2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

2017

Samuel N. Steerman, MD, FACS, RPVI

EVMS Assistant Professor of Surgery

Sentara Vascular Specialists

Renal Denervation For Hypertension: Status Update

Disclosures

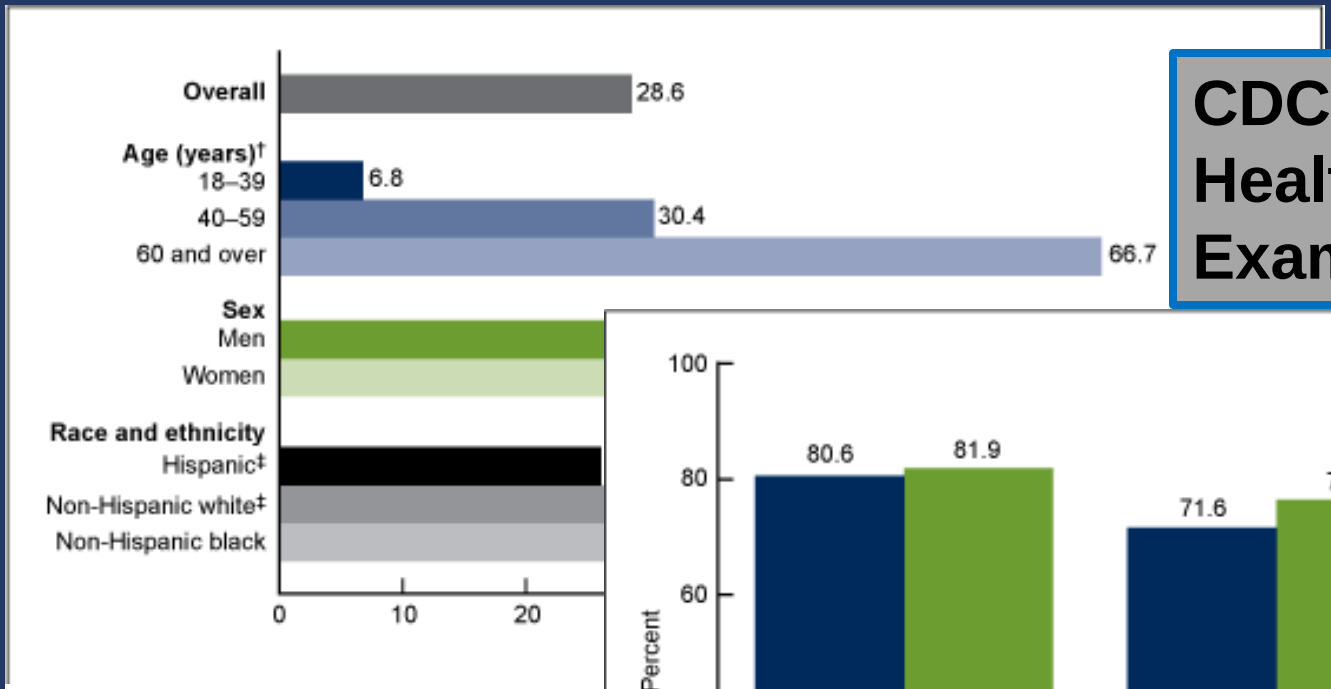
- Disclosures
  - Speaker's Panel – Medtronic, Abbott Vascular, Penumbra
  - Clinical Instructor – Bard, Medtronic

- Some devices discussed are not approved by the FDA or currently available in the United States.

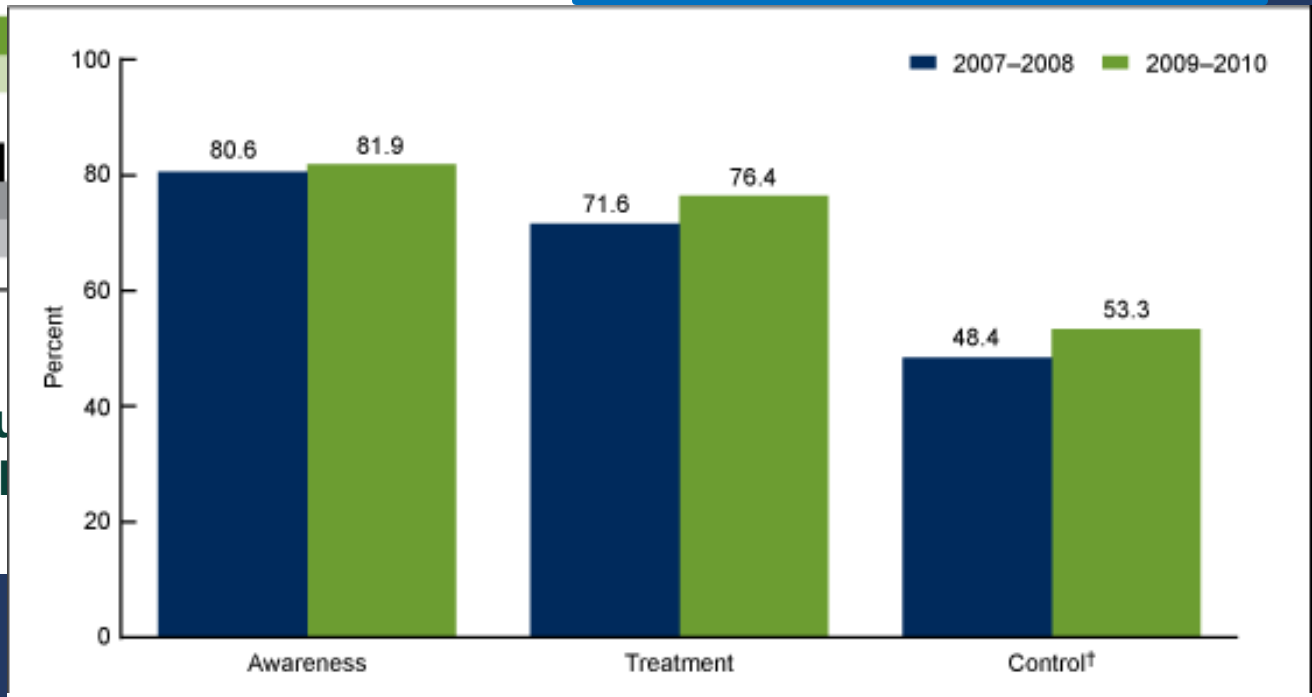
Outline

- “Resistant Hypertension” Prevalence and Impact
- Denervation Mechanism
- Current Technology
- Denervation literature
- Future Technology

CDC - National Health and Nutrition Examination Survey



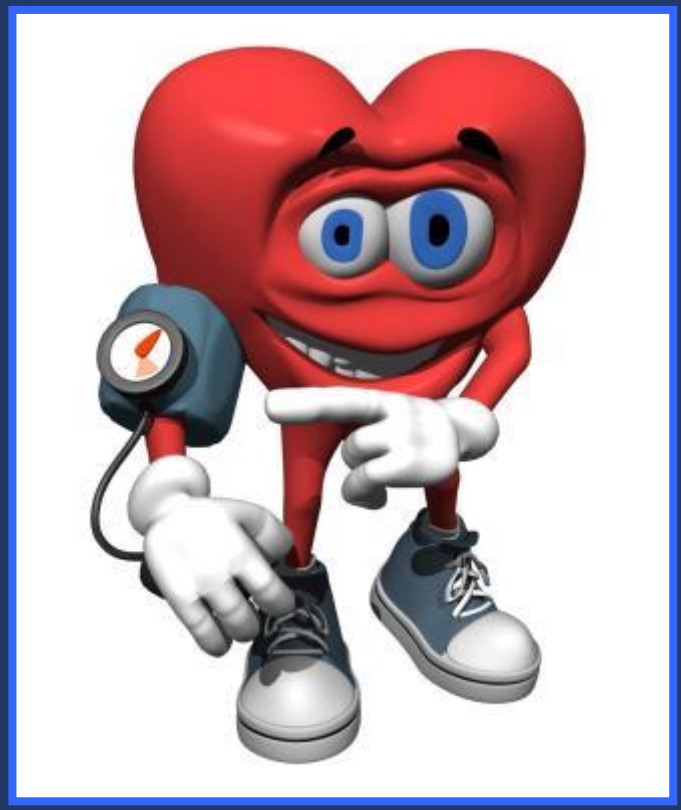
Age-specific and age-adju hypertension among adul 2009–2010



Age-adjusted awareness, treatment, and control of hypertension among adults with hypertension: US, 2007–2010

Impact of Hypertension

- Framingham Heart Study
  - CHF related mortality 2.3-3x in Pt's with HTN
- Multiple Risk Factor Intervention Trial
  - ↑RR 2.3-6.9 - CAD mortality
  - ↑RR 3.6 to 19.2 – stroke
- JNC-7 - Benefit for anti-Hypertensive's:
  - 35-40% reduction in CVA
  - 20-25% reduction in MI
  - >50% reduction in CHF



Global Impact

- Prevalence of adult HTN: 30.4% (66.9 million)
- Uncontrolled HTN: 53.5% of HTN patients (35.8 million)
- 85.2% of uncontrolled HTN patients had health insurance
- Worldwide Burden of Hypertension:
  - 7.6 million premature deaths each year attributed to high blood pressure
  - About 54% of stroke and 47% of ischemic heart disease attributable to high blood pressure

Table 2. Dates of Discovery of Antihypertensive Drugs or Drug Classes

Year(s)	Antihypertensive Agent(s)
1900	Sodium thiocyanate
1931	Reserpine
1947–1950	Ganglion blocking drugs
1958	Thiazide-type diuretics
1950s	Hydralazine
1950s	Guanethidine
1957	Spironolactone
1960	Methyldopa
1973	β-Receptor blockers (eg, propranolol)
1970s	Central α_2 agonists (eg, clonidine)
1975	Peripheral α_1 receptor blockers (eg, prazosin)
1977	ACE inhibitors (eg, captopril)
1977	Calcium channel blockers (eg, verapamil, nifedipine)
1993	Angiotensin II receptor blockers (eg, losartan)
2000	Renin inhibitors (eg, aliskiren)

ACE indicates angiotensin-converting enzyme. Data derived from Freis.[39]

Historical Trends and Milestones in Hypertension Research: A Model of the Process of Translational Research

