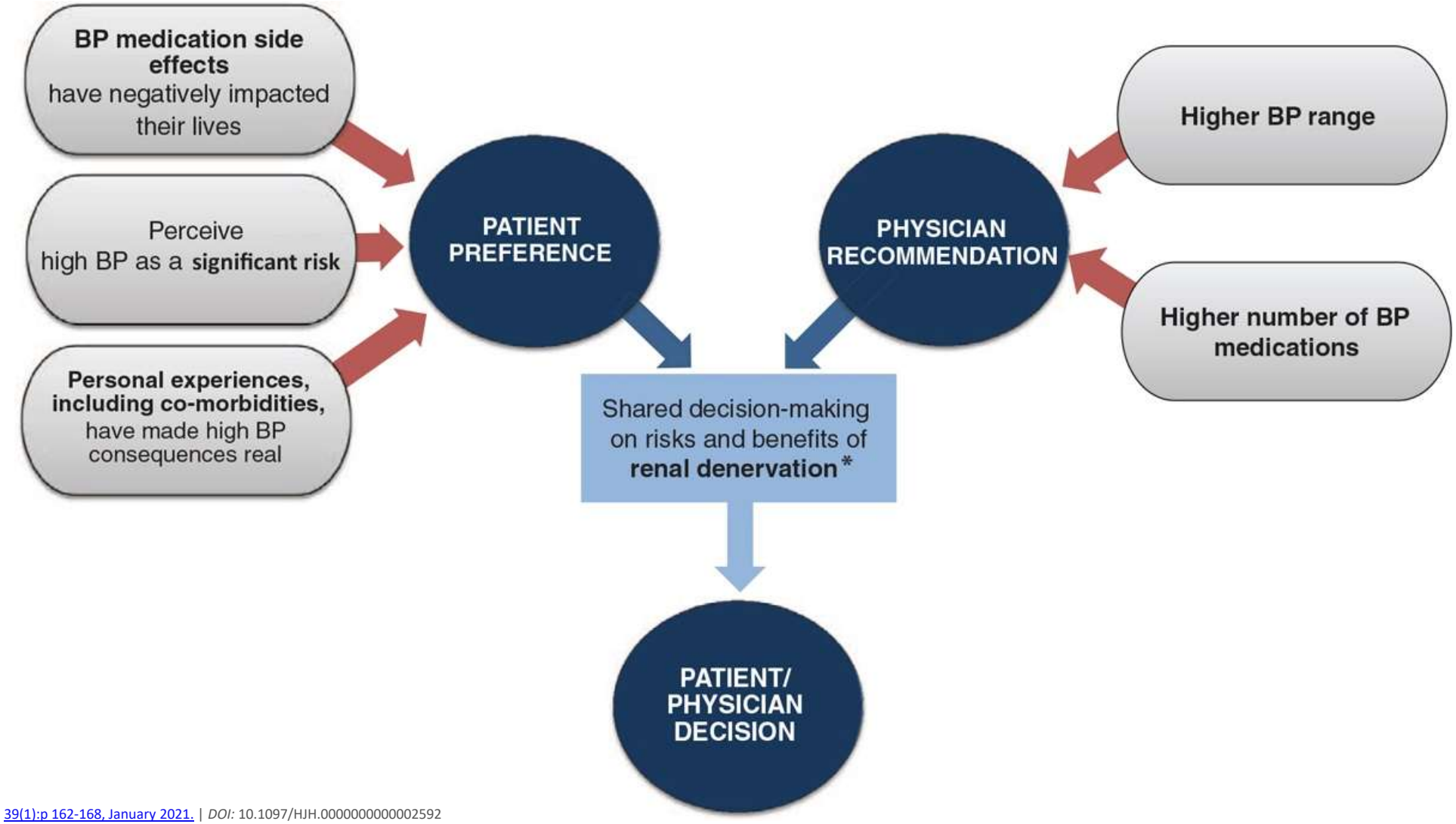
2025

Recommendations for Resistant Hypertension and Renal Denervation

1 B-NR	5. All patients with hypertension who are being considered for RDN should be evaluated by a multidisciplinary team with expertise in resistant hypertension and RDN.[12-14]
1 C-EO	6. For patients with hypertension for whom RDN is contemplated, the benefits of lowering BP and potential procedural risks compared with continuing medical therapy should be discussed as part of a shared decision-making process to ensure patients choose the therapy that meets their expectations.

Medtronic

Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults JACC 25



Journal of Hypertension 39(1):p 162-168, January 2021. | *DOI:* 10.1097/HJH.0000000000002592

Medtronic

Revised recommendations (15)

2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation)					
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	**III**	**B**	To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	**IIb**	**A**

Revised recommendations (15)

2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation)					
Use of device-based therapies is not recommend[illegible] for t[illegible]utine treatmen[illegible] unless in the co[illegible] and RCTs, un[illegible]e regarding their saf[illegible]omes availab[illegible]	III	B	To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	A

IIb – May be considered

A- Multiple RCTs or Meta-analyses

ESC 2024 / AHA ACC 2025

Recommendations for RDN

1. Performed in a medium-to-high volume center
   Once / Twice a week (50 to 100 /y). IIb - B

2. May be considered for RHTN pts with uncontrolled BP despite a 3 BP drug combination (+ thiazide), as an adjunct treatment. IIb – B

3. Patients with both, increased CVD risk and uncontrolled BP on fewer than 3 BP drugs and express a preference to undergo RDN / shared risk-benefit discussion and multi-disciplinary assessment. IIb – A.  B/C 

Revised recommendations (16)

