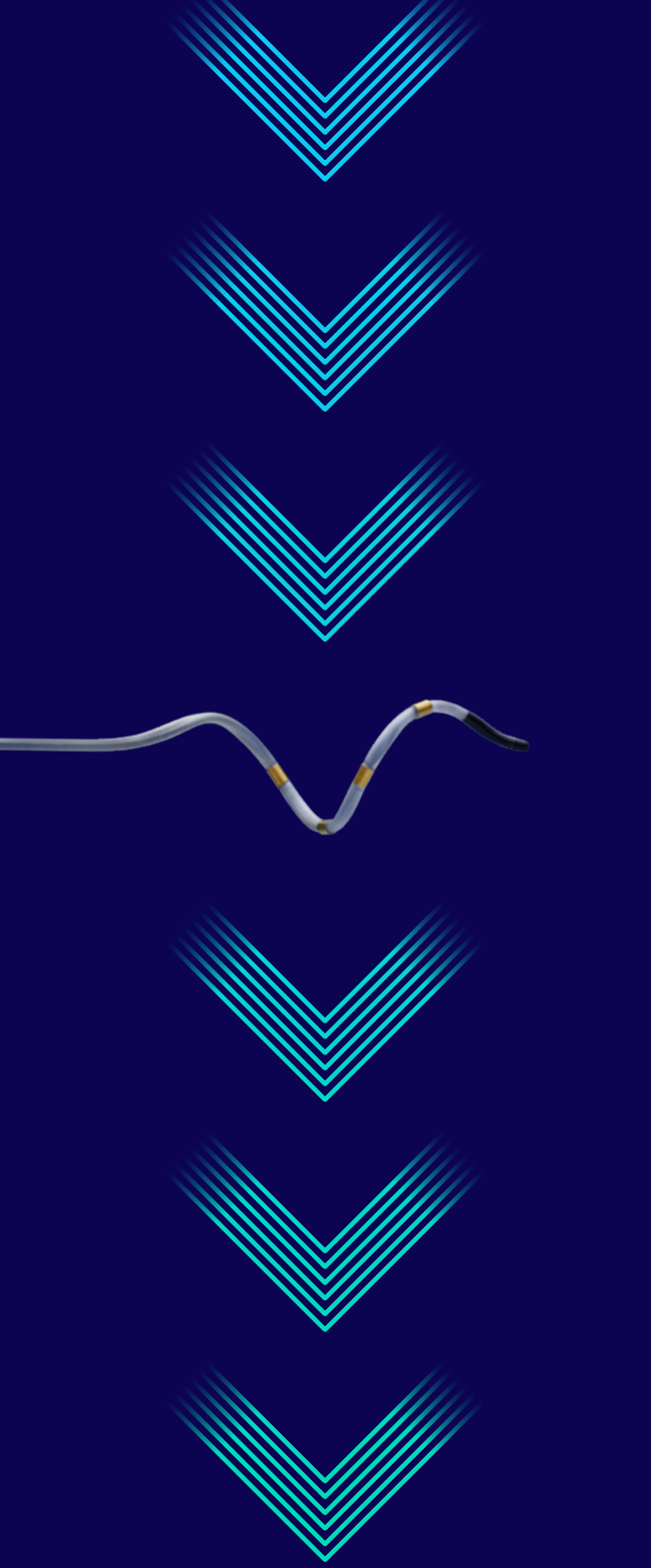


>9 mmHg

mean reduction in office SBP on and off medication at primary endpoints in multiple clinical trials[†3,4]

Medtronic

Symplicity™
blood pressure procedure

This is the turning point

in hypertension care

The Symplicity blood pressure procedure – featuring the Symplicity Spyral™ renal denervation system – is proven to deliver significant, safe, and sustained blood pressure reductions.[1-4]

Teaming up to take control of hypertension

Hypertension has been managed with lifestyle changes and medications for decades, but patients continue to fight to control their hypertension.

