RENAL DENERVATION FOR RESISTANT HYPERTENSION REALLY WORKS AS SHOWN BY RCTS: WHAT ARE THE TECHNIQUES AND DEVICES: WHEN SHOULD THEY BE USED

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Eric A. Secemsky, MD, MSc, RPVI, FACC, FSCAI, FSVM
Director I Vascular Intervention I Beth Israel Deaconess Medical Center
Section Head I Interventional Cardiology & Vascular Research I
Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology
Associate Professor of Medicine I Harvard Medical School

Beth Israel Lahey Health

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2 RDN Devices Approved by FDA in November 2023

November 7, 2023

FDA Approves Recor Medical's Paradise Renal Denervation System for Hypertension Treatment

November 7, 2023—Recor Medical announced it has received United States FDA approval for its Paradise ultrasound renal denervation (RDN) system for the treatment of hypertension. A subsidiary of Otsuka Medical Devices Co. Ltd., Recor notes that the Paradise system is intended as an adjunctive treatment option when lifestyle changes and medications have not adequately controlled a patient's blood pressure.

An FDA Advisory Committee Panel reviewed data supporting the Paradise system in August 2023, resulting in a favorable vote. The company's RADIANCE II clinical trial met its primary safety and efficacy endpoints, and its data were published in the *Journal of the American Medical Association*. At TCT 2023 in October, Ajay Kirtane, MD, presented positive results from a combined analysis of 6-month follow-up data from the three RADIANCE global clinical studies evaluating the Paradise system. The data demonstrated maintenance of blood pressure reduction compared to sham, with fewer hypertensive treatments. The study results were simultaneously published by Michel Azizi, MD, et al online in *Circulation*.

Recor says its ultrasound-based Paradise system denervates the sympathetic nerves that surround the renal arteries, the overactivity of which can lead to hypertension. It includes a HydroCooling system that circulates sterile water through the balloon catheter to help protect the renal artery wall, the company notes. The platform gained CE Mark in 2012 and is available in Europe. It is currently an investigational device in Japan, the company notes.

"It is truly remarkable to witness the approval o difficult-to-control hypertension who are in nee medications," said Dr. Kirtane in comments to C thank all of the collaborators and the many pati this technology, allowing this to come to fruitio Vagelos College of Physicians and Surgeons anc

November 17, 2023

Medtronic's Symplicity Spyral Renal Denervation System Gains FDA Approval for Hypertension Treatment

November 17, 2023—Medtronic announced it has received United States Food and Drug Administration (FDA) approval for its Symplicity Spyral Renal Denervation System for the treatment of hypertension. The company plans to begin United States commercialization immediately.

The Symplicity procedure denervates the renal arteries using radiofrequency energy to reduce blood pressure. Medtronic's SPYRAL HTN Global Clinical Program includes more than 25,000 patients over 10 years of study, including those both on and off blood pressure medications. A patient preference study was also conducted, which the company notes showed that when presented with an interventional treatment with blood pressure reduction and potential risks in line with those of the procedure, approximately one-third of patients were likely to choose the intervention.

Results from Medtronic's clinical program were presented at a 2-day FDA advisory panel session in August 2023, along with those of Recor Medical, which has also gained approval for its renal denervation system.

"The Symplicity blood pressure procedure is safe and effective, providing significant 'always on' blood pressure reductions for patients," said David Kandzari, MD, in Medtronic's announcement. Dr. Kandzari is Chief of Piedmont Heart Institute and Cardiovascular Service and Co-Principal Investigator of the SPYRAL clinical program. "This landmark approval is the culmination of rigorous scientific study and clinical trials, including long-term, sham-controlled studies in the presence and absence of medication, and the largest real-world study."

"This approval paves the way for a transformation in hypertension treatment, offering a solution that complements medication and lifestyle changes," added Raymond Townsend, MD, in the release. Dr. Townsend is from the Hypertension Section in the Department of Internal Medicine/Renal, at the University of Pennsylvania School of Medicine. He is also Co-Principal Investigator of the SPYRAL clinical program. "The Symplicity blood pressure procedure is a promising treatment option for clinicians and patients alike and offers opportunity to fulfill a significant unmet need in hypertension care, especially for those patients who are desperately seeking additional approaches to get their blood pressure down."

