Medtronic

Symplicity Spyral™
renal denervation system

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.[1-5]

When typical hypertension treatments aren't enough

Lifestyle changes and medications have defined hypertension treatment, but they are not always enough to help patients achieve control.

50%
of adults in the U.S.
have high blood pressure[6]

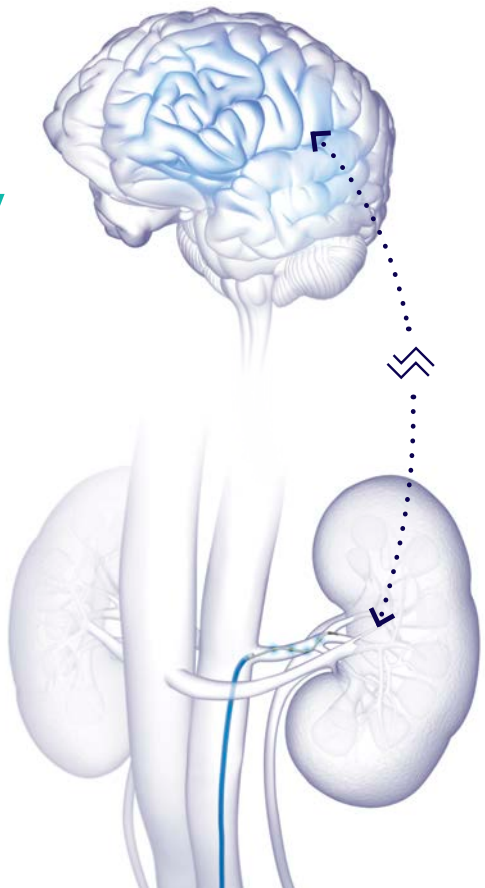
~80%
of hypertension patients
do not have their blood pressure under control[7]

50%
of hypertension patients
become non-adherent to their medication within one year[8]

Turn to a proven, complementary approach to treat hypertension

How renal denervation (RDN) with Symplicity Spyral works:

- Supplies precisely controlled and targeted radiofrequency energy to the renal nerves[9]
- Safely disrupts the overactive sympathetic signaling between the kidneys and brain to reduce blood pressure[3,4,9]

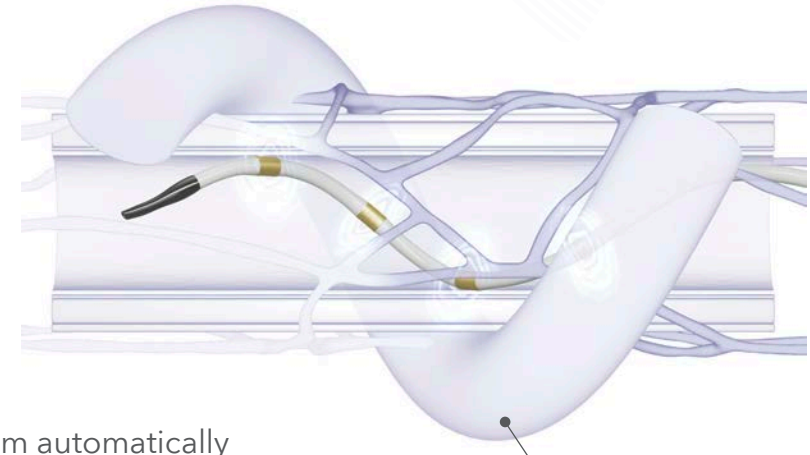


Setting the standard in renal denervation

>25,000 patients treated globally with the Symplicity RDN system[10]

Simple and versatile

- One catheter size fits vessels 3–8 mm[11]
- 4 F catheter,† compatible with 6 F guide catheter, 0.014" guidewire
- Easy-to-use, plug-and-play design
- Nonocclusive design allows for continuous blood flow to naturally protect the vessel wall[9]



Targeted circumferential ablation coverage area

Safe and precise[3,4]

- Unique, real-time, and responsive algorithm automatically adjusts power by monitoring temperature and impedance for safe energy distribution[9]
- Multi-electrode, helical design covers four quadrants simultaneously for a circumferential ablation[9,11]
- Radiofrequency energy preferentially heats fat tissue where renal nerves are located and avoids non-target structures‡,[12]
- Only the Symplicity Spyral RDN system allows for denervation throughout the renal anatomy, including the distal branches,[11] where late arriving nerves are accessible and total nerve density is highest.[13,14]

Results may vary.