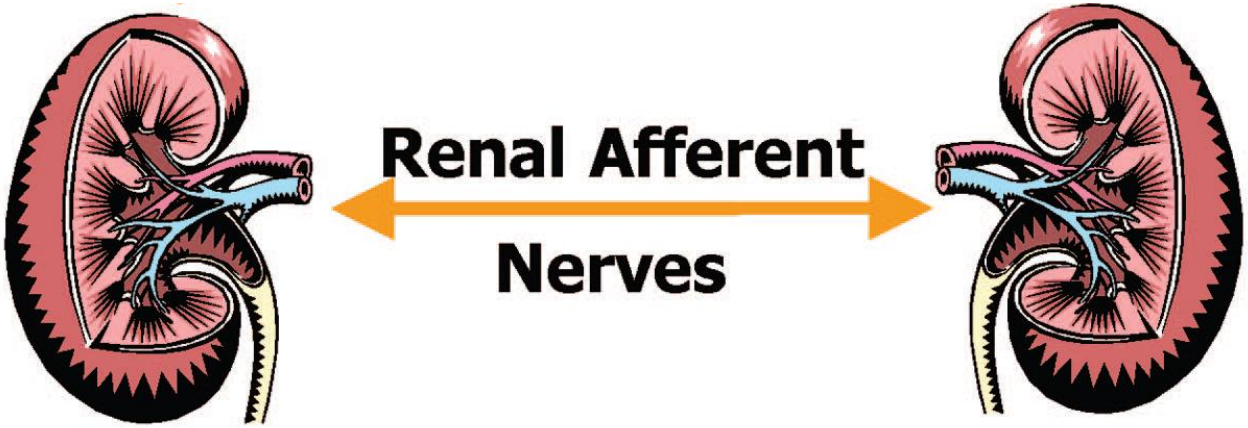
Theodore A. Kotchen

Hypertension. 2011;58:522-538

Hypertension

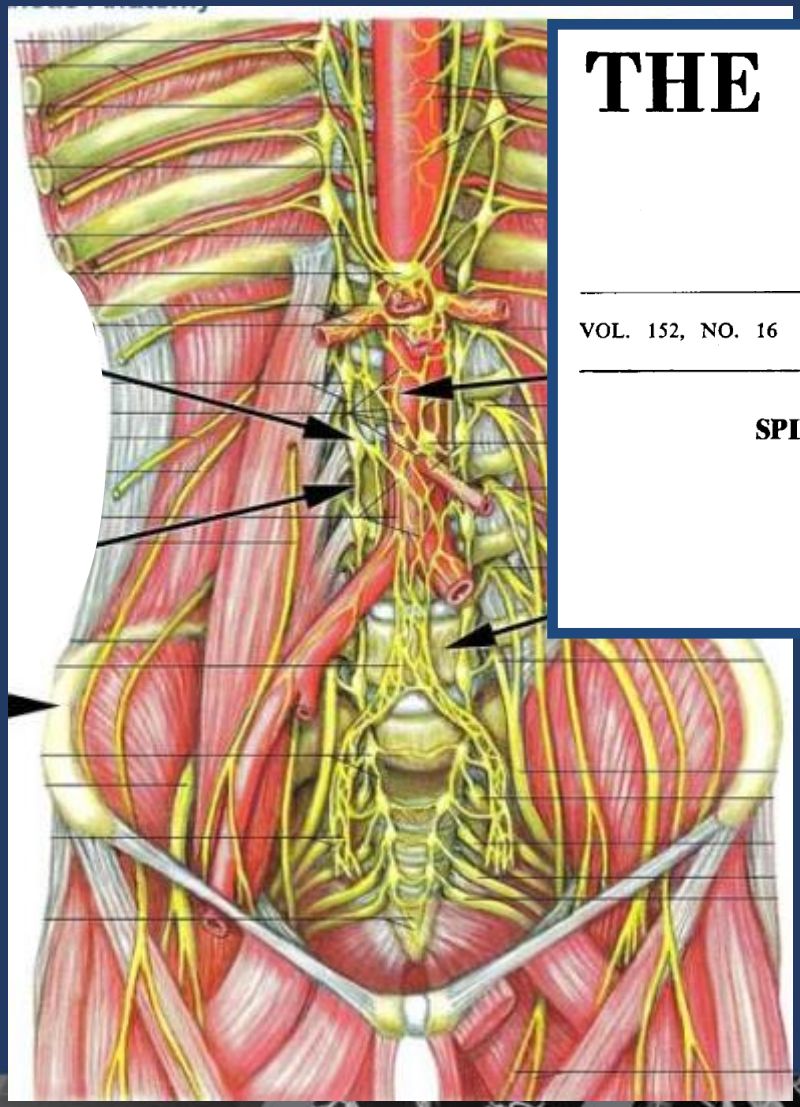
Journal of the American Heart Association

Renal Sympathetic Innervation and Hypertension



Krum et al. Circulation 2011;123:209-215

Anatomic Considerations



THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 152, NO. 16 — CHICAGO, ILLINOIS — AUGUST 15, 1953

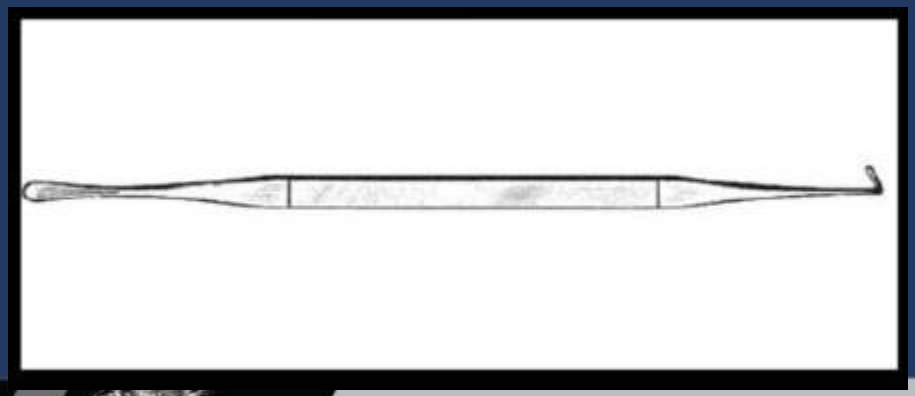
SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Smithwick, M.D.

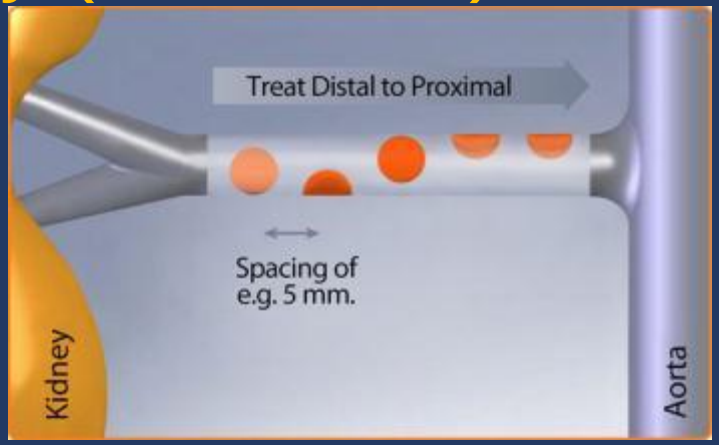
and

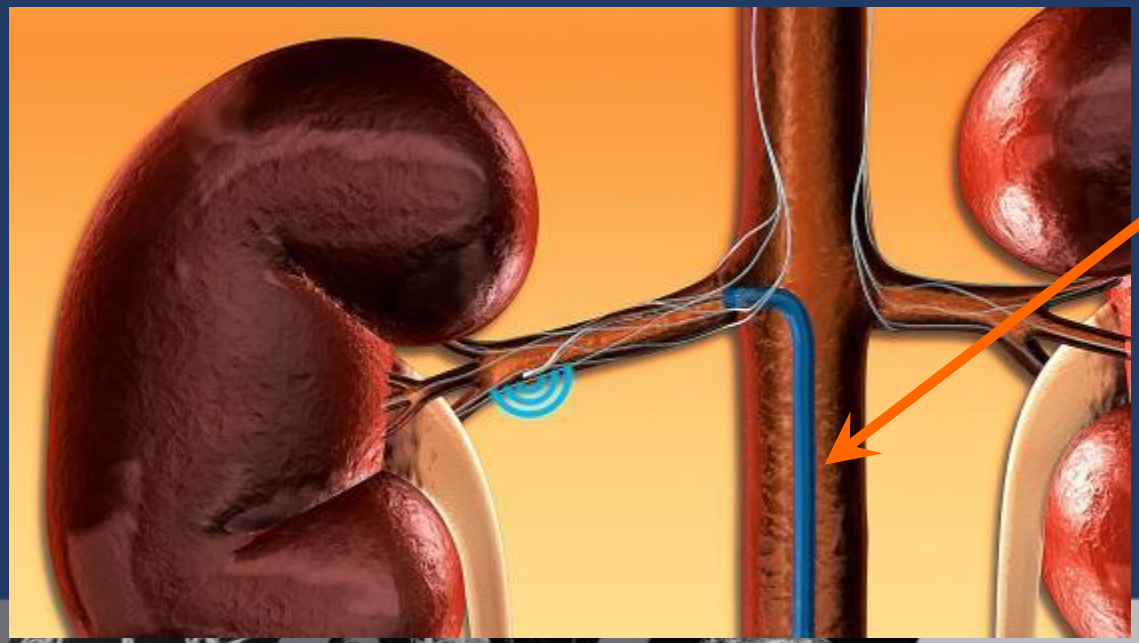
Jesse E. Thompson, M.D., Boston



Catheter Based Renal Sympathetic Denervation – Symplicity (Medtronic)

