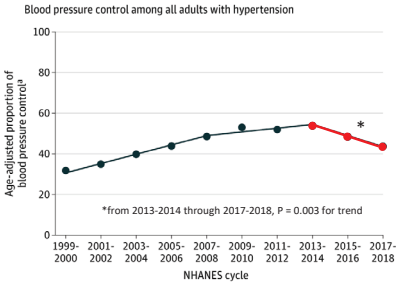
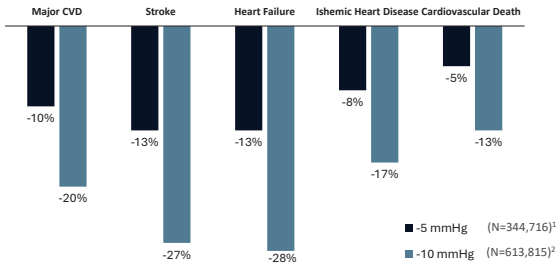
US BLOOD PRESSURE CONTROL RATES ARE DECREASING

- Over **56%** of US hypertensive patients are **not controlled to below 140 mmHg**
- Over **35%** of US *treated* hypertensive patients are uncontrolled



Muntner P, et al. JAMA. 2020. doi:10.1001/jama.2020.14545

Relative Risk Reduction Proportional to Decrease in OSBP
Irrespective of Baseline BP or CVD History in 2 Meta-Analyses



[1] Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2021;397(10285):1625-36
[2] Ettehad D, et al. *Lancet*. 2016;387(10022):957-67

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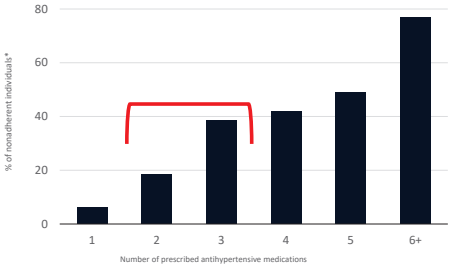
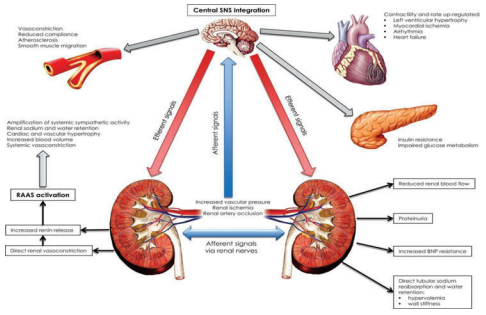


History of Renal Denervation: Mechanistic Reasoning



THE EFFECT OF RENAL DENERVATION ON THE LEVEL OF ARTERIAL BLOOD PRESSURE AND RENAL FUNCTION IN ESSENTIAL HYPERTENSION

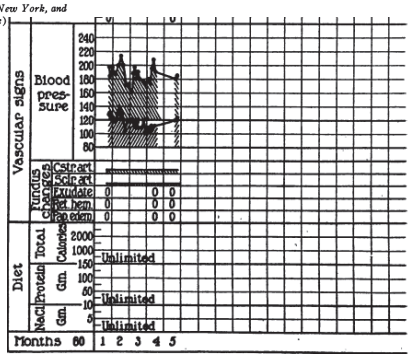
By IRVINE H. PAGE and GEORGE J. HEUER

(From the Hospital of the Rockefeller Institute for Medical Research, New York, and the Department of Surgery, New York Hospital, New York)

(Received for publication September 12, 1934)

JCI 1935

25-year–old woman who reported easy fatigability and had severe headaches and BP in the range of 208/140 mm Hg. The patient underwent surgical staged, bilateral renal sympathectomy



AJS The American Journal of Surgery

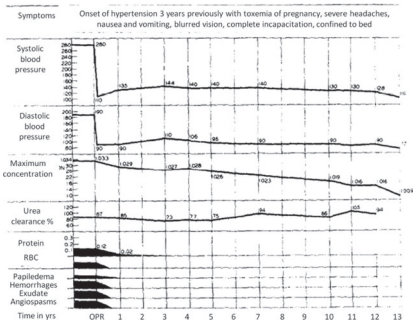
Hypertension and its surgical treatment by bilateral supradiaphragmatic splanchnicectomy

Max Minor Peet, M.D.

