ReCor Medical

# Paradise

Ultrasound Renal Denervation System

**INSTRUCTIONS FOR USE**

## Paradise® Catheter

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PRDS-063-02
PRDS-064-02
PRDS-065-02
PRDS-066-02
PRDS-067-02
PRDS-068-02

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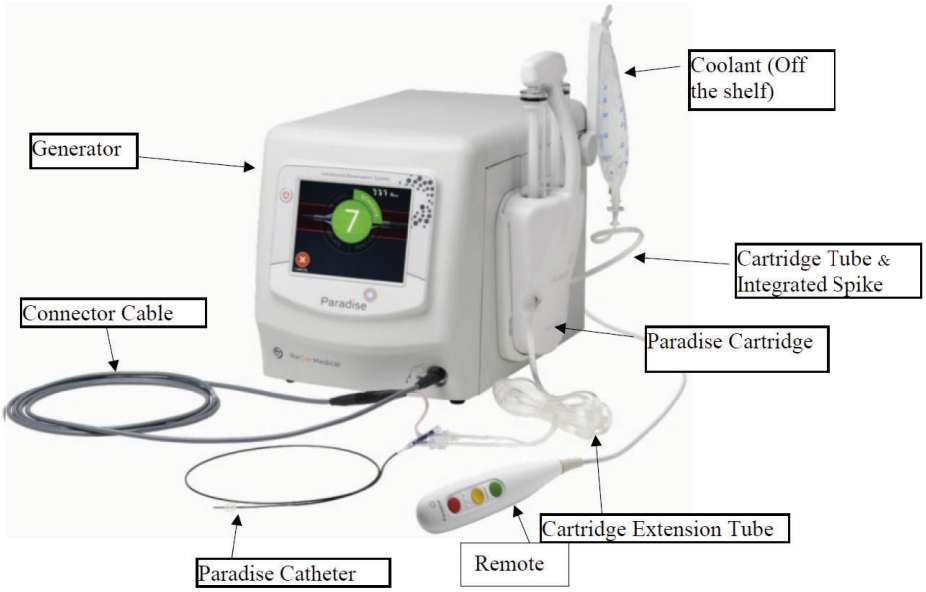


℞ ONLY

**General safety**

THE PARADISE CATHETER IS SPECIFICALLY DESIGNED FOR USE WITH THE PARADISE GENERATOR AND OTHER ACCESSORIES SPECIFIED BY RECOR MEDICAL, INC.

DISREGARDING THE WARNINGS AND PRECAUTIONS COULD ENDANGER THE PATIENT, THE USERS, OR OTHERS, AS WELL AS THE EQUIPMENT.

**Required Expertise**

The Paradise Catheter is to be operated only under direct physician supervision. In addition to medical knowledge, the user must know the proper operation of the paradise catheter and the necessary conditions for its application. Hospital personnel operating the Paradise Catheter shall be trained in the proper use of the paradise system.

## Contents

## 1. Device Description

The Paradise Ultrasound Renal Denervation System is a catheter-based system that delivers ultrasound energy circumferentially to thermally ablate and disrupt the renal sympathetic nerves.

### Paradise® Catheter

The Paradise Catheter consists of a multi-lumen shaft with a cylindrical piezoelectric ceramic transducer located at the distal end of the catheter. The Paradise Catheter has a distal balloon which is pressurized by the Paradise System to a range of 1.4 ATM– 2.0 ATM using coolant fluid. The Paradise Catheter is available in multiple balloon diameters. The Paradise Catheter is designed to be connected to the extension tubing of the Paradise Cartridge which connects with the Paradise Generator. The Paradise Catheter contains a through lumen which is compatible with a 0.014" guidewire. Using a 0.014" guidewire, the Paradise Catheter can be tracked into position for delivery of ultrasound energy. The Paradise Catheter is supplied sterile using Ethylene Oxide (EtO) and is single use only.

The Paradise Catheter is available with different balloon diameters, designated by the product codes listed below:

**Table 1: Paradise Catheter sizes**

| Reference Number | Balloon Diameter Size |
|---|---|
| PRDS-063-02 | 3.5mm |
| PRDS-064-02 | 4.2mm |
| PRDS-065-02 | 5mm |
| PRDS-066-02 | 6mm |
| PRDS-067-02 | 7mm |
| PRDS-068-02 | 8mm |

### Paradise® Cartridge

The Paradise Cartridge when used in conjunction with the Paradise Generator controls the fluid flow into and out of the Paradise Catheter. The Paradise Cartridge contains tubing and an integrated spike to connect to the sterile water supply. The Paradise Cartridge also contains a 3 meters (10') long tube to connect to the Paradise Catheter in the sterile field. Fluid flows through the Paradise Cartridge and catheter body to the balloon at the distal end of the Paradise Catheter and returns to the Paradise Cartridge. The Paradise Cartridge is supplied sterile using Ethylene Oxide (EtO) and is single use only.

### Paradise® Connection Cable

The Paradise Connection Cable transfers electrical energy from the Paradise Generator to the Paradise Catheter. The Paradise Connection Cable connects to the connector on the proximal end

of the Paradise Catheter and to the front panel of the Paradise Generator. The Paradise Connection Cable is supplied sterile using Ethylene Oxide (EtO) and is single use only.

## Paradise® Generator Description

The Paradise Generator is designed to be used in conjunction with the Paradise Cartridge and Paradise Connection Cable to circulate coolant fluid and electrical energy to the Paradise Catheter. The Paradise Generator uses a series of sensors and control software for management of fluid flow and ultrasound energy delivery to the Paradise Catheter. Fluid flow through the system allows for the transmission of ultrasound from the Paradise Catheter and removes unwanted heat during treatment. The Paradise Generator has a touch screen which allows users to operate the Paradise System through a sequence of steps.

## 2. General Information

The Paradise™ Catheter is used with the following devices:

**Table 2: Compatible devices**

| Reference Number | Product Description |
|---|---|
| PRDS-USG-2X | Paradise™ Generator |
| PRDS-CT-02 | Paradise™ Cartridge |
| PRDS-CC-02 | Paradise™ Connection Cable |

## 3. Definitions

Sonication – The delivery of ultrasound energy by the Paradise System.

Radiopaque transducer length – The length of the Paradise Catheter's ultrasound transducer (~5mm) that is easily visible under fluoroscopy. It can be used as a measurement guide for treatment locations within the renal artery.

## 4. How Supplied

**Sterile**- Sterilized with ethylene oxide gas. Non-pyrogenic. Do not use any Paradise Catheter, Paradise Cartridge, or Paradise Connecting Cable or Paradise Generator power cable that show any signs of damage or are expired based on the product label expiration date.

**Contents**- One (1) Paradise Catheter

**Storage** - Store in a dry, dark, cool place. Protect from light. Do not remove from carton until ready for use. Store at room temperature; excursions permitted to 18 – 55°C.

## 5. Indications for Use

The Paradise Ultrasound Renal Denervation System (Paradise System) is indicated to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

## 6. Contraindications

The Paradise Catheter is contraindicated in any of the following:

- Renal arteries with diameter <3 mm and >8mm
- Renal artery with Fibromuscular disease (FMD)
- Stented renal artery
- Renal artery with aneurysm
- Renal artery with stenosis of any origin >30%
- Pregnancy
- Presence of abnormal kidney (or secreting adrenal) tumors
- Iliac/femoral artery stenosis precluding insertion of the catheter

## 7. Catheter sizing considerations

The Paradise System is intended to be used in renal arteries of diameters ranging from 3.0 to 8.0 mm.

**Table 3: Catheter sizing**

| Balloon Diameter Size | Artery Diameter Range (mm) |
|---|---|
| 3.5 mm | 3 to <3.5 |
| 4.2 mm | 3.5 to <4.2 |
| 5 mm | 4.2 to <5 |
| 6 mm | 5 to <6 |
| 7 mm | 6 to <7 |
| 8 mm | 7 to ≤8 |

## 8. Warnings

1. Failure to use the recommended balloon size may result in renal artery stenosis, dissection, perforation, aneurysm, significant vasospasm requiring intervention, ablation of unintended tissues or structures, and/or no ablation of target tissue achieved.
2. Energy emission in an unintended location may result in unintended tissue damage.
3. Do not move the Paradise Catheter during sonication.
4. Do not sonicate in renal artery at locations with visible plaque.
5. Do not deliver sonications in an overlapping arterial target zone.
    a. In case of partial energy emissions, move the catheter to a new location prior to next sonication in order to avoid sonications in overlapping arterial target zone.

# 9. Precautions

## 9.1. Paradise System

1. Do not attempt to operate the Paradise Generator before thoroughly reading the Paradise Generator Operator's Manual (IFU-0107).

2. Paradise Catheters are to be used only with Paradise Cartridges and Paradise Connection Cables and listed accessories in conjunction with the Paradise Generator.

3. Anxiolytic and analgesic medications should be given prior to and/or during treatment per standard institutional practice.

4. Patients with known allergy to contrast medium may be at increased risk of hypersensitivity reactions.

5. Appropriate systemic anticoagulation shall be administered prior to and/or during treatment to minimize the risk of thrombus formation. The risks of using the Paradise System in patients who cannot be anticoagulated are unknown.

6. Sonication in air will result in damage to the Paradise Catheter.

7. Use of power injectors with the Paradise Catheter can lead to excessive pressure on the balloon causing a generator error and potentially causing procedural delay.

8. Do not use any Paradise Catheter, Paradise Cartridge, or Paradise Connecting Cable or Paradise Generator power cable that show any signs of damage or are expired based on the product label expiration date.

9. Only use specified coolant (Sterile water) for fluid supply. DO NOT USE SALINE.

10. Do not use the Paradise System in the presence of flammable anesthetics.

## 9.2. Paradise Catheter

11. Avoid touching the balloon with sharp instruments or metal objects.

12. Do not use guide catheters less than 7 French.

13. Use only a "push/pull style" hemostasis valve with no manual tightening feature for the guide catheter. Standard hemostasis valves can affect the performance of the Paradise System when over-tightening of the threaded valve occurs.

14. The Paradise Catheter is only compatible with 0.014" diameter guidewire.

15. When positioned outside the guide catheter, never advance, withdraw, or rotate the Paradise Catheter without fluoroscopic visualization.

16. Never advance or withdraw the Paradise Catheter against unknown or excessive resistance.

17. The Paradise Catheter balloon size should be carefully selected for each renal artery diameter size to minimize the risk of balloon oversizing or undersizing.

18. Once the Paradise Catheter is placed in the artery and inflated, do not move the device until device is deflated. To deflate the device, press the DEFLATE button on the Paradise Generator touch screen.

19. Ensure that the inflated balloon is apposed to the wall of the renal artery to ensure proper cooling and protection of the arterial wall.

20. Avoid multiple balloon inflations to achieve apposition of the balloon to the renal artery wall; multiple balloon inflations may result in increased vessel trauma.

21. In the event of persistent Paradise Generator errors, deflate the balloon and withdraw the Paradise Catheter from the patient. Do not reuse the catheter.

22. In the event that the balloon does not deflate, detach the 2 cartridge fluid lines from the hub of the Paradise Catheter and replace one line with a closed-end Luer cap (or stop cock) and the other with an empty 10 cc syringe. Pull vacuum on the syringe to manually deflate the balloon. If the balloon does not deflate, switch locations of the closed-end Luer cap and the 10 cc syringe, then retry to deflate.

23. In the event that the Paradise Catheter should become kinked or damaged during manipulation, deflate the balloon and withdraw the Paradise Catheter from the patient. Do not reuse.

24. In an emergency, sonication can be immediately halted at any time by pressing the CANCEL button on the touch screen, pressing the emergency stop button on the front of the Paradise Generator, or pressing the orange-red button on the optional handheld remote.

25. The Paradise Catheter is for single use only. Do not resterilize or reuse. Reuse, reprocessing, or resterilization will compromise device integrity which may result in patient injury, illness, or death.

26. Do not touch the Paradise Catheter balloon during sonication, as it may result in serious injury.

27. Trapped air within the catheter may impede energy delivery resulting in undertreatment.

28. Rough handling of the catheter may adversely affect its characteristics; handle the catheter with care.

29. The Paradise System may interfere with or adversely affect the operation of cardiac pacemakers or other active implants, unless proper precautions have been taken or managed per the manufacturer's instructions. When in doubt regarding possible hazards, seek qualified advice and/or consult with the manufacturer(s) prior to initiating a procedure. The Paradise Catheter is a Type CF, defibrillation-proof Applied Part.

30. The Paradise Catheters must not be used in the presence of the high magnetic field created by a Magnetic Resonance Imaging (MRI) device.

## 9.3. Use in Special Patient Populations

***Pregnancy***

The Paradise System has not been tested in pregnant women. Effects on the developing fetus have not been studied. The risks and reproductive effects are unknown at this time.

***Diabetes Mellitus***

The Paradise System has not been studied in patients with Type I Diabetes Mellitus. Type II diabetes patients comprised approximately 12% of the patient population studied in the clinical studies. No safety or effectiveness related differences were observed between the Type II diabetic and non-diabetic population in clinical studies.

***Black/ African Americans Patients***

Black/African American patients comprised approximately 20% of patient population studied in the clinical studies. No safety or effectiveness related differences were observed in black patients compared to the overall patient population.

***Ethnicity***

Insufficient subject numbers in a range of ethnicities (e.g. Hispanic) prevent ethnicity-related analyses on clinical safety and effectiveness.

***Pediatrics***

The Paradise System has not been studied in pediatric patients.

***Isolated systolic hypertension***

The safety and effectiveness of the Paradise System has not been established in patients with isolated systolic hypertension.

***Secondary Hypertension***

The Paradise System was not studied in patients with known primary aldosteronism, Pheochromocytoma/paraganglioma, Cushing's syndrome, Primary hyperparathyroidism and Mineralocorticoid excess syndromes. The safety and effectiveness of the Paradise System in patients with these conditions has not been established.

***Chronic Kidney Disease***

The Paradise System was not studied in patients with eGFR < 40 mL/min/1.73m$^2$. The safety and effectiveness of the Paradise System in this patient population has not been established.

***Prior Renal Interventions***

The Paradise System was not studied in patients with pre-existing renal stents, history of renal angioplasty, or history of prior renal denervation. The safety and effectiveness of the Paradise System in these patients has not been established.

### *Active Infection*

The Paradise System was not studied in patients with evidence of active infection within 7 days of the renal denervation procedure. The safety and effectiveness of the Paradise System in these patients has not been established.

### *Angina*

The Paradise System was not studied in patients with documented, confirmed episode(s) of stable or unstable angina. The safety and effectiveness of the Paradise System in these patients has not been established.

## 10. PATIENT SELECTION FOR TREATMENT

In diagnosing and treating hypertension, proper blood pressure measurement techniques are essential to confirm the diagnosis and manage the condition. Medical professional society guidelines[1] provide recommendations regarding accurate and reproducible blood pressure assessment equipment and proper blood pressure measurement methods.

Medical professional society guidelines[2][3] provide target blood pressure goals that reduce end organ damage and cardiovascular risks and blood pressure lowering medication strategies.

Lifestyle modifications (e.g., dietary salt restriction, heathy diet, weight loss in overweight individuals, exercise, and limited alcohol intake) and medical therapy are the first-line approaches to lower blood pressure. In hypertensive patients, these interventions reduce the risk of mortality, myocardial infarction, heart failure, stroke, and kidney disease. In general, meta-analyses of randomized hypertension treatment trials show a 2% cardiovascular absolute risk reduction for every 1 mmHg reduction in systolic blood pressure.

In hypertensive patients who are unable to achieve blood pressure goals with lifestyle modifications and an adequate trial of medical therapy, health care providers should consider whether:

- Patients are compliant with prescribed blood pressure medications. Patient counseling and the use of once daily fixed-dose combination antihypertension strategies are among the strategies that can improve medication adherence.
- Blood pressure control may be improved via up-titration of medication dosages or adding antihypertensive medications having a different mechanism of action from the current regimen
- Blood pressure measurements are accurate (e.g., using a proper cuff size)

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[1]Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association
Paul Muntner, PhD, MHS, FAHA, Chair, Daichi Shimbo, MD, Vice Chair, Robert M. Carey, MD, FAHA, Jeanne B. Charleston, PhD, Trudy Gaillard, PhD, Sanjay Misra, MD, FAHA, Martin G. Myers, MD, Gbenga Ogedegbe, MD, FAHA, Joseph E. Schwartz, PhD, Raymond R. Townsend, MD, FAHA, Elaine M. Urbina, MD, MS, FAHA, Anthony J. Viera, MD, MPH, FAHA, William B. White, MD, FAHA, Jackson T. Wright Jr, MD, PhD, FAHA, on behalf of the American Heart Association Council on Hypertension; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; and Council on Quality of Care and Outcomes Research

[2]Whelton PK et al.. 2018. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation and management of high blood pressure in adults. *Hypertension.* **71:** e13-e115

[3]Mancia G, Kreutz R, Brunstrom M, Burnier M, Grassi G, Januszewicz A, Muiesant ML, Tsioufis K, Agabiti-Rosei E, Algharably EAE, et al. 2023 ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension [published online June 21, 2023]. J Hypertens. doi: 10.1097/HJH.0000000000003480

- Patients are taking agents that can elevate blood pressure (e.g., nonsteroidal anti-inflammatory drugs or stimulants)
- Secondary causes of hypertension are present

Renal denervation with the Paradise System is a treatment option in selected patients if blood pressure remains elevated despite: (1) lifestyle modifications and antihypertensive medical therapy; (2) addressing potential factors that may be contributing to inadequate blood pressure control; or (3) strategies to address potential contributing factors are ineffective, not feasible, or not aligned with the patient's interests.

## 11. PATIENT COUNSELING

Treatment with the Paradise System should be based on a joint decision between the physician and the patient, considering the benefits and risks of the device and following a review of the device indications for use (Section 5), contraindications (Section 6), warnings (Section 8), precautions (Section 9), adverse events (Section 14.2), and clinical study data (Section 14). Patient consultation should include a comprehensive discussion of treatment options, an individualized benefit-risk assessment, and post-procedure follow-up recommendations.

