HTH Technology Matters. Return on experience  
*The Vessix technology*

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Faculty disclosure

I disclose the following financial relationships:

I have no financial relationships to disclose.
Vessix Renal Denervation System

- Balloon-based technology
  - 4 to 7 mm diameters
  - Helical pattern of bipolar radiofrequency electrodes
- 30 second treatment time
- All electrodes are activated simultaneously

- Bipolar energy delivery, ~1 Watt
- Temperature-controlled algorithm
- ensures energy delivery at 68°C
- One button operation
**Vessix™ System: Intuitive User interface**

- **Splash Screen**
- **Image flashes prompting user to connect catheter**
- **Confirms catheter is connected**
- **Electrode pairs light up to confirm apposition inside renal artery**
- **Treatment screen, indicates temperature, time, power, and # of electrodes treating**
- **End of treatment screen, displaying average treatment temperature, time, power and # of electrodes activated**
**Fixed Pattern**

Vessix System treats the full length of the artery in a fixed helical pattern.

**Bipolar**

Bipolar electrodes on a balloon platform enable targeted, temperature controlled energy delivery.

**Balloon**

Balloon provides firm vessel apposition of electrodes and occludes blood flow, for predictable treatment.
The Vessix™ System: Treatment of the full length of artery

Automatic de-activation of unapposed electrodes
For longer length renal arteries, 1-2 treatments can be applied
Balloon inflated to a maximum of 3 Atm
# Renal Denervation Technologies

<table>
<thead>
<tr>
<th></th>
<th>BSC Vessix</th>
<th>MDT Flex</th>
<th>MDT Spyral</th>
<th>STJ EnlightN</th>
<th>JNJ RenLane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter Design</td>
<td>Balloon catheter, 4-8 electrodes</td>
<td>Single electrode</td>
<td>Pigtail Catheter, 4 electrodes</td>
<td>Basket, 4 electrodes</td>
<td>Pigtail Catheter, 5 electrodes, irrigated</td>
</tr>
<tr>
<td>Balloon</td>
<td>✓</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Guidewire</td>
<td>✓</td>
<td>--</td>
<td>✓</td>
<td>--</td>
<td>✓</td>
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<tr>
<td>Energy</td>
<td>Bipolar RF</td>
<td>Monopolar RF</td>
<td>Monopolar RF</td>
<td>Monopolar RF</td>
<td>Monopolar RF</td>
</tr>
<tr>
<td>Power</td>
<td>~1W</td>
<td>~8W</td>
<td>6.5W</td>
<td>8W</td>
<td>Unknown</td>
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<tr>
<td>Total Treatment Time</td>
<td>1-2 min.</td>
<td>16-24 min.</td>
<td>2-4 min.</td>
<td>4 min.</td>
<td>Unknown</td>
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</table>
Boston Scientific Renal Denervation Program

Vessix™ Global Clinical Program

> 1200 Patients planned worldwide

REDUCE-HTN Clinical Series

Studies evaluating the Vessix System technology in the currently defined hypertension space:

- REDUCE-HTN FIM Study
- REDUCE-HTN Post Market Study
- REDUCE-HTN Global Pivotal Study
- REDUCE-HTN Regional Reg. Approval Studies
- REDUCE-HTN EU Post Market Trial

RELIEVE Clinical Series

Includes pre-clinical, clinical and investigator initiated research evaluating the Vessix System technology in additional disease states:

- RELIEVE - End Stage Renal Disease
- RELIEVE - Heart Failure
- RELIEVE - Atrial Fibrillation
- RELIEVE - Diabetes