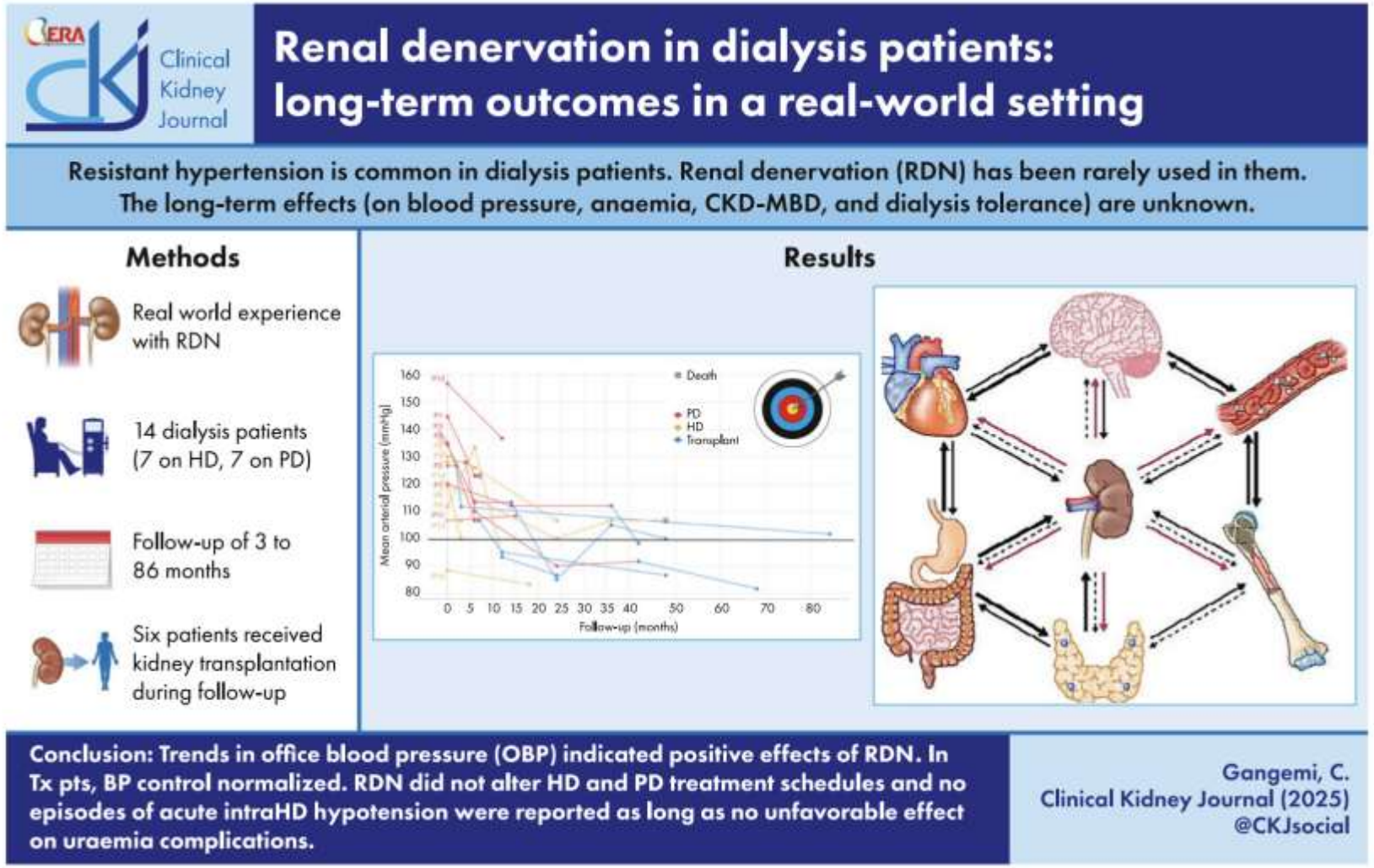
2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation) cont.					
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	**III**	**B**	Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension.	**III**	**C**
			Renal denervation is not recommended for treating hypertension in patients with moderately to severely impaired renal function (eGFR <40 mL/min/1.73 m^2) or secondary causes of hypertension, until further evidence becomes available.	**III**	**C**

Revised recommendations (16)

2018 Guidelines	Class	Level	2024 Guidelines	Class	Level
Preventing and treating elevated blood pressure (renal denervation) cont.					
Use of de ies is not recom e treatmen , unless in the cont and RCTs, u regarding their safet becomes available.	III	B	Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension.	III	C
			Renal denervation is not recommended for treating hypertension in patients with moderately to severely impaired renal function (eGFR <40 mL/min/1.73 m^2) or secondary causes of hypertension, until further evidence becomes available.	III	C

Renal denervation in dialysis patients: long-term outcomes in a real-world setting

Concetta Gangemi[1,*], Alessia Gambaro[2,*], Vittorio Ortalda[1], Domenico Tavella[2], Chiara Caletti[1], Simone Fezzi[2], Beatrice Bianco[1], Elisa De Tomi[1], Giovanni Gambaro[1,†] and Flavio Luciano Ribichini[2,†]; on behalf of the GITIAR team



Journal of Nephrology
https://doi.org/10.1007/s40620-025-02406-2

POSITION PAPERS AND GUIDELINES

The role of renal denervation for the treatment of hypertension in patients with chronic kidney disease: a position paper of the Italian Society of Nephrology

THE ROLE OF RENAL DENERVATION FOR THE TREATMENT OF HYPERTENSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A POSITION PAPER OF THE ITALIAN SOCIETY OF NEPHROLOGY

Feriozzi S, Battaglia Y, Cirami CL , Gangemi C, La Manna G, Gesualdo L, Muiesan ML Pani A, Pieruzzi F, Ribichini F. Taddei S, Bianchi S, on behalf of the Italian Society of Nephrology

BACKGROUND

Renal denervation is an effective therapeutic option to improve blood pressure control in patients with resistant or uncontrolled hypertension. Its use in patients with advanced chronic kidney disease or on replacement therapy is not currently supported by international guidelines, but growing evidence from scientific literature allows us, on behalf of the Italian Society of Nephrology, to outline its use also in these patients.