4-6 two minute treatments per artery

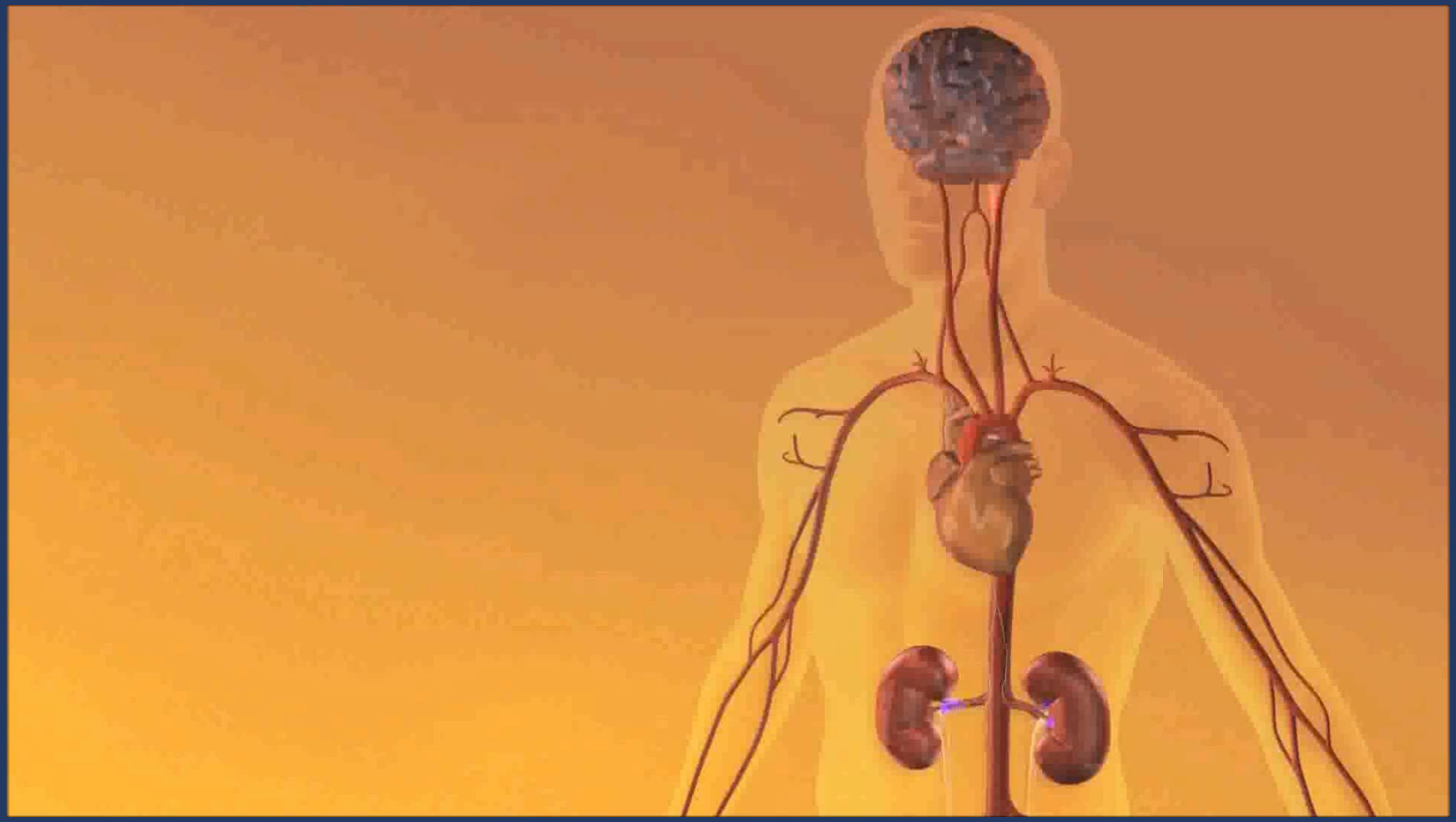




6F Guide Cath

$800 million

Catheter Based Renal Sympathetic Denervation – Symplicity (Medtronic)



Hypertension
Journal of the American Heart Association

American Heart Association®

Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension : Durability of Blood Pressure Reduction Out to 24 Months

Symplicity HTN-1 Investigators

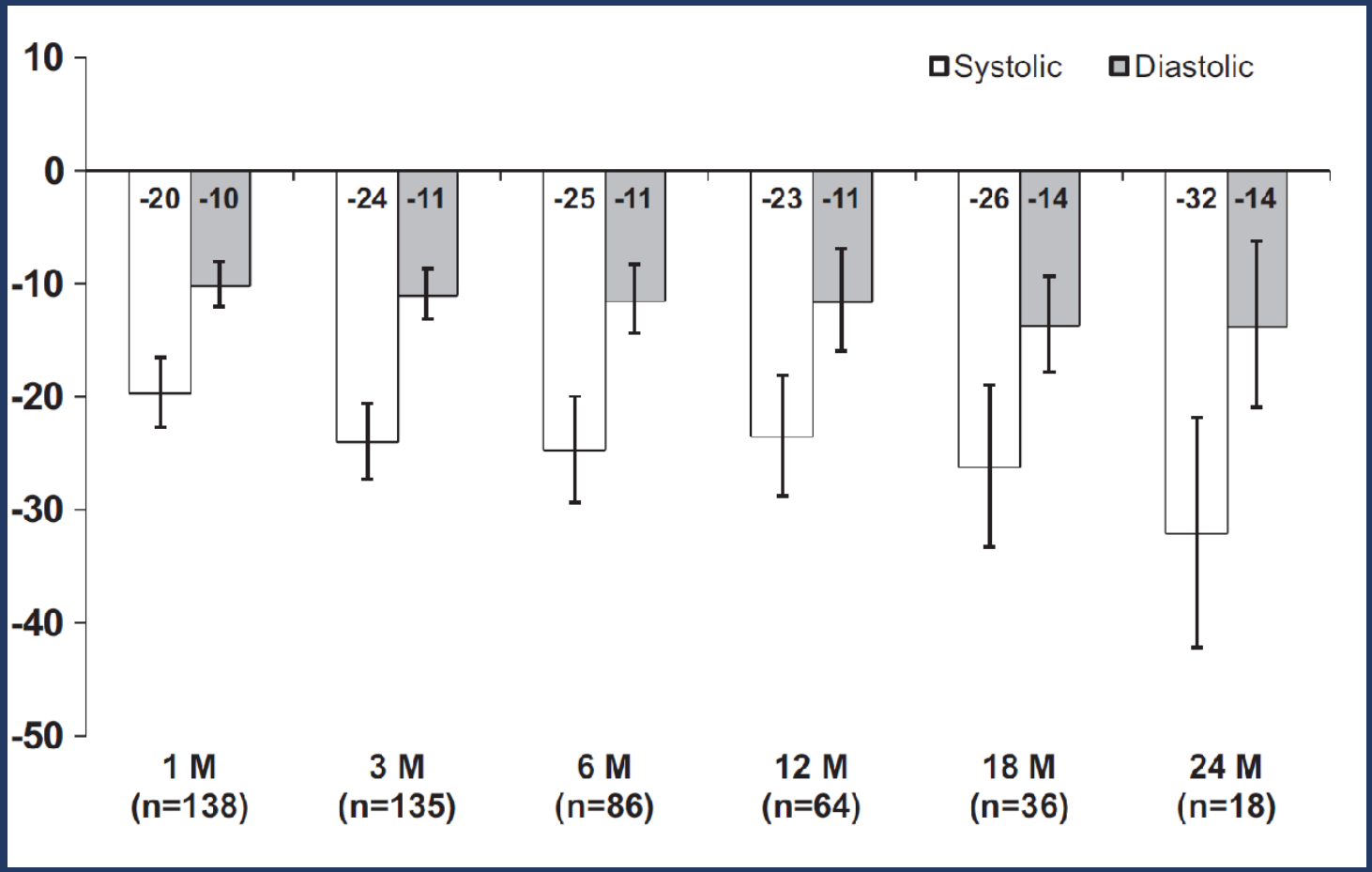
Hypertension. 2011;57:911-917; originally published online March 14, 2011;

- 19 centers in Australia, Europe, and the United States
- 153 patients with catheter-based renal sympathetic denervation

Baseline BP (mm Hg)	176/98 ± 17/15
# of anti-HTN meds (mean)	5.1 ± 1.4

Symplicity HTN-1 Results

BP change (mm Hg)



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Renal Sympathetic Denervation for Treatment of Drug-Resistant Hypertension : One-Year Results From the Symplicity HTN-2 Randomized, Controlled Trial

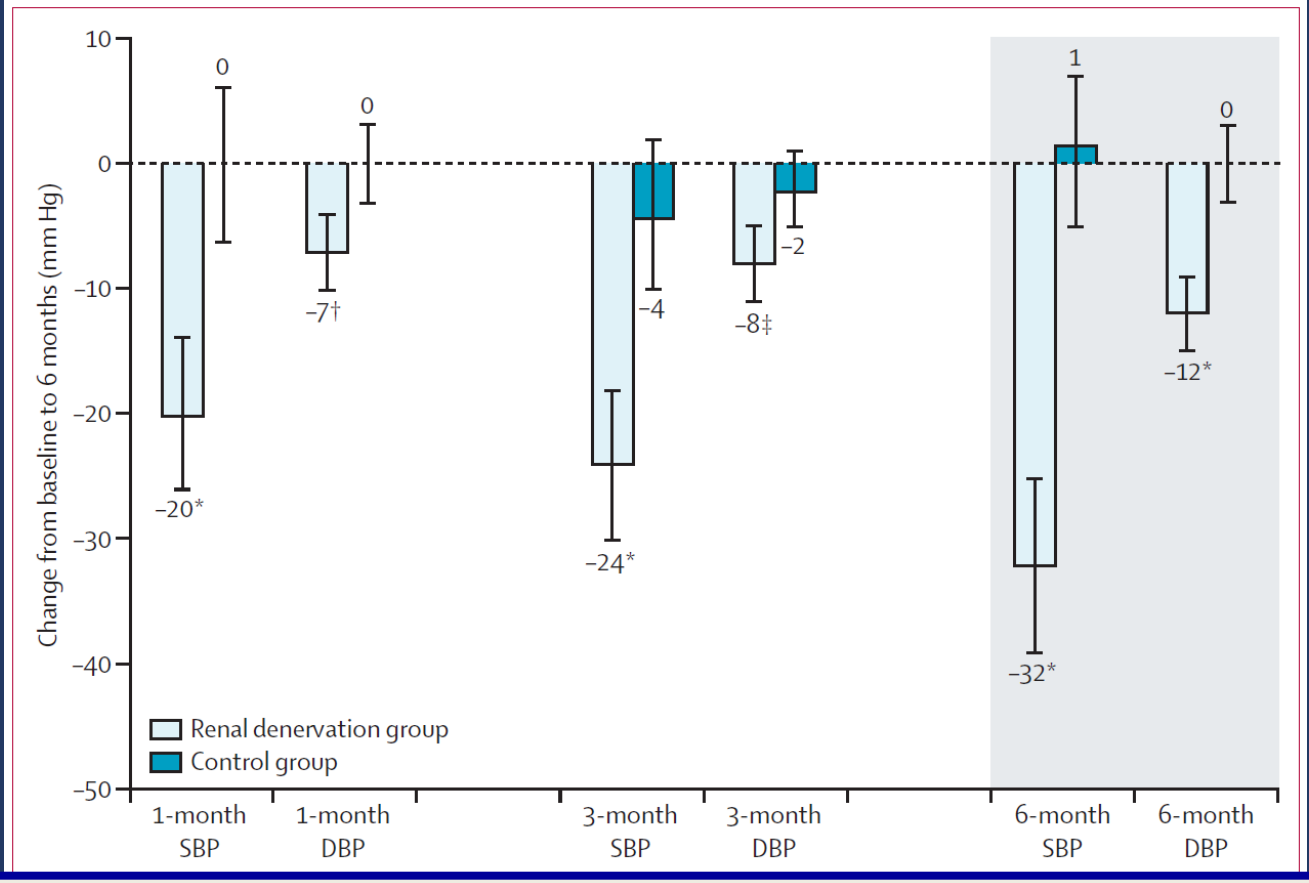
Murray D. Esler, Henry Krum, Markus Schlaich, Roland E. Schmieder, Michael Böhm and Paul A. Sobotka
for the Symplicity HTN-2 Investigators