ORIGINAL ARTICLE | VOLUME 75, ISSUE 1, P48-68, JANUARY 1948

22-year-old patient with known severe hypertension for >3 years.

- Bedrest for 8 months because of the severity of symptoms
- BP remained at 280/190 mm Hg.
- Fundoscopic examination revealed stage IV retinopathy with evidence of early papilledema, flame-shaped hemorrhages, and cotton wool exudates.



SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Smithwick, M.D.
and
Jesse E. Thompson, M.D., Boston

JAMA. 1953;152(16):1501-1504.

Many forms of therapy have been used in an effort to control hypertension. The principal ones may be classified under three headings: (1) diets low in sodium and fat, (2) drugs with a hypotensive or sedative effect, and (3) surgery. The form of surgical therapy that has been used most extensively is intervention on the sympathetic nervous system. There are many data in the literature

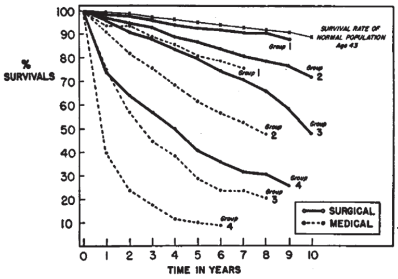


TABLE 1.—*Numerical Value of Various Factors That Influence Prognosis*

	Numerical Value of Each Factor
Cerebrovascular accident with or without minor residual	1
Abnormal electrocardiogram	
Enlarged heart	
Impending congestive failure	
Phenolsulfonphthalein excretion, less than 25% in 15 min. or less than 60% in 2 hr.	
Age 50 or over	
Mild angina	
Cerebrovascular accident, with residual *	2
Frank congestive failure, moderate angina	
Phenolsulfonphthalein excretion, less than 20% in 15 min.	
Unsatisfactory response to sedation	
Phenolsulfonphthalein excretion, less than 15% in 15 min.	3
Nitrogen retention	4

* Cerebral deterioration or definite involvement of arm and/or leg.

- Unfortunately, this was a morbid surgery and frequently resulted is severe orthostatic hypotension and syncope

Thoracolumbar splanchnicectomy was the standard of care for malignant hypertension for 20 years, until…

TREATMENT OF ESSENTIAL HYPERTENSION WITH CHLOROTHIAZIDE (DIURIL)

ITS USE ALONE AND COMBINED WITH OTHER ANTIHYPERTENSIVE AGENTS

Edward D. Freis, M.D., Annemarie Wanko, M.D., Ilse M. Wilson, M.D.
and
Alvin E. Parrish, M.D., Washington, D. C.

J.A.M.A., Jan. 11, 1958

TABLE 1.—*Antihypertensive Effects of Chlorothiazide Alone in Ten Hypertensive Patients*

Blood Pressure Levels	Av.	Range
Pretreatment, mm.Hg	175/108	140/94 to 187/127
Post-treatment, mm.Hg	136/93	129/78 to 162/104
% decrease in systolic	—18.7	(—10 to —37)
% decrease in diastolic	—13.9	(— 5 to —20)
% decrease in mean*	—16.9	(— 9 to —25)

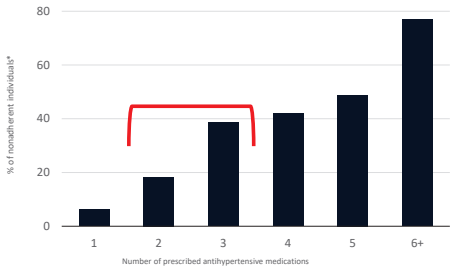
* Mean blood pressure $= \frac{\text{systolic} + \text{diastolic}}{2}$.

TABLE 2.—*Addition of Chlorothiazide to Other Antihypertensive Regimens*

Antihypertensive Regimen	No. of Patients	Av. Pretreatment Blood Pressure, Mm. Hg: Systolic	Av. Pretreatment Blood Pressure, Mm. Hg: Diastolic	% Decrease in Blood Pressure Level: Before Chlorothiazide	% Decrease in Blood Pressure Level: After Chlorothiazide	% Decrease in Blood Pressure Level: Difference
Ganglionic blocker alone	10	225	135	12.5	28.7	16.2
with reserpine	12	214	130	9.6	25.7	16.1
with reserpine & hydralazine	8	236	134	20.9	34.8	13.9
with hydralazine	3	203	115	7.5	18.3	10.8
Veratrum alone	5	210	120	9.7	25.4	15.7
with reserpine	12	208	122	6.8	22.6	15.8
with reserpine & hydralazine	2	240	152	15.6	32.9	17.3
Reserpine	7	175	120	12.3	26.2	13.9
Reserpine & hydralazine	14	198	118	8.9	28.3	19.4
Total	73					
Mean		211	126	11.0	27.0	16.0