IFU/Indications for RDN Devices

Indications:

"…..indicated to reduce blood pressure as an adjunctive treatment in patients with hypertension in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure."

Contraindications:

- Renal artery diameter <3 mm or >8 mm
- Renal artery fibromuscular dysplasia (FMD)
- Stented renal artery (>3 months prior to Spyral RDN procedure OK)
- Renal artery aneurysm
- Renal artery diameter stenosis of >30 (Paradise) or >50% (Spyral)
- Pregnancy
- Presence of abnormal kidney (or secreting adrenal) tumors
- Iliac/femoral artery stenosis precluding insertion of the catheter

****Not studied in patients with eGFR <45 mL/min/1.73 m2 (Spyral) or eGFR <40 mL/min/1.73 m2 (Paradise)****

SCAI Position Statement on RDN

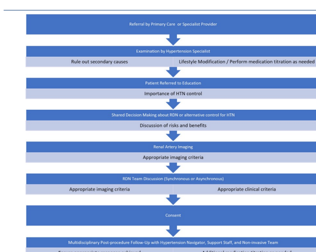
Standards and Guidelines

SCAI Position Statement on Renal Denervation for Hypertension: Patient Selection, Operator Competence, Training and Techniques, and Organizational Recommendations

Rajesh V. Swaminathan, MD, FSCAI (Vice-Chair)[a,*], Cara Anne East, MD[b], Dmitriy N. Feldman, MD, FSCAI[c], Naomi D. Fisher, MD[d], Joseph M. Garasic, MD, FSCAI[e], Jay S. Giri, MD, MPH, FSCAI[f], David E. Kandzari, MD, FSCAI[g], Ajay J. Kirtane, MD, SM, FSCAI[h], Andrew Klein, MD, FSCAI[g], Taisei Kobayashi, MD, FSCAI[f], Gerald Koenig, MD, FSCAI[i], Jun Li, MD, FSCAI[j], Eric Secemsky, MD, MSc, FSCAI[k], Raymond R. Townsend, MD[f], Herbert D. Aronow, MD, MPH, FSCAI (Chair)[l,m]

SCAI = Society for Cardiovascular Angiography and Interventions.
Swaminathan RV, et al. *J Soc Cardiovasc Angiogr Interv.* 2023;101121 [Epub ahead of print].

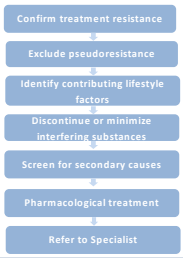
SCAI Position Statement on RDN



Key Takeaways:

1) **Need a Non-Invasive Hypertension Lead**
2) **Need an Invested Endo-competent Proceduralist**
3) **Need Hospital/ Administrative Buy-In**

ACC/AHA Approach to Resistant Hypertension



SCAI Position Statement on RDN

Skillset	Training modality
- Arterial vascular access and hemostasis - Vascular access site complication management - Experience and knowledge of analgesia or sedation - Periprocedural hypertension management - Radiation and contrast-sparing measures	Prerequisite (current interventional or endovascular experience)
- Knowledge of aortic, renal, and visceral anatomy - Understanding of renal sympathetic nervous system anatomy and pathophysiology - Understand renal denervation indications - Know the risks and benefits of available renal denervation platforms	Didactic modules, simulation
- Understand catheter selection and technique for renal angiography - Know device-specific renal denervation set-up and technique - Recognize and treat potential renovascular complications, including balloon angioplasty and stenting	Simulation, observerships, and supervision

Goal is for proceduralists to have some endovascular experience or achieve experience by proctorship

- **For those with endovascular privileges:**
  - **5 proctored RDN cases**
- **For those without endovascular privileges:**
  - **10 supervised renal angiograms in calendar year and 5 proctored RDN cases**

Must Haves for the Proceduralist

- **High-quality imaging with DSA**
- **Trained staff for "deep" conscious sedation**
- **Technical familiarity with:**
  - Aorta/Renal anatomy
    - Identification of accessory renal arteries
  - Multiple renal guides
  - 014 support and non-support wires
  - Renal stents, glue and coils

Who Should Be Considered for RDN?