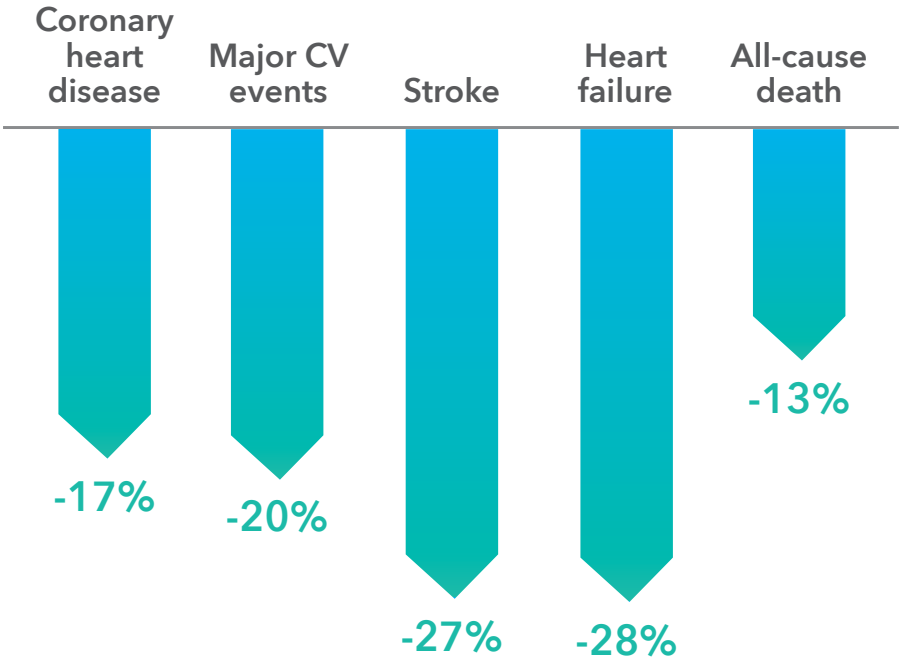
~50%
of U.S. adults have hypertension[5]
(120 million)

~80%
of HTN patients
do not have their blood pressure under control[6]

50%
of HTN patients
become non-adherent to their medication within one year[7]

Even a small drop in BP can make a big impact

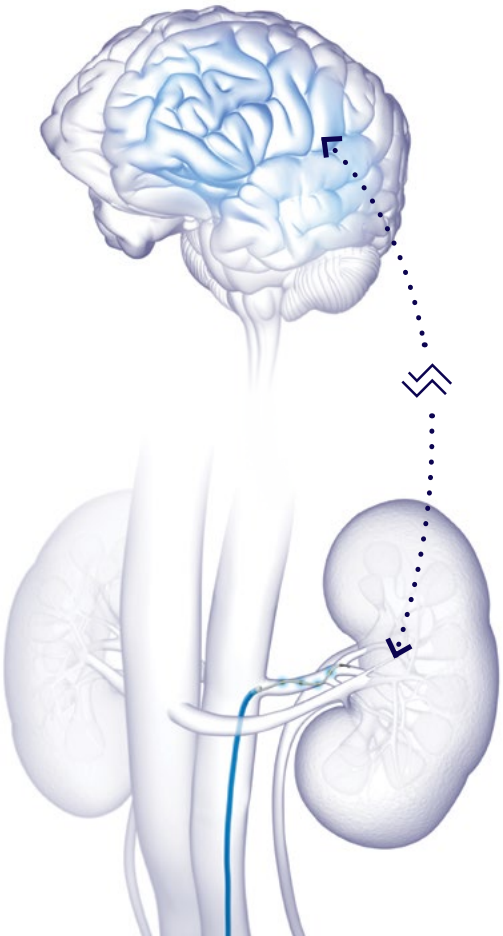
A 10 mmHg reduction in office systolic blood pressure reduces the risk of cardiovascular events.[8]