Circulation. 2012;126:2976-2982

- **Prospective, randomized trial in 24 centers in Europe, Australia and New Zealand**
- **106 patients randomized**

	RDN (n=52)	Control (n=54)
Baseline BP (mm Hg)	178/97	178/98
# of Anti-HTN Meds	5.2 ±1.5	5.3 ±1.8

Symplicity HTN-2 Results

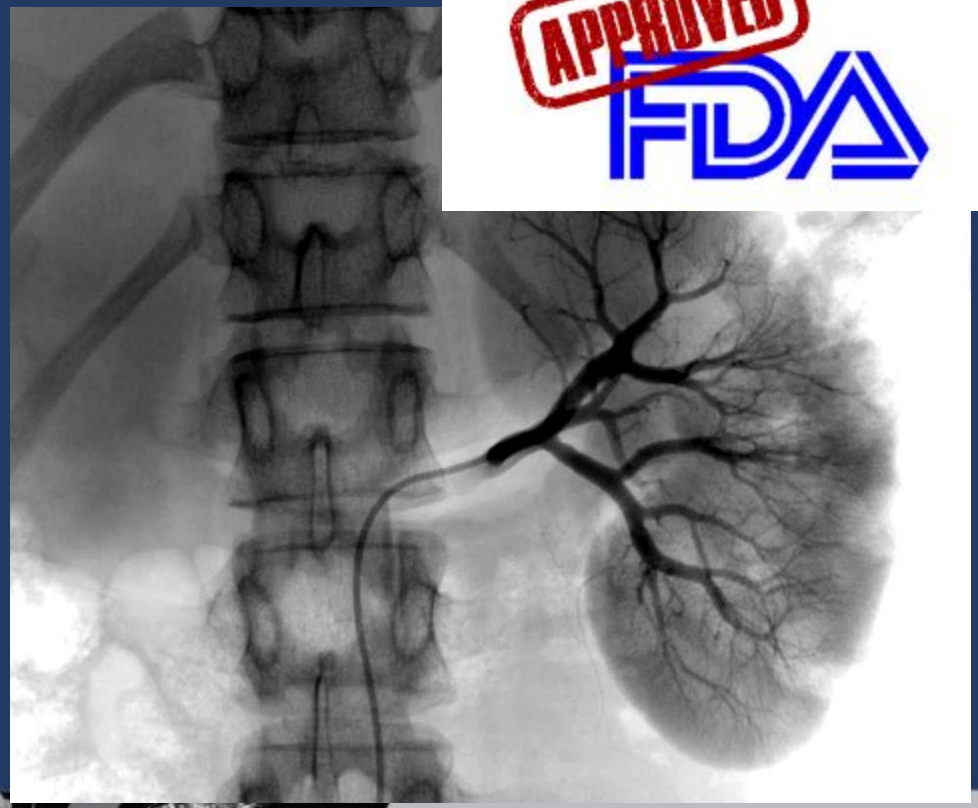


- **84% of RDN patients had ≥ 10 mmHg reduction in SBP**
- **10% of RDN patients had no reduction in SBP**


Preclinical
First-in-Man Trial
CE Mark Approval
Clinical Trials USA
FDA Approval
Post Marketing Trial Data
Radio Frequency
Symplicity™

Renal Denervation in Patients with Uncontrolled Hypertension
Symplicity HTN-3

- Prospective, double blinded study
- Randomization is accomplished at the time of angiogram



A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., and George L. Bakris, M.D., for the SYMPLICITY HTN-3 Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

March 29, 2014

- 535 patients
- 88 sites in the United States

	RDN (n=364)	Sham (n=171)
# of Anti-HTN Meds	5.1 ±1.4	5.2 ±1.4

Results of Simplicity HTN-3

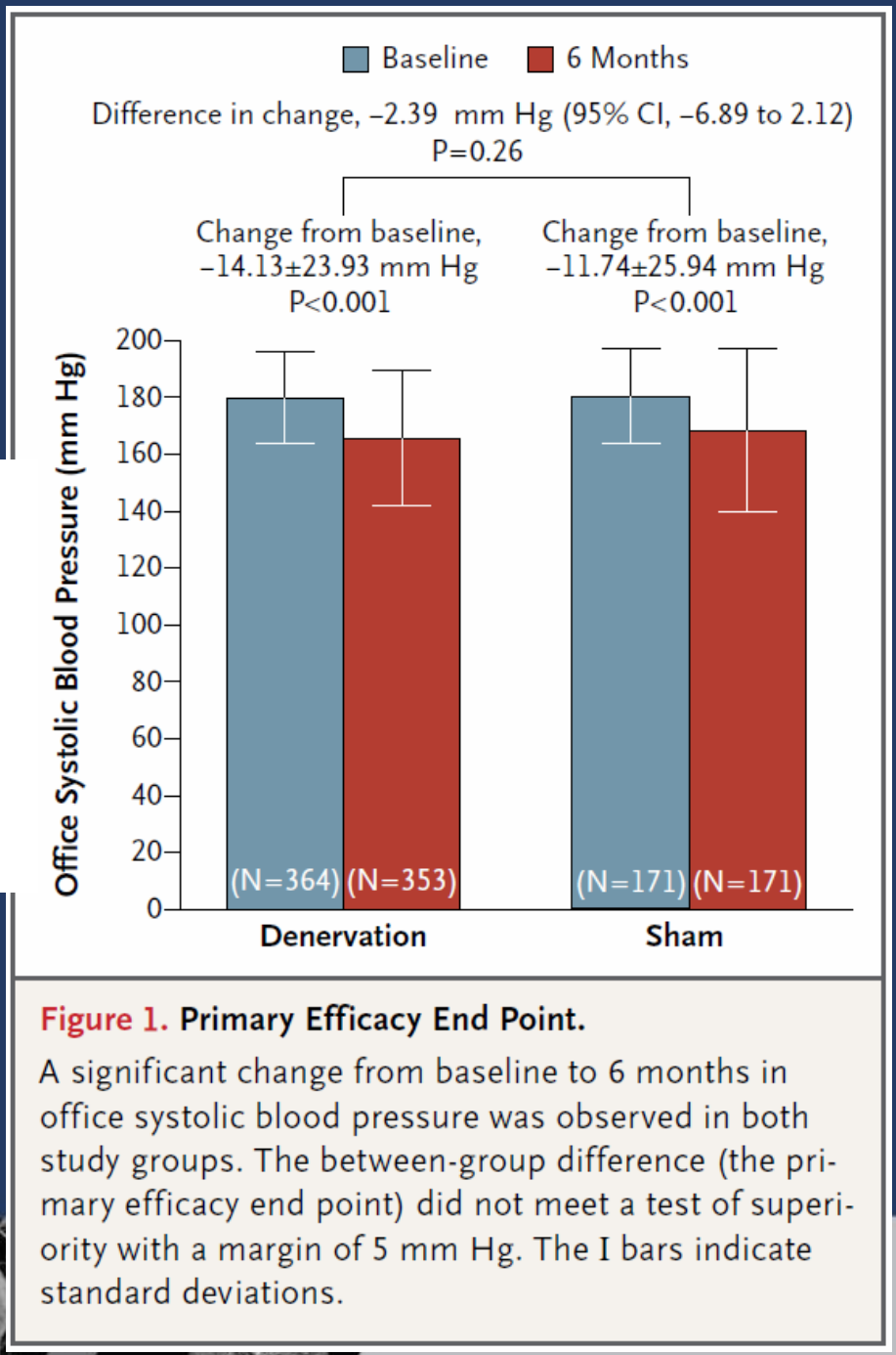


Figure 1. Primary Efficacy End Point.

A significant change from baseline to 6 months in office systolic blood pressure was observed in both study groups. The between-group difference (the primary efficacy end point) did not meet a test of superiority with a margin of 5 mm Hg. The I bars indicate standard deviations.

Explanations

- 137 Operators
  - 111 operators who did at least one procedure (31% did only 1 procedures)
  - 26 operators who did ≥5 procedures
- Good medical care
  - Without a control group, the observed treatment effect may have been a result of trial participation
  - Reduction in SBP could be due to good care and a high degree of adherence to antihypertensive therapy as a result of close follow-up (i.e., the Hawthorne effect)

Renal Denervation

Predictors of Response: RDN Device?

