The next steps in renal denervation – update on Medtronic SPYRAL HTN program

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Faculty Disclosure

• Thomas Zeller, MD

For the 12 months preceding this presentation, I disclose the following types of financial relationships:

• **Honoraria received from:** Abbott Vascular, Angioslide, Bard Peripheral Vascular, Veryan, Biotronik, Boston Scientific Corp., Cook Medical, Cordis Corp., Covidien, Gore & Associates, Medtronic, Spectranetics, Straub Medical, TriReme, VIVA Physicians

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Hypertension Remains a Major Health Burden

• Astonishing prevalence of hypertension:\(^2\)
  – 1 in 3 adults
  – 1 billion people worldwide → 1.6 billion by 2025

• Single largest contributor to death\(^3\)

• Dramatically increases risk of heart attack, stroke, heart failure, and kidney failure\(^4\)

• Direct costs: $500B worldwide

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\(^1\)Uncontrolled defined as \(\geq 140\) mm Hg systolic or \(\geq 90\) mm Hg diastolic. CDC Vital Signs September 2012, NHANES 2003–2010.


Small Reductions in Blood Pressure Reduce Risk of Cardiovascular Mortality

- 10% Reduction in Risk of Stroke Mortality
- 7% Reduction in Risk of Ischemic Heart Disease Mortality

Meta-analysis of 61 prospective, observational studies
- 1 million adults (40–89 years; 70% Europe, 20% North America or Australia, 10% Japan or China)
- 12.7 million person-years

SBP = systolic blood pressure
SPRINT: Systolic Blood Pressure Intervention Trial Showed Lower Risk and Improved Mortality with More Aggressive BP Targets

9361 Patients with HTN
Exclusions: DM, prior stroke
Inclusion: age >50 and CAD, CKD, ≥75 (~25%) or Framingham risk ≥15% over 10 years

<table>
<thead>
<tr>
<th>SBP Goal &lt;120</th>
<th>SBP Goal &lt;140</th>
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<tbody>
<tr>
<td>chlorthalidone, amlodipine, lisinopril</td>
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</table>

Primary endpoint: MI, CV death, ACS, heart failure, stroke
↓25%

Secondary endpoint: all-cause mortality
↓27%

SPYRAL HTN Global Clinical Trial Program

SYMPLECTICITY
HTN-3 Factor Identified

Medications
- Obtain off-med data
- Standardise meds
- No max dose titration
- Measure adherence

Study population
- Less severe HTN
- Fewer prescribed meds
- Focus on ABPM
- Patients from across globe
- Avoid changing patient behavior

Procedural
- Symplicity Spyral™ catheter
- Main and branch vessel treatment
- Experienced proceduralists

SPYRAL HTN

Medication Study Population Procedural
Simplicity Spyral™ Multi-Electrode Renal Denervation Catheter

- Consistent four-quadrant ablation pattern
- 4 F catheter profile
- 6 F guide catheter compatible
- 0.014” over-the-wire rapid exchange delivery
- 60-second simultaneous energy delivery
- Vessel diameter range: 3–8 mm
- Multisensor feedback to control energy delivery

Performance data on file at Medtronic.
Renal Sympathetic Innervation

- Renal nerves generally originate from the aorta and arborise towards the kidney.
- Nerve fibers do not completely converge on the renal artery until beyond the main bifurcation.
- Accessory arteries, when present, have similar anatomical innervation patterns that mimic the main renal arteries.
- Renal denervation within the post-bifurcation branches may increase the likelihood of achieving complete renal denervation.

Our View of Renal Nerve Distribution Has Changed

Renal nerves may have a positional bias on radial distance from arterial lumen; distal nerves are closer.

Prior concept—uniform radial distribution

Current concept—nonuniform radial distribution

Sakakura K et al. JACC. 201464:634–643.
Preclinical data show significantly greater reductions in renal sympathetic activity with combined proximal and distal therapy application.

<table>
<thead>
<tr>
<th>%NE Change ± SD</th>
<th>-71 ± 27%</th>
<th>-83 ± 21%</th>
<th>-92 ± 9%</th>
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Note: Preclinical data may not be representative of human data.
**SPYRAL HTN**

Global Clinical Trial Program

**First Phase Includes Two Parallel Trials**
Up to 25 Sites Globally

**SPYRAL HTN–OFF MED**
- 100 patients
- Sham RCT (1:1)
- Main body and branch ablation
- No specific baseline medication requirement
- Compare ABPM change at 3 months

**SPYRAL HTN–ON MED**
- 100 patients
- Sham RCT (1:1), 1–3 medications
- Main body and branch ablation
- No max tolerated dose
- Compare ABPM change at 3 months

**Second**

**SPYRAL HTN Pivotal**
- Based on OFF/ON trial results
- Cost effectiveness data/QOL to be measured
Enrolling in all geographies:
- USA
- Europe
- Japan
- Australia
### Summary

| The SPYRAL HTN Global Clinical Trial Program is intended to address the confounding factors identified in SYMPLICITY HTN-3. | The ON- and OFF- antihypertensive studies will allow better understanding of the impact of medication on renal denervation. | The SPYRAL HTN program is designed to obtain evidence required for future regulatory approvals and reimbursement. |
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