What is the potential relative benefit-risk of adding another antihypertensive medication vs Renal Denervation?	
Efficacy	Roughly Equivalent
Tolerability	May Favor Renal Denervation
Safety	Both Demonstrating Overall Safety to Date
Adherence	Favors Renal Denervation
Durability	Unclear for RDN, Dependent Upon Adherence for Medication
Cost	Likely Favors Medication
Patient Preference	Varies Among Individuals

SCAI Position Statement on RDN

Table 1. Selection criteria appropriate for renal denervation.

Patients with resistant hypertension, defined by blood pressure >130/80 mm Hg despite being on 3 medications with maximally tolerated doses from classes with outcomes data (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, calcium channel blockers, thiazide diuretics, and beta blockers)

Patients with uncontrolled hypertension despite attempting lifestyle modification and antihypertensive medication but who are either intolerant of additional medication or do not wish to be on additional medications and who are willing to undergo renal denervation after shared decision-making

Priority may be appropriately given to patients with higher cardiovascular risk (eg, comorbidities of coronary artery disease, diabetes, prior transient ischemic attack/ cerebrovascular accident, or chronic kidney disease) who may have the greatest benefit from blood pressure reduction

BIDMC Experience

- Enrolling in Spyral AFFIRM Study (pre and post approval)
- Performed first commercial case November 28, 2023 (3rd in US)
- 17 cases done to date

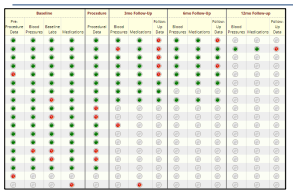
BIDMC Average Case Experience

- **Examples of Commercial Case Experience:**
  - 75 yo F, resistant HTN on 3+ meds (doxazosin, clonidine), Stage II CKD
  - 63 yo F, resistant HTN on 3+ meds (clonidine), multiple drug intolerances
  - 71 yo F, resistant HTN on 3+ meds (clonidine), multiple drug intolerances
  - 65 yo F, uncontrolled HTN on 2 meds (minoxidil), multiple drug intolerances
  - 62 yo M, resistant HTN on 3+ meds (labetalol)
  - –All cases <90 minutes
  - –No procedural complications
  - –All discharged same day

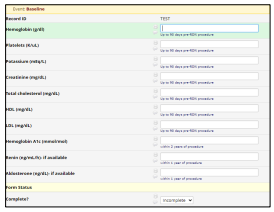
Post-procedure monitoring

Assessments	Baseline	Procedure	Post-procedure						
			3M	6M	12M	24M	36M	48M	60M
Demographic data	x								
Medical History	x								
Baseline Labs	x								
Renal Denervation Procedure		x							
Blood Pressures and HR	x		x	x	x	x	x	x	x
Post-Procedure Labs			x	x	x	x	x	x	x
Medication Review	x		x	x	x	x	x	x	x
Event Review		x	x	x	x	x	x	x	x

Smith Center Renal Denervation Registry



REDCap



BIDMC Experience through RDN Registry

Variable	Overall (N = 8 Subjects)
Change in AOBP systolic blood pressure at 6 mos compared to baseline	-16.0±41.6
Change in AOBP diastolic blood pressure at 6 mos compared to baseline	-9.3±15.3
Change in office systolic blood pressure at 6 mos compared to baseline	-24.2±23.7
Change in office diastolic blood pressure at 6 mos compared to baseline	-10.0±12.4
>5mmHg absolute change in AOBP systolic blood pressure between 6 mos and baseline	5 (62.5%)
>10mmHg absolute change in AOBP systolic blood pressure between 6 mos and baseline	4 (50.0%)
Change in number of anti-hypertensive meds between 6 mos and baseline	0.3±1.0

Thank you

esecemsk@bidmc.harvard.edu
@EricSecemskyMD

Smith Center for Outcomes Research in Cardiology
375 Longwood Avenue, 4th Floor
Boston, Massachusetts 02215