EnligHTN (St. Jude Medical)

EnligHTN-1: **(n =46)**

ΔoSBP at 6 month: -26mmHg

Response Rate: 76%

OneShot (Covidien)

RHAS: **(n = 8)**

ΔoSBP at 6 month: -42mmHg

ΔoDBP at 6 month: -15mmHg

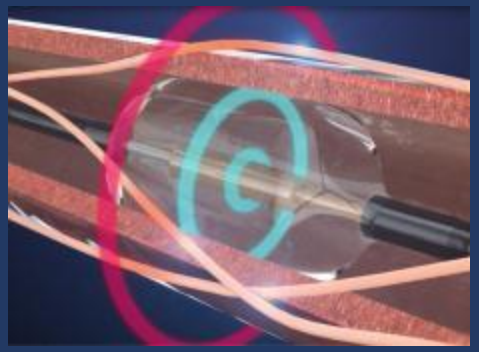
Vessix V2 (Boston Scientific)

ReduceHTN: **(n = 10)**

ΔoSBP at 1 month: -30mmHg

ΔoDBP at 1 month: -11mmHg
Response Rate: 100% at 1 month

Paradise (ReCor)



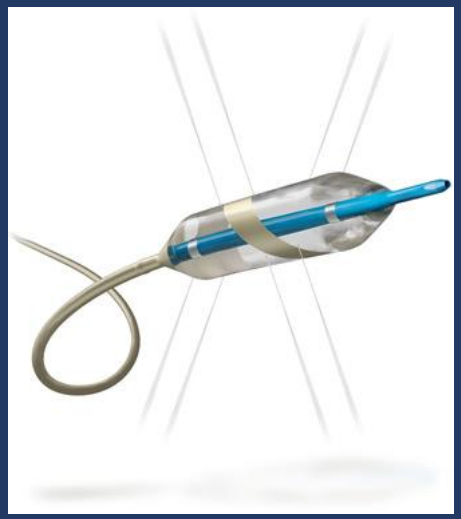
REALISE: **(n = 20)**

Δ BP at 6 month: -21/9mmHg

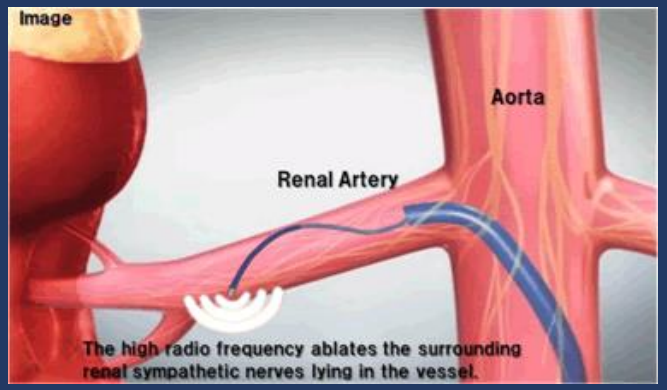
Δ ABP at 6 month: -9/4mmHg

Downstream effects of “HTN-3”

Cordis Renlane
10 patient German study, removed from market



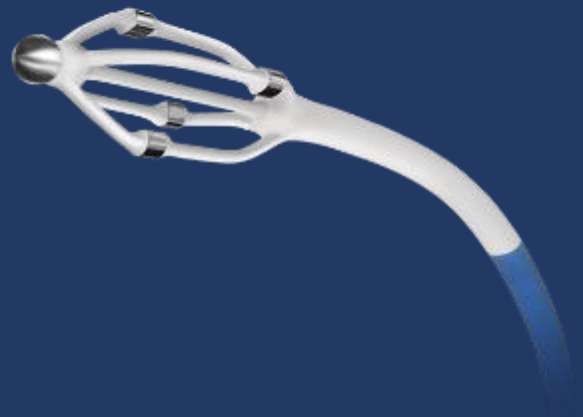
Covidien OneShot
Discontinued product in 2014 due to slow market development

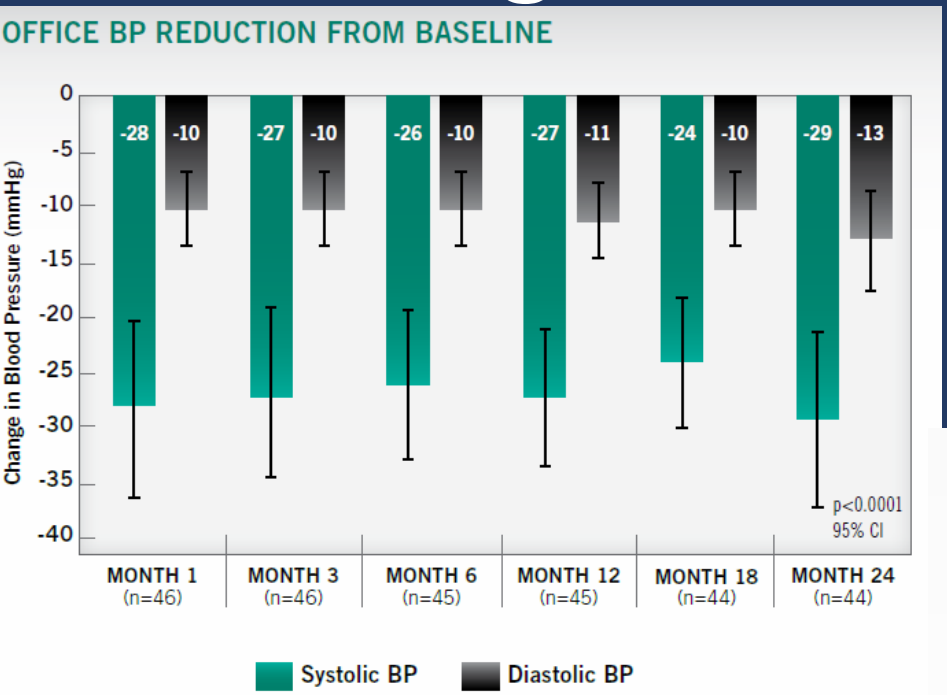


Terumo Iberis
2 case reports in 2013, no ongoing studies

EnligHTN – St. Jude

EnligHTN – St. Jude

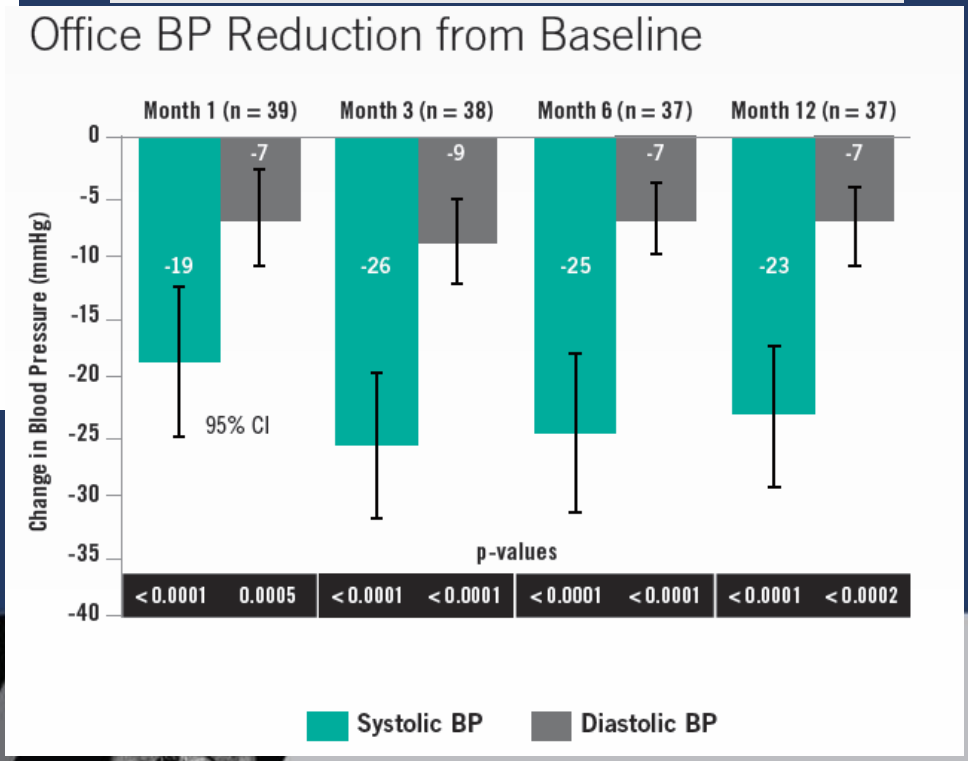


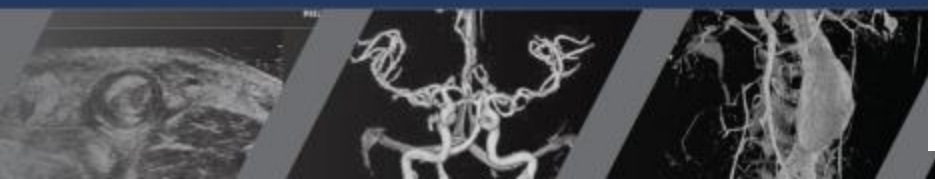


EnligHTN therapy delivers a rapid significant reduction in Office BP that is sustained through the 24-month timeframe.

EnligHTN I: 24-Month Clinical Data[1]