GENERAL STEPS FOR THE RENAL DENERVATION PROCEDURE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

1. Renal denervation is currently not recommended for patients with resistant or uncontrolled hypertension and eGFR <40 mL/min/1.73 m².
2. Multiple studies in patients with eGFR <40 mL/min/1.73 m² highlighted renal denervation efficacy and safety.
3. Renal denervation should be considered on a case-by-case basis. Patients must be fully informed of the potential clinical benefits and risks.
4. Patients should be hospitalized following investigation of the anatomic status of the renal arteries.
5. Preventive measures for minimizing the risk of kidney damage induced by contrast media are recommended. Patients should be hydrated to minimize contrast-induced kidney injury
6. Antihypertensive medications should be continued.
7. After the procedure, strict control of clinical and laboratory parameters is recommended. Kidney function should be checked 24 and 72 hours after the procedure
8. Antiplatelet therapy should be added for at least one month after renal denervation.
9 . Monthly laboratory tests and frequent blood pressure measurements should be checked for 12 months after the procedure.

SPECIFIC STEPS FOR THE PROCEDURE IN PATIENTS ON DIALYSIS

1. Follow all steps listed in the general procedure, except for point 5
2. Schedule the next dialytic session at least 24 hours after the procedure, with minimal anticoagulation. In peritoneal dialysis, the exchanges can follow the usual schedule.
3. The patient's blood pressure values should be monitored frequently during the following dialysis sessions and in the interdialytic periods.

SPECIFIC STEPS FOR THE PROCEDURE IN KIDNEY TRANSPLANT

1. Considering all physiopathological aspects, there is evidence for encouraging a wise and weighted approach to renal denervation in transplant patients
2. All steps (1-9) of the procedure for chronic kidney disease should be followed.

CONCLUSIONS

Renal denervation is a safe and effective procedure in the treatment of uncontrolled or resistant hypertension, also in patients with advanced CKD. In addition, in dialysis patients, renal denervation improves intradialytic vascular stability. In kidney transplant patients, more evidence is still needed before making specific recommendations.

Journal of NEPHROLOGY
official journal of the Italian Society of Nephrology

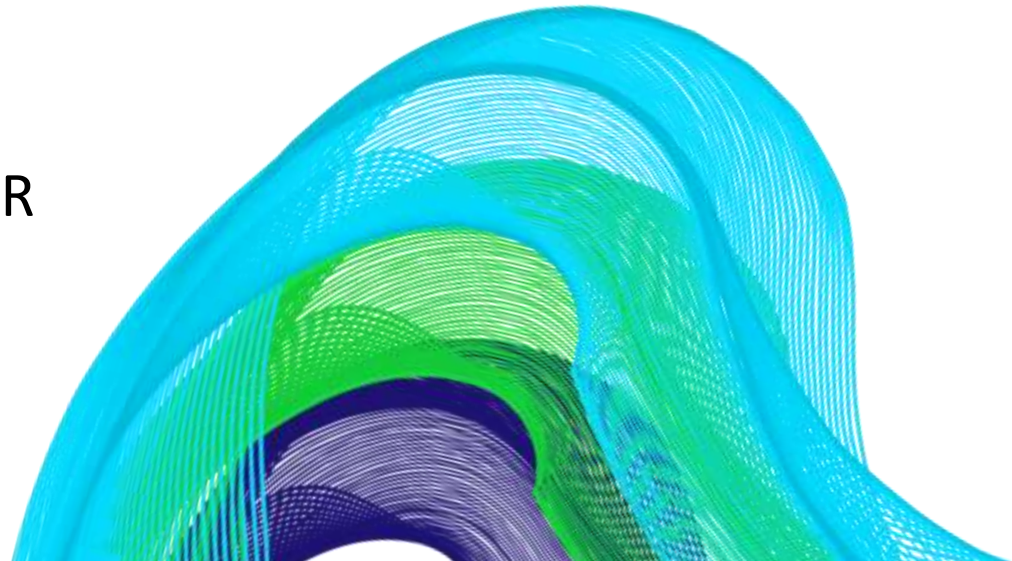
Puibished online 8 sep 2025

Evidencia Actual de RDN y Criterios de selección de pacientes.

1. Todo lo que si sabemos hoy en DSR…

2. Lo que está pendiente por saber de la DSR (perspectivas futuras)…

3. Selección del candidato para DSR



Hypertension management with renal denervation

Unmet need:

- There is no direct parameter of successful renal nerve ablation (blinded procedure)
- Response to renal denervation varies