## 12. Possible Risks

The following are possible risks associated with the renal denervation procedure/response to treatment. These potential risks may include:

Ablation or thermal injury to vessel, adjacent tissue or other structures
Acute kidney injury
Angina
Anxiety
Arrhythmia
Atrial tachycardia
Bradycardia
Gastrointestinal complications (diarrhea, nausea, vomiting)
Hypotension/ Dizziness and/or Headaches
Hypertension
Hyperhidrosis
Pain (transient abdominal, lower back)
Renal failure or renal insufficiency
Renal artery aneurysm or pseudoaneurysm
Renal infarction
Renal artery dissection, or perforation
Renal artery stenosis
Vasospasm
Vasovagal response
Stroke or transient ischemic event

Additionally, there are risks of the renal denervation procedure which are similar to the risks of all procedures requiring arterial catheterization. The following are potential risks of the catheterization procedure (including renal angiography):

Allergic reaction to contrast
Arterio-enteric fistula
Arterio-venous fistula
Bleeding
Cardiopulmonary arrest
Complications related to pain and anti-anxiety medications
Death
Deep vein thrombosis
Edema
Embolism (pulmonary, renal, peripheral vasculature, plaque)
Hematuria
Infection
Myocardial infarction
Pain
Vascular access site complications (pseudoaneurysm, pain, swelling, hematoma)

## 13. Overview of RADIANCE Clinical program

The clinical evidence supporting the safety and effectiveness of the Paradise Ultrasound Renal Denervation System for the treatment of hypertension is based on data collected from three IDE clinical studies – RADIANCE-HTN SOLO, RADIANCE-HTN TRIO, and RADIANCE II.

### 13.1. Objective, Study Design, Study Population

All three clinical studies were prospective, multi-center, randomized, double-blind, sham controlled and independently powered to demonstrate a reduction in daytime ambulatory systolic blood pressure (BP) at 2 months and to demonstrate the safety profile of the Paradise System.

#### RADIANCE-HTN SOLO

Subjects were consented between March 2016 and December 2017. Subjects had their antihypertensive medication discontinued for a period of 4 weeks prior to a reassessment of their hypertension to determine randomization eligibility. One hundred forty-six (146) subjects were randomized to either uRDN treatment (n=74) or Sham control (n=72) at 21 investigational sites in the United States and 18 sites in Europe. The data presented include information collected through August 22, 2022 with subjected follow-up through 36 months.

#### RADIANCE-HTN TRIO

Subjects were consented between March 2016 and March 2020. Subjects had their current hypertensive regimen replaced with a single pill (a fixed dose antihypertensive combination of a calcium channel blocker, angiotensin II receptor blocker, and hydrochlorothiazide diuretic) administered once daily during a 4-week stabilization period prior to a reassessment of their hypertension to determine randomization eligibility. One hundred thirty-six (136) subjects were randomized to either uRDN treatment (n=69) or Sham control (n=67) at 28 investigational sites in the United States and 25 sites in Europe. The data presented include information collected through August 22, 2022 with subjected follow-up through 24 months.

## RADIANCE II

Subjects were consented between January 14, 2019, and May 6, 2022. Subjects had their antihypertensive medication discontinued for a period of 4 weeks prior to a reassessment of their hypertension to determine randomization eligibility. Two hundred twenty-four (224) subjects were randomized to either uRDN treatment (n=150) or Sham control (n=74) at 37 investigational sites in the US and 24 sites in Europe. The data presented include information collected through February 23, 2023 with subjected follow-up through 6-months.

Following enrollment, patients were either withdrawn from medications (SOLO and RADIANCE-II) or had their anti-hypertensive medications standardized (TRIO) for four weeks. They were then randomized and underwent either uRDN treatment or a sham procedure (renal angiogram). Subjects were not to make any changes in BP medications prior to 2-months post-uRDN treatment or the sham procedure unless they met elevated blood pressure safety escape criteria. After the collection of the primary endpoint data at 2-months, subjects in the three studies underwent guideline-based antihypertensive medication escalation (as needed) between 2- and 6-months post-uRDN treatment or sham procedure to optimize blood pressure control (target home systolic blood pressure ≤135 mmHg and diastolic blood pressure ≤85 mmHg), with TRIO subjects remaining on the standardized triple pill and having medications added as needed between 2- and 6-months. Beyond 6-months, blood pressure was managed medically per physician discretion. Subjects in SOLO and TRIO remained blinded to treatment assignment for 6 months following uRDN or sham procedure, while RADIANCE-II subjects remained blinded for 12 months.

**Table 4** provides an overview of the three uRDN trials.

**Table 4: Summary of Clinical Studies**

| Study Design Parameters | RADIANCE- HTN SOLO (SOLO) | RADIANCE- HTN TRIO (TRIO) | RADIANCE II (R-II) |
|---|---|---|---|
| Patient Population | Uncontrolled (OBP ≥140/90 & <180/110 mmHg) on 0-2 anti-hypertensive medications<br>or<br>Controlled (OBP ≤140/90 mmHg) on 1-2 anti-hypertensive medications | Uncontrolled (OBP ≥140/90 mmHg) on 3 or more anti-hypertensive medications | Uncontrolled OBP ≥140/90 mmHg & <180/110 mmHg) on 0-2 anti-hypertensive medications |
| Randomized patients | 146 (1:1 uRDN:Sham) | 136 (1:1 uRDN:Sham) | 224 (2:1 uRDN:Sham) |
| Medications through primary endpoint at 2m | No anti-hypertensive medications | Single , fixed dose anti-hypertensive medication combination triple pill | No anti-hypertensive medications |
| Medications 2-6m | Standardized guideline driven medication escalation to target BP control | | |
| Medications beyond 6m | Medications prescribed per physician discretion | | |

| Study Design Parameters | RADIANCE- HTN SOLO (SOLO) | RADIANCE- HTN TRIO (TRIO) | RADIANCE II (R-II) |
|---|---|---|---|
| Primary Effectiveness Endpoint | The difference in the reduction in average daytime ambulatory systolic BP between uRDN and Sham control, from baseline to 2 months post procedure | | |
| Follow up schedule | 2, 6, and 12 months and annually through 3 years | 2, 6, and 12 months and annually through 5 years | |
| Safety | All adverse events collected and reviewed | | |
| Primary Safety Endpoint: | None | None | Patient level composite of the incidence of Major Adverse Events (MAE) at 30 days and the incidence of new renal artery stenosis (>70% diameter stenosis) at 6-months |
| Imaging | • Renal duplex ultrasound performed for all randomized subjects at 2 and 6 months and for uRDN-treated subjects at 24 and 36 months; CTA/MRA was obtained if specific duplex ultrasound parameters (e.g., PSV) were elevated<br>• CTA/MRA at 12 months for subjects treated with uRDN | | CTA/MRA at 6 months for all randomized subjects and at 12 months for subjects treated with uRDN |
| Study Duration | 3 years | 3 or 5 years | 5 years |
| Status | Complete follow up available through 36 months | Complete follow up available through 24 months | Complete follow up available through 6 months |

uRDN: ultrasound renal denervation; BP: blood pressure; OBP: Office BP; CTA: computed tomography angiography; MRA: magnetic resonance angiography; PSV: peak systolic velocity

## 13.2. Clinical Study Endpoints

### 13.2.1. Safety

All adverse clinical events were collected and reported for the duration of all three studies. Severity was determined, as was device and/or procedure relatedness for each event. Events were assessed by an Independent Data Safety Monitoring Board (DSMB) quarterly. Event rates were calculated for each study arm, RDN and sham throughout the duration of the study.

In RADIANCE (SOLO and TRIO), pre-specified adverse events included:

- All-cause mortality
- Hypertensive emergency resulting in hospitalization
- Hospitalization for heart failure
- Stroke, transient ischemic attack, cerebrovascular accident
- Acute myocardial infarction (STEMI/non-STEMI)
- Any coronary revascularization
- End stage renal disease; the need for permanent renal replacement therapy (i.e. the need for dialysis); doubling of plasma creatinine

- Any renal artery complication requiring intervention (e.g. dissection; perforation)
- Major access site complications requiring intervention
- Significant embolic events resulting in end organ damage
- Procedure-related pain lasting for > 2 days
- Acute renal injury
- Significant renal artery stenosis (>50% diameter stenosis) diagnosed by duplex ultrasound and confirmed by renal CTA/MRA or diagnosed/confirmed by renal CTA/MRA
- Severe (>75%) renal stenosis as diagnosed by duplex ultrasound and confirmed by renal CTA/MRA or as diagnosed and confirmed by renal CTA/MRA
- Need for renal artery angioplasty or stenting

*Primary Safety Endpoint*

RADIANCE II included the primary safety endpoint consisting of a patient level composite of the incidence of Major Adverse Events (MAE) within 30 days and at 6 months (there was no pre-specified safety endpoint for SOLO and TRIO).

The 30-day post randomization safety event rate consisted of the incidence of:

- All-cause mortality
- New onset (acute) end-stage renal disease (eGFR< 15 mL/min/m2 or need for renal replacement therapy)
- Significant embolic event resulting in end-organ damage (e.g., kidney/bowel infarct, lower extremity ulceration or gangrene, or doubling of serum creatinine)
- Renal artery perforation requiring an invasive intervention
- Renal artery dissection requiring an invasive intervention
- Major vascular complications (e.g., clinically significant groin hematoma, arteriovenous fistula, pseudoaneurysm) requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion (requiring more than 2 units of packed red blood cells within any 24-hr period during the first 7 days post randomization)
- Hospitalization for hypertensive or hypotensive crisis
- Hospitalization for major cardiovascular- or hemodynamic- related events (e.g. HF; MI; Stroke)
- New onset Stroke,
- New onset Myocardial Infarction.

The 6-month post randomization safety event rate consisted of the incidence of renal artery stenosis (>70% diameter stenosis) confirmed by CT or MR angiography

The MAE rate was compared to a pre-specified performance goal of 9.8%, derived from a review of adverse events in studies of renal artery angioplasty or stenting, estimated to be 14.2% (ranging from 9.5 to 23.2%).

To assess the safety across the RADIANCE studies, a Pooled Safety Analysis was performed. The analysis consisted of an MAE composite endpoint consisting of 30-day

events and 6-month renal artery stenosis (based on the RADIANCE II study definition), and an assessment of 12-month CTA/MRA imaging studies. The events for the MAE composite endpoint were adjudicated by the RADIANCE II Clinical Events Committee (CEC) run by Cardiovascular Research Foundation (CRF). All 12-month CTA/MRA were assessed by the CRF Imaging Core Lab to ensure a consistent evaluation of the renal arteries post-procedure.

### 13.2.2. **Effectiveness**

The primary effectiveness endpoint was the reduction in the average daytime ambulatory systolic BP (SBP) at 2-months post procedure. The study success criterion was a statistically significant difference in the decrease in average daytime ambulatory SBP from baseline to 2-months between uRDN treatment and Sham groups.

The mean difference between randomized groups for the change in daytime ambulatory systolic BP at 2 months post-procedure was compared via a linear regression (ANCOVA) model adjusted for subjects' baseline daytime ambulatory systolic BP. Statistical analyses were performed on each study at a two-sided 0.05 alpha level.

In SOLO and TRIO, a value of zero was used for the reduction in BP in the intention-to-treat (ITT) analysis for patients missing the 2-month follow-up BP value. In RADIANCE II, multiple imputation was used for BP in the ITT analysis for patients missing the 2-month follow-up BP value.

In all RADIANCE studies, for patients that met the protocol defined "High BP Action" changes, their last BP measurement prior to the medication change was used in calculating the reduction in BP in the analysis.

The primary effectiveness analyses were performed on the ITT Cohort, which was comprised of all randomized patients regardless of whether they received the assigned study treatment. Additional effectiveness analyses were conducted on the following:

- Per-Protocol (PP) population – all randomized patients with successful treatment delivery (defined as a minimum of 2 emissions bilaterally) and who were free from major protocol deviations.

- Complete ABP (CA) population – all randomized patients with ABP values at both baseline and follow-up.

### 13.2.3. **Secondary Effectiveness**

The following secondary effectiveness endpoints were evaluated:

<u>RADIANCE-HTN SOLO and TRIO</u>:

- Reduction in average 24-hr/night-time ambulatory SBP at 2 months post-procedure (2 assessments)
- Reduction in average daytime/24-hr/night-time ambulatory DBP at 2 months-post procedure (3 assessments)

RADIANCE II:

- Reduction in average 24-hr ambulatory SBP at 2 months post-procedure (1 assessment)
- Reduction in average 24-hr/daytime ambulatory DBP at 2 months post-procedure (2 assessments)
- Reduction in average home SBP and DBP at 2 months post-procedure (2 assessments)
- Reduction in average office SBP and DBP at 2 months post-procedure (2 assessments)

## Subjects studied

*RADIANCE-HTN SOLO*

A total of 804 subjects were consented and screened for eligibility into the SOLO Study. One hundred forty-six (146) subjects were randomized (74 uRDN; 72 Sham) from 21 centers in the United States and 18 in Europe. At the time of the database lock on August 22, 2022, 146 patients were available for the primary analyses, and 84 subjects had reached the 36-month post-randomization visit. Thirty-seven (37) patients originally randomized to Sham group have crossed over to uRDN treatment. Cross-over subjects restarted the required post-procedure follow-up schedule, and 34 are continuing to be followed. All other subjects have completed study participation. Subject accountability post randomization is shown in **Figure 1**.

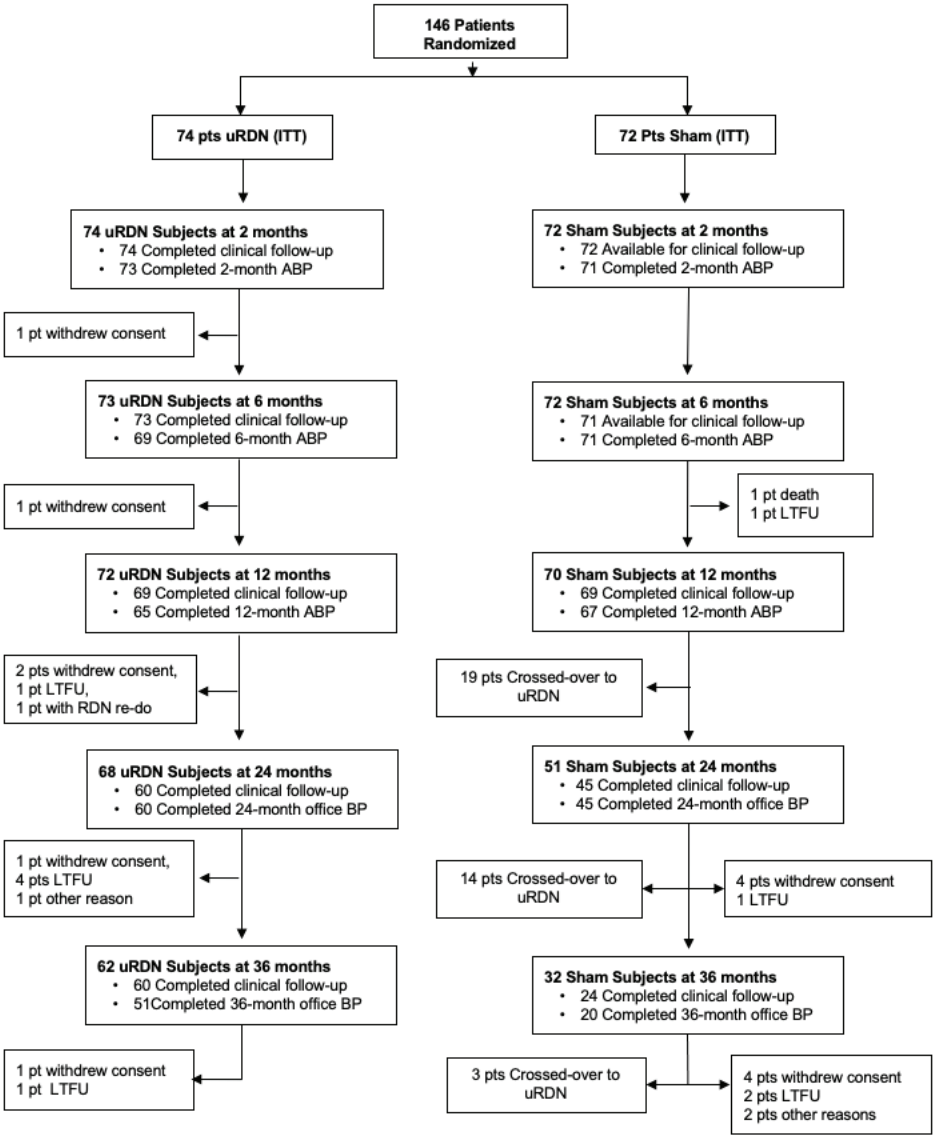



**Figure 1: SOLO Subject Accountability**

## *RADIANCE-HTN TRIO*

A total of 990 patients were consented and screened for eligibility into the TRIO Study. One hundred thirty-six (136) subjects were randomized (69 uRDN; 67 Sham) from 28 sites in the US and 25 sites in Europe. At the time of the database lock on August 22, 2022, 78 patients were available for analysis at the 24-month post-randomization visit. Follow-up is on-going. Twenty-one (21) Sham subjects crossed over to treatment to date. Cross over subjects restarted the required post-procedure follow-up schedule. Subject accountability post randomization is shown in **Figure 2.**