Non-Adherence Increased with Pill Burden

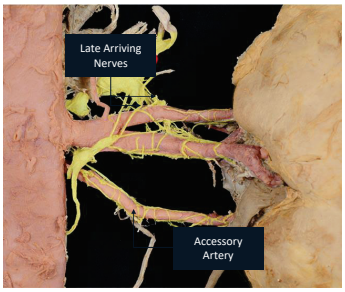
- Going from 2 to 3 medications doubled non-adherence
- Patients on 5 medications are nearly 50% non-adherent
- Majority of patients prescribed 6+ medications were nonadherent



Beth Israel Deaconess Medical Center | Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology | HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Renal nerve anatomy

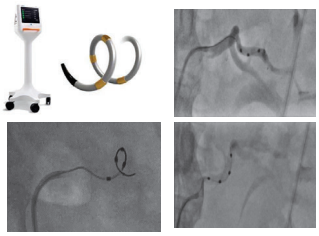
- Renal nerves often bypass the main renal artery and converge on the branches[1]
- 63% of kidneys had renal nerves that joined distal to the main renal artery bifurcation[2]
- 30% of cadavers had accessory arteries and were highly innervated[3]



[1]In human cadaver kidneys.
[2]Garcia-Touchard A, et al. *Hypertension.* 2020;76:1240–1246.
[3]Garcia-Touchard, et al. *Rev Esp Cardiol (Engl Ed).* 2019;72:531-534.
[4]Kompanje B, et al. *Clin Anat.* 2006;19:660–664.

Medtronic SPYRAL HTN Catheter

SYMPLICITY SPYRAL ™ CATHETER AND SYMPLICITY G3 ™ GENERATOR

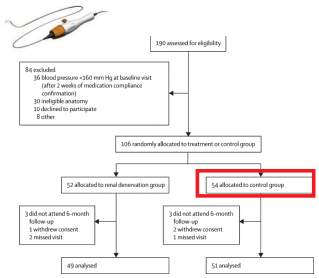


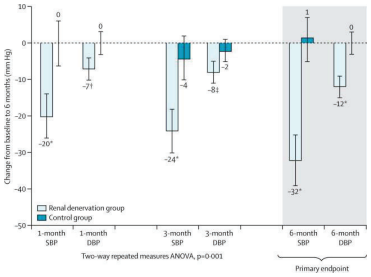
Nitinol catheter automatically positions electrodes to generate 360-degree ablations
- Consistent, repeatable four-quadrant ablation pattern
- 60-second simultaneous energy delivery
- Temperature and impedance feedback to control energy delivery

Able to ablate distal main renal artery branches, and accessories
- Vessel diameter range: 3–8 mm

CAUTION: Investigational device.

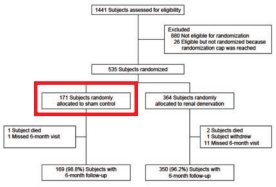
Symplicity HTN-2 Trial: The Impact of No Sham

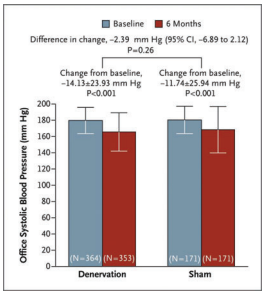




Symplicity HTN-2 Investigators. Lancet 2010.

Symplicity HTN-3 Trial: Sham Controlled

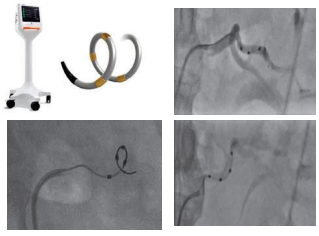




DL Bhatt, et al. NEJM 2014.