Help patients achieve control with the Symplicity blood pressure procedure

This minimally invasive procedure works in tandem with lifestyle management and medication to help patients achieve blood pressure control, which may reduce the risk of heart attack and stroke.[3,4,8]

The Symplicity procedure uses the Symplicity Spyral renal denervation system



Turn to a proven, complementary approach to treat hypertension

How renal denervation (RDN) with the Symplicity System works:

- A catheter-based procedure where **no device is left behind**
  - The catheter delivers precisely controlled radio-frequency (RF) energy to the renal nerves[9]
  - This energy reduces blood pressure by safely disrupting the sympathetic signal between the brain and the kidney[9]
- For most patients, it's a **one-hour procedure,** not including procedure preparation and recovery time
  - An overnight stay may be needed
- After procedure follow-up, the patient is **returned to the referrer for ongoing care**

Significant, safe, and sustained blood pressure reductions

>4,000 patients enrolled in the global clinical program[‡§2–4]

Significant

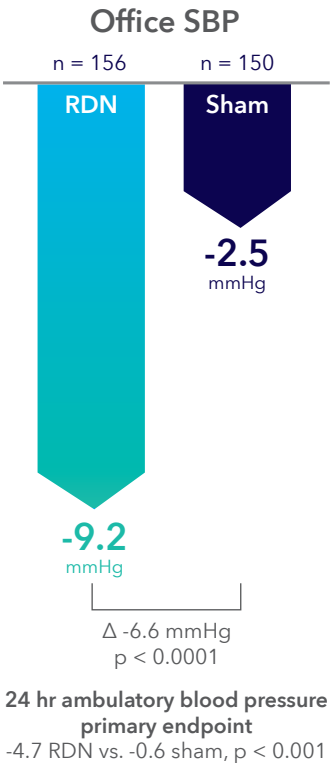
SPYRAL HTN-OFF MED[3]

Pivotal Trial
Significant blood pressure reduction in the **absence of medication** at 3 months

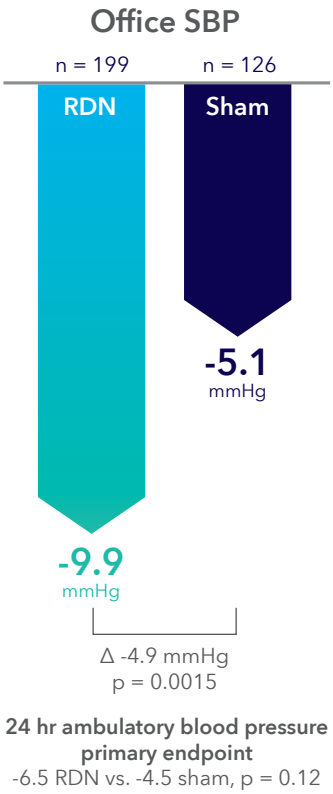
SPYRAL HTN-ON MED[4]

Significant blood pressure reductions with **20% lower medication burden at 6 months** with RDN (2.9 RDN vs. 3.5 sham, p = 0.04)

Average baseline office systolic blood pressure (OSBP) for both RDN and Sham arms in both trials = 163 mmHg



24 hr ambulatory blood pressure primary endpoint
-4.7 RDN vs. -0.6 sham, p < 0.001



24 hr ambulatory blood pressure primary endpoint
-6.5 RDN vs. -4.5 sham, p = 0.12

>9 mmHg

mean reduction in office SBP in patients off and on medications[†3,4]