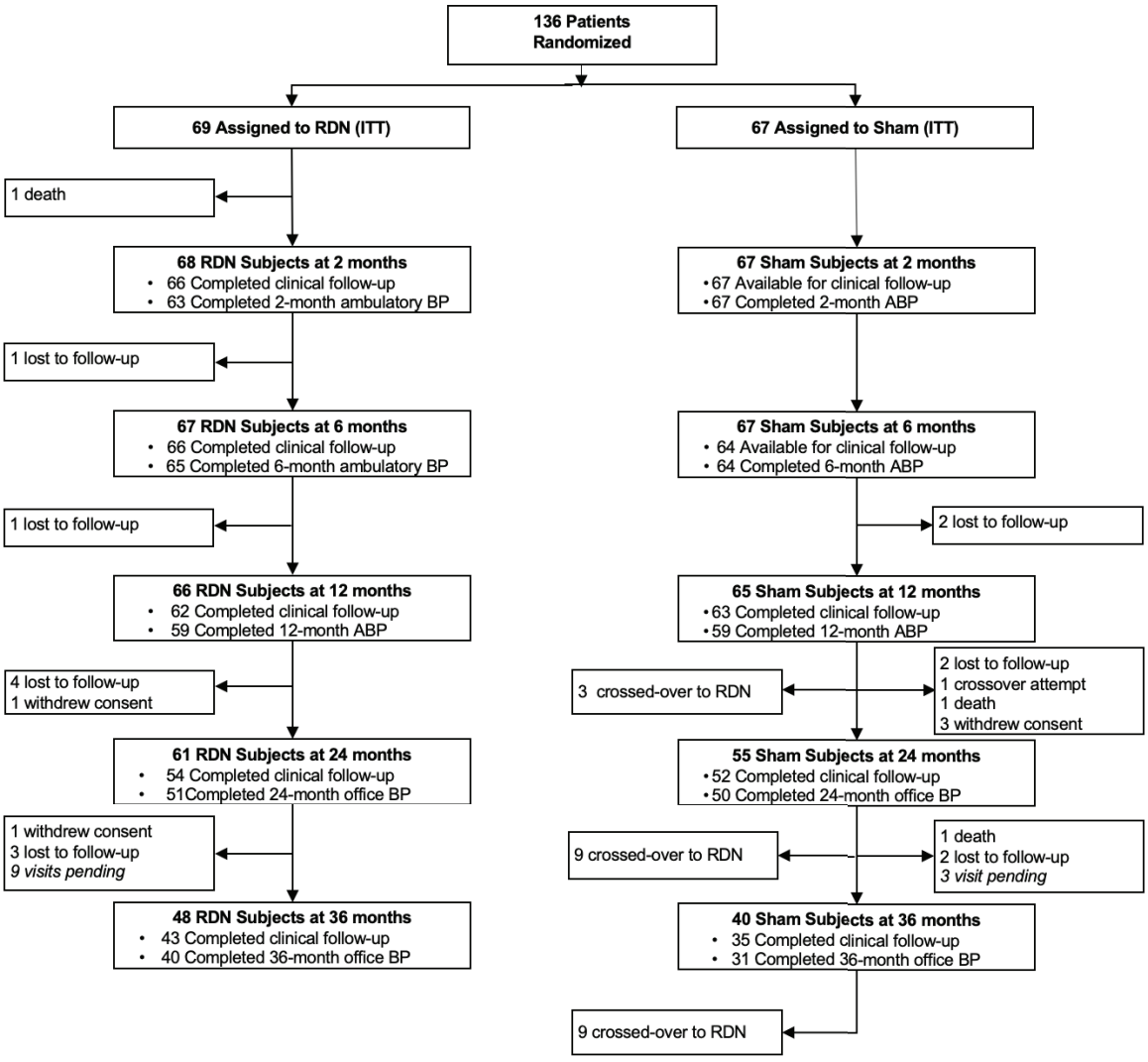



**Figure 2: TRIO Subject Accountability**

*RADIANCE II*

A total of 1,038 patients were consented and screened for eligibility. Two hundred twenty-four (224) subjects were randomized (150 uRDN: 74 Sham) at 37 centers in the United States and 24 in Europe. At the time of the database lock on August 13, 2022, all patients had completed their two- month post-procedure visit. An updated database lock was performed on February 23, 2023, at which time all patients had completed their 6-month follow up visit. Twenty-eight patients originally randomized to the Sham group have crossed over to treatment. Crossover subjects restarted the required post-procedure assessment schedule, and all are continuing to be followed. Subject accountability post-randomization is shown in **Figure 3.**

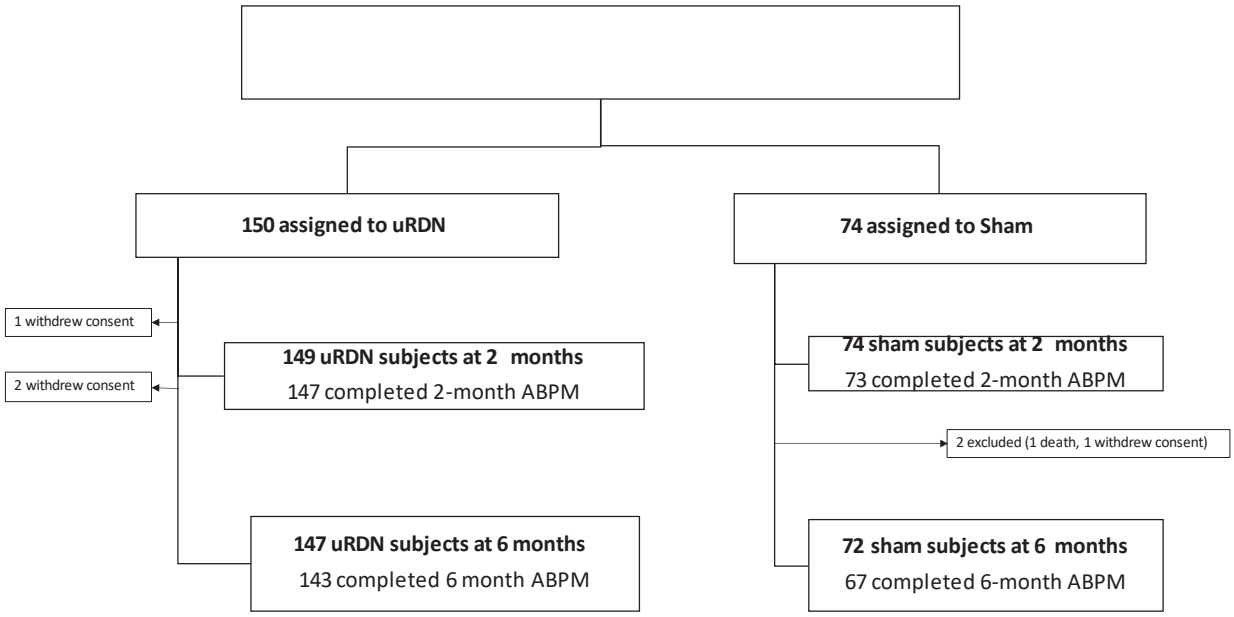



**Figure 3: RADIANCE II Subject Accountability**

### 13.2.4. Study Population Demographics and Baseline Parameters

**Table 5** and **Table 6** show baseline demographics and medical history, respectively, for RADIANCE study subjects.

The studies enrolled a majority of male patients with an average age in the mid 50's. Fifteen to 20% of patients self-identified as Black or African American.

**Table 5: Baseline Demographics, ITT, RDN vs Sham**

| | SOLO | | TRIO | | RADIANCE II | |
|---|---|---|---|---|---|---|
| Measure | Renal Denervation (n=74) | Sham Procedure (n=72) | Renal Denervation (n=69) | Sham Procedure (n=67) | Renal Denervation (n=150) | Sham Procedure (n=74) |
| Sex | | | | | | |
| Male | 62.1% (46 / 74) | 54.1% (39 / 72) | 81.1% (56 / 69) | 79.1% (53 / 67) | 68.6% (103 / 150) | 77% (57 / 74) |
| Female | 37.8% (28 / 74) | 45.8% (33 / 72) | 18.8% (13 / 69) | 20.9% (14 / 67) | 31.3% (47 / 150) | 22.9% (17 / 74) |
| Age | 54.4 ± 10.2 | 53.8 ± 10.0 | 52.3 ± 7.5 | 52.8 ± 9.1 | 55.1 ± 9.9 | 54.9 ± 7.9] |
| Race | | | | | | |
| American Indian or Alaska Native | 0.0% (0 / 74) | 0.0% (0 / 72) | 0.00% (0 / 68) | 1.52% (1 / 66) | 0% (0 / 150) | 0% (0 / 74) |
| Asian | 1.3% (1 / 74) | 0.0% (0 / 72) | 1.47% (1 / 68) | 1.52% (1 / 66) | 0.0% (0 / 150) | 1.3% (1 / 74) |
| Black | 16.2% (12 / 74) | 18.0% (13 / 72) | 20.59% (14 / 68) | 19.70% (13 / 66) | 14.0% (21 / 150) | 20.2% (15 / 74) |

| | SOLO | | TRIO | | RADIANCE II | |
|---|---|---|---|---|---|---|
| Measure | Renal Denervation (n=74) | Sham Procedure (n=72) | Renal Denervation (n=69) | Sham Procedure (n=67) | Renal Denervation (n=150) | Sham Procedure (n=74) |
| Caucasian | 81.0% (60 / 74) | 72.2% (52 / 72) | 66.18% (45 / 68) | 77.27% (51 / 66) | 76.0% (114 / 150) | 75.6% (56 / 74) |
| Hispanic or Latino | 1.3% (1 / 74) | 5.5% (4 / 72) | 7.35% (5 / 68) | 0.00% (0 / 66) | 10.0% (15 / 150) | 2.7% (2 / 74) |
| Native Hawaiian or other Pacific Islander | 0.0% (0 / 74) | 0.0% (0 / 72) | 0.00% (0 / 68) | 0.00% (0 / 66) | 0.00% (0 / 150) | 0.00% (0 / 74) |
| Other/Mixed Race | 0.0% (0 / 74) | 4.17% (3 / 72) | 4.41% (3 / 68) | 0.00% (0 / 66) | 10.00% (15 / 150) | 2.70% (2 / 74) |
| BMI | 29.9 ± 5.9 | 29.0 ± 5.0 | 32.8 ± 5.7 | 32.6 ± 5.4 | 30.1 ± 5.2 | 30.6 ± 5.2 |
| Abdominal circumference (cm) | 101.5 ± 14.2 | 98.5 ± 15.1 | 109.4 ± 15.5 | 109.2 ± 12.9 | 102.4 ± 12.3 | 104.3 ± 13.1 |
| Office Systolic blood pressure (mmHg)* - Screening | 142.6 ± 14.7 | 144.6 ± 15.9 | 161.9 ± 15.5 | 163.6 ± 16.8 | 155.8 ± 11.1 | 154.3 ± 10.6 |
| Office Diastolic blood pressure (mmHg)* - Screening | 92.3 ± 10.1 | 93.6 ± 8.3 | 105.1 ± 11.6 | 103.3 ± 12.7 | 101.3 ± 6.7 | 99.1 ± 5.6 |
| Pulse* - Screening | 73.2 ± 12.4 | 73.2 ± 12.4 | 74.5 ± 11.0 | 77.6 ± 12.9 | 74.1 ± 12.0 | 73.6 ± 11.9 |
| Pulse* - Baseline | 72.0 ± 12.1 | 72.6 ± 12.3 | 76.9 ± 12.2 | 82.0 ± 12.1 | 74.3 ± 11.3 | 72.5 ± 11.5 |

## Baseline Medical History

Medical history of randomized subjects is shown in **Table 6**.

### Table 6: Baseline Medical History and Comorbidities (ITT)

| | SOLO | | TRIO | | RADIANCE II | |
|---|---|---|---|---|---|---|
| **Measure** | **Renal Denervation (n=74)** | **Sham Procedure (n=72)** | **Renal Denervation (n=69)** | **Sham Procedure (n=67)** | **Renal Denervation (n=150)** | **Sham Procedure (n=74)** |
| History of Hypertension | 100% (74 / 74) | 100% (72 / 72) | 100% (69 / 69) | 100% (67 / 67) | 100% (150 / 150) | 100% (74 / 74) |
| Hospitalization for hypertensive crisis | 2.7% (2 / 74) | 2.7% (2 / 72) | 21.7% (15 / 69) | 16.4% (11/67) | 6% (9 / 150) | 4% (3 / 74) |
| Peripheral vascular disease | 2.7% (2 / 74) | 0% (0 / 72) | 1.4 %(1 / 69) | 4.48% (3 / 67) | 0% (0 / 150) | 0% (0 / 74) |
| Primary pulmonary hypertension | 0.0% (0 / 74) | 0.0% (0 / 72) | 0.0% (0 / 69) | 0.0% (0/67) | 0.0% (0 / 150) | 0.0% (0 / 74) |
| Cerebrovascular event(s) | 0.0% (0 / 74) | 0.0% (0 / 72) | 8.7% (6 / 69) | 5.9% (4 /67) | 0.0% (0 / 150) | 0.0% (0 / 74) |
| Type II Diabetes | 2.7% (2 / 74) | 6.9% (5 / 72) | 30.4% (21 / 69) | 25.3% (17 /67) | 6.0% (9 / 150) | 8.1% (6 / 74) |
| Sleep Apnea | 8.1% (6 / 74) | 11.1% (8 / 72) | 27.5% (19 / 69) | 16.4% (11/67) | 14.0% (21 / 150) | 17.5% (13/74) |
| Chronic kidney disease | 0.00% (0 / 74) | 0.00% (0 / 72) | 4.35% (3 / 69) | 5.97% (4 / 67) | 5.33% (8 / 150) | 4.05% (3 / 74) |
| Ischemic heart disease | 0.00% (0 / 74) | 0.00% (0 / 72) | 2.90% (2 / 69) | 1.49% (1 / 67) | 0.00% (0 / 150) | 0.00% (0 / 74) |
| Document episodes of Angina | 0.00% (0 / 74) | 0.00% (0 / 72) | 5.80% (4 / 69) | 1.4% (1 / 67) | 0.6% (1 / 150) | 2.70% (2 / 74) |
| Prior myocardial infarction | 0.0% (0 / 74) | 0.0% (0 / 72) | 2.9% (2 / 69) | 5.9% (4 / 67) | 0.0% (0 / 150) | 0.0% (0 / 74) |

| | SOLO | | TRIO | | RADIANCE II | |
|---|---|---|---|---|---|---|
| Measure | Renal Denervation (n=74) | Sham Procedure (n=72) | Renal Denervation (n=69) | Sham Procedure (n=67) | Renal Denervation (n=150) | Sham Procedure (n=74) |
| History of heart failure | 0.0% (0 / 74) | 0.0% (0 / 72) | 1.4% (1 / 69) | 4.4% (3 / 67) | 0.6% (1 / 150) | 0.0% (0 / 74) |
| Bradycardia | 1.3% (1 / 74) | 2.7% (2 / 72) | 1.4% (1 / 69) | 0.0% (0 / 67) | 1.3% (2 / 150) | 4.0% (3 / 74) |
| Atrial arrhythmias | 0.0% (0 / 74) | 0.0% (0 / 72) | 0.0% (0 / 69) | 4.4% (3 / 67) | 0.0% (0 / 67) | 0.0% (0 / 28) |
| Prior atrial ablation | 0.0% (0 / 74) | 0.0% (0 / 72) | 0.0% (0 / 69) | 1.4% (1 / 67) | 0.6% (1 / 150) | 0.0% (0 / 74) |
| Ventricular arrhythmias | 0.0% (0 / 74) | 0.0% (0 / 72) | 1.4% (1 / 69) | 2.9% (2 / 67) | 0.0% (0 / 150) | 1.3% (1 / 74) |

### Treatment and Procedural characteristics

The treatment and procedural characteristics of the subjects treated in the RADIANCE studies are shown below in **Table 7**. The majority of patients were treated under conscious sedation (83% in SOLO, 63% in TRIO, and 76% in RADIANCE II). The remaining patients were treated under general anesthesia or monitored anesthesia care due to regional hospital practice (OUS). Procedure success in the studies was defined as delivery of a minimum of two emissions bilaterally, which was achieved in greater than 96% of uRDN subjects across the three studies. In four patients (2 SOLO, 1 TRIO, 1 RADIANCE II), zero or 1 renal artery was treated at time of procedure due to difficulty accessing the renal artery.

**Table 7: Treatment and Procedure Characteristics**

| | SOLO (N=74) | TRIO (N=69) | RADIANCE II (N=150) |
|---|---|---|---|
| Procedure time (sheath removal - sheath insertion) (min) | 71.9 ± 23.2 | 83.0 | 76.7 ± 25.2 |
| Contrast volume (cc) | 138.5 ± 66.6 | 176.9 ± 77.0 | 135.7 ± 67.4 |
| Fluoroscopy exposure (minutes) | 13.7 ± 6.8 | 19.0 ± 11.5 | 15.9 ± 8.6 |
| Total Number of Emissions[1] | 5.3 ± 1.1 | 5.8 ± 1.2 | 5.6 ± 1.0 |
| Total Number of Subjects with Accessory and/or Proximal Side Branch Emissions | 9/74 (12.1%) | 17/69 (24.6%) | 30/150 (20.0%) |
| Treatment successfully delivered (minimum 2 emissions bilateral) | 71/74 (95.9%) | 67/69 (97.1%) | 148/150 (98.6%) |
| Total Emission Time (seconds)[1] | 37.4 ± 8.0 | 40.7 ± 8.1 | 38.9 ± 7.3 |

Data displayed as either n/N (%), Mean±SD, or Median [IQR] (Minimum, Maxiumum).
[1]Procedure time was defined as the time from arterial sheath placement to sheath removal.
[2]Includes main renal and accessory artery emissions.

## 14. Clinical Study Safety and Effectiveness Results

### 14.1. Safety Results

The safety analysis was based on all available data on enrolled subjects in each of the three studies at the time of the database lock (August 13, 2022 for SOLO and TRIO, and February 23, 2023 for RADIANCE II) and included a pooled cohort of 367 uRDN-treated patients with 30-day and 6-month evaluations.

*Primary Safety Results*

In RADIANCE II, the primary safety endpoint was defined as a patient level composite of the incidence of the Major Adverse Events (MAE) at 30 days and at 6-months post-randomization. No events met the definition of an MAE in either uRDN or Sham patients in RADIANCE II. The composite MAE rate was 0% (95% CI 0.0% - 1.63%). Based on the performance goal of 9.8%, the primary safety endpoint was met (0.0% vs 9.8%, **Table 8)**.

The pooled safety analysis was conducted on all uRDN-treated patients enrolled in the RADIANCE studies. As of August 8, 2022, 367 subjects were treated with the Paradise System and received at least one ultrasound emission. These 367 patients were randomized to renal denervation (n=290) during their Index procedure or crossed over to uRDN treatment from the Sham group (n=77). Six (6) events in 367 patients met the definition of an MAE per the independent CEC. The MAE composite rate was 1.1% with a 95% confidence interval of 0.3% - 2.77% (**Table 9**).

**Table 8. Primary Safety Results (ITT)**

| | MAE Rate | 95% CI | Performance Goal | Result |
|---|---|---|---|---|
| RADIANCE-II | 0.0% | 0 - 1.63% | 9.8% | Met |
| Pooled uRDN subjects | 1.1% | 0.3% - 2.77% | -- | -- |

The Pooled safety analysis with individual events is reported in **Table 9**.