The solution: Renal nerve stimulation for RDN

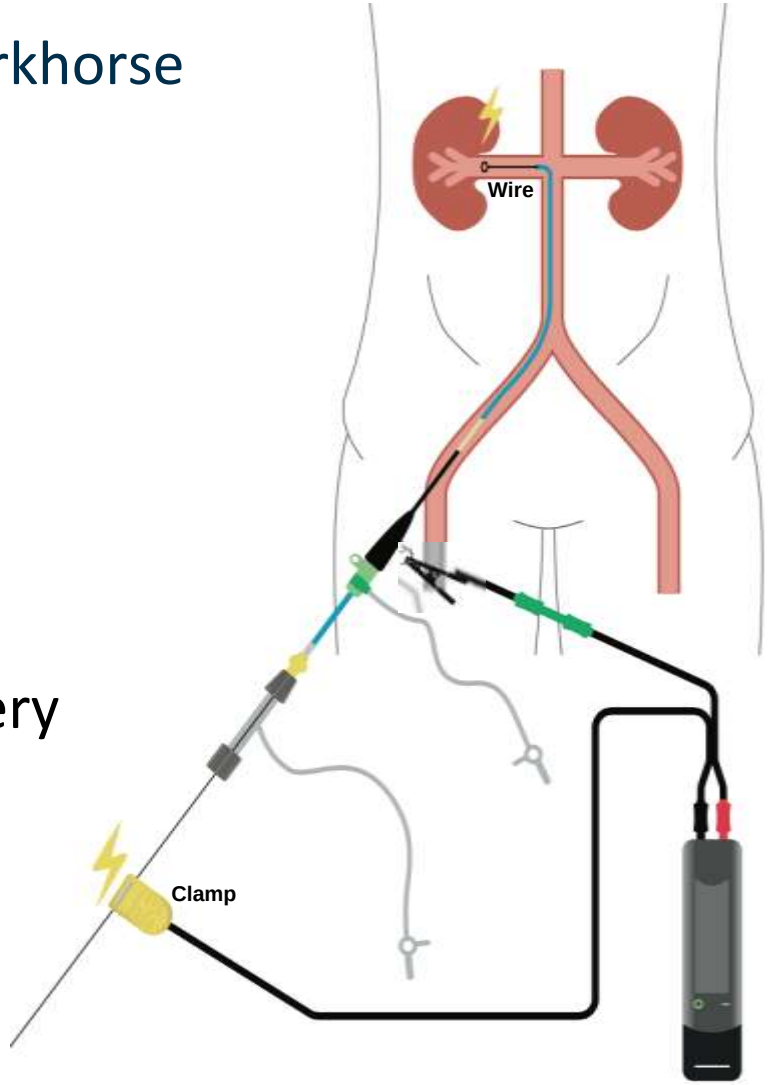
- *Identifies* good responders
- *Maps* target areas
- *Verifies* the completeness of the procedure

Safety and Efficacy of Renal Stimulation with Direct Wire Pacing during Renal Denervation procedure

Design: Unipolar Renal Nerves Stimulation (RNS) using a workhorse guidewire and an external pacemaker

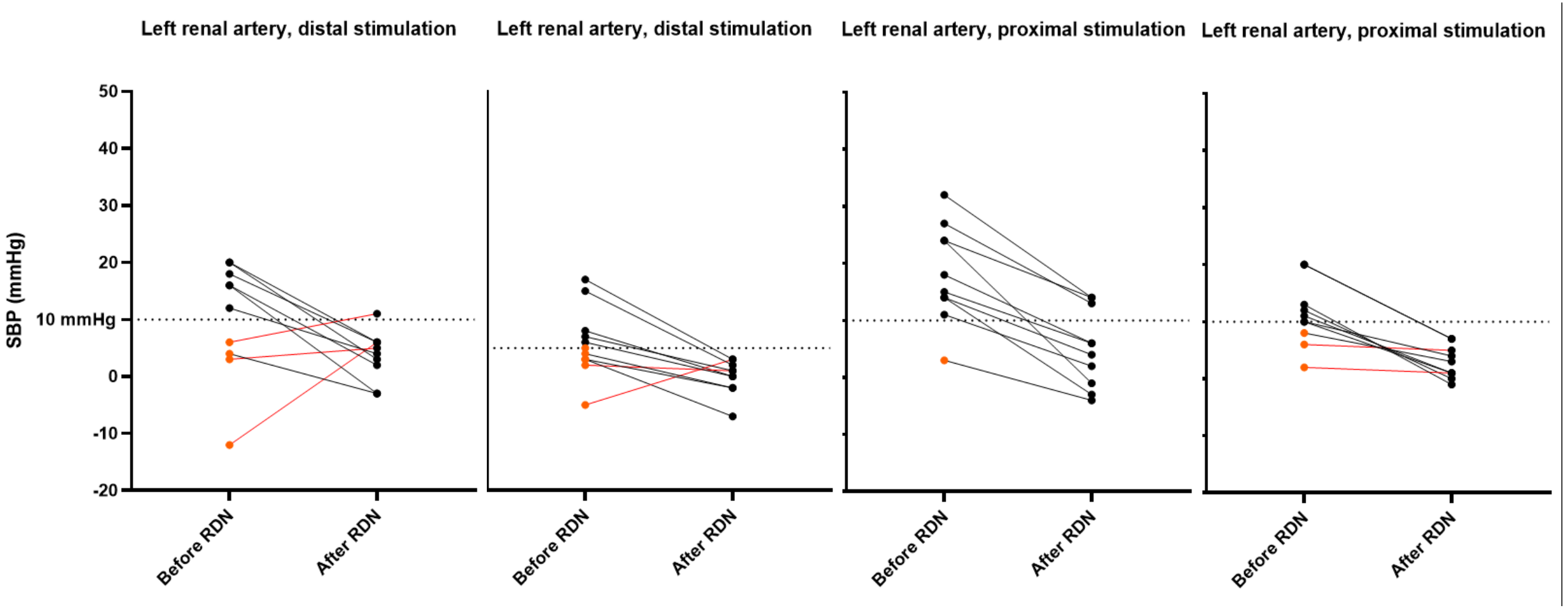
Study population: 11 patients undergoing uRDN procedure