Safe

Excellent safety profile

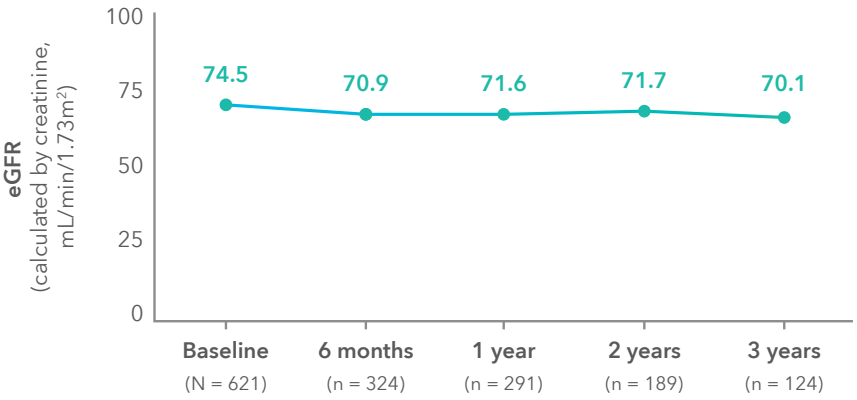
Pooled data from the **SPYRAL HTN-OFF MED** and **SPYRAL HTN-ON MED** trials indicated low incidence of procedural related and clinical adverse events.[4]

0.4%

major adverse event rate at composite endpoint, including no new incidence of renal artery stenosis (>70%) at 6 months[4]

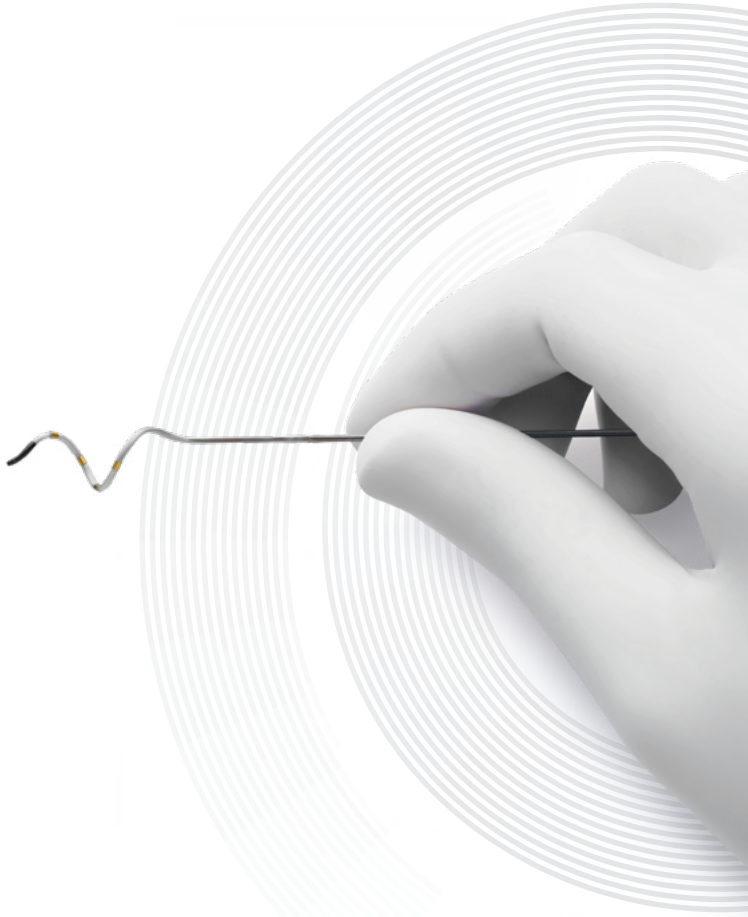
Stable kidney function in real-world patients

The Global SYMPLICITY Registry study showed stable kidney function at 3-year follow-up.[10]



Sustained

Only the Symplicity Spyral RDN system has demonstrated sustained blood pressure reductions **through 3 years in real-world patients.[11]**



18
mmHg

mean reduction in office SBP real-world patients at 3 years with the Symplicity Spyral catheter, n = 267†[11]

†Results may vary across patients.

Patients who may benefit from the Symplicity procedure

Have uncontrolled hypertension

Consider patients where lifestyle modifications and medications haven't adequately controlled blood pressure.

Are willing to undergo an interventional procedure

Consider patients who opt for the Symplicity procedure following shared decision-making and an attempt at lifestyle modifications and medical therapy.