**Table 9. Pooled Primary Safety Endpoint for uRDN-treated (Initial Procedure and Crossover)**

| | SOLO | | TRIO | | RADIANCE-II | | |
|---|---|---|---|---|---|---|---|
| **Number of Events (% Subjects with Event)** | **Initial** | **Crossover** | **Initial** | **Crossover** | **Initial** | **Crossover** | **Combined** |
| **30-day events** | | | | | | | |
| All-cause mortality | 0 | 0 | 1 (1.4%) | 1 (4.8%) | 0 | 0 | 2 (0.5%) |
| New onset (acute) end-stage renal disease (eGFR< 15 mL/min/$m^2$ or need for renal replacement therapy) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Significant embolic event resulting in end-organ damage (e.g., kidney/bowel infarct, lower extremity ulceration or gangrene, or doubling of serum creatinine) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Renal artery perforation requiring an invasive intervention | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Renal artery dissection requiring an invasive intervention | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Number of Events (% Subjects with Event) | SOLO | | TRIO | | RADIANCE-II | | Combined |
|---|---|---|---|---|---|---|---|
| | Initial | Crossover | Initial | Crossover | Initial | Crossover | |
| Major vascular complications (e.g., clinically significant groin hematoma, arteriovenous fistula, pseudoaneurysm) requiring surgical repair, interventional procedure, thrombin injection, or blood transfusion (requiring more than 2 units of packed red blood cells within any 24-hr period during the first 7 days post randomization) | 0 | 0 | 2 (1.4%) | 0 | 0 | 0 | 2 (0.3%) |
| Hospitalization for hypertensive or hypotensive crisis | 0 | 0 | 1 (1.4%) | 0 | 0 | 0 | 1 (0.3%) |
| Hospitalization for major cardiovascular- or hemodynamic- related events (e.g., HF; MI; Stroke) | 1 (1.4%) | 0 | 0 | 0 | 0 | 0 | 1 (0.3%) |
| New onset Stroke | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| New onset Myocardial Infarction | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **6-month events** | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| New onset renal artery stenosis of more than 70%, confirmed by CT or MR angiography | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Overall Composite*** | 1 (1.4%) | 0 | 4 (2.9%) | 1 (4.8%) | 0 | 0 | **6 (1.1%) Exact 95% CI 0.30% - 2.77%** |

## 14.2. Adverse effects in the PMA clinical studies:

Specific events of interest pre-specified in the study protocol summarized by treatment group (based on the percentage of subjects experiencing events) (**Table 10**)

Adverse Device Events (ADEs) and Serious Adverse Device Events (SADEs) are reported in **Table 11**, **Table 12** and **Table 13** and for all three studies.

In the SOLO Study, there were few post-procedure SAEs and SADEs, 1.4% and 3.4%, respectively. ADEs within the first 30 days were reported in 42% of randomized uRDN and Sham patients, with the majority associated with vascular access site complications (hematoma, swelling, pain). ADEs were primarily procedure-related, and no events were classified as only device-related based on assessment by the treating physician (**Table 11**).

In the TRIO Study, there were few serious events during the post-procedure period – 3% rate of SAE and 3% rate of SADE. ADEs were reported in 41% of the randomized population in both the uRDN and Sham groups, with the majority associated with vascular access site complications (hematoma, pain) and self-limited vasospasm. ADEs were primarily procedure-related (e.g., access site complications), and not device-related, based on assessment by the treating physician (**Table 12**).

In the RADIANCE II Study, there were few serious events during the post-procedure period – 9% rate of SAE and 5% rate of SADE. ADEs were reported in 56% of the randomized population in both the uRDN and Sham groups, with the majority associated with vascular access site complications (hematoma, pain), back pain, and self-limited vasospasm. ADEs were primarily procedure-related (e.g., access site complications), and not device-related, based on assessment by the treating physician (**Table 13**)

**Table 10: Prespecified Safety Events (Randomized Subjects) – SOLO, TRIO, and RADIANCE-II**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Number of Events (% Subjects with Event) 95%CI[1]** | **RDN (n=74)** | **Sham (n=72)** | **RDN (n=69)** | **Sham (n=67)** | **RDN (n=150)** | **Sham (n=74)** |
| All-cause mortality | 0 (0%) | 1 (1.39%) | 1 (1.45%) | 1 (1.49%) | 1 (0.67%) | 1 (1.35%) |
| Hypertensive emergency resulting in hospitalization | 1 (1.35%) | 2 (1.39%) | 3 (4.35%) | 2 (2.99%) | 1 (0.67%) | 1 (1.35%) |
| Hospitalization for heart failure | 0 (0%) 0.00% - 4.86% | 0 (0%) 0.00% - 4.99% | 4 (1.45%) 0.04% - 7.81% | 0 (0.00%) 0.00% - 5.36% | 0 (0.00%) 0.00% - 2.43% | 0 (0.00%) |
| Stroke, transient ischemic attack, cerebrovascular accident | 1 (1.35%) | 1 (1.39%) | 0 (0%) | 2 (2.99%) | 2 (1.33%) | 1 (1.35%) |
| Acute myocardial infarction (STEMI/non-STEMI) | 0 (0%) | 1 (1.39%) | 2 (2.90%) | 1 (1.49%) | 0 (0%) | 0 (0%) |
| Any coronary revascularization | 0 (0%) | 0 (0%) | 2 (2.90%) | 1 (1.49%) | 2 (1.33%) | 0 (0%) |
| End stage renal disease, the need for permanent renal replacement therapy (i.e., the | 0 (0%) | 0 (0%) | 2 (1.45%) | 0 (0%) | 0 (0%) | 0 (0%) |

| | SOLO | | TRIO | | RADIANCE II | |
|---|---|---|---|---|---|---|
| **Number of Events (% Subjects with Event) 95%CI[1]** | **RDN (n=74)** | **Sham (n=72)** | **RDN (n=69)** | **Sham (n=67)** | **RDN (n=150)** | **Sham (n=74)** |
| need for dialysis); doubling of plasma creatinine | | | | | | |
| Any renal artery complication requiring intervention (e.g., dissection; perforation) | 0 (0%) 0.00% - 4.86% | 0 (0%) 0.00% - 4.99% | 0 (0%) 0.00% - 5.21% | 0 (0%) 0.00% - 5.36% | 0 (0%) 0.00% - 2.43% | 0 (0%) |
| Major access site complications requiring intervention | 0 (0%) | 0 (0%) | 1 (1.45%) | 1 (1.49%) | 1 (0.67%) | 0 (0%) |
| Significant embolic events resulting in end organ damage | 0 (0%) | 0 (0%) | 1 (1.45%) | 1 (1.49%) | 1 (0.67%) | 1 (1.35%) |
| Procedure-related pain lasting for > 2 days | 12 (16.22%) | 4 (5.56%) | 12 (17.39%) | 10 (14.93%) | 40 (25.33%) | 13 (16.22%) |
| Acute renal injury | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Significant (>50%) and severe (>75%) new onset renal stenosis diagnosed by duplex ultrasound & confirmed by renal CTA/ MRA or diagnosed/confirmed by renal CTA/MRA | 1 (1.35%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Need for renal artery angioplasty or stenting | 1 (1.35%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

Table excludes events occurring post-crossover in subjects who cross-over.
See separate tables for events occurring post cross-over in cross-over subjects.
[1]Exact 95% confidence interval.

## Table 11: Adverse Device and Serious Adverse Device Effects by Term and Treatment Group (Randomized Subjects) - SOLO

| | Renal Denervation (n=74) | | | |
|---|---|---|---|---|
| | Adverse Device Event | | Serious Adverse Device Event | |
| **Event type** | **# Events** | **% Subjects** | **# Events** | **% Subjects** |
| Abdominal pain | 1 | 1.35 % | 0 | 0.00 % |
| Angina pectoris | 1 | 1.35 % | 0 | 0.00 % |
| Asthenia | 1 | 1.35 % | 0 | 0.00 % |
| Atrial fibrillation | 0 | 0.00 % | 1 | 1.35 % |
| Atrioventricular block - Drug therapy | 0 | 0.00 % | 1 | 1.35 % |
| Back pain | 4 | 5.41 % | 0 | 0.00 % |
| Bradycardia | 2 | 2.70 % | 0 | 0.00 % |
| Bradycardia - Drug therapy | 0 | 0.00 % | 2 | 2.70 % |
| Contrast media allergy | 1 | 1.35 % | 0 | 0.00 % |
| Dizziness postural | 0 | 0.00 % | 0 | 0.00 % |
| Endotracheal intubation complication | 1 | 1.35 % | 0 | 0.00 % |
| Haematuria | 0 | 0.00 % | 0 | 0.00 % |
| Headache | 1 | 1.35 % | 0 | 0.00 % |
| Hypotension | 1 | 1.35 % | 0 | 0.00 % |
| Hypotension - Orthostatic Hypotension | 2 | 2.70 % | 0 | 0.00 % |
| Post procedural complication | 0 | 0.00 % | 0 | 0.00 % |
| Presyncope - Drug therapy | 0 | 0.00 % | 1 | 1.35 % |
| Pyrexia | 1 | 1.35 % | 0 | 0.00 % |
| Renal artery stenosis | 1 | 1.35 % | 0 | 0.00 % |
| Sedation complication | 1 | 1.35 % | 0 | 0.00 % |
| Sinus tachycardia | 1 | 1.35 % | 0 | 0.00 % |
| Thrombophlebitis superficial | 0 | 0.00 % | 0 | 0.00 % |
| Vascular access site dissection | 1 | 1.35 % | 0 | 0.00 % |
| Vascular access site haematoma | 11 | 14.86 % | 0 | 0.00 % |
| Vascular access site pain | 13 | 17.57 % | 0 | 0.00 % |

| | Renal Denervation (n=74) | | | |
|---|---|---|---|---|
| | Adverse Device Event | | Serious Adverse Device Event | |
| Event type | # Events | % Subjects | # Events | % Subjects |
| Vascular access site swelling | 0 | 0.00 % | 0 | 0.00 % |
| Vasospasm | 15 | 20.27 % | 0 | 0.00 % |
| Vasospasm - Drug therapy | 5 | 6.76 % | 0 | 0.00 % |
| Vessel puncture site paraesthesia | 1 | 1.35 % | 0 | 0.00 % |
| Vomiting | 2 | 2.70 % | 0 | 0.00 % |

*Renal artery stenosis ~50% observed in imaging study; no treatment or intervention required

## Table 12: Adverse Device and Serious Adverse Device Effects by Term and Treatment Group (Randomized Subjects)- TRIO

| | Renal Denervation (n=69) | | | |
|---|---|---|---|---|
| | Adverse Device Event | | Serious Adverse Device Event | |
| Event type | # Events | % Subjects | # Events | % Subjects |
| Air embolism | 1 | 1.45 % | 0 | 0.00 % |
| Back pain | 4 | 5.80 % | 0 | 0.00 % |
| Bradycardia | 7 | 10.14 % | 0 | 0.00 % |
| Bradycardia - Drug therapy | 1 | 1.45 % | 0 | 0.00 % |
| Dizziness | 0 | 0.00 % | 0 | 0.00 % |
| Drug hypersensitivity - Morphine | 0 | 0.00 % | 0 | 0.00 % |
| Ecchymosis | 1 | 1.45 % | 0 | 0.00 % |
| Headache | 1 | 1.45 % | 0 | 0.00 % |
| Hematoma Infection | 0 | 0.00 % | 0 | 0.00 % |
| Hyperhidrosis | 0 | 0.00 % | 0 | 0.00 % |
| Hypotension | 4 | 5.80 % | 1 | 1.45 % |
| Infection | 0 | 0.00 % | 1 | 1.45 % |
| Inflammation | 1 | 1.45 % | 0 | 0.00 % |
| Investigation normal | 1 | 1.45 % | 0 | 0.00 % |
| Pain in extremity | 1 | 1.45 % | 0 | 0.00 % |
| Palpitations | 1 | 1.45 % | 0 | 0.00 % |
| Post procedural complication | 2 | 2.90 % | 0 | 0.00 % |
| Renal artery dissection | 1 | 1.45 % | 0 | 0.00 % |
| Renal artery thrombosis | 1 | 1.45 % | 0 | 0.00 % |
| Sedation complication - Drug therapy | 0 | 0.00 % | 1 | 1.45 % |
| Supraventricular tachycardia | 1 | 1.45 % | 0 | 0.00 % |
| Vascular access site bruising | 1 | 1.45 % | 0 | 0.00 % |
| Vascular access site dissection | 0 | 0.00 % | 0 | 0.00 % |
| Vascular access site haematoma | 10 | 14.49 % | 1 | 1.45 % |
| Vascular access site haemorrhage | 1 | 1.45 % | 0 | 0.00 % |
| Vascular access site pain | 9 | 13.04 % | 0 | 0.00 % |
| Vascular access site swelling | 1 | 1.45 % | 0 | 0.00 % |
| Vascular dissection | 1 | 1.45 % | 0 | 0.00 % |
| Vascular pseudoaneurysm | 0 | 0.00 % | 1 | 1.45 % |
| Vasospasm | 13 | 18.84 % | 0 | 0.00 % |
| Vasospasm - Drug therapy | 3 | 4.35 % | 0 | 0.00 % |
| Vomiting | 1 | 1.45 % | 0 | 0.00 % |

## Table 13: Adverse Device and Serious Adverse Device Effects by Term and Treatment Group (Randomized Subjects)- RADIANCE-II

| | Renal Denervation (n=150) | | | |
|---|---|---|---|---|
| | Adverse Device Event | | Serious Adverse Device Event | |
| Event type | # Events | % Subjects | # Events | % Subjects |
| Abdominal pain | 0 | 0.00 % | 0 | 0.00 % |
| Allergic reaction | 1 | 0.67 % | 0 | 0.00 % |
| Anesthesia intubation complication | 0 | 0.00 % | 0 | 0.00 % |
| Aortic dissection | 0 | 0.00 % | 1 | 0.67 % |
| Asystole | 1 | 0.67 % | 1 | 0.67 % |
| Back pain | 12 | 8.00 % | 0 | 0.00 % |
| Back pain aggravated | 1 | 0.67 % | 0 | 0.00 % |
| Blood in stool | 0 | 0.00 % | 1 | 0.67 % |
| Bradycardia | 3 | 2.00 % | 0 | 0.00 % |
| Catheter site pain | 0 | 0.00 % | 0 | 0.00 % |
| Chest pain | 1 | 0.67 % | 0 | 0.00 % |
| Contrast media allergy | 1 | 0.67 % | 0 | 0.00 % |
| Deep vein thrombosis leg | 0 | 0.00 % | 1 | 0.67 % |
| Diaphoresis | 1 | 0.67 % | 0 | 0.00 % |
| Dizziness aggravated | 1 | 0.67 % | 0 | 0.00 % |
| Fatigue | 1 | 0.67 % | 0 | 0.00 % |
| Femoral artery pseudoaneurysm | 1 | 0.67 % | 0 | 0.00 % |
| Flank pain | 0 | 0.00 % | 0 | 0.00 % |
| Groin pain | 8 | 5.33 % | 0 | 0.00 % |
| Headache | 1 | 0.67 % | 0 | 0.00 % |
| Hypertension aggravated | 2 | 1.33 % | 1 | 0.67 % |
| Hypertensive crisis | 0 | 0.00 % | 0 | 0.00 % |
| Hypotension | 1 | 0.67 % | 0 | 0.00 % |
| Inguinal pain | 4 | 2.67 % | 0 | 0.00 % |
| Low back pain | 6 | 4.00 % | 0 | 0.00 % |
| Low blood pressure | 1 | 0.67 % | 0 | 0.00 % |
| Orthostatic hypotension | 1 | 0.67 % | 0 | 0.00 % |
| Pain in leg | 1 | 0.67 % | 0 | 0.00 % |
| Pain loin | 3 | 2.00 % | 0 | 0.00 % |
| Palpitations | 0 | 0.00 % | 0 | 0.00 % |
| Post procedural bleeding | 1 | 0.67 % | 0 | 0.00 % |
| Post procedural complication | 0 | 0.00 % | 1 | 0.67 % |
| Post procedural dizziness | 1 | 0.67 % | 0 | 0.00 % |
| Post procedural headache | 4 | 2.67 % | 0 | 0.00 % |
| Post procedural nausea | 5 | 2.67 % | 1 | 0.67 % |
| Post procedural pain | 11 | 7.33 % | 0 | 0.00 % |
| Post procedural vomiting | 4 | 2.67 % | 0 | 0.00 % |
| Postoperative hip pain | 1 | 0.67 % | 0 | 0.00 % |
| Premature ventricular contractions | 0 | 0.00 % | 0 | 0.00 % |
| Renal colic | 1 | 0.67 % | 0 | 0.00 % |
| Shingles | 1 | 0.67 % | 0 | 0.00 % |
| Sinus bradycardia | 3 | 2.00 % | 0 | 0.00 % |
| Somnolence | 1 | 0.67 % | 0 | 0.00 % |
| Syncope | 0 | 0.00 % | 2 | 1.33 % |
| Throat pain | 1 | 0.67 % | 0 | 0.00 % |
| Vascular access site bleeding | 1 | 0.67 % | 0 | 0.00 % |
| Vascular access site bruising | 7 | 4.67 % | 0 | 0.00 % |
| Vascular access site haematoma | 13 | 8.67 % | 3 | 2.00 % |
| Vascular access site pain | 16 | 10.67 % | 0 | 0.00 % |
| Vascular access site swelling | 1 | 0.67 % | 0 | 0.00 % |
| Vascular injury | 3 | 1.33 % | 0 | 0.00 % |
| Vasospasm | 7 | 4.67 % | 0 | 0.00 % |
| Vertigo | 1 | 0.67 % | 0 | 0.00 % |
| Vessel puncture site induration | 0 | 0.00 % | 0 | 0.00 % |

*Renal Artery Stenosis Analysis*

For SOLO and TRIO, the per protocol assessment required renal duplex ultrasound (DUS) for all randomized subjects at 2-months and 6-months and for uRDN-treated subjects at 24-months and 36-months. CTA/MRA was required for all uRDN-treated subjects at 12 months. For RADIANCE II, the per protocol assessment required CTA/MRA for all randomized subjects at 6-months and for uRDN-treated subjects at 12-months.

Renal imaging results

Across all timepoints in SOLO and TRIO, 10-13% of renal DUS studies triggered an MRA/CTA evaluation. 118 of 119 (99%) of these CTA/MRA were within normal limits, defined as the absence of significant (>50%) or severe (>75%) renal artery stenosis.

*SOLO*

At 12 months, 65 of 69 eligible subjects had an MRA/CTA completed, and 98.5% (64 of 65) of evaluable CTA/MRA were within normal limits per site radiologists. Through 36 months, MRA/CTAs in 5 subjects showed mild narrowing (<50% diameter stenosis), most often at the renal artery ostium and not at the site of ultrasound emissions. There was one case of renal artery stenting at 5 months post-procedure due to progression of preexisting ostial stenosis (>30% diameter stenosis), which should have excluded this subject from enrollment. There were no cases of clinically significant renal artery stenosis at 12, 24, and 36 months and no renal artery interventions through 36 months.

*TRIO*

At 12 months, 54 of 62 subjects had CTA/MRAs, and 100% (54/54) of evaluable CTA/MRA were within normal limits. Through 24 months, MRA/CTAs in 3 subjects showed mild narrowing (<25% diameter stenosis) near the ostium and not at the site of emissions. There were no cases of clinically significant renal artery stenosis at 12 and 24 months and no renal artery interventions through 24 months.