- >2 antihypertensive drugs
- Office BP >140/90 mmHg and 24-hour systolic BP >130
- Glomerular filtration rate >40 mL/min
- Main renal artery diameter ≥3 mm & max 1 accessory artery



Presented by F. Mahfoud at TCT 2024

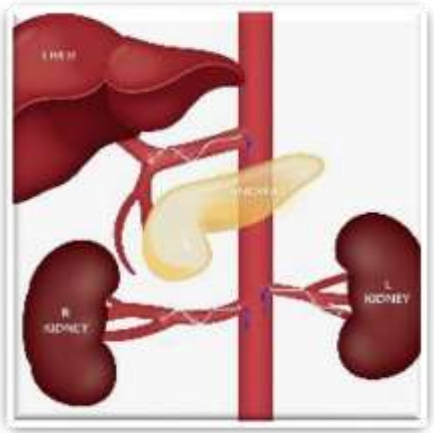
RNS by DWP: Primary results



Presented by F. Mahfoud at TCT 2024

Multi-organ Denervation Offers a New Sympathetic Nerve System Target

Multi-organ
(hepatic + renal) denervation



Rationale

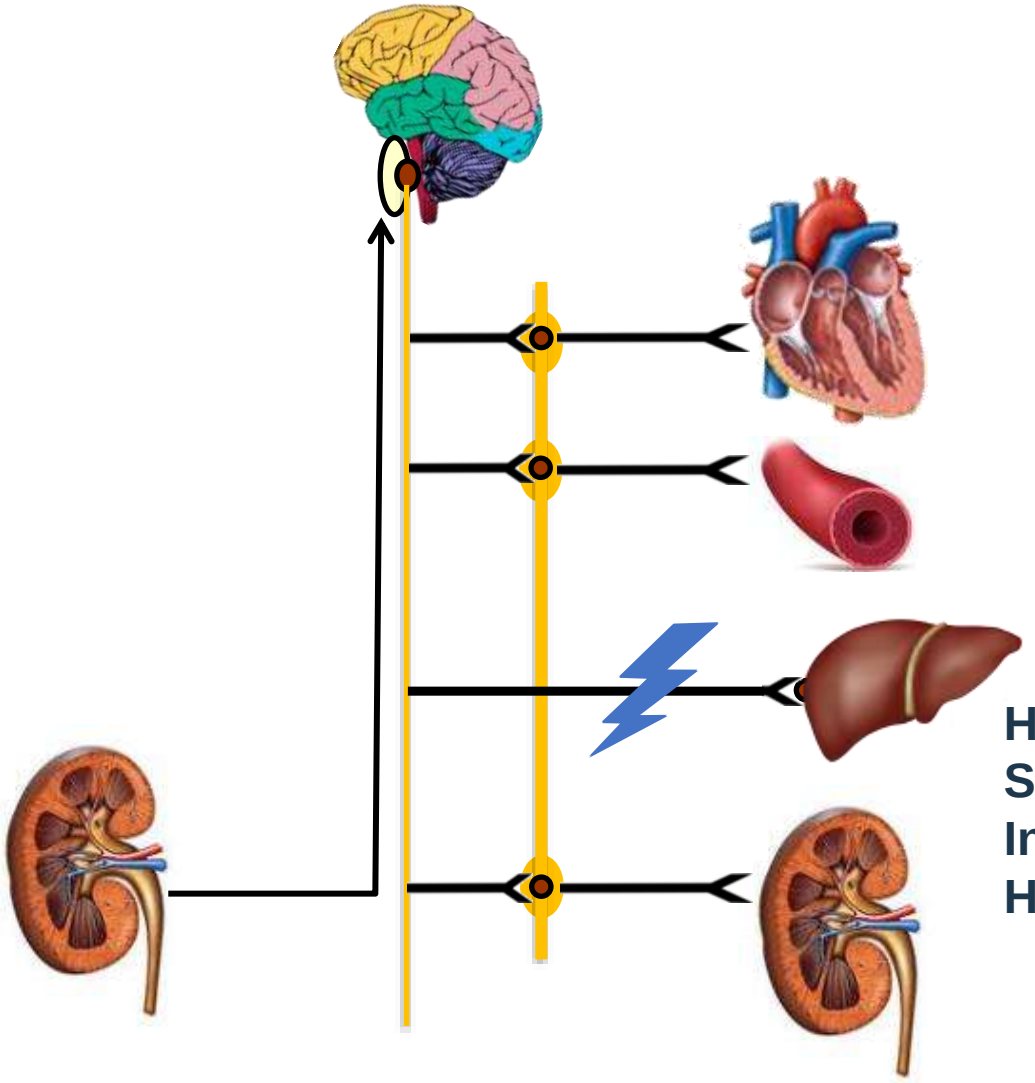
Target peri-vascular bed that may be more richly innervated than current targets

Initial pilot and pre-clinical studies support approach

Symplicity Spyral catheter potential for both hepatic and renal anatomy

Presented Oct 28/2024 at TCT by Dr. Raven Voora

Sympathetic Neural Mechanisms of BP Regulation



Hypothesis:
Smooth muscle relaxation ->
Increase hepatic blood flow ->
Hepatic blood pool becomes larger