30%
of patients
would be willing to consider an interventional approach to manage hypertension versus an additional medication[12]

3x
as many patients vs. sham were able to get their **blood pressure under control (<140 mmHg) at 6 months**[4]
(20% RDN vs. 6% sham, p = 0.001)

What patients can expect following the Symplicity procedure

Patients on one or more antihypertensive medications who underwent the Symplicity procedure as a complementary treatment (N = 199) experienced the following reductions in office systolic blood pressure at 6 months[4,13]:

61%	51%	37%	24%
of patients	of patients	of patients	of patients
>5 mmHg	>10 mmHg	>15 mmHg	>20 mmHg

Recommended by cardiovascular experts

The 2023 Society for Cardiovascular Angiography & Interventions (SCAI) position statement recognizes renal denervation as a promising therapy for treating hypertension. Read the full statement to review recommendations for success, including patient selection, operator competency, procedural training and techniques, and organizational recommendations.

SCAI

Scan to access the statement

>25,000 patients treated globally with the Symplicity RDN system[14]

We're here for you at every turn so you can:

1 **Activate**
a hypertension care pathway or a Symplicity™ renal denervation program

2 **Advance**
clinical expertise with education and training

3 **Accelerate**
patient access with physician education and communication resources, and targeted patient outreach

4 **Optimize**
hypertension and Symplicity programs

Combined with exclusive one-on-one support from:

- Experienced **sales representatives** providing case support and product training
- Accomplished **market development specialists** helping overcome barriers and expand patient access to care
- Expert **field medical education representatives** sharing deep technical knowledge
- Seasoned **regional economic managers** supporting you throughout the reimbursement process

Find a physician experienced in the Symplicity blood pressure procedure

Connect with your Medtronic representative to learn more

Explore education and training opportunities at Hypertension Headquarters

Hypertension Headquarters offers all inclusive, on-demand education for all things relating to hypertension:

- Archived webinars with hypertension KOLs
- CEU-based modules
  - Hypertension disease state
  - Anatomy and physiology
  - Symplicity blood pressure procedure
- Information to help healthcare professionals not only understand the gravity of the hypertension challenge, but what they can do to help

Find resources

Medtronic Academy account required

Notes

†Results may vary across patients.
‡Includes Symplicity Spryal and Flex catheters.
§Study follow-up is ongoing. Data does not represent follow-up for all patients.

[1] Mahfoud F, Kandzari DE, Kario K, et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): a randomised, sham-controlled trial. *Lancet.* 2022; 399(10234):1401–1410.
[2] Mahfoud F, et al. Outcomes following radiofrequency renal denervation according to antihyptensive medications: subgroup analysis of the Global SYMPLICITY Registry DEFINE. EuroPCR 2023.
[3] Böhm M, Kario K, Kandzari DE, et al. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED Pivotal): a multicentre, randomised, sham-controlled trial. *Lancet.* 2020;395(10234):1444–1451.
[4] Kandzari D, Townsend R, Kario K, et al. Safety and Efficacy of Renal Denervation in Patients Taking Antihypertensive Medications. *J Am Coll Cardiol.* 2023 Nov, 82 (19) 1809–1823.
[5] U.S. Department of Health and Human Services. The Surgeon General's Call to Action to Control Hypertension. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General; 2020.
[6] World Health Organization. Hypertension fact sheet. https://www.who.int/news-room/fact-sheets/detail/hypertension. Accessed August 23, 2023
[7] Jung O, Gechter JL, Wunder C, et al. Resistant hypertension? Assessment of adherence by toxicological urine analysis. *J Hypertens.* April 2013;31(4):766-774.
[8] Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet.* March 5, 2016;387(10022):957-967.
[9] Coates P, Tunev S, Trudel J, Hettrick DA. Time, temperature, power, and impedance considerations for radiofrequency catheter renal denervation. *Cardiovasc Revasc Med.* September 2022;42:171-177.
[10] Schlaich M, et al. Long-term safety and efficacy of renal denervation with the Symplicity Spyral catheter in the Global SYMPLICITY Registry. Presented at American Society of Nephrology Kidney Week, San Diego, CA. November 4–7, 2021.
[11] Medtronic data on file. Global Symplicity Registry clinical data snap, March 2023.
[12] Kandzari DE, Weber MA, Poulos C, et al. Patient Preferences for Pharmaceutical and Device-Based Treatments for Uncontrolled Hypertension: Discrete Choice Experiment. *Circ Cardiovasc Qual Outcomes.* January 2023;16(1):e008997.
[13] CSDP Sponsor Executive Summary: Symplicity Spyral Renal Denervation System. Medtronic. Available at: www.fda.gov/media/171412/download. Accessed on November 17, 2023.
[14] Medtronic data on file. RDN Catheter Historical Data, June 2023. Data includes both Symplicity Flex and Symplicity Spyral.