Significant, safe, and sustained blood pressure reductions[1–5]

>4,000 patients enrolled in the SPYRAL HTN clinical program[§, ◊, 3–5]

Significant

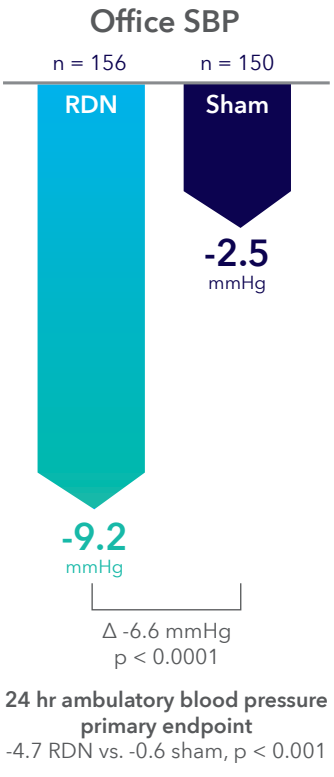
SPYRAL HTN-OFF MED[3]

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

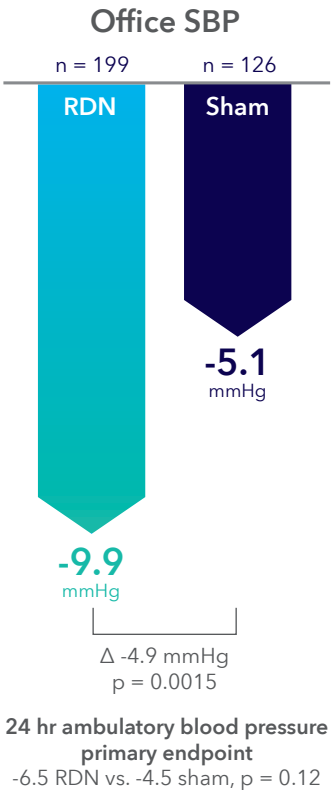
SPYRAL HTN-ON MED[4]

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 (SBP) 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]

Results may vary.

Safe

Excellent safety profile

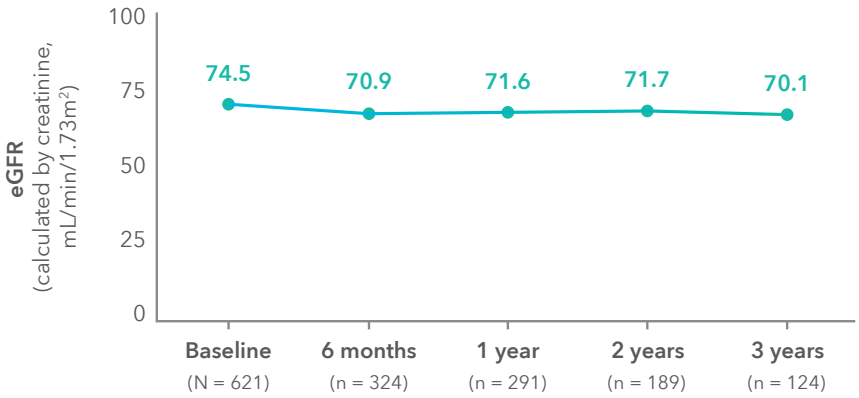
Pooled data from the **SPYRAL HTN-OFF MED** and **SPYRAL HTN-ON MED** trials indicated low incidence of procedural related and clinical adverse events.[4]

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.[15]



Sustained

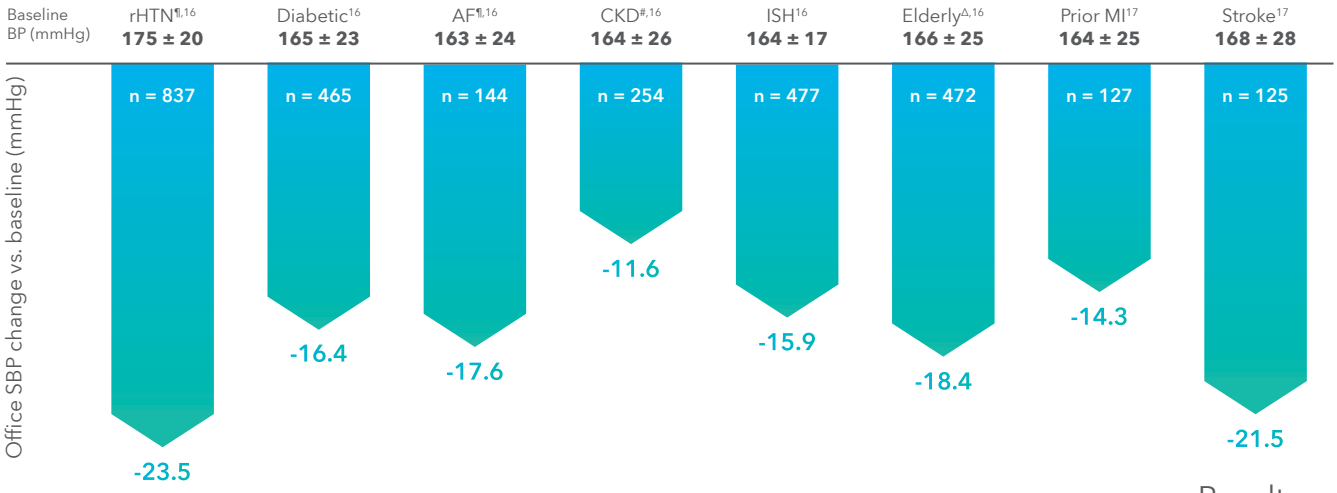
Only the Symplicity RDN system has demonstrated sustained blood pressure reductions **through 3 years in real-world patients.**[§,2]

17

mmHg

mean reduction in office SBP in real-world patients at 3 years
n = 1,337[§,2]

Blood pressure reductions across high-risk subgroups at 3 years in the Global SYMPLICITY Registry (GSR-DEFINE)[§]



Results may vary.