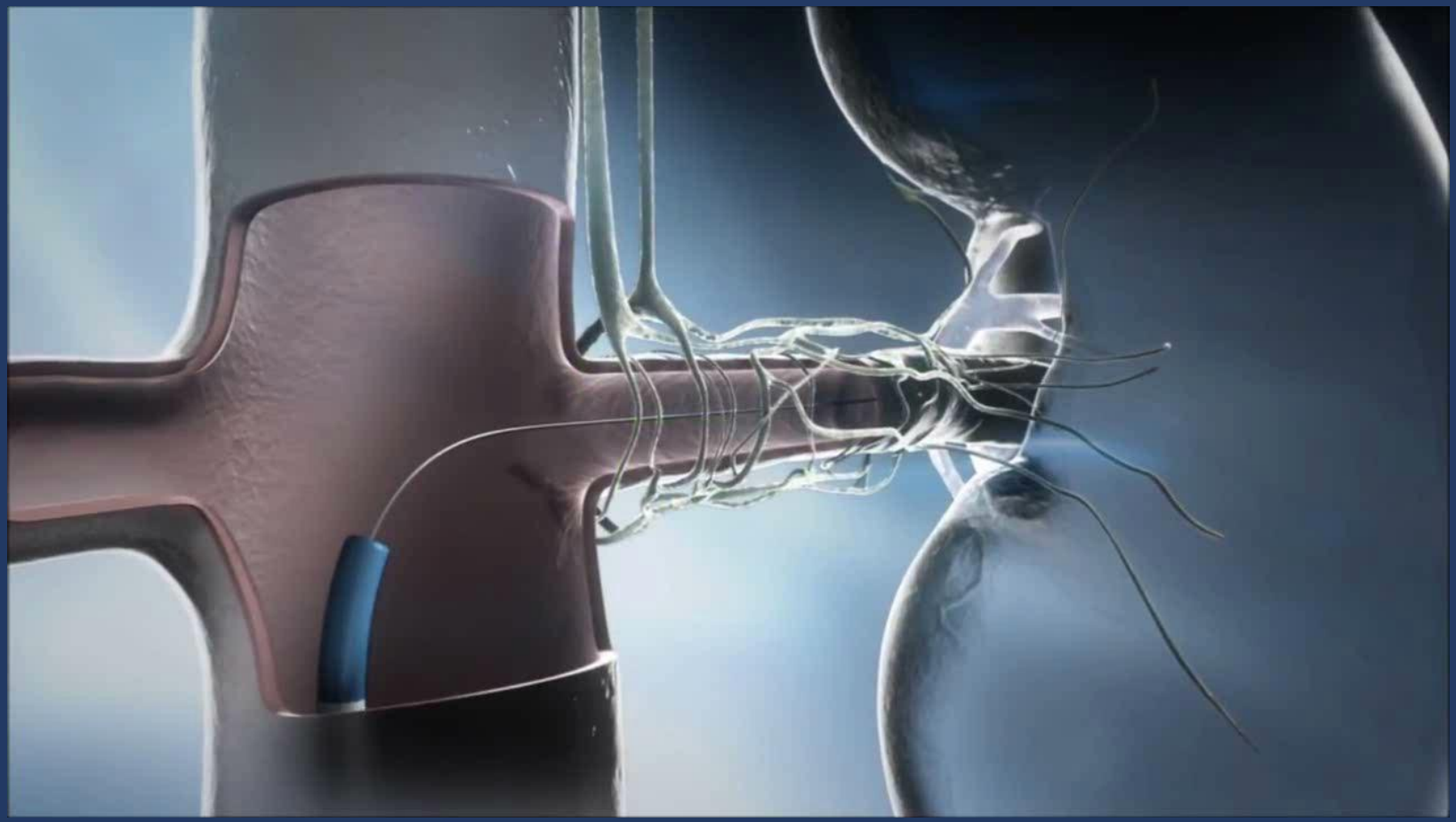
EnligHTN III: Twelve-Month Clinical Data

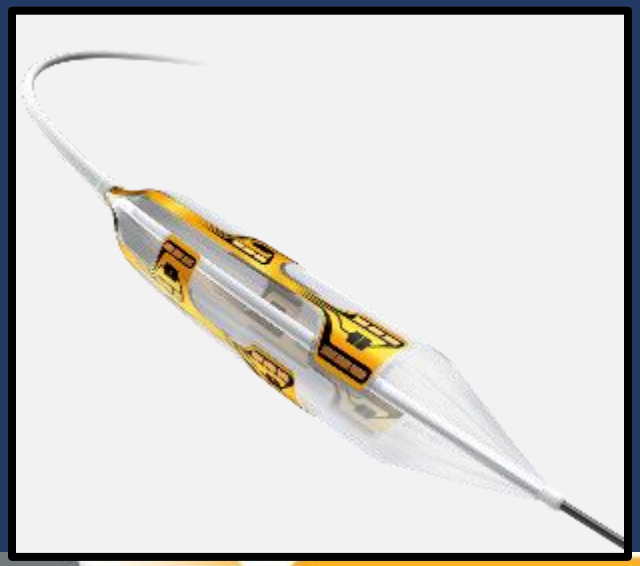




Boston Scientific
Advancing science for life™

Vessix





Vessix Global Clinical Program

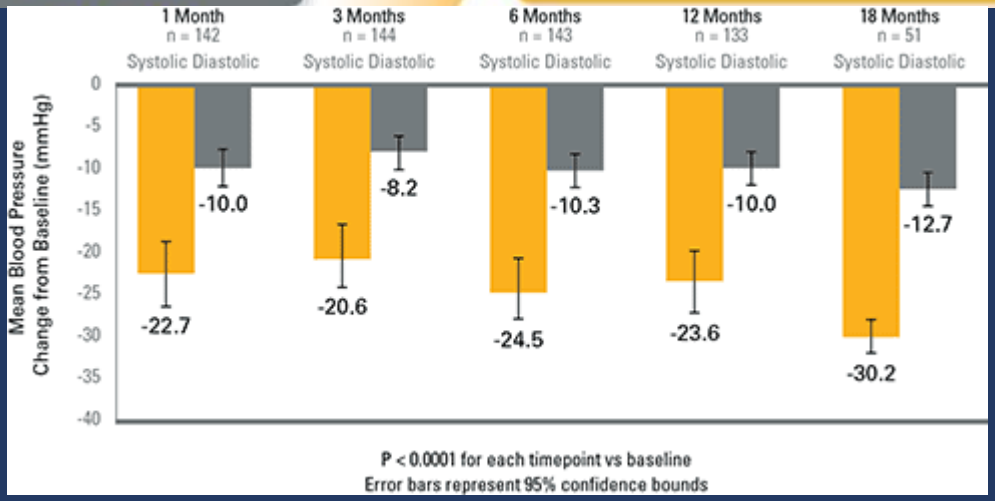
REDUCE HTN

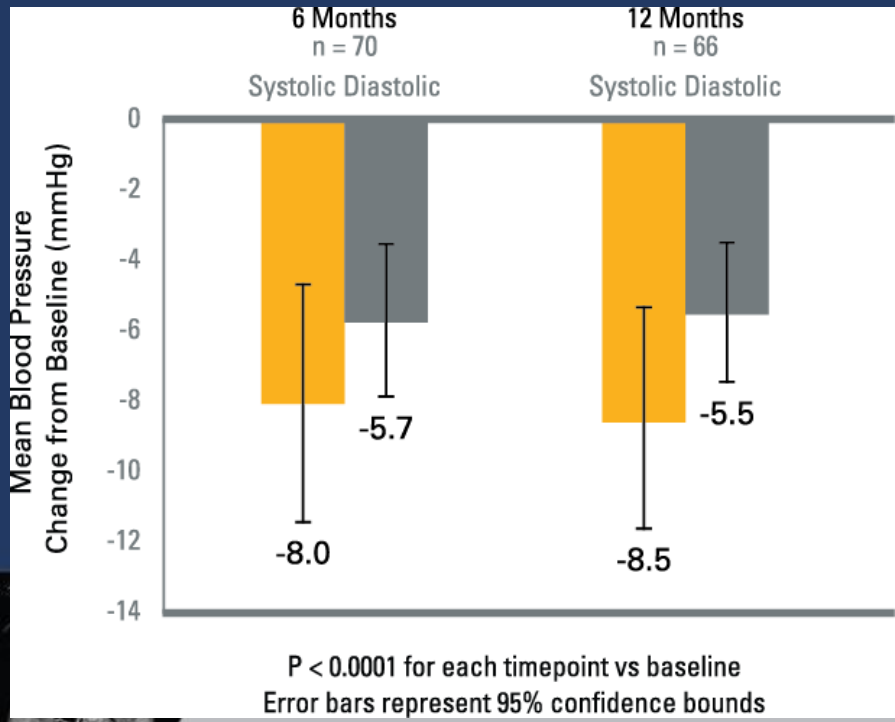
FIM + Post-Market Study

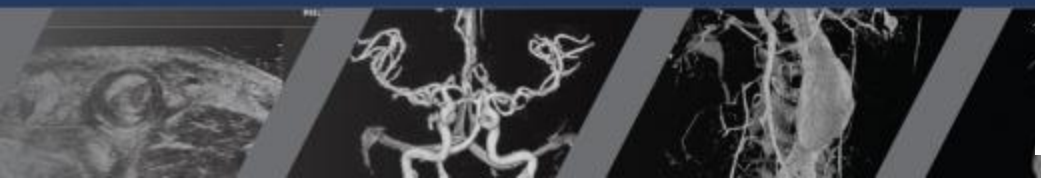
REDUCE-HTN FIM n = 18

REDUCE-HTN PMS n = 128

REDUCE-HTN FIM + PMS
n = 146





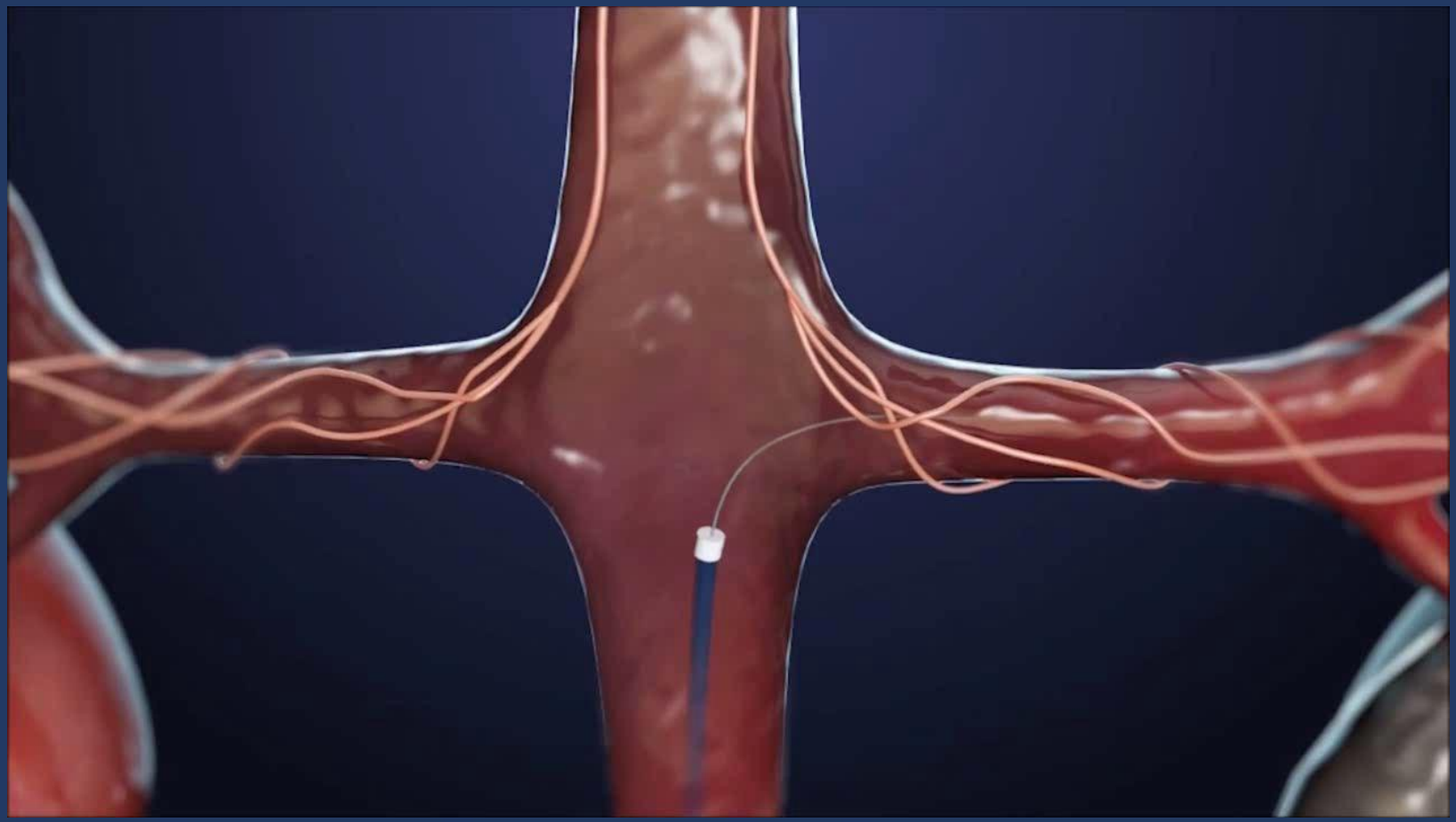


Renal Denervation Using the Vessix Renal Denervation System for the Treatment of Hypertension (REDUCE HTN:REINFORCE)