Medtronic SPYRAL HTN Catheter

SYMPLICITY SPYRAL ™ CATHETER AND SYMPLICITY G3 ™ GENERATOR



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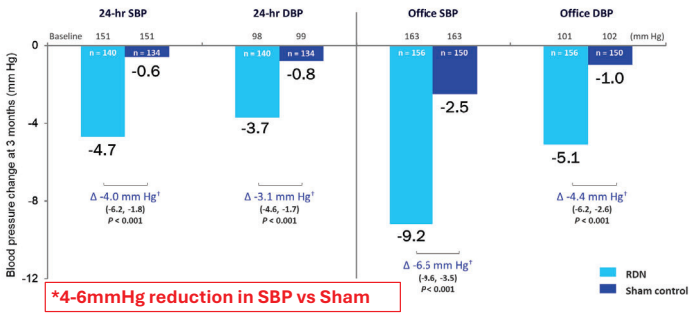
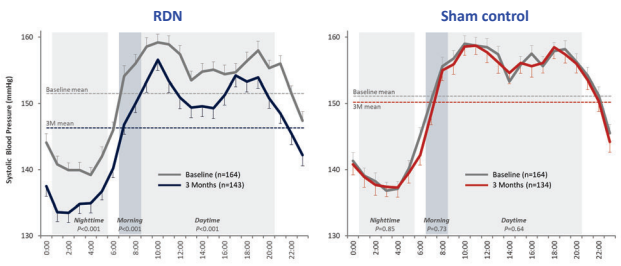
SPYRAL HTN-OFF MED Pivotal Study Results: 3 Months



***4-6mmHg reduction in SBP vs Sham**

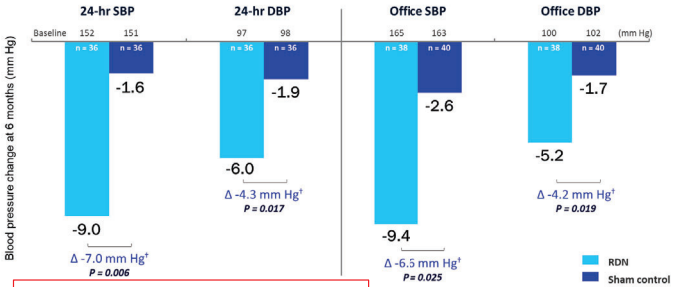
SPYRAL HTN-OFF MED Pivotal Study Results: 3 Months



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

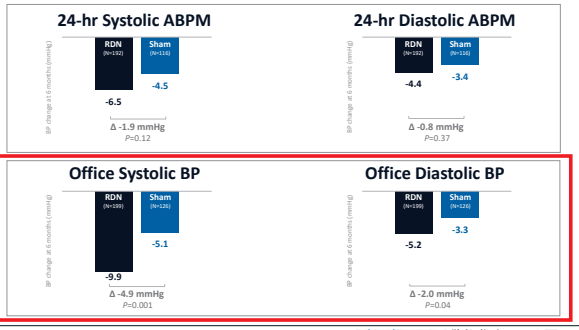
[1] Bohm M, et al. *Lancet*. 2020;395:1444-1451.
[2] Amodeo C. *Blood Press Monit*. 2014;19:199-202.
[3] Boggia J, et al. *Lancet*. 2007;370:1219-1229.

SPYRAL HTN-ON MED Pilot Study Results: 6 Months



*4-7mmHg reduction in SBP vs Sham

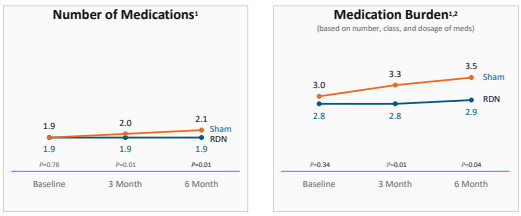
SPYRAL HTN-ON MED Study Results: 6 Months



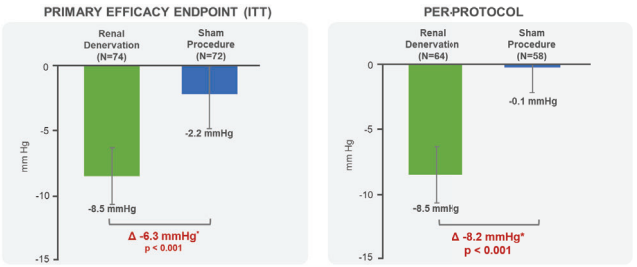
SPYRAL HTN-ON MED Study Results: 6 Months

