Medtronic

Our journey to help transform hypertension care

Symplicity Spyral™ renal denervation system

2010

Ardian Symplicity™ renal denervation acquisition

We got to work applying our expertise to further develop a catheter-based procedure for uncontrolled hypertension patients.

Our commitment to developing a safe, novel, and effective renal denervation (RDN) system never wavered — even with detours along the way. When others gave up, we remained dedicated to:

- Redesigning our clinical studies
- Refining how to perform the procedure
- Advancing our technology

2014

Symplicity HTN-3 trial[1]

Did not demonstrate superiority of the Symplicity RDN system over a sham procedure and medical therapy in reducing office and ambulatory blood pressure at six months in patients with severe, resistant hypertension

Learning from the past to inform our future

While we did not meet the primary endpoint of our HTN-3 trial, it showed[1,†]:

- A significant difference in nighttime blood pressure (a "high-risk" zone) between the RDN group and the sham group (p = 0.015).[2] We also met our safety endpoint.[1,‡] **These milestones signaled the promising impact of RDN and incentivized us to continue our research and design.**
- Through patient journaling, we saw ~40% of patients had their medications changed during the study. **Because of this, we made sure future studies included a plasma/urine draw to understand medication variance.**[3]

Peer-reviewed, preclinical research showed that treating both the branch vessels and main renal artery resulted in greater nerve destruction and less variability in the reduction of renal norepinephrine. This showed an increased benefit compared to ablating the main renal artery alone.[4]

Preclinical data may not be representative of clinical performance in human subjects.

With these learnings, we redesigned our catheter into a spiral shape to provide **360-degree ablations,**[5,6] **resulting in significant, sustained, and safe blood pressure reductions.**[7-10]

Results may vary.

2015

SPYRAL HTN clinical program begins

Spyral HTN-OFF MED trial
Pivotal, randomized, sham-controlled trial studying safety and efficacy in the absence of antihypertensive medication

Spyral HTN-ON MED trial
Prospective, randomized, sham-controlled trial studying safety and efficacy in the presence of antihypertensive medication

Global SYMPLICITY Registry (GSR) Denervation Findings in the Real World (DEFINE)[3,7,11]
Prospective, single-arm, all-comer, real-world registry to demonstrate long-term durability and safety in over 3,900 patients with uncontrolled hypertension treated with the Symplicity RDN system

2020

SPYRAL HTN-OFF MED pivotal results

Significant blood pressure reductions in the absence of medication at three months[§]

SPYRAL HTN-OFF MED[9]
Pivotal Trial
Absence of antihypertensive medications

SPYRAL HTN-ON MED[9]
Full Cohort
Presence of antihypertensive medications

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

Office SBP (mmHg), n = 156

Δ -6.6 mmHg
p < 0.0001

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

Office SBP (mmHg), n = 129

Δ -4.9 mmHg
p = 0.0015

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

Excellent safety profile[9]

Pooled data from the SPYRAL HTN-OFF MED and SPYRAL HTN-ON MED trials **showed fewer than 0.4% major adverse events** at composite endpoint including no new incidents of renal artery stenosis (> 70%) at six months

Adverse events include, but are not limited to, pain and hematoma. Results may vary.

2021

Clinical evidence expansion begins

SPYRAL AFFIRM Global Clinical Post-approval Study

Single-arm interventional study, evaluating the long-term safety, efficacy, and durability of the Symplicity Spyral system

GSR-DEFINE expansion[3,12]
2,000 patients added

2022

Initial SPYRAL HTN-ON MED results presented

Blood pressure reductions with 20% lower medication burden at six months with RDN (2.9 RDN vs. 3.5 sham, p = 0.04)[9]

2023

FDA approval of the Symplicity Spyral system

Long-term SPYRAL HTN-ON MED data presented[10]

Durable blood pressure reductions in the presence of medication out to three years. At three years, 74% of patients treated in the sham arm elected to undergo the Symplicity procedure.

18.5
mmHg
mean reduction in office systolic blood pressure at 3 years.[10] (N = 175)

2025

Hypertension guidelines recommend renal denervation

Published by the American Heart Association (AHA) and the American College of Cardiology (ACC)[6,13]

Medicare covers renal denervation

The Centers for Medicare & Medicaid Services (CMS) issued positive coverage for renal denervation for uncontrolled hypertension, including the Symplicity blood pressure procedure.[6,14]

Visit our website

to stay up to date on the latest developments for the **Symplicity Spyral renal denervation system** and **Symplicity blood pressure procedure.**

† The primary efficacy endpoint was the mean change in office systolic blood pressure from baseline to six months in the denervation group, as compared with the mean change in the sham control group, with a superiority margin of 5 mmHg.

‡ Includes Symplicity Spyral and Flex catheters.

§ See ACC/AHA hypertension guidelines for specific patient selection recommendations.

¶ Refer to the national coverage determination for full coverage criteria, including patient, physician, and facility requirements.

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3. Kandzari DE, Kario K, Mahfoud F, et al. 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. *Am Heart J*. January 2016;171(1):82-91.

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5. Coates P, Tunev S, Trudel J, Hettrick DA. Time, Temperature, Power, and Impedance Considerations for Radiofrequency Catheter Renal Denervation. *Cardiovasc Revasc Med*. September 2022;42:115-117.

6. Symplicity Spyral™ multi-electrode renal denervation catheter instructions for use. November 18, 2023.

7. Mahfoud F, Schlaich M, Schmieder RE, et al. Long-term outcomes in ESC guideline-recommended patients for RDN from Global SYMPLICITY Registry DEFINE. Presented at: EuroPCR 2025; May 20-23, 2025; Paris, France.

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9. 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.

10. Kandzari D, Mahfoud F, Townsend R, et al. Durable safety and efficacy of renal denervation using the Symplicity Spyral catheter in patients taking antihypertensive drugs: final, 3-year results from the SPYRAL HTN-ON MED randomized study. Presented at: TCT 2025; October 25-28, 2025; San Francisco, CA.

11. Mahfoud F, Townsend RR, Kandzari DE, et al. Long-Term, Patient-Level Analysis of Radiofrequency Renal Denervation in the SYMPLICITY Clinical Trial Program. *JACC Adv*. March 2025;4(3):101666.

12. National Library of Medicine Clinical Trials. Global SYMPLICITY REGISTRY (GSR) DEFINE. Accessed January 21, 2026. https://clinicaltrials.gov/study/NCT06999616

13. Jones DW, Ferdinand KC, Taler SJ, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/ASG/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. November 4, 2025;86(18):1567-1678.

14. Centers for Medicare and Medicaid Services. Renal denervation for uncontrolled hypertension: Final Decision Memo. Published October 28, 2025. Accessed January 21, 2026.

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, type 1 diabetes, secondary hypertension (including renal artery stenosis, 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-anxiogenic medications • Death • Deep vein thrombosis • Edema
• Electrolyte imbalance • Heart rhythm disturbances, including bradycardia • Hematoma
• Hemorrhage requiring transfusion • Infection • Kidney damage, including renal artery end organ hypoperfusion • Infection • Kidney damage including renal failure or perforation
• Myocardial infarction • Nausea or vomiting • Pain or discomfort • Peripheral ischemia
• Pulmonary embolism • Pyelonaus • 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.

Medtronic

medtronic.com/SymplicityProcedure

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