*RADIANCE II*

At 6 months, based on core lab review of CTA/MRA imaging, there was no evidence of clinically significant renal artery stenosis in uRDN-treated patients, of which 98% had no measurable stenosis. The proportion of patients with any measureable renal artery narrowing was similar between uRDN and Sham groups.

*Pooled Analysis*

A total of 238 CTA/MRAs performed 12 months post-procedure were reviewed by the CRF Imaging Core Lab (**Figure 4**). Ninety six percent (96%) had no evidence of any renal artery narrowing (Figure 4). There were no subjects with renal artery stenosis (>70% diameter stenosis).

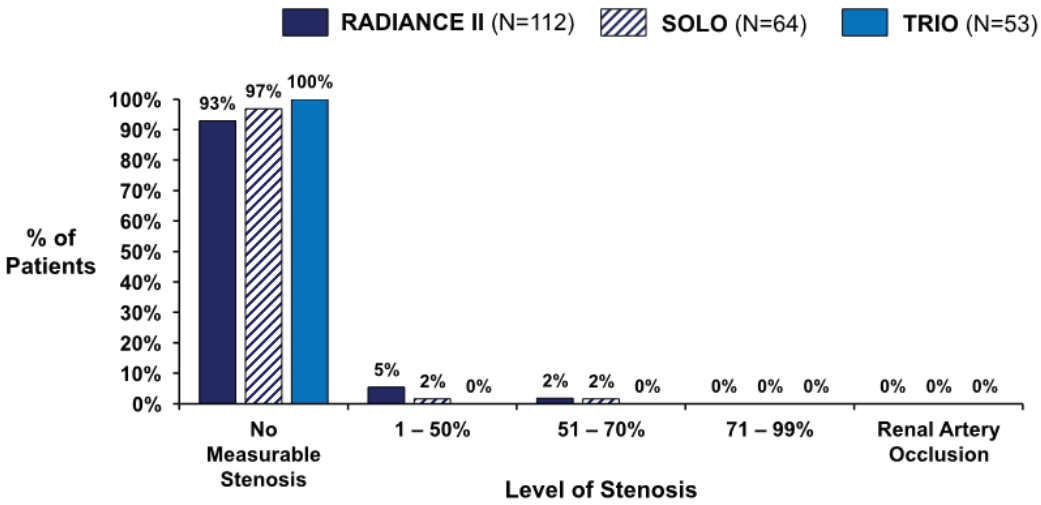



**Figure 4: Pooled safety analysis at 12 months**

*Renal Function*

Renal function was assessed by estimated glomerular filtration rate (eGFR), which was calculated from serum creatinine at various time points in all 3 trials. 12-month eGFR data and serum creatinine were available for the SOLO and TRIO trials. Table 14 shows renal function results for the SOLO trial, which are similar to the TRIO results. The mean change in eGFR at 12 months in uRDN subjects was –0.99 ml/min and was +3.40 in Sham subjects, with a mean difference of 3.79. Statistically significant differences in renal function are not necessarily clinically significant.

**Table 14: Renal Function at 12 months**

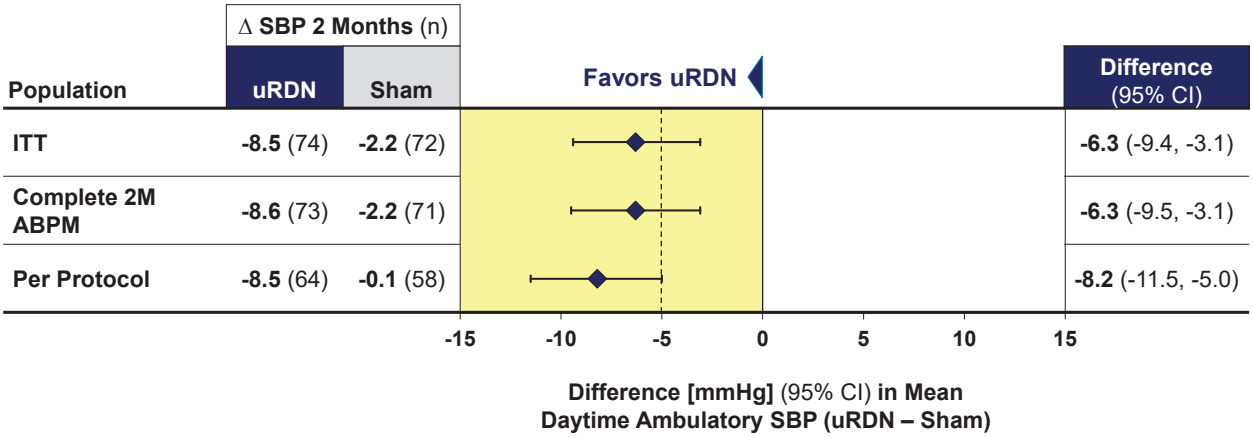
| | uRDN (n = 68) | | | Sham (n = 67) | | | Baseline Adjusted | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | 12 months | Change | Baseline | 12 months | Change | Mean Difference (95% CI) (RDN - Sham)[1] | p-value |
| eGFR | 84.46 ± 16.47 | 83.47 ± 14.61 | -0.99 ± 11.18 | 82.23 ± 15.79 | 85.63 ± 16.99 | 3.40 ± 11.53 | -3.79 (-7.40, -0.19) | 0.0391 |
| Serum Creatinine | 0.90 ± 0.18 | 0.90 ± 0.18 | 0.01 ± 0.11 | 0.90 ± 0.18 | 0.87 ± 0.17 | -0.03 ± 0.10 | 0.04 (0.00, 0.07) | 0.0326 |

## 14.3. Primary Effectiveness Endpoint

The Primary effectiveness endpoint for the three studies was the difference in average daytime ambulatory systolic BP between uRDN treatment with the Paradise System and Sham control (renal angiogram) from baseline to 2-months post procedure.

### *RADIANCE-HTN SOLO*

In the ITT cohort, SOLO showed a statistically significant ($p < 0.001$) reduction in daytime ambulatory SBP in the renal denervation group compared with Sham. Similar results were observed for the CA and PP populations (**Figure 5**).




ITT p<0.001
2M=2-month; ABPM=ambulatory blood pressure measurement; CI=confidence interval; ITT=intention-to-treat; SBP=systolic blood pressure; uRDN=ultrasound renal denervation.

**Figure 5: SOLO: Change from Baseline in Average Daytime Ambulatory SBP at 2 Months**

### RADIANCE-HTN TRIO

TRIO showed a reduction in daytime ambulatory SBP in the uRDN group compared with Sham group in patients with uncontrolled hypertension treated with a standardized triple antihypertensive pill (**Figure 6 and Figure 7**).

Because the residuals of ANCOVA results of the ITT population were non-normally distributed, the median difference was also evaluated, which yielded the same difference of -4.5 mmHg between groups in favor of the uRDN group. In the ITT population, 6 uRDN patients (8.7%) compared with 0 Sham patients (0%) had missing ABPM values at 2 months; thus, more patients in the uRDN group had their ABPM imputed at 2 months to baseline values (no change) due to missing data. Analyses of the CA and PP populations showed median between-group reductions of -5.8 mmHg and -5.4 mmHg, respectively, in favor of the uRDN group.. For TRIO, the fully BP-medication adherent* population (as demonstrated by medication testing) was also evaluated and showed a median between-group difference of -5.5 mmHg in favor of the uRDN group (**Figure 7**).

*Not a pre-specified endpointn. Subjects were considered “fully adherent” if presence of all prescribed drugs was verified via urine testing at both baseline and 2 months.

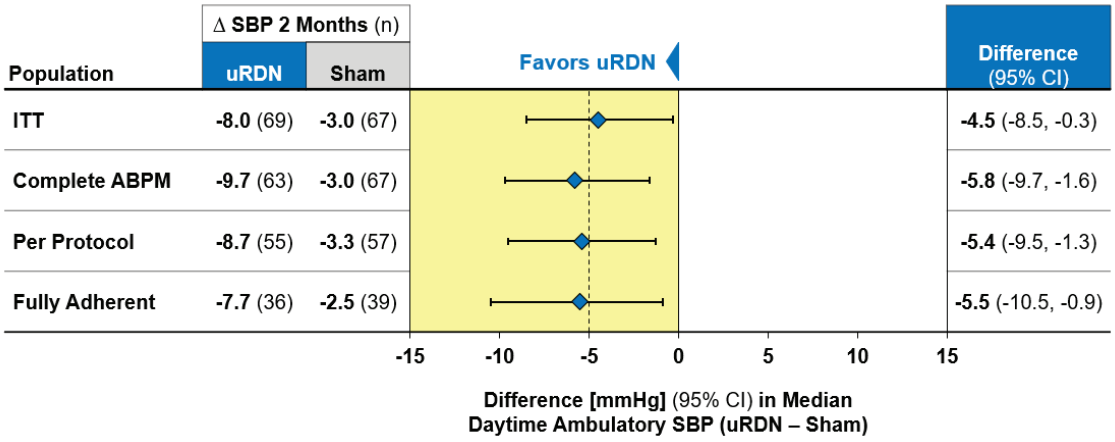



**Figure 6: TRIO: Mean Change from Baseline in Average Daytime Ambulatory SBP at 2 Months**

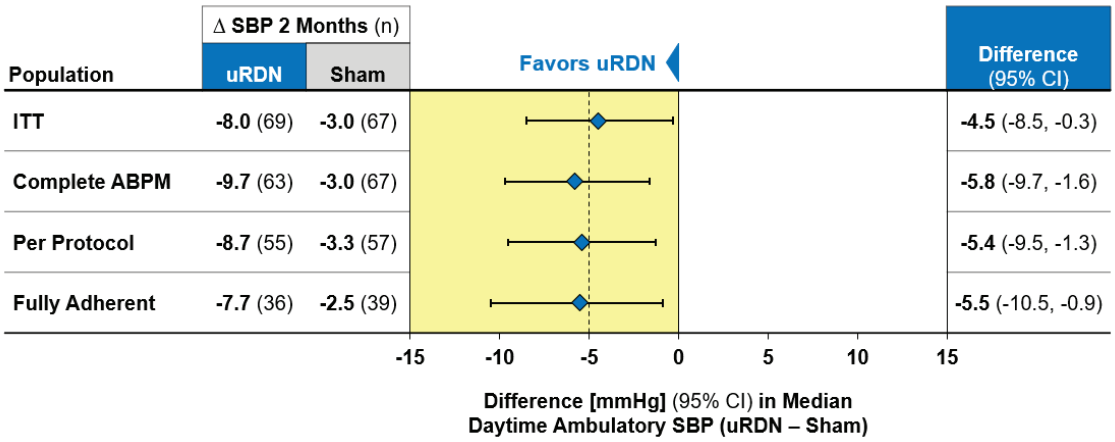
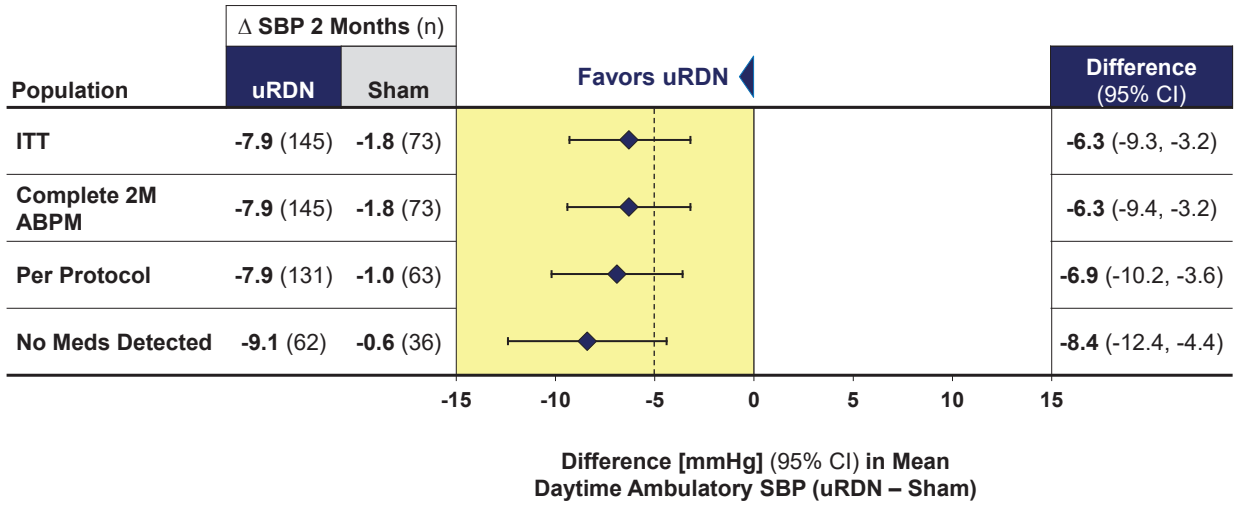



**Figure 7: TRIO: Median change from Baseline in Average Daytime Ambulatory SBP at 2 Months**

## RADIANCE II

In the ITT cohort, RADIANCE II showed a statistically significant (p <0.001) reduction in daytime ambulatory SBP in the uRDN group compared to Sham **(Figure 8** ). The results were similar in the CA and PP populations.




ITT p<0.001

"No Meds Detected" means subjects for whom urine testing showed a lack of adherence to medications at both baseline and 2 months

ABPM=ambulatory blood pressure measurement; CI=confidence interval; ITT=intention-to-treat; SBP=systolic blood pressure; uRDN=ultrasound renal denervation

**Figure 8: RADIANCE-II: Change from Baseline in Average Daytime Ambulatory SBP at 2 Months**

## 14.4. Secondary and Observational Effectiveness Endpoints

Secondary effectiveness endpoints specified for hierarchical testing were changes in average 24-hr ambulatory systolic BP, average 24-hr ambulatory diastolic BP, average night-time ambulatory systolic BP, average night-time ambulatory diastolic BP, and average daytime ambulatory diastolic BP at 2 months. Observational endpoints included home SBP and DBP and Office SBP and DBP for SOLO, TRIO, and RADIANCE-II. For TRIO, there were missing data for 6 out of 69 uRDN subjects. Results for these endpoints are shown in Table 15 (ITT population).

**Table 15: Secondary and Observational BP Effectiveness Endpoints at 2 months for ITT Population**

| | SOLO | | TRIO | | RADIANCE-II | |
|---|---|---|---|---|---|---|
| | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] |
| Daytime Ambulatory DBP (mmHg) | -2.6 (-4.6, -0.6) | 0.0118 (0.0060*) | -1.6 (-4.9, 1.7) | 0.3415 (0.1835*) | -3.9 [-5.6, -2.2] | <.0001 |
| 24 Hour Ambulatory SBP (mmHg) | -4.1 (-7.1, -1.2) | 0.0061 | -4.3 (-9.3, 0.7) | 0.0895 (0.0162*) | -6.2 [-9.1, -3.4] | <.0001 |
| 24 Hour Ambulatory DBP (mmHg) | -1.8 (-3.7, 0.2) | 0.0715 | -1.7 (-4.9, 1.5) | 0.3054 (0.1228*) | -4.1 [-5.7, -2.4] | <.0001 |

| | SOLO | | TRIO | | RADIANCE-II | |
|---|---|---|---|---|---|---|
| | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] | Mean Difference (95% CI) (uRDN - Sham)[1] | p-value[1] |
| Nighttime Ambulatory SBP** (mmHg) | -2.5 (-6.0, 0.9) | 0.1534 | -4.4 (-9.9, 1.2) | 0.1213 (0.0441*) | -5.8 [-9.0, -2.6] | 0.0004 (<.0001*) |
| Nighttime Ambulatory DBP** (mmHg) | -1.4 (-3.8, 1.0) | 0.2492 | -2.2 (-5.8, 1.4) | 0.2242 (0.0534*) | -4.2 [-6.3, -2.2] | <.0001 (<.0001*) |
| Home SBP** (mmHg) | -7.1 (-10.4, -3.8) | <.0001 (<.0001*) | -4.3 (-8.6, 0.0) | 0.0524 | -7.6 [-10.1, -5.0] | <.0001 |
| Home DBP** (mmHg) | -3.6 (-5.6, -1.5) | 0.0009 (<.0001*) | -2.6 (-5.2, 0.0) | 0.0527 | -4.3 [-5.9, -2.8] | <.0001 |
| Office SBP** (mmHg) | -6.5 (-11.3, -1.8) | 0.0073 (0.0007*) | -5.4 (-11.9, 1.1) | 0.1042 (0.0374*) | -5.4 [-9.0, -1.8] | 0.0035 |
| Office DBP** (mmHg) | -4.1 (-7.0, -1.3) | 0.0045 | -3.2 (-7.5, 1.1) | 0.1375 (0.1598*) | -2.3 [-4.9, 0.2] | 0.0755 |

[1] p-value from baseline adjusted ANCOVA. In the event that change from baseline in either cohort is non-normal, the p-value (*) from a baseline adjusted ANCOVA on the ranks (observed data) is also provided.

*24-Hour Ambulatory Systolic Blood Pressure*

Ambulatory systolic blood pressure curves at 2 months are shown in Figures 8 - 10. The uRDN group showed a greater mean decrease in SBP throughout the 24-hour period compared to Sham in all studies.