Antihypertensive Medication Use

Significantly Higher Medication Number and Burden in Sham Control Over Follow-up



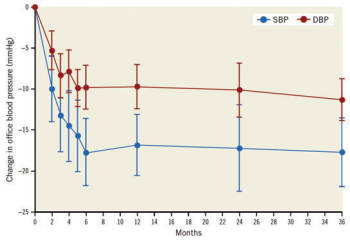
RADIANCE HTN SOLO (Off Med) Results: 2 Months



8.5 mmHg reduction in ABP in the RDN group at 2 months

RADIANCE HTN SOLO (Off Med) Results: 3 Years

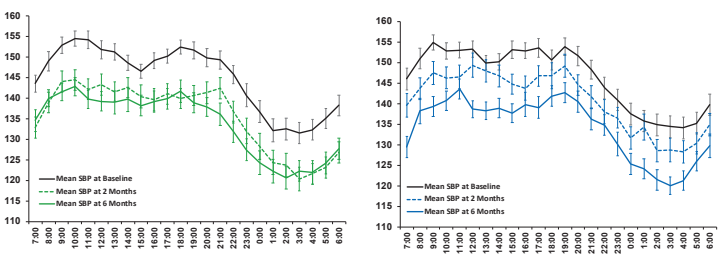
Persistent reduction in both SBP/DBP out to 3 years



Number of antihypertensive medications (mean)					
BL	2M	6M	12M	24M	36M
0.0	0.1	0.9	1.0	1.2	1.3

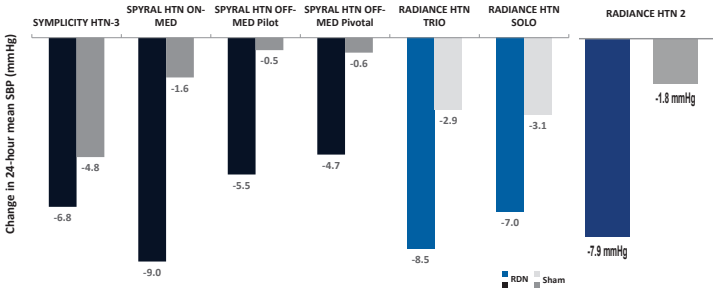
- Rader et al. EuroIntervention 2022.

RADIANCE-HTN TRIO (On Med) Results: 6 Months



Always On: 24 hour BP reduction

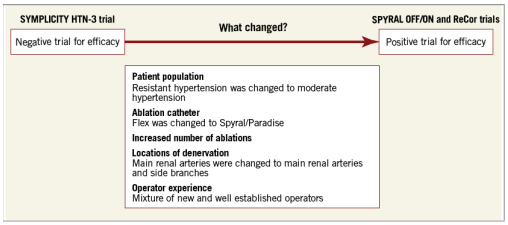
SUMMARY OF RDN TRIALS



Renal denervation reliably reduces BP across different patient populations and device platforms

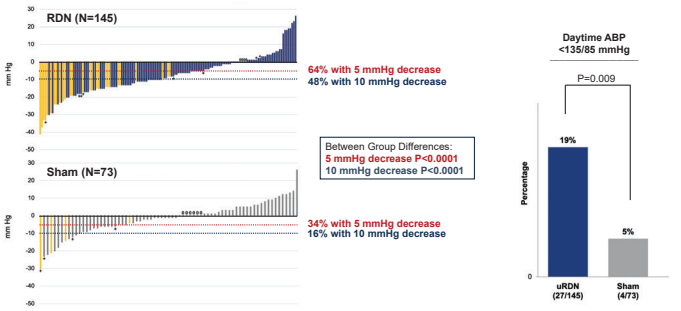
Adapted from: Kandzari D.....Secemsky EA. CCI 2021.

So what happened



https://eurointervention.pcronline.com/article/renal-artery-denervation-a-lot-done-and-more-to-do

MORE WINNERS THAN LOSERS



Kirtane A, et al. TCT 2022.