Patient selection

Patients may benefit from this procedure if they:

Have uncontrolled hypertension

Consider patients where lifestyle modifications and antihypertensive 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[18,19] (N = 400)

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)

Recommended by cardiovascular experts

The **2023 SCAI position statement** recognizes renal denervation as a promising therapy for treating hypertension.[20] Read the full statement to review recommendations for success, including patient selection, operator competency, procedural training and techniques, and organizational recommendations.

Scan to access the statement

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

Components and ordering information

RDN016 Symplicity Spyral multi-electrode renal denervation catheter: single-use RDN catheter for use only with the Symplicity G3 renal denervation RF generator
RDNG3A Symplicity G3 generator: reusable RF generator, power cable, remote control, and DVI-D output for use with the Symplicity Spyral catheter
RDN019 Mobile cart for Symplicity G3 generator (optional accessory)
0.014" guidewire (recommend non-hydrophilic with a supportive shaft and floppy tip)
4 F catheter,† compatible with 6 F guide catheter (90 cm max length)
Dispersive Electrode for RDNG3A: Compatible with Covidien ValleyLab Polyhesive™ adult patient return electrode (Model E7507, E7507DB)

† Catheter dimension of 0.052" is average maximum diameter determined during design verification. Upper bound allowable is 0.061".

‡ Preclinical data may not be indicative of clinical performance.

§ Includes Symplicity Spyral and Flex catheters.

◊ Study follow-up is ongoing. Data does not represent follow-up for all patients.

¶ Resistant hypertension defined as OSBP > 150 mmHg, ≥ 3 antihypertensive medications.

CKD defined as eGFR < 60 mL/min/1.73m^2.

Δ Elderly defined as 65 years or older.

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.* April 9, 2022;399(10234):1401–1410.

2. Mahfoud F, et al. Outcomes following radiofrequency renal denervation according to antihypertensive 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.* May 2, 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.* November 7, 2023;82(19):1809–1823.

5. Mahfoud F, Mancia G, Schmieder RE, et al. Outcomes Following Radiofrequency Renal Denervation According to Antihypertensive Medications: Subgroup Analysis of the Global SYMPLICITY Registry DEFINE. *Hypertension*. August 2023;80(8):1759-1770.

6. 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.

7. Hypertension fact sheet. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/hypertension. Accessed August 23, 2023.

8. Berra E, Azizi M, Capron A, et al. A. Evaluation of Adherence Should Become an Integral Part of Assessment of Patients With Apparently Treatment-Resistant Hypertension. *Hypertension*. August 2016;68(2):297-306.

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. Medtronic data on file. RDN Catheter Historical Data, June 2023. Data includes both Symplicity Flex and Symplicity Spyral.

11. Medtronic Symplicity Spyral multi-electrode renal denervation catheter Instructions for Use.

12. Sato Y, Sharp A, Mahfoud F, et al. Translational value of preclinical models for renal denervation: a histological comparison of human versus porcine renal nerve anatomy. *Eurointervention.* February 6, 2023;18(13):e1120–e1128.

13. García-Touchard A, Maranillo E, Mompeo B, Sañudo JR. Microdissection of the human renal nervous system : Implications for performing renal denervation procedures. *Hypertension.* October 2020;76(4):1240–1246.

14. Struthoff H, Lauder L, Hohl M, et al. Histological examination of renal nerve distribution, density, and function in humans. *EuroIntervention.* September 18, 2023;19(7):612–620.

15. 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.

16. Mahfoud F, Mancia G, Schmieder R, et al. Renal Denervation in High-Risk Patients With Hypertension. *J Am Coll Cardiol.* June 16, 2020;75(23):2879–2888.

17. Mahfoud F, et al. Blood pressure reduction after catheter-based renal denervation in patients with cardiovascular disease in the Global SYMPLICITY Registry. ESH 2022.

18. 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.

19. Symplicity Spyral™ Renal Denervation System. Sponsor Presentation. US FDA Circulatory Systems Devices Panel. Meeting date August 23, 2023. Available at: https://www.fda.gov/media/171691/download. Accessed July 8, 2024.

20. Swaminathan RV, East CA, Feldman DN, et al. SCAI Position Statement on Renal Denervation for Hypertension: Patient Selection, Operator Competence, Training and Techniques, and Organizational Recommendations. *JSCAI*. November 2023;2(6).

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 800-633-8766 or the Medtronic website at medtronic.com.

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medtronic.com/SymplicityProcedure

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