Indications
The Symplicity Spyral™ renal denervation system is indicated to reduce blood pressure as an adjunctive treatment in patients with hypertension in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

Contraindications
The Symplicity Spyral system is contraindicated in patients with any of the following conditions: • Renal artery diameter < 3 mm or > 8 mm • Renal artery fibromuscular dysplasia (FMD) • Stented renal artery (< 3 months prior to RDN procedure) • Renal artery aneurysm • Renal artery diameter stenosis > 50% • Pregnancy • Presence of abnormal kidney (or secreting adrenal) tumor • Iliac/femoral artery stenosis precluding insertion of the catheter.

Warnings and Precautions
A thorough understanding of the technical principles, clinical applications, and risks associated with vascular access techniques and percutaneous transluminal catheterization in renal arteries is necessary before using this device.

The safety and efficacy of the Symplicity Spyral system has not been established in patients with isolated systolic hypertension or in patients with prior renal artery interventions including renal stents, renal angioplasty, or prior renal denervation. The Symplicity Spyral system has not yet been studied in patients who are breastfeeding, under the age of 18, or with secondary hypertension. • Avoid treatment with the Symplicity Spyral™ catheter within 5 mm of any diseased area or stent. • Implantable pacemakers (IPGs) and implantable cardioverter defibrillators (ICDs) or other active implants may be adversely affected by RF ablation. Refer to the implantable device's *Instructions for Use*. • The patient's heart rate may drop during the ablation procedure. • Proper pain medication should be administered at least 10 min before ablating renal nerves.

Potential Adverse Events
Potential adverse events associated with use of the renal denervation device or the interventional procedures include, but are not limited to, the following conditions: • Allergic reaction to contrast • Arterial damage, including injury from energy application, dissection, or perforation • Arterial spasm or stenosis • Arterio-enteric fistula • AV fistula • Bleeding • Blood clots or embolism • Bruising • Cardiopulmonary arrest • Complications associated with medications commonly utilized during the procedure, such as narcotics, anxiolytics, or other pain or anti-vasospasm medications • Death • Deep vein thrombosis • Edema • Electrolyte imbalance • Heart rhythm disturbances, including bradycardia • Hematoma • Hematoma – retroperitoneal • Hematuria • Hypertension • Hypotension (may cause end organ hypoperfusion) • Infection • Kidney damage including renal failure or perforation • Myocardial infarction • Nausea or vomiting • Pain or discomfort • Peripheral ischemia • Pulmonary embolism • Proteinuria • Pseudoaneurysm • Radiocontrast nephropathy • Renal artery aneurysm • Skin burns from failure of the dispersive electrode pad • Stroke • Other potential adverse events that are unforeseen at this time.

Please reference appropriate product *Instructions for Use* and *User Manual* for more information regarding indications, contraindications, warnings, precautions, and potential adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

For further information, please call and/or consult Medtronic at 707-525-0111 or Medtronic's website at medtronic.com.

Medtronic

Medtronic
Tel: 707.525.0111

LifeLine Customer Support
Tel: 877.526.7890

Product Services
Tel: 888.283.7868

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