2 RDN Devices Approved by FDA in November 2023

November 7, 2023

FDA Approves Recor Medical's Paradise Renal Denervation System for Hypertension Treatment

November 7, 2023 – Recor Medical announced it has received United States FDA approval for its Paradise ultrasound renal denervation (RDN) system for the treatment of hypertension. A subsidiary of Otsuka Medical Devices Co. Ltd., Recor notes that the Paradise system is intended as an adjunctive treatment option when lifestyle changes and medications have not adequately controlled a patient's blood pressure.

An FDA Advisory Committee Panel reviewed data supporting the Paradise system in August 2023, resulting in a favorable vote. The company's RADIANCE II clinical trial met its primary safety and efficacy endpoints, and its data were published in the *Journal of the American Medical Association*. At TCT 2023 in October, Ajay Kirtane, MD, presented positive results from a combined analysis of 6-month follow-up data from the three RADIANCE global clinical studies evaluating the Paradise system. The data demonstrated maintenance of blood pressure reduction compared to sham, with fewer hypertensive treatments. The study results were simultaneously published by Michel Azizi, MD, et al online in *Circulation*.

Recor says its ultrasound-based Paradise system denervates the sympathetic nerves that surround the renal arteries, the overactivity of which can lead to hypertension. It includes a HydroCooling system that circulates sterile water through the balloon catheter to help protect the renal artery wall, the company notes. The platform gained CE Mark in 2012 and is available in Europe. It is currently an investigational device in Japan, the company notes.

"It is truly remarkable to witness the approval o difficult-to-control hypertension who are in nee medications," said Dr. Kirtane in comments to C thank all of the collaborators and the many pati this technology, allowing this to come to fruitio Vagelos College of Physicians and Surgeons and

ReCor Medical
Paradise

November 17, 2023

Medtronic's Symplicity Spyral Renal Denervation System Gains FDA Approval for Hypertension Treatment

November 17, 2023 – Medtronic announced it has received United States Food and Drug Administration (FDA) approval for its Symplicity Spyral Renal Denervation System for the treatment of hypertension. The company plans to begin United States commercialization immediately.

The Symplicity procedure denervates the renal arteries using radiofrequency energy to reduce blood pressure. Medtronic's SPYRAL HTN Global Clinical Program includes more than 25,000 patients over 10 years of study, including those both on and off blood pressure medications. A patient preference study was also conducted, which the company notes showed that when presented with an interventional treatment with blood pressure reduction and potential risks in line with those of the procedure, approximately one-third of patients were likely to choose the intervention.

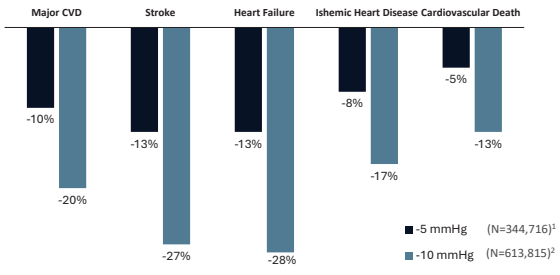
Results from Medtronic's clinical program were presented at a 2-day FDA advisory panel session in August 2023, along with those of Recor Medical, which has also gained approval for its renal denervation system.

"The Symplicity blood pressure procedure is safe and effective, providing significant 'always on' blood pressure reductions for patients," said David Kandzari, MD, in Medtronic's announcement. Dr. Kandzari is Chief of Piedmont Heart Institute and Cardiovascular Service and Co-Principal Investigator of the SPYRAL clinical program. "This landmark approval is the culmination of rigorous scientific study and clinical trials, including long-term, sham-controlled studies in the presence and absence of medication, and the largest real-world study."

"This approval paves the way for a transformation in hypertension treatment, offering a solution that complements medication and lifestyle changes," added Raymond Townsend, MD, in the release. Dr. Townsend is from the Hypertension Section in the Department of Internal Medicine/Renal, at the University of Pennsylvania School of Medicine. He is also Co-Principal Investigator of the SPYRAL clinical program. "The Symplicity blood pressure procedure is a promising treatment option for clinicians and patients alike and offers opportunity to fulfill a significant unmet need in hypertension care, especially for those patients who are desperately seeking additional approaches to get their blood pressure down."

Relative Risk Reduction Proportional to Decrease in OSBP

Irrespective of Baseline BP or CVD History in 2 Meta-Analyses



[1] Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2021;397(10285):1625-36
[2] Ettehad D, et al. *Lancet*. 2016;387(10022):957-67