Penn Medicine

CLINICAL BRIEFING™

Penn Heart and Vascular • Renal-Electrolyte and Hypertension Division

Enrolling Clinical Trials: SPYRAL HTN — Renal Denervation with or without Antihypertensive Therapy

Cardiologists and nephrologists at Penn Medicine are conducting a pair of studies to evaluate the safety and effectiveness of the SPYRAL™ multi-electrode renal denervation system.* The studies, which are ongoing simultaneously, will investigate the use of the device both with (HTN ON-MED) and without (HTN OFF-MED) adjunctive antihypertensive therapy.

The SPYRAL HTN-3 trials are global and phased. Their objective is to arrive at a conclusive determination of the efficacy of renal denervation, a procedure by which the nerves of the renal arteries are ablated to attenuate renin secretion from the juxtaglomerular kidney cells. Renin contributes to hypertension by provoking vasoconstriction and sodium and water retention.

Renin production is stimulated by (among other forces) activation of the sympathetic nerves of the kidney, which occur as a dense network adjacent to the renal arteries. Ablation of these nerves (renal denervation) has been found to result in reductions in renin output, with consequent reductions in blood pressure in individuals with hypertension.

Efforts to establish the efficacy of renal denervation over medical treatment of hypertension, however, have been hampered in clinical studies by a variety of barriers. These include measurement bias, placebo effect, the complexity of prescribing and monitoring drug regimens, and adverse events resulting in variable adherence to therapy and the need to alter drug therapy.

The SPYRAL-HTN trials have thus been designed to eliminate potential impediments to a definitive conclusion. To ensure the largest perceived benefit, only patients with moderate to high-risk hypertension will be included (systolic blood pressure ≥150 & <180 mmHg; diastolic blood pressure ≥90 mmHg). The use of 24-hour ambulatory monitoring (ABPM) devices will ensure comprehensive, accurate blood pressure measurement. Both trials will be blinded to eliminate the placebo effect, meaning that some patients will have "sham" procedures consisting of renal angiography only. The potential confounding effect of regression to the mean on trial results will be circumvented by randomization between active and control arms and the use of treatment effect as the efficacy endpoint (defined as the difference in response between active and control arms).

The procedures for both studies will be performed using the SPYRAL renal denervation catheter. The SPYRAL employs four radiofrequency electrodes mounted ~5 mm apart in a helical pattern to provide automated 4-quadrant ablation treatments in the main, branch, and accessory renal arteries in vessels ranging in diameter between 3 and 8 mm.

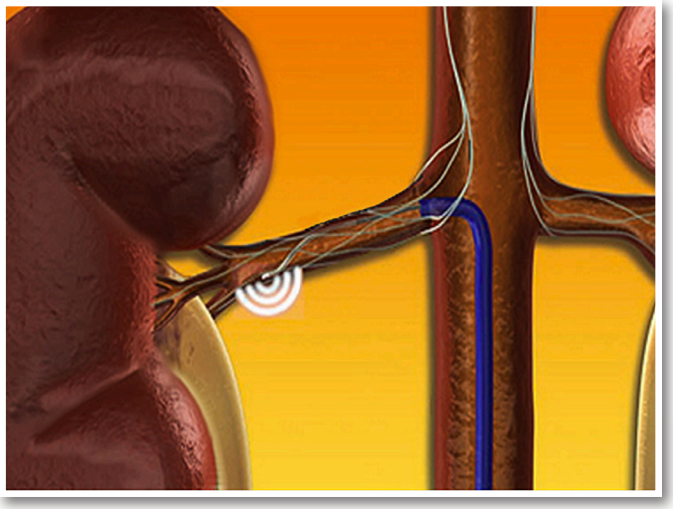

Figure 1: The SPYRAL™ System consists of a small percutaneous catheter and a controlled treatment delivery generator that provides ~8 watts of energy to ablate the renal sympathetic nerves.

ABOUT SPYRAL HTN-OFF-MED

Objectives: The goal of the SPYRAL HTN-OFF MED study is to confirm that renal denervation therapy lowers blood pressure in patients with hypertension in the absence of antihypertensive treatment. Acute and chronic safety will be measured, as will change in systolic blood pressure as measured by 24-hour ambulatory blood pressure monitoring.

Methods: Participants between 20-80 years of age will discontinue antihypertensive therapy, and following a two-week washout will be randomized to either treatment or a sham procedure. Changes in 24-hour ambulatory and office blood pressure will be compared between therapy and sham groups at 3, 6, and 12-month intervals following the procedure.

ABOUT SPYRAL HTN-ON-MED

Objectives: The purpose of this study is to obtain an assessment of the efficacy and safety of renal denervation in the presence of three standard antihypertensive medications.

Methods: Participants will achieve stable treatment on an antihypertensive regimen consisting of a thiazide-type diuretic, a calcium channel blocker and an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker. Stable therapy must be maintained at dosages at least 50% of the maximal dose from 6 weeks prior to the initial screening until 6 months after the procedure.

PARTICIPATING IN THE SPYRAL HTN STUDIES

Individuals seeking information about participation in the SPYRAL-HTN Studies at Penn Medicine may contact principal investigators Debbie Cohen, MD, and Robert Wilensky, MD, at 215-615-0794, or research coordinator Edith Fletcher, RN, BSN, CCRC, at 215-662-6590.

FACULTY TEAM

Penn Heart and Vascular combines the renowned expertise of clinicians, researchers and educators to provide comprehensive, high quality care to all patients. Interventional cardiologists at Penn Heart and Vascular are currently teaming with specialists from the Renal Electrolyte and Hypertension Division to treat uncontrolled hypertension. The Renal Electrolyte and Hypertension Division treats patients with acute and chronic diseases of the kidneys and complex hypertension problems, among many other conditions.

SPYRAL HTN Study Team

Debbie Cohen, MD
Director, Hypertension; Co-Director, Neuroendocrine Tumor Program

Jay S. Giri, MD, MPH
Assistant Professor of Clinical Medicine

Robert L. Wilensky, MD
Director, Interventional Cardiology Research
Professor of Medicine

Research Nurse Coordinators

Robin Neubauer, RN
Clinical Research Coordinator

ACCESS

Penn Heart and Vascular Center
Perelman Center for Advanced Medicine
East Pavilion, 2nd Floor
3400 Civic Center Boulevard
Philadelphia, PA 19104

Renal Electrolyte and Hypertension
Perelman Center for Advanced Medicine
South Pavilion, 1st Floor
3400 Civic Center Boulevard
Philadelphia, PA 19104

FY-16-9984_03.16