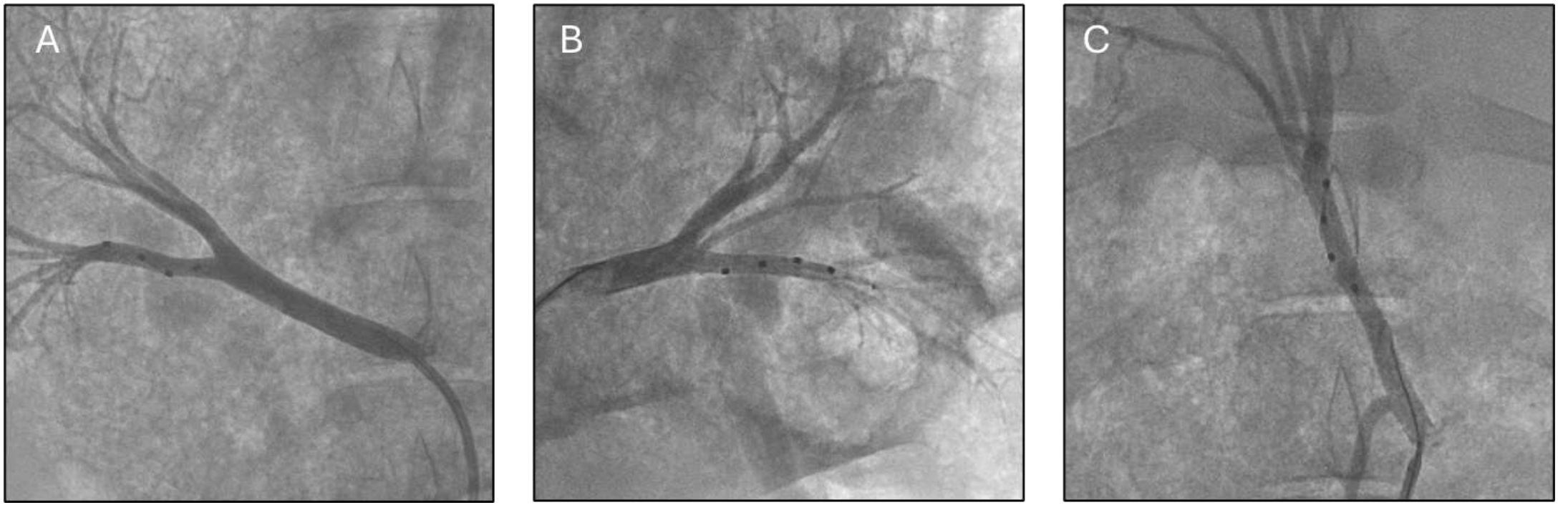
Presented Oct 28/2024 at TCT by Dr. Raven Voora

Multi-electrode Spyral Catheter placement in the Right and Left Renal Arteries and Common Hepatic Artery

Right renal artery

Left renal artery

Common Hepatic Artery



Medtronic data on file. Preclinical imaging

Presented Oct 28/2024 at TCT by Dr. Raven Voora

Evidencia Actual de RDN y Criterios de selección de pacientes.