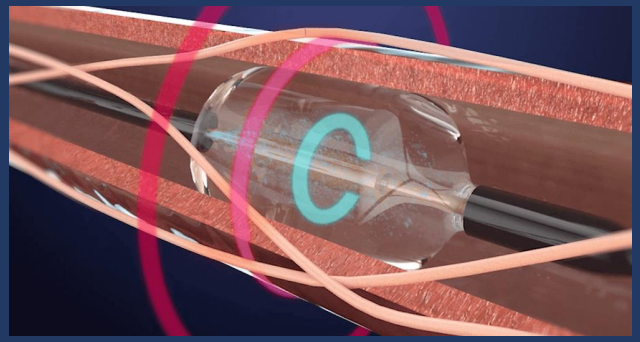
- Randomized, sham-controlled, multicenter study
- The primary efficacy assessment is the mean reduction in average 24-hour ambulatory systolic blood pressure (ASBP) at eight weeks post randomization.

Estimated Enrollment:	100
Study Start Date:	April 2015
Estimated Study Completion Date:	March 2021
Estimated Primary Completion Date:	February 2018 (Final data collection date for primary outcome measure)

ReCor Medical Paradise System



A Study of the ReCor Medical Paradise System in Clinical Hypertension (RADIANCE-HTN)



- Randomized, double-blind, sham controlled
- Primary Outcome Measures: Mean reduction in average daytime ambulatory systolic BP: from baseline to 2 months post procedure

Estimated Enrollment:	292
Study Start Date:	March 2016
Estimated Study Completion Date:	August 2021
Estimated Primary Completion Date:	August 2018 (Final data collection date for primary outcome measure)

Hypertension
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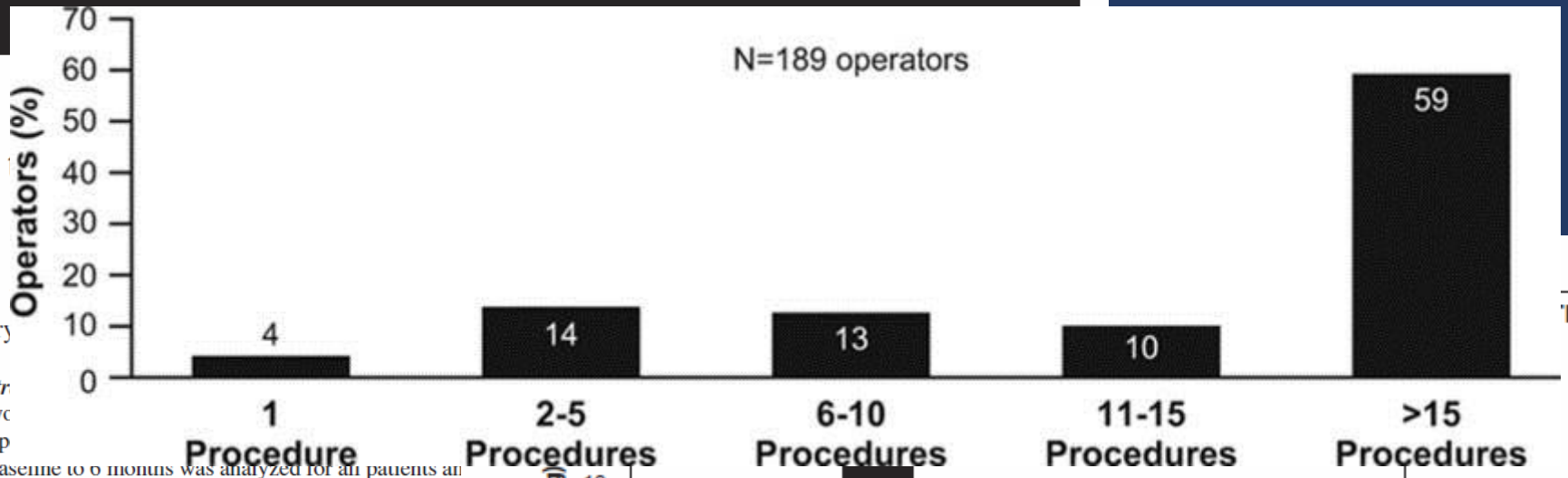

Bry

Abstr
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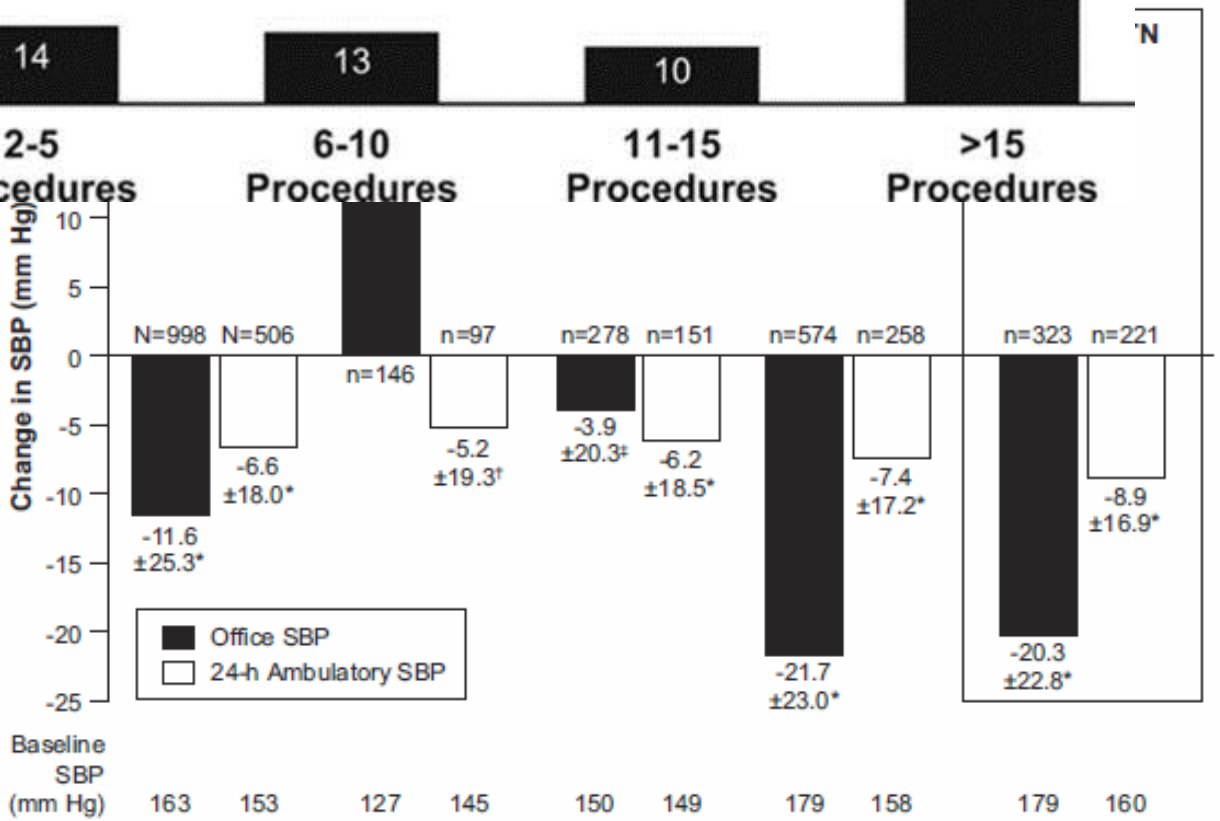
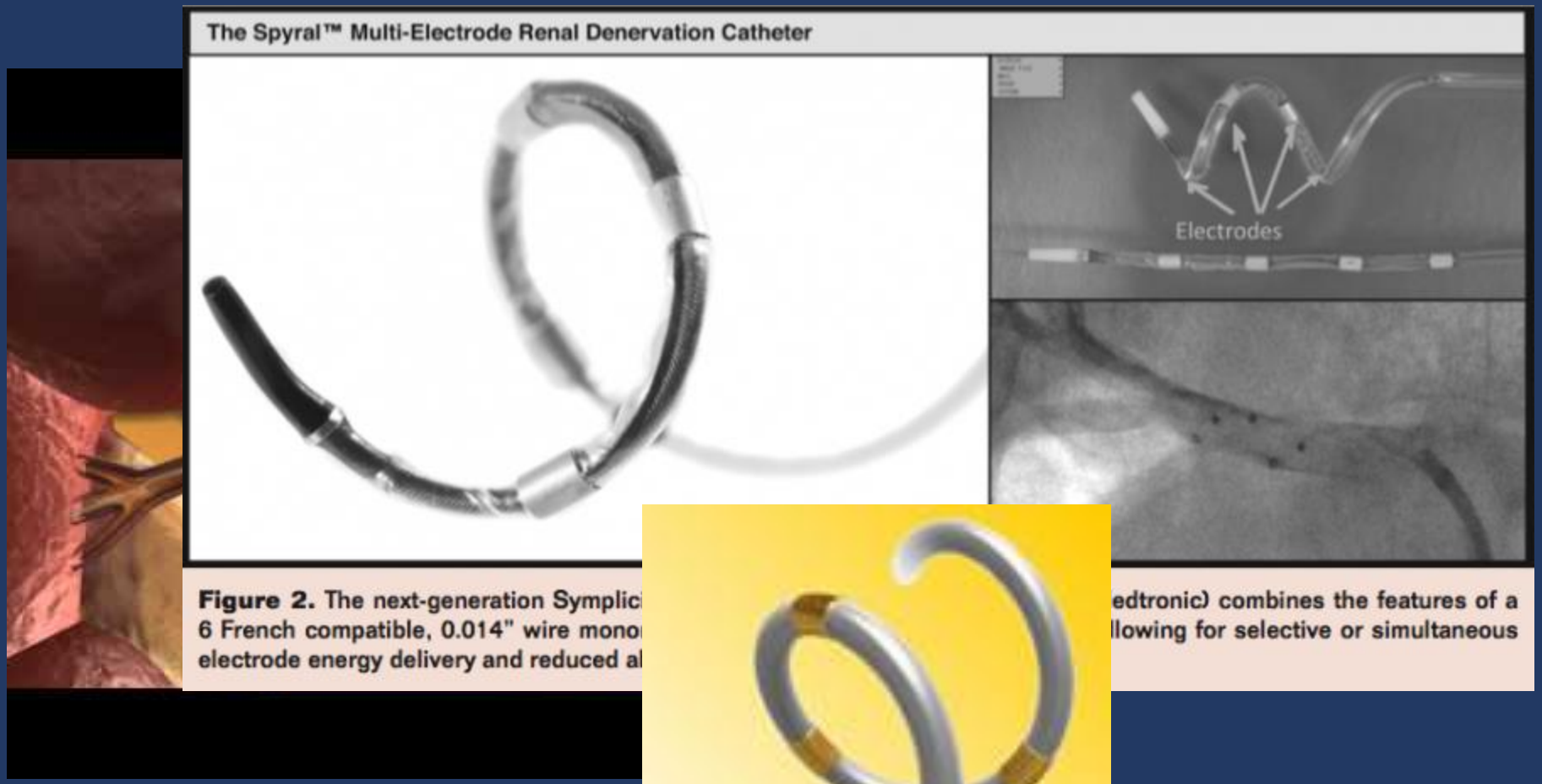
baseline to 6 months was analyzed for all patients an
and renal function; a cohort with severe hypertensic
≥135 mm Hg; and ≥3 antihypertensive medication
safety events. Six-month outcomes for 998 patients,
baseline office systolic BP was 163.5±24.0 mm Hg
corresponding baseline 24-hour mean systolic BPs w
office and 24-hour systolic BPs were −11.6±25.3 and
and −8.9±16.9 mm Hg for those with severe hyperter
rates of adverse events. After the procedure through
of hospitalization for a hypertensive emergency. In
in office and 24-hour BPs with a favorable safety p
baseline pressures.