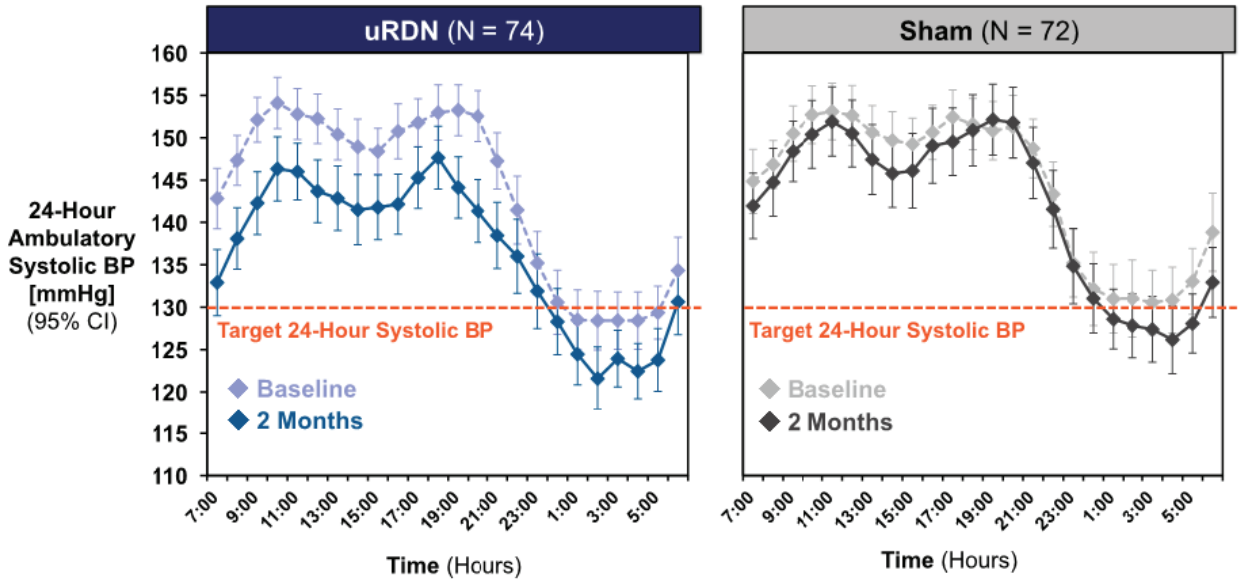



**Figure 9: SOLO 24-Hour Ambulatory SBP**

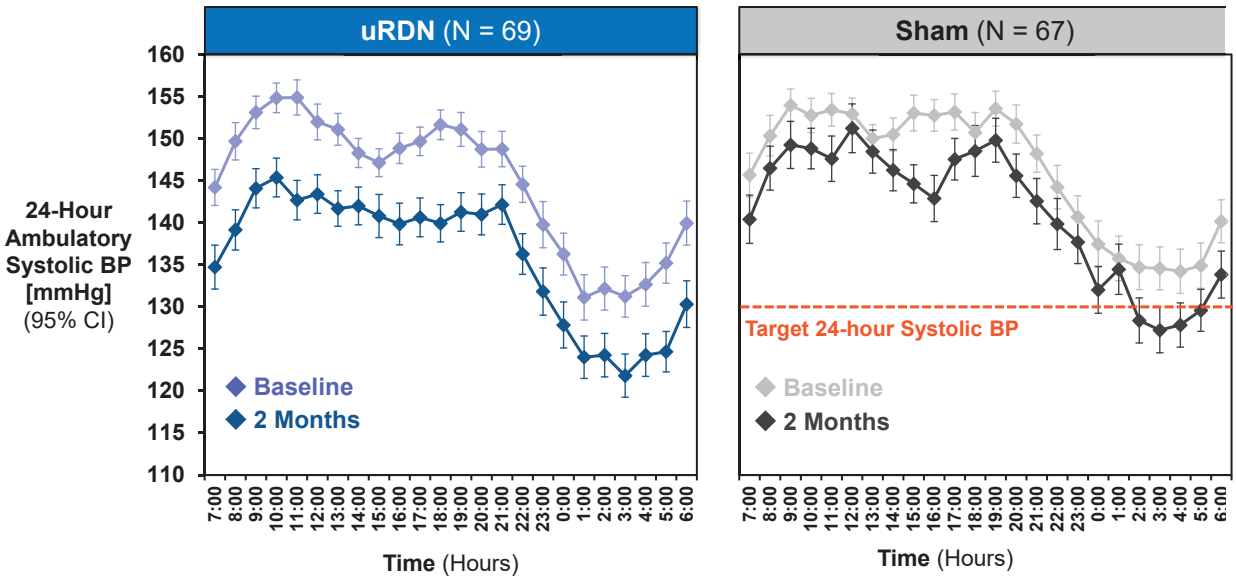



**Figure 10: TRIO 24-Hour Ambulatory SBP**

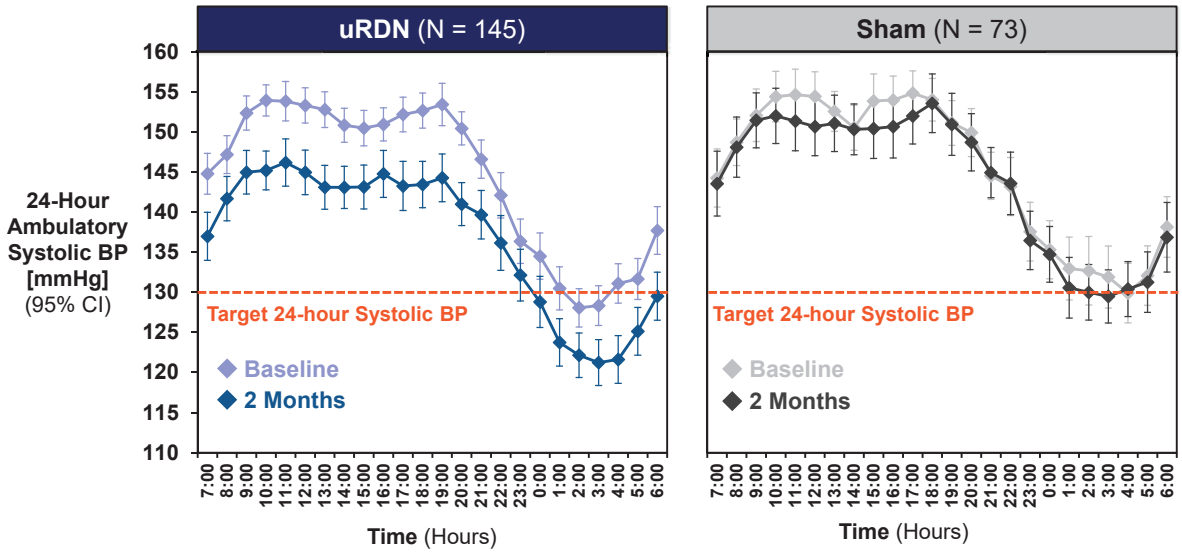



**Figure 11 RADIANCE-II 24-Hour Ambulatory SBP**

*Blood Pressure Reduction Magnitude*

**Figure 11, Figure 12, and Figure 13** show the changes in daytime ambulatory SBP from baseline to 2-months for individual subjects in each trial. For all three trials, more uRDN subjects experienced a decrease in daytime ambulatory systolic BP compared with Sham patients, and they had a BP reduction of greater magnitude.

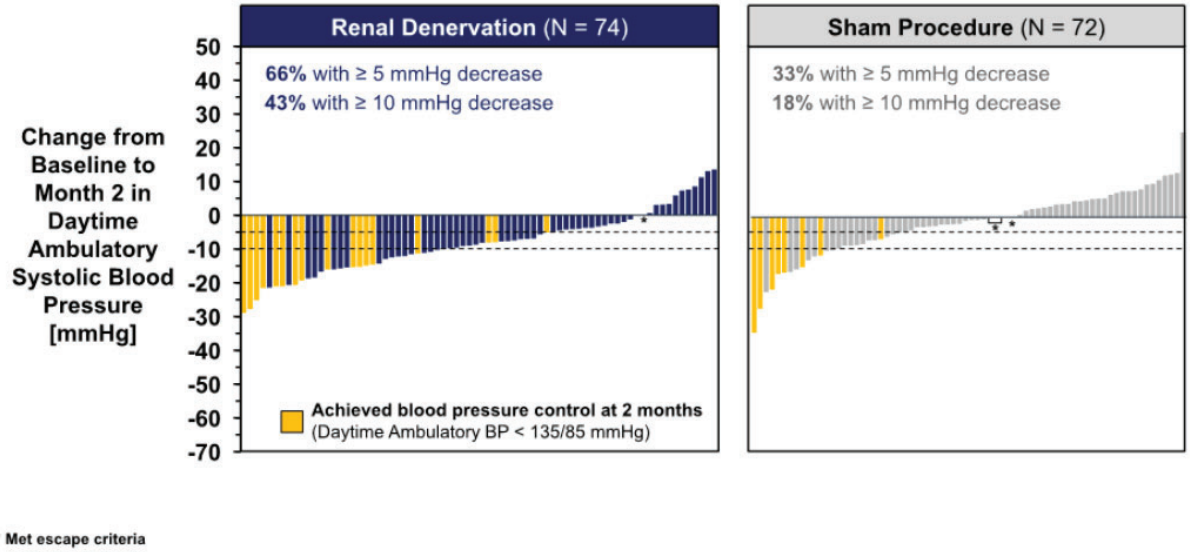



**Figure 12: SOLO Daytime Ambulatory SBP Response by Individual at 2 Months**

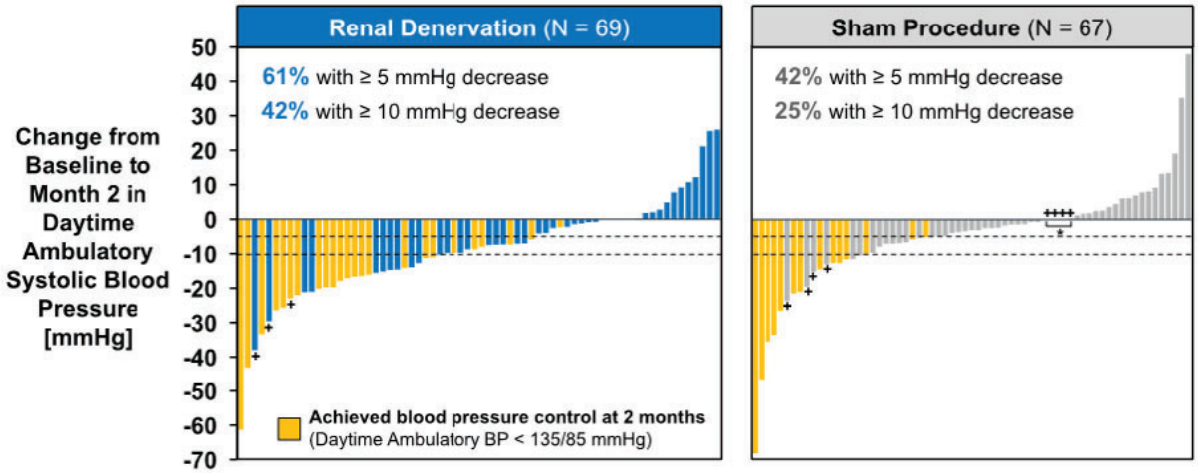



**Figure 13: TRIO Daytime Ambulatory SBP Response by Individual at 2 months**

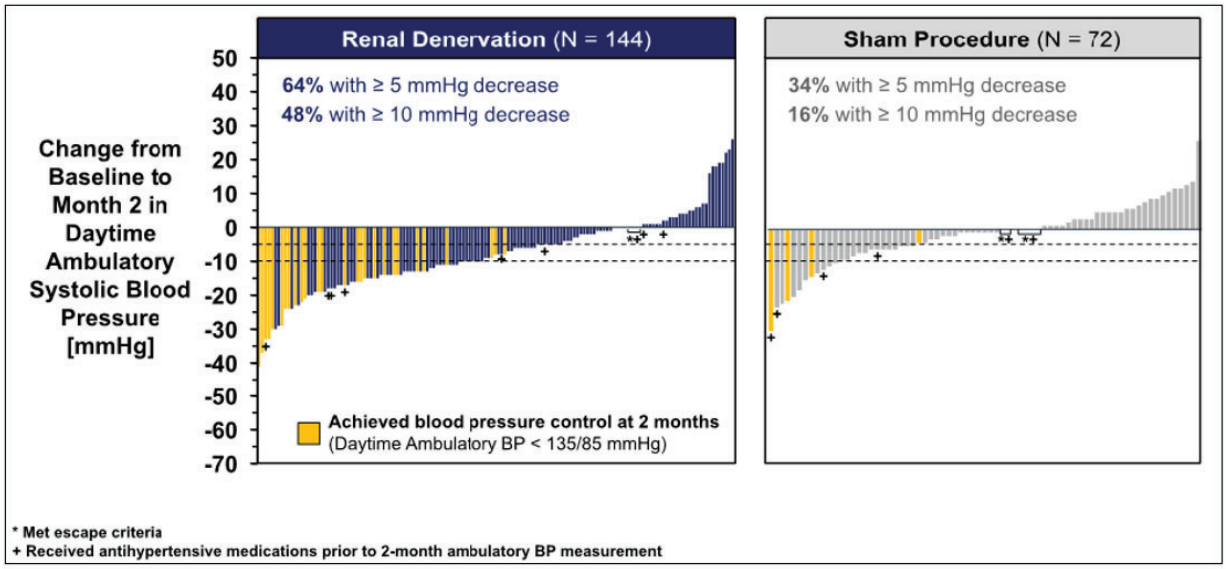



**Figure 14: RADIANCE-II- Daytime Ambulatory SBP Response by Individual at 2 months**

*Blood Pressure Targets and Blood Pressure Reduction Magnitude*

**Figure 15** shows the proportion of subjects who met specific targets for daytime SBP at 2 months for SOLO, TRIO, and RADIANCE II.

| | | RADIANCE II | | SOLO | | TRIO | |
|---|---|---|---|---|---|---|---|
| Measure | Target (mmHg) | uRDN N = 138 | Sham N = 64 | uRDN N = 69 | Sham N = 59 | uRDN N = 69 | Sham N = 67 |
| Daytime | < 135 / 85 | 19% | 5% | 22% | 3% | 35% | 21% |
| 24-hour | < 130 / 80 | 23% | 5% | 26% | 3% | 30% | 22% |
| Night-time | < 120 / 70 | 24% | 8% | 19% | 8% | 30% | 18% |
| Home | < 135 / 85 | 12% | 0% | 25% | 8% | 22% | 21% |
| Office | <140 / 90 | 23% | 21% | 16% | 0 | 26% | 13% |

**Figure 15: Proportion of ITT Subjects Achieving BP Targets at 2-Months**

For all 3 studies two months after the procedure, a higher proportion of uRDN patients had a decrease of ≥5 mmHg, ≥10 mmHg, or ≥15 mmHg in daytime ambulatory SBP compared with Sham patients (**Figure 16)**.

| Reduction in Daytime Ambulatory Systolic BP | RADIANCE II | | SOLO | | TRIO | |
|---|---|---|---|---|---|---|
| | uRDN N = 150 | Sham N = 74 | uRDN N = 74 | Sham N = 72 | uRDN N = 69 | Sham N = 67 |
| ≥ 5 mmHg | 64% | 34% | 66% | 33% | 61% | 42% |
| ≥ 10 mmHg | 48% | 16% | 43% | 18% | 42% | 25% |
| ≥ 15 mmHg | 26% | 10% | 26% | 11% | 30% | 15% |

**Figure 16: Blood Pressure Reduction Magnitude at 2-Months (ITT Population)**

***Durability of Blood Pressure Reduction***

The RADIANCE HTN studies were not primarily designed to assess the durability of blood pressure reduction, as the effect of uRDN at later timepoints may be challenging to interpret because of the use and escalation of BP medications after 2 months, unblinding of study subjects to their treatment assignment, and crossover of some Sham subjects to uRDN treatment.

SOLO and RADIANCE-II
Figure 17 and Figure 18 show office SBP through available follow-up in SOLO and RADIANCE-II, including medication changes in both uRDN and Sham groups.

At two months, uRDN subjects in SOLO (FIGURE 16) and RADIANCE II (FIGURE 17) had a significantly greater decline in office SBP compared to sham subjects. After two months, BPs continued to decline in both groups following use of a standardized medication titration protocol, with a greater relative decline in Sham subjects, resulting in a small BP reduction difference between uRDN and Sham groups at 6 months. However, there were more BP medications added in the Sham group compared to the uRDN group. In SOLO, treatment differences were observed for office SBP at 12 months and 24 months favoring uRDN.

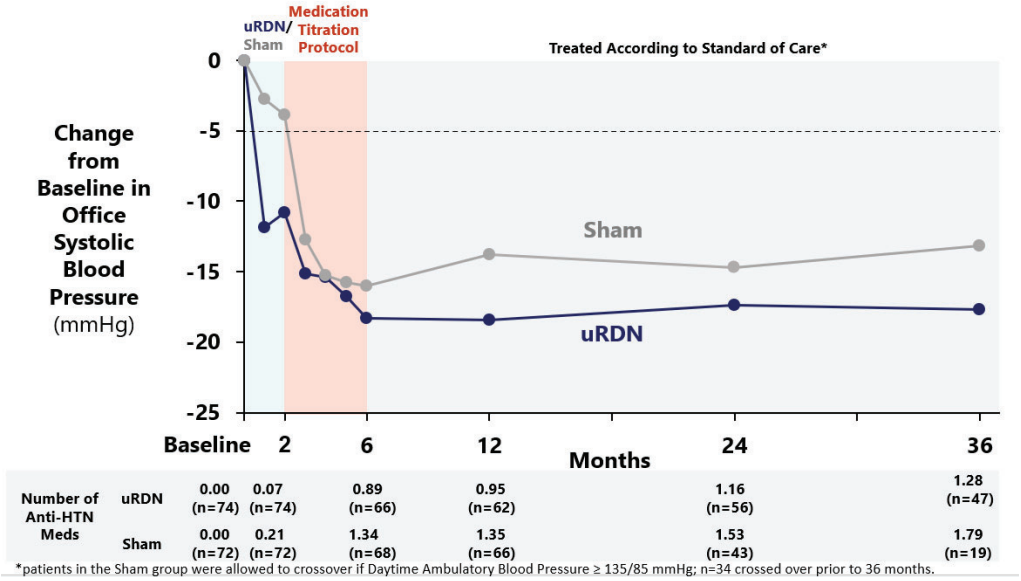



**Figure 17: SOLO Change in Office Blood Pressure from Baseline through 36 Months**

RADIANCE-II

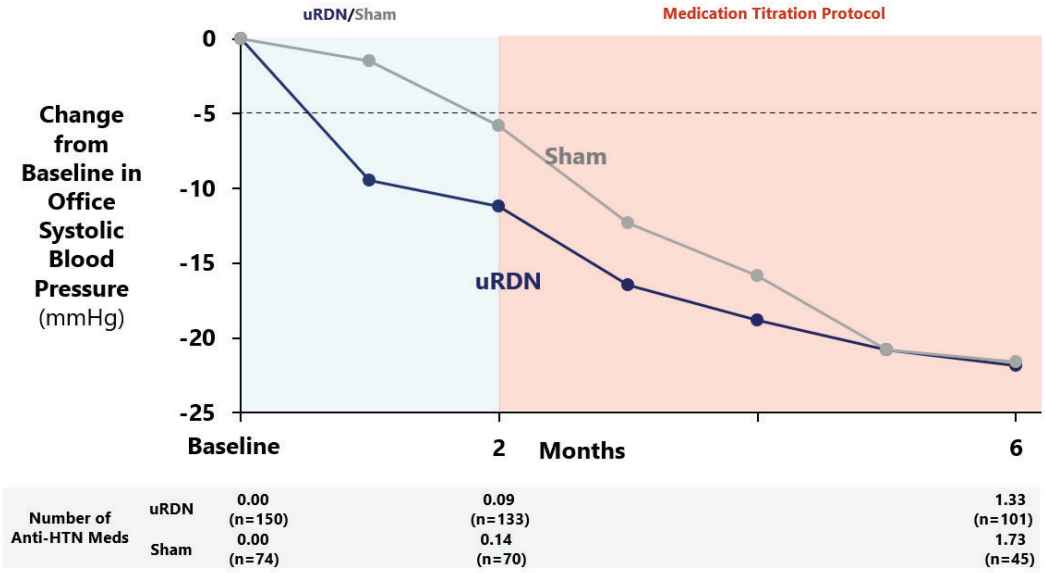



**Figure 18: RADIANCE-II Change in Office Blood Pressure from Baseline Through 6 Months**

TRIO

Figure 18 shows office SBP through available follow-up. At two months, there was a greater decline in uRDN versus Sham subjects. Systolic BPs continued to decline in both treatment groups through 6 months following use of a standardized medication titration protocol with a greater relative decline in Sham subjects, resulting in a similar BP reduction in the two treatment groups at 6 months.