1. Todo lo que si sabemos hoy en DSR…

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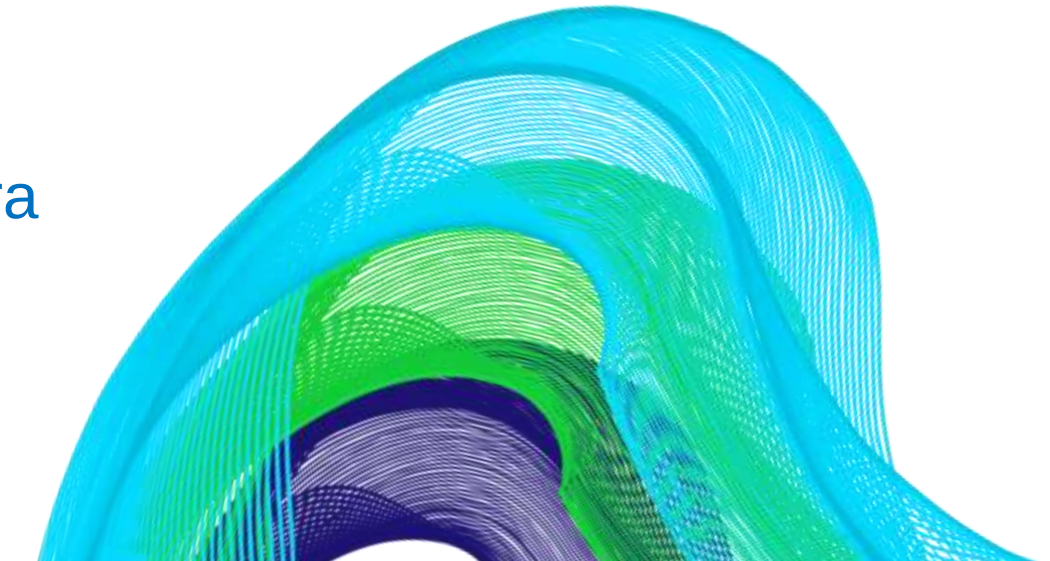
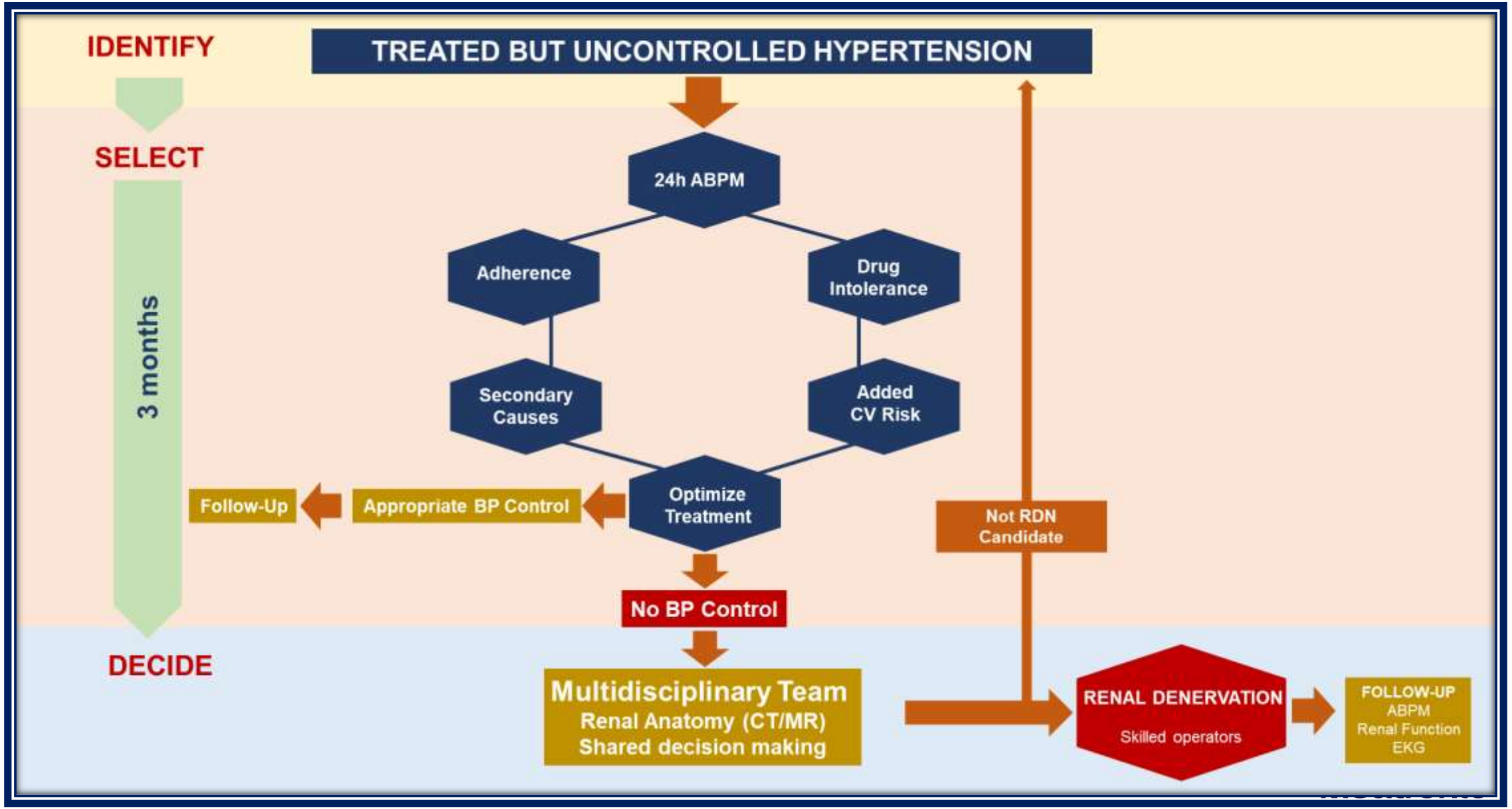


STEP 1: Patient Selection



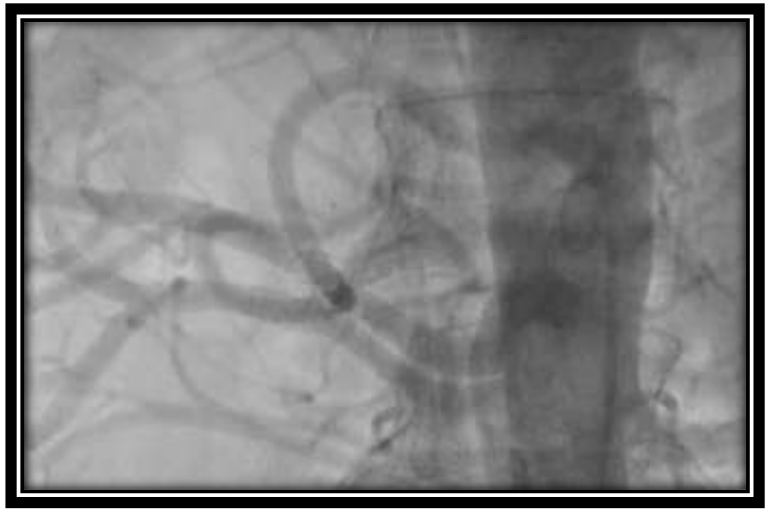
Rodríguez-Leor O, et al. *REC Interv Cardiol*. 2021. https://doi.org/10.24875/RECICE.M21000235

STEP 2: Anatomy evaluation

- Femoral Approach (6Fr)
- Pigtail Catheter
- Aortogram
  - Rule out stenosis
  - Evaluate Take-off of the renal arteries
  - Look for accessory renal arteries