Clinical Trial Registration—URL: www.clinicaltrials.
(*Hypertension*. 2015;65:766-774. DOI: 10.1161/H

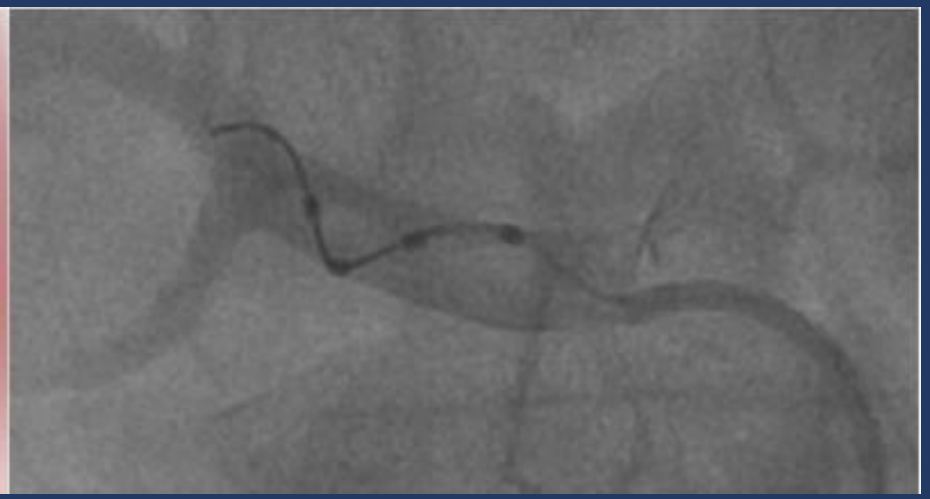
Key Words: denervation ■ hy



December 5, 2013 - Symplicity Spyral - Medtronic



The SPYRAL HTN Global Clinical Trial Program: Rationale and design for studies of renal denervation in the absence (SPYRAL HTN OFF-MED) and presence (SPYRAL HTN ON-MED) of antihypertensive medications



SPYRAL HTN-ON MED Study

Patients to be treated with a consistent triple therapy antihypertensive regimen

SPYRAL HTN-OFF MED Study

3- to 4-week drug washout period followed by a 3-month efficacy and safety end point in the absence of antihypertensive medications

- Primary Outcome Measures:
  - Major Adverse Events
  - Change in SBP

Estimated Enrollment:	100
Study Start Date:	June 2015
Estimated Study Completion Date:	July 2020
Estimated Primary Completion Date:	July 2017 (Final data collection date for primary outcome measure)

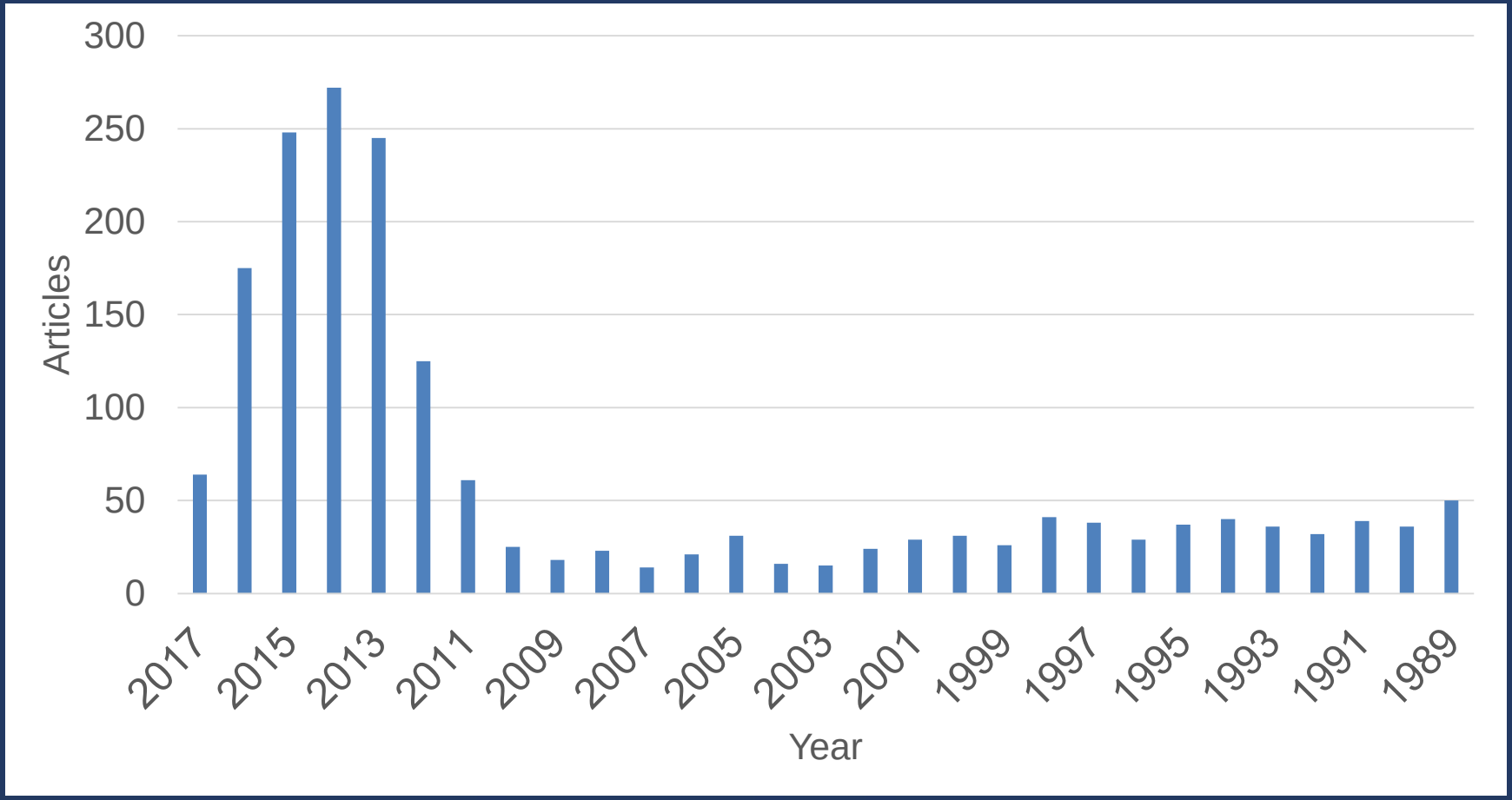
Estimated Enrollment:	120
Study Start Date:	June 2015
Estimated Study Completion Date:	July 2020
Estimated Primary Completion Date:	July 2017 (Final data collection date for primary outcome measure)

A Prospective, Post-marketing, Single-arm, Open Label, Multi-center Clinical Study to Evaluate the Safety and Efficacy of the ReDy™ Renal Denervation System in the Treatment of Patients With Uncontrolled Hypertension

Primary Outcome Measures:
Device-related adverse events at 1-month follow-up post treatment

Estimated Enrollment:	55
Study Start Date:	April 2016
Estimated Study Completion Date:	August 2017
Estimated Primary Completion Date:	April 2017 (Final data collection date for primary outcome measure)

Annual Publications on "Renal Sympathetic Denervation" from PubMed



Conclusions

- Uncontrolled hypertension is a global epidemic that, for a significant portion of the population, is inadequately managed
- Future studies on Renal Denervation are necessary for mainstream use
- The saga continues…