However, there were more medications added in the Sham group compared to the uRDN group. There was a difference in reduction of office SBP at 12 and 24 months favoring uRDN.

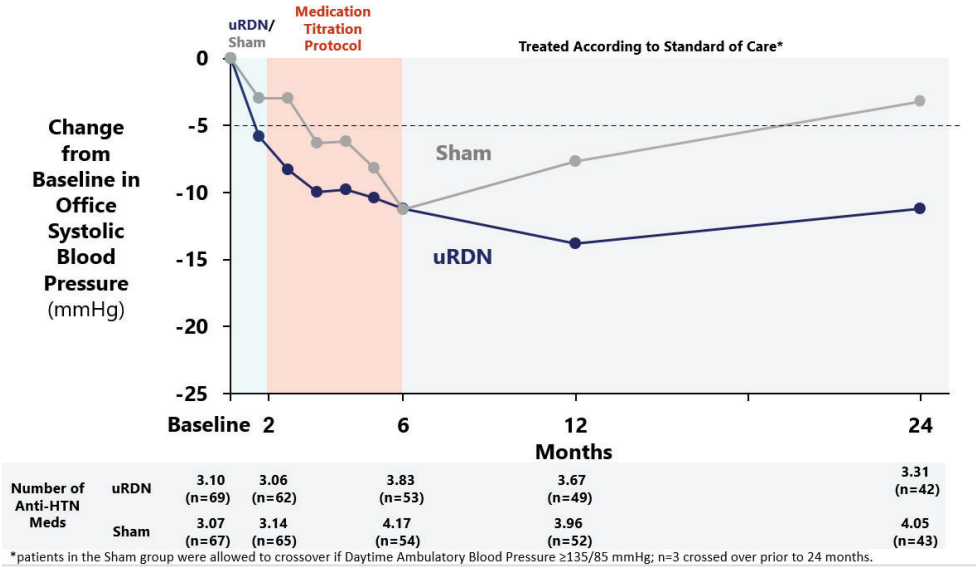


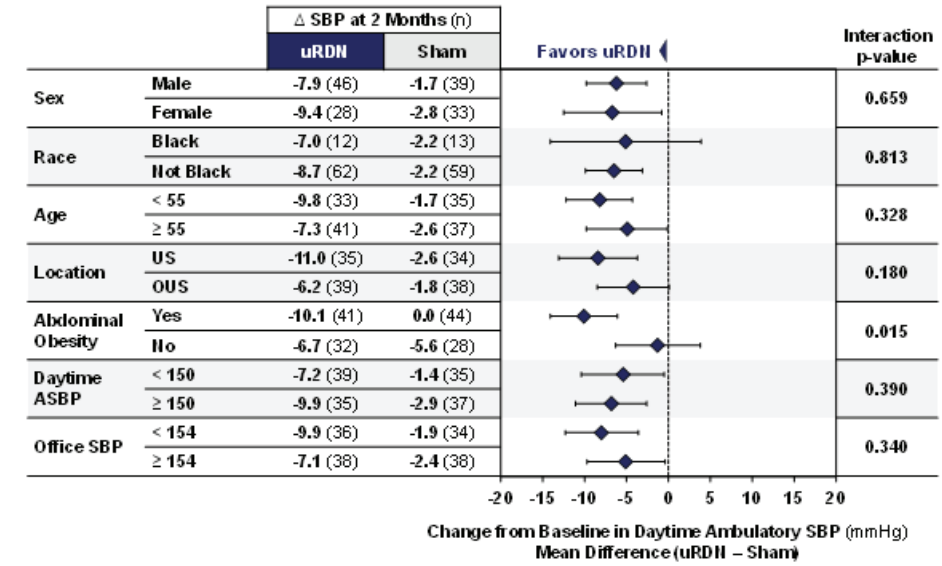

**Figure 19 : TRIO Change in Office Blood Pressure from Baseline Through 24 Months**

***Subgroup Analyses***

Treatment interactions were assessed with linear regression models adjusting for baseline daytime ambulatory systolic BP for the following pre-specified subgroups: ethnicity, age, sex, geography, baseline daytime ambulatory SBP, baseline office blood pressure, abdominal obesity, heart rate (RADIANCE II only) and eGFR (<60 versus ≥ 60).

**RADIANCE-HTN SOLO (Figure 20)**

The effect of uRDN on the primary effectiveness endpoint was generally consistent with reductions in daytime ambulatory SBP across prespecified subgroups, except in the abdominal obesity subgroup, in which a greater treatment effect was observed in subjects with a waist circumference >102 cm for men and >88 cm for women. Although subjects with and without abdominal obesity in the uRDN group each had reductions in daytime ambulatory SBP, this interaction seemed to be related to a larger than expected daytime ambulatory SBP reduction in subjects without abdominal obesity in the Sham group. The difference in daytime ambulatory SBP reduction in Black subjects was not considered significant likely due to the sample size and the BP decrease being similar to that observed in other subgroups.

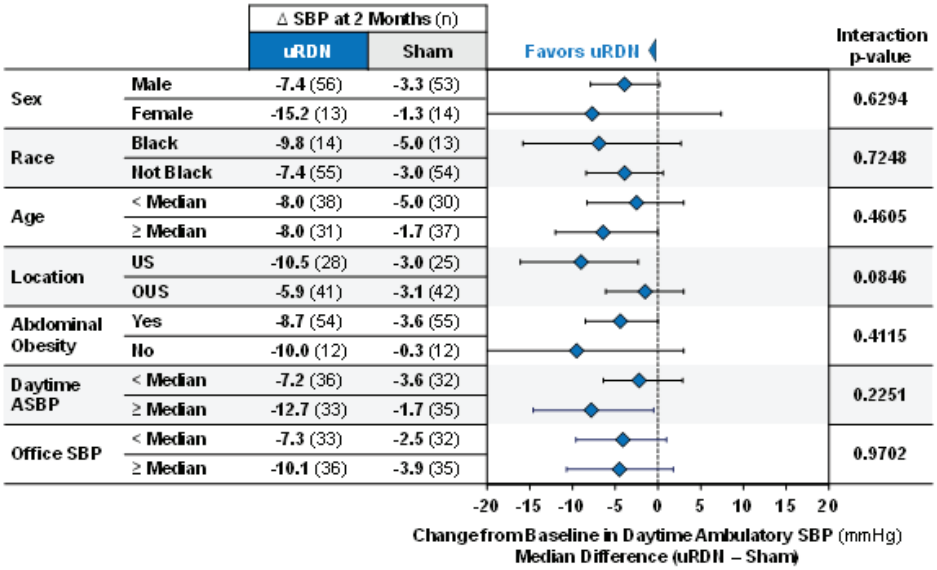



AHR=ambulatory heart rate; OUS=outside United States; SBP=systolic blood pressure; uRDN=ultrasound renal denervation, US=United States

**Figure 20: SOLO Change in Daytime Ambulatory SBP from Baseline to 2-months by Subgroup**

### RADIANCE-HTN TRIO (Figure 21)

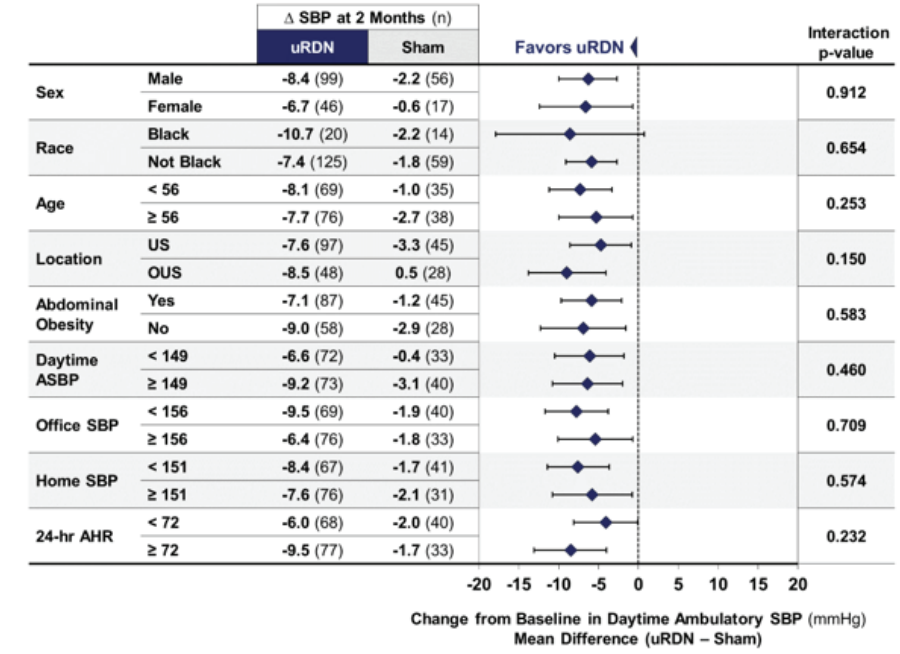
There was no heterogeneity in the between-group difference in daytime ambulatory SBP changes from baseline to 2 months according to sex, ethnicity, age, abdominal obesity, baseline BP, and geography. Results favoring uRDN vs. Sham were generally consistent across subgroups.




AHR=ambulatory heart rate; OUS=outside United States; SBP=systolic blood pressure; uRDN=ultrasound renal denervation, US=United States

**Figure 21: TRIO Change in Daytime Ambulatory SBP from Baseline to 2-Months by Subgroup**

**RADIANCE-II (Figure 22)**
The effect of uRDN on the primary effectiveness endpoint was consistent across pre-specified subgroups. There was no heterogeneity in the between-group difference in daytime ambulatory SBP changes from baseline to 2 months according to sex, ethnicity, age, abdominal obesity, baseline BP, baseline eGFR and geography. Results favoring uRDN vs. Sham were consistent across subgroups.




AHR=ambulatory heart rate; OUS=outside United States; SBP=systolic blood pressure; uRDN=ultrasound renal denervation, US=United States

**Figure 22: RADIANCE-II, Mean Change in Daytime Ambulatory SBP from Baseline to 2-Months by Subgroup**

## 15. Shipping and Storage

1. The Paradise Catheter is delivered in packaging that protects the product during shipping. Please report any packaging damage to ReCor Medical or your distributor and do not use. The contents are sterile if the packaging is unopened and undamaged at the time of use.
2. Ambient conditions during shipping and storage
   - -18°C to +55°C
   - 15% to 90% relative humidity
   - Avoid direct sunlight
   - Store in a cool dry place

### Paradise Catheter Care

1. The Paradise Catheter contains delicate components and must be handled with care.
2. Never use excessive force to advance, withdraw, or rotate the Paradise Catheter.

## 16. TREATMENT PROCEDURE

### 16.1.1. Paradise Catheter Preparation, Insertion, and Placement Procedure

1. Administer both anxiolytic and analgesic medications to the patient as per standard institutional practice.
2. Prior to the procedure, appropriate systemic anticoagulation should be administered and verified by ACT monitoring or other similar testing. Attach a push/pull style hemostasis valve (non-tightening valve feature) e.g. Merit Medical Honor® hemostasis valve.

Y **CAUTION: If a hemostasis valve with threaded closure mechanism is used, clinicians must not over-tighten the valve as this will restrict the catheter's cooling capabilities.**

3. Using standard interventional technique, gain access to femoral artery and place a 7-French (or larger) guide catheter.
4. Using standard interventional technique, carefully advance 7-French guide catheter into the left or right renal artery under fluoroscopic guidance.
5. Verify the patency of the left or right renal artery by performing an angiogram.
6. Measure arteries based on the angiogram utilizing the fluoroscopic system recording and measurement capability.

   6.1. Measure the distal, mid, and proximal artery diameters to select the appropriate Paradise Catheter balloon size per the following table:

| Balloon Diameter Size | Artery Diameter Range (mm) | Reference Number |
|---|---|---|
| 3.5mm | 3 to <3.5 | PRDS-063-02 |
| 4.2mm | 3.5 to <4.2 | PRDS-064-02 |
| 5 mm | 4.2 to <5 | PRDS-065-02 |
| 6 mm | 5 to <6 | PRDS-066-02 |
| 7 mm | 6 to <7 | PRDS-067-02 |
| 8 mm | 7 to ≤8 | PRDS-068-02 |

   6.2. Select the Paradise catheter based on the smallest measured diameter of the artery.

7. Prepare and attach the Paradise Cartridge, Paradise Connection Cable, and sterile water supply as per the Paradise Generator Operator's Manual (IFU-0107).
8. Using aseptic technique, open the Paradise Catheter package and carefully remove the device.
9. Connect the Paradise Cartridge extension tubing to the fluid Luer connections of the Paradise Catheter. The order of connections is not important.

10. Prepare the Paradise Catheter according to the instructions in the Paradise Generator Operator's Manual.
11. Flush the center lumen of the Paradise Catheter prior to tracking over a wire.
12. Remove access devices from lumen of guide catheter and insert a 0.014" guidewire.
13. Verify the balloon on the Paradise Catheter is deflated. If balloon is not deflated, press RE-PREP button on the Generator touchscreen.
14. Track Paradise Catheter over the 0.014" guidewire and gently insert the Paradise Catheter into the push/pull style hemostasis valve and guide catheter.
15. Advance the Paradise Catheter into the renal artery.
16. See the Paradise Generator Operator's Manual (IFU-0107) for balloon inflation, sonication, and balloon deflation instructions.

### 16.2. Delivery of Treatment

16.1. Target delivery of 2-3 sonications in each of the left and right renal arteries.

16.1.1. Each sonication should be delivered distal to proximal in **non-overlapping** target arterial zones. Do not cross a treated location to perform additional treatments.

16.1.2. Maintain at least one (1) radiopaque transducer length (5mm) between a sonication and the kidney parenchyma

16.1.3. Maintain at least one (1) radiopaque transducer length (5mm) between a sonication and the renal artery/aorta ostium

16.1.4. Avoid placement at branchpoints and bifurcations

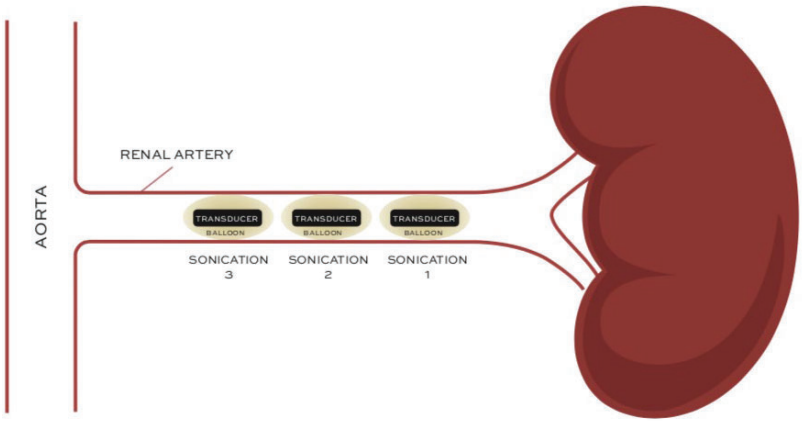



Figure 1: Example Treatment Strategy of Renal Artery

16.2. Target delivery in other renal anatomy

16.2.1. If an accessory renal artery (directly from the aorta) is present and has a treatable artery diameter ≥3mm, one (1) sonication should be delivered at least one (1) radiopaque transducer length from the kidney parenchyma and one (1) radiopaque transducer length from the accessory artery/aorta ostium (Figure 2)

16.2.2. If proximal artery branching is present and diameter of branch is ≥3mm, one (1) sonication should be delivered in the branch at a location at least one (1) radiopaque transducer length from the kidney parenchyma (Figure 3).

16.2.3. Emission zones should not overlap between adjacent vessels. Maintain a minimum of two (2) radiopaque transducer lengths (10 mm) apart or stagger sonications.

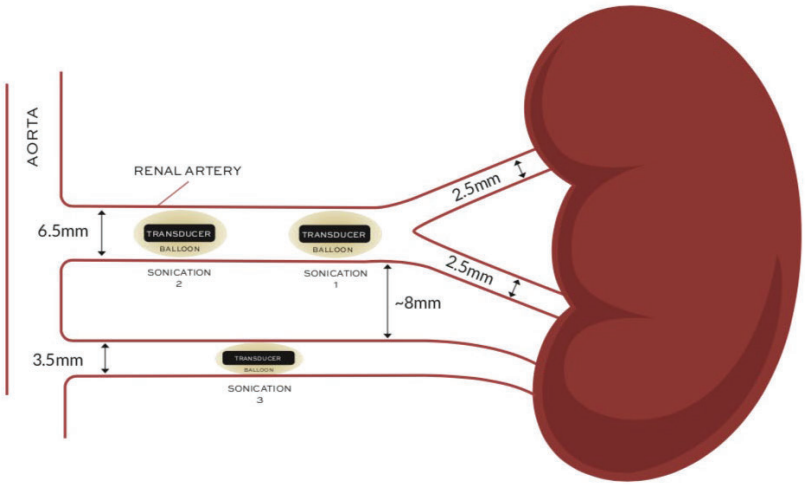



Figure 2: Example Treatment Strategy of Renal Artery with Treatable Accessory Artery

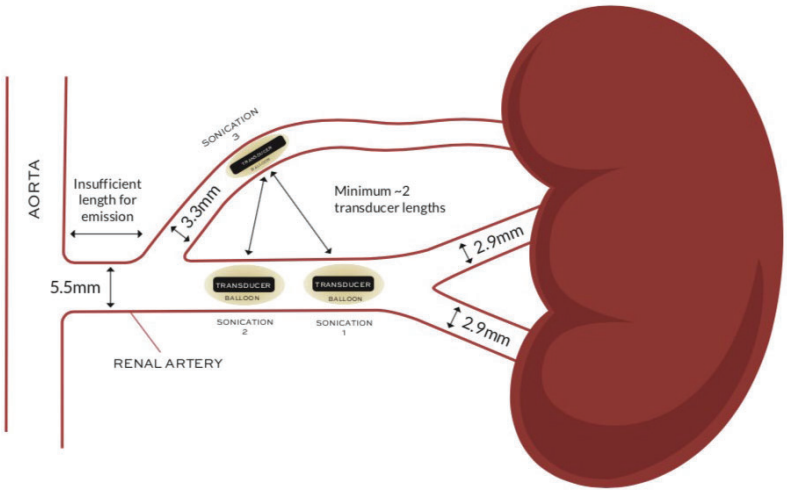



Figure 3: Example Treatment Strategy of Renal Artery with Treatable Proximal Branch

17. After positioning the Paradise Catheter transducer per the above steps:
    - Inflate the balloon.
    - Verify the position of balloon and transducer via fluoroscopy and contrast injection.
    - Perform denervation of left and/or right renal artery by delivering ultrasound energy.
    - Verify if the balloon is deflated via fluoroscopy before moving to the next location.
18. Withdraw the Paradise Catheter back into the guide catheter prior to moving the device into an alternate artery or accessory vessel for treatments.
19. Position the guidewire and guiding catheter into the contralateral artery for treatment and repeat the procedure starting at step 5.
20. Remove the Paradise Catheter, guidewire, and guide catheter after treatment of both arteries.
21. Close the wound per standard practice.
22. Follow standard-of-care post-intervention monitoring procedures.