Double Renal Arteries

Triple Renal Arteries



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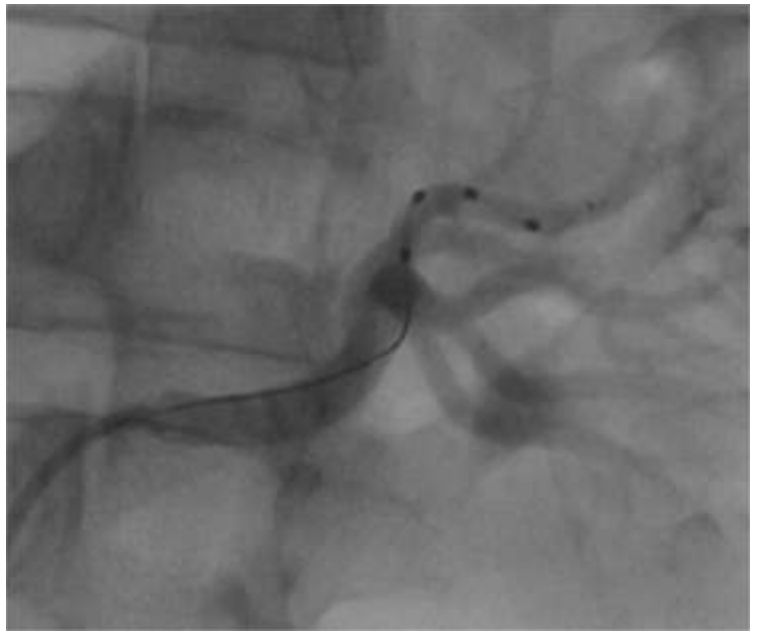
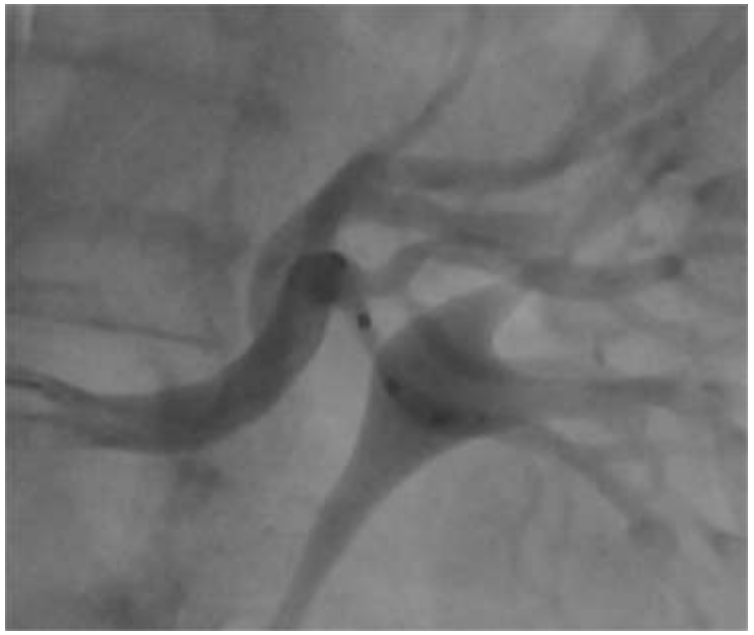
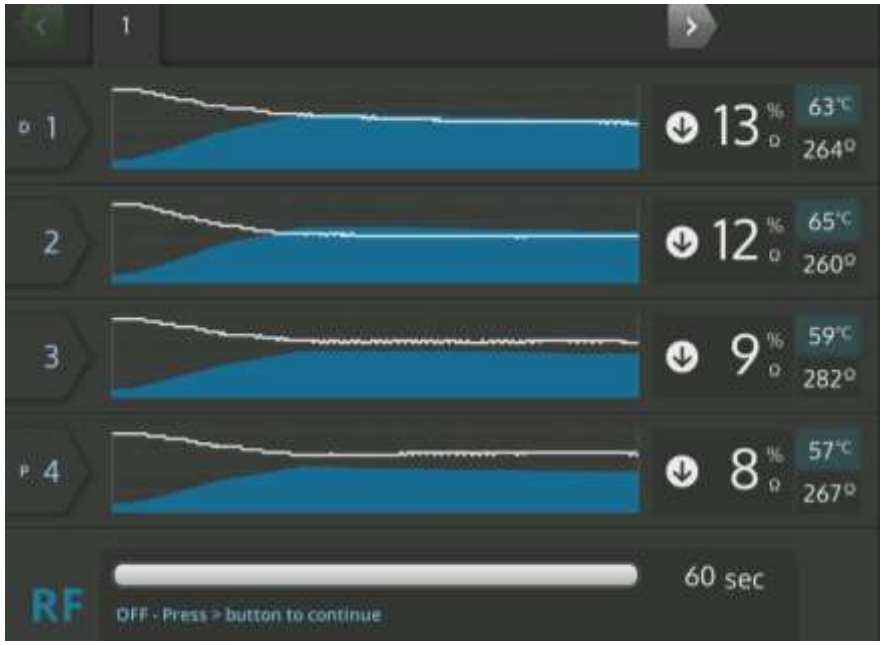
STEP 3: Anatomy evaluation

- **AVOID**
  - Stents
  - Stenosis
  - Aneurism
  - Fibromuscular dysplasia






1
13 %
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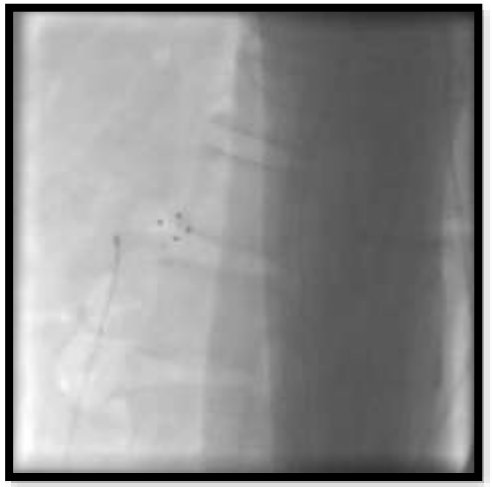


RF


292Ω
290Ω
299Ω
284Ω
RF

After the procedure

Handle pain after the procedure

- It may hurt for 48 hrs after.

Do not take off meds…..

- Results are not immediate
- RDN is not intended to skip meds, but to control the patient BP.

Thank you