**CAUTION: Ensure that the balloon is properly positioned in the renal artery and that the ultrasound energy is delivered into the renal artery and not into the kidney.**

**CAUTION: In the event of persistent Paradise Generator errors, deflate and withdraw the Paradise Catheter from the patient. Do not reuse.**

**Disposal of Catheter: Discard the Catheter according to standard hospital protocol.**

## 17. PARADISE SYSTEM REQUIRED ACCESSORIES

### Paradise™ Cartridge

**Intended Use**

The Paradise Cartridge, when used in conjunction with the Paradise Generator, controls the fluid flow into and out of the Paradise Catheter.

### Paradise™ Connection Cable

**Intended Use**

The Paradise Connection Cable is an accessory device to the Paradise System. The Paradise Connection Cable carries power to the Paradise Catheter from the Paradise Generator.

### Warnings and Precautions

- Use only with Paradise Generators and Catheters.
- Never use excessive force to attach or remove the Paradise Cartridge.
- Do not attempt to operate the Paradise System before thoroughly reading the Paradise Generator Operator's Manual.
- The Paradise Connection Cable and Paradise Cartridge are delivered in packaging that protects the product during shipping. Do not use if package shows signs of damage.
- Do not alter this device.
- Thorough cleaning of biological and foreign material of the Paradise Cartridge is not possible. Adverse patient reactions may result from reuse of this device.
- The Paradise Cartridge and Connection Cable are intended for single use only. Do not resterilize or reuse. Reuse, reprocessing, or resterilization may compromise device integrity and may result in the transmission of infectious diseases from one patient to another, which may result in patient injury, illness, or death.

### Shipping and Storage

The Paradise Connection Cable is supplied in a sterile, single-pouched package in a labeled carton and is delivered in packaging that protects the product during shipping. Store in original packaging until use at ambient temperature. Store in a cool, dry place.

The Paradise Cartridge is delivered in packaging that protects the product during shipping. Please report any packaging damage to ReCor Medical or your distributor upon receipt and do not use. Store in original packaging until use at ambient temperature. Store in a cool, dry place.

Please report any product damage to your distributor or ReCor Medical and do not use. The contents are sterile if the packaging is unopened and undamaged at the time of use.
Avoid exposing the Paradise System to direct sunlight.
Ambient conditions during shipping and storage:

- -18°C to +55°C
- 15% to 90% relative humidity

- Avoid direct sunlight
- Store in a cool, dry place

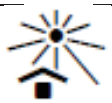
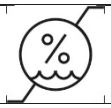
**Disposal:** Discard the cartridge according to standard hospital protocol.

Dispose of electrical cables according to standard procedures and in accordance with local laws and regulations.

## 18. Troubleshooting

All known error conditions are automatically detected by the Paradise Generator which will display any actions a user should take to correct the error condition. Refer to IFU-0107 for list of error codes and instructions.

## 19. SYMBOLS/ICONS, AND DEFINITIONS

| | |
|---|---|
|  | Manufacturer |
|  | Do not use if package is damaged and consult instructions for use |
|  | Caution |
|   | US Federal law restricts this device to sale by or on the order of a physician. |
|  | Catalog number |
|  | Serial number |
|  | Do not reuse |
|  | Do not resterilize |
|  | Use-by date |
|   | Batch code |
|   | Sterilized using ethylene oxide |
|  | Temperature limitations |
|  | Keep dry |
|  | Keep away from sunlight |
|  | Humidity limitation |
|  | Consult instructions for use |
|  | Defibrillation proof type CF Applied Part |
|  | Single sterile barrier system with protective packaging inside |
|  | Single sterile barrier system |
|   | Medical device |
|   | MR Unsafe |

## 20. Limited Warranty, Disclaimer, and Patents

ReCor Medical warrants that this product, the Paradise Catheter, is free from defects in original workmanship and materials through its date of expiration. If this product is proven to be defective in original workmanship or original materials, ReCor Medical, in its absolute and sole discretion, will replace or repair it, less charges for transportation and labor costs incidental to inspection, removal, or restocking of product. This limited warranty applies only to original factory delivered products which have been used for their normal and intended uses. ReCor Medical's limited warranty shall not apply to ReCor Medical products which have been repaired, altered, or modified in any way, unless done so by a ReCor Medical authorized service representative, and shall not apply to ReCor Medical products which have been improperly stored or improperly installed, operated, or maintained contrary to ReCor Medical's instruction. RECOR MEDICAL MAKES NO OTHER WARRANTIES, EXPRESS, IMPLIED OR STATUTORY REGARDING THE PRODUCTS PROVIDED HEREUNDER INCLUDING, BUT NOT LIMITED TO IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE WHICH ARE HEREBY EXPRESSLY DISCLAIMED. RECOR MEDICAL DOES NOT REPRESENT THAT THE PRODUCTS WILL OPERATE ERROR-FREE OR THAT THEY WILL OPERATE WITHOUT INTERRUPTION, OR THAT THEY WILL FUNCTION IN ACCORDANCE WITH USER'S REQUIREMENTS. IN NO EVENT SHALL MANUFACTURER HAVE ANY LIABILITY FOR, NOR SHALL ANY THIRD PARTY HAVE ANY REMEDY AGAINST RECOR MEDICAL FOR CONSEQUENTIAL DAMAGES, ANY LOSS OF PROFITS OR SAVINGS, LOSS OF USE, OR ANY OTHER COMMERCIAL LOSS



## 21. Customer Support and Contact Information

For customer support, contact ReCor Medical.

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Recor Medical®

# A proven approach to lower blood pressure

## Paradise® Ultrasound Renal Denervation (RDN)

Actual patient not pictured.

At age 50, people without high blood pressure have a **life expectancy**

# 5 YEARS LONGER

than people with high blood pressure.[1]

When not controlled, high blood pressure can lead to heart disease, stroke, heart failure, kidney disease, and dementia.

With treatment and management, you can lower your blood pressure to help you live a longer and healthier life.

## Reducing your blood pressure by 10 mmHg can lower your risk of[2]:

**HEART FAILURE BY ↓ 28%**

**STROKE BY ↓ 27%**

**CARDIAC EVENT BY ↓ 20%**

# The Paradise ultrasound RDN treatment

In addition to lifestyle changes and medications, the Paradise Ultrasound RDN treatment is now available to help lower blood pressure.

**Lifestyle Changes**

**Medications**

**Paradise ultrasound RDN treatment**

## What is the Paradise ultrasound RDN treatment?

- One-time, safe, minimally invasive treatment proven to reduce high blood pressure[3-6]
- Fast recovery allows for an easy return to regular life[7]
- Provides 24-hr blood pressure reductions without the side effects of medications.[3-6]


## How does the Paradise ultrasound RDN treatment work?

In many people with high blood pressure, the nerves leading to the kidneys have become overactive causing blood pressure to increase.

The Paradise procedure uses ultrasound energy to calm the nerves near the kidneys to help lower blood pressure.

> *While I still take medication now, I have an excellent control of my blood pressure, I consider this procedure as a true gift of good medical sciences and the application of scientific learning.*
>
> **Gerard,** 73 years old

# What to expect if you choose this treatment

## Before the procedure

- You and your healthcare professional will discuss the procedure to determine if this is the right treatment for you. You may need additional testing and verification of coverage benefits before deciding the next steps.
- Once you and your healthcare professional agree that it is the right treatment for you, the procedure will be scheduled.

## Day of the procedure

- Treatment is usually done in an outpatient setting and typically takes about an hour to perform.
- As a part of the treatment, a small flexible tube (catheter) is guided into the blood vessels near the kidneys and 7 seconds of ultrasound energy is applied 2-3 times. Both sides are treated and then the tube is removed, leaving nothing behind.
- After the procedure, some people go home the same day or some stay overnight.

## After the procedure

- Most people are able to return to their usual activities within a few days after the treatment.
- Talk with your care team about when you can resume your day-to-day activities.

> *Going for treatment with the Paradise Ultrasound RDN procedure was a great decision for me because now I have only one blood pressure medication. Prior to it, it was all over the board, I was taking all those medications and my blood pressure was up and down. For me personally, it is a lifesaver.*
>
> **David,** 48 years old

## Learn how it works

Scan the QR Code

**www.recormedical.com**

Recor Medical®

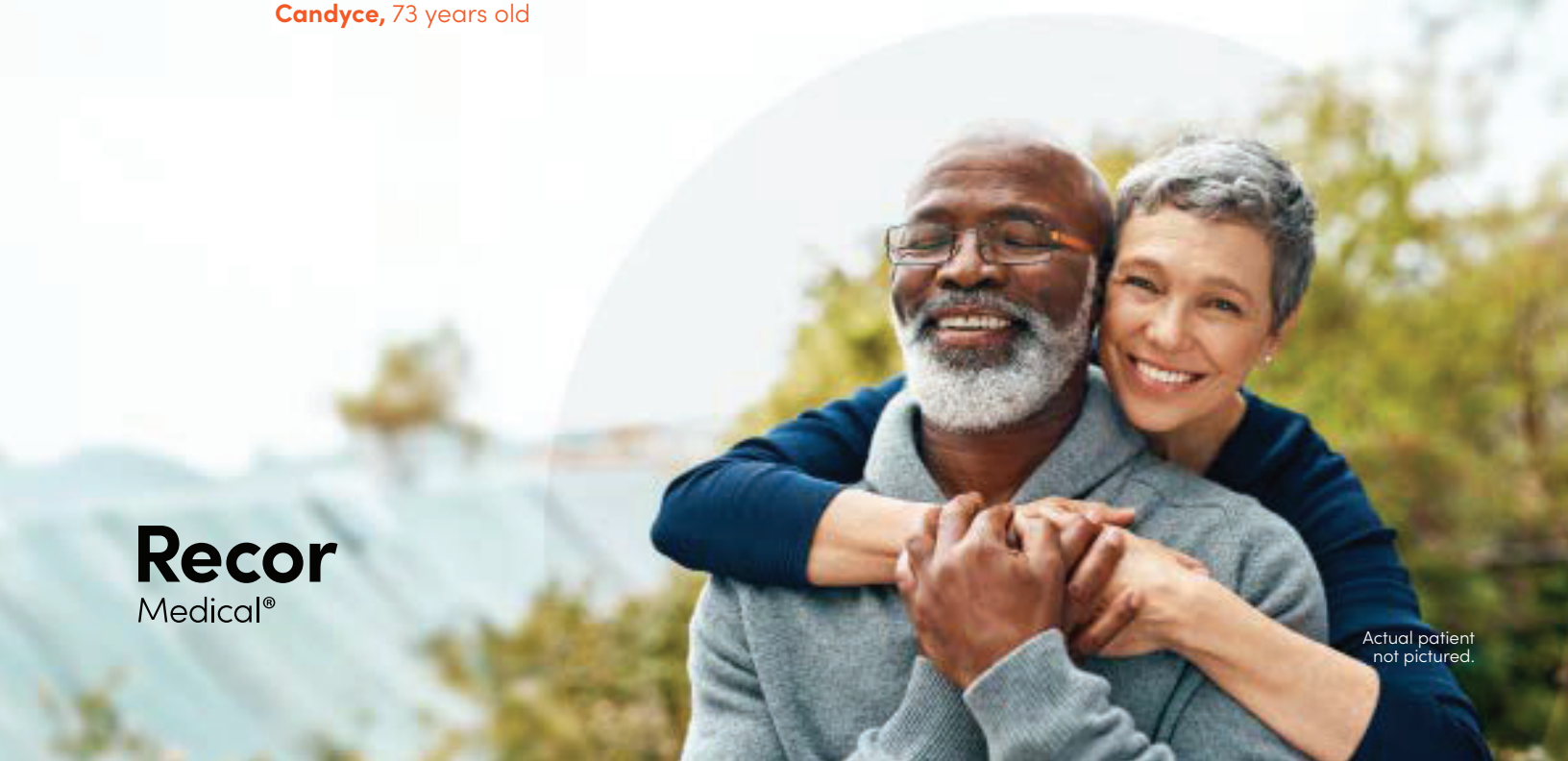
# Managing high blood pressure can be challenging

> *I have been on blood pressure medication ever since [college] and after a while I was taking 2 medications daily. One of the side effects of taking medication was frequent trips to the bathroom so I didn't want to take the medication at bedtime, but then I had an hour commute to work, so I didn't want to take it in the morning either.*
>
> **Gene,** 62 years old

Whether you were recently diagnosed with high blood pressure or have had it for years, managing high blood pressure is not an easy task. Controlling your blood pressure may be a struggle despite making changes to what you eat, exercising more, and taking your medications as prescribed.

If you are looking for an additional way to lower your blood pressure, the **Paradise ultrasound renal denervation (RDN) treatment** may be the right choice for you.

> *Following my procedure with Paradise ultrasound RDN, my blood pressure is better controlled.*
>
> **Candyce,** 73 years old



Actual patient not pictured.

Recor Medical®

# Notes

This patient brochure is intended for informational purposes only and does not contain medical advice. This brochure should not be used as an alternative to consulting with your healthcare professional. Speak to your healthcare professional to obtain additional information or to discuss any questions that you may have. You should discuss with your healthcare professional questions specific to your health and the treatment options that are appropriate for you. Always talk with your healthcare professional about diagnosis and treatment, including medications, and ensure you understand and carefully follow the information you are given.

**References: 1.** Stroke and High Blood pressure correlation – AHA - High Blood Pressure and Stroke Infographic | American Stroke Association **2.** Ettehad D, et al. *The Lancet.* 2016;387:957-67. **3.** Azizi M. *JAMA.* 2023;329(8):651-661 **4.** Azizi M. et al. *Lancet.* 2018 Jun 9;391(10137):2335-2345. **5.** Azizi M. et al. *Lancet.* 2021 Jun 26;397(10293):2476-2486. **6.** Kirtane A. et al. *JAMA Cardiol.* 2023;8(5):464-473

**IMPORTANT SAFETY INFORMATION**

**Rx Only. Brief Summary - Prior to use, please reference the Instructions for Use**

**Indications for Use**
The Paradise™ Ultrasound Renal Denervation System (Paradise System) is indicated to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

**Contraindications**
The Paradise Catheter is contraindicated in any of the following: • Renal arteries diameter <3 mm and >8 mm • Renal artery Fibromuscular disease (FMD) • Stented renal artery • Renal artery aneurysm • Renal artery diameter stenosis >30% • Pregnancy •Presence of abnormal kidney (or secreting adrenal) tumors • Iliac/femoral artery stenosis precluding insertion of the catheter

**Warnings**
• Failure to use the recommended balloon size may result in renal artery stenosis, dissection, perforation, aneurysm, significant vasospasm requiring intervention, ablation of unintended tissues or structures, and/or no ablation of target tissue achieved. • Energy emission in an unintended location may result in unintended tissue damage. • Do not move the Paradise Catheter during sonication. • Do not sonicate in renal artery at locations with visible plaque. • Do not deliver sonications in an overlapping arterial target zone.

**Precautions**
• Patients with known allergy to contrast medium may be at increased risk of hypersensitivity reactions. • Only use specified coolant (Sterile water) for fluid supply. DO NOT USE SALINE. • Avoid multiple balloon inflations to achieve apposition of the balloon to the renal artery wall; multiple balloon inflations may result in increased vessel trauma. • The Paradise Catheter is for single use only. Do not resterilize or reuse. Reuse, reprocessing, or resterilization will compromise device integrity which may result in patient injury, illness, or death. •Do not touch the Paradise Catheter balloon during sonication, as it may result in serious injury. • The Paradise System may interfere with or adversely affect the operation of cardiac pacemakers or other active implants, unless proper precautions have been taken or managed per the manufacturer's instructions. When in doubt regarding possible hazards, seek qualified advice and/or consult with the manufacturer(s) prior to initiating a procedure. The Paradise Catheter is a Type CF, defibrillation-proof Applied Part.

**Potential risks of renal denervation procedure/response to treatment**
Ablation or thermal injury to vessel, adjacent tissue or other structures, Acute kidney injury, Angina, Anxiety, Arrhythmia, Atrial tachycardia, Bradycardia, Gastrointestinal complications (diarrhea, nausea, vomiting), Hypotension/ Dizziness and/or Headaches, Hypertension, Hyperhidrosis, Pain (transient abdominal, lower back), Renal failure or renal insufficiency, Renal artery aneurysm or pseudoaneurysm, Renal infarction, Renal artery dissection, or perforation, Renal artery stenosis, Vasospasm, Vasovagal response, Stroke or transient ischemic event

**Potential risks of arterial catheterization procedure**
Allergic reaction to contrast, Arterio-enteric fistula, Arterio-venous fistula, Bleeding, Cardiopulmonary arrest, Complications related to pain and anti-anxiety medications, Death, Deep vein thrombosis, Edema, Embolism (pulmonary, renal, peripheral vasculature, plaque), Hematuria, Infection, Myocardial infarction, Pain, Vascular access site complications (pseudoaneurysm, pain, swelling, hematoma)

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