Vessix™ Global Clinical Program
# REDUCE-HTN Clinical Sites

<table>
<thead>
<tr>
<th>Institution</th>
<th>Principal Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parcelsus Medical University</td>
<td>Prof. Dr. Uta C. Hoppe</td>
</tr>
<tr>
<td>Allgemein Affentliches Krankenhaus der Stadt Linz</td>
<td>Prof. Dr. Clemens Steinwender</td>
</tr>
<tr>
<td>Onze-Lieve-Vrouwziekenhuis, (OLVZ)</td>
<td>Dr. Eric Wyffels</td>
</tr>
<tr>
<td>Monash Heart Southern Health</td>
<td>Prof. Dr. Ian Meredith</td>
</tr>
<tr>
<td>CardioVasculares Centrum (CVC) Frankfurt</td>
<td>Prof. Dr. med Horst Sievert</td>
</tr>
<tr>
<td>George Pompidou Hospital</td>
<td>Prof. Dr. Michel Azizi</td>
</tr>
<tr>
<td>The Prince Charles Hospital</td>
<td>Associate Prof. Darren Walters</td>
</tr>
<tr>
<td>Cardiology Center Geneva university Hospitals</td>
<td>Dr. Georg Ehret</td>
</tr>
<tr>
<td>Auckland City Hospital</td>
<td>Dr. Mark Webster</td>
</tr>
<tr>
<td>Flinders Medical Centre</td>
<td>Dr. Ajay Sinhal</td>
</tr>
<tr>
<td>Erasmus Medical Center</td>
<td>Dr. Joost Daemen</td>
</tr>
<tr>
<td>Vascular Center Berlin</td>
<td>Dr. Ralf Langhoff</td>
</tr>
<tr>
<td>Main Tanus Kliniken</td>
<td>Prof. Dr. med. Nicolaus Reifart</td>
</tr>
<tr>
<td>St. Vincent's</td>
<td>Dr. David Muller</td>
</tr>
<tr>
<td>Zentrum für Gefäßmedizin</td>
<td>Prof. Dierk Scheinert</td>
</tr>
<tr>
<td>Academic Medical Center</td>
<td>Prof. Robbert-Jan de Winter</td>
</tr>
<tr>
<td>Cliniques Universitaires Saint Luc</td>
<td>Prof. dr. Alexandre Persu</td>
</tr>
<tr>
<td>Clinique Pasteur</td>
<td>Prof. Jean Fajadet</td>
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<tr>
<td>German Heart Centre</td>
<td>Prof. Dr. med. Ilka Ott</td>
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<tr>
<td>Universitäres Herz- und Gefäßzentrum Hamburg</td>
<td>Prof. Dr. med. Joachim Schofer</td>
</tr>
<tr>
<td>Zentralklinik Bad Berka GmbH</td>
<td>Dr. med. Ahmed Farah</td>
</tr>
<tr>
<td>Royal Adelaide Hospital</td>
<td>Prof. Steven Worthley</td>
</tr>
<tr>
<td>Mercy Angiography - Auckland</td>
<td>Dr. John Ormiston</td>
</tr>
</tbody>
</table>
Key Inclusion Criteria

- Office-based blood pressure (average of 3 readings):
  - First in Man (FIM): systolic blood pressure ≥ 160 mmHg
  - Post-Market Study (PMS): systolic/diastolic ≥ 160/90 mmHg
- ≥ 3 antihypertensive drugs at maximally tolerated doses with stable regimen for at least 2 weeks prior to enrollment
- Renal artery length:
  - FIM: ≥ 20 mm
  - PMS: ≥ 15 mm
- Renal artery without significant stenosis (i.e., baseline diameter stenosis <30%)
- Main renal artery diameter of ≥ 3.5 mm and ≤ 7.0 mm for each kidney:
  - FIM: Single renal artery
  - PMS: Subjects with accessory renal arteries were enrolled

Efficacy Measures

- Office blood pressure (through 18 months)
- 24-hour ambulatory blood pressure (6 and 12 months)

35% of patients (51/146) have completed 18 month follow-up to date
## Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>N=146</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Characteristics</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender (male)</td>
</tr>
<tr>
<td>Ethnic origin (white)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
</tr>
<tr>
<td><strong>Kidney Function</strong></td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L)</td>
</tr>
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</table>
18 month f/u results

<table>
<thead>
<tr>
<th>Time Point</th>
<th>N</th>
<th>Mean BP Change (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Month</td>
<td>142</td>
<td>-10,0</td>
</tr>
<tr>
<td>3 Months</td>
<td>144</td>
<td>-8,2</td>
</tr>
<tr>
<td>6 Months</td>
<td>143</td>
<td>-10,3</td>
</tr>
<tr>
<td>12 Months</td>
<td>133</td>
<td>-10,0</td>
</tr>
<tr>
<td>18 Months</td>
<td>51</td>
<td>-12,7</td>
</tr>
</tbody>
</table>

P < .0001 for each time point vs baseline. Error bars represent 95% confidence bounds.

- Change in Office Systolic BP
- Change in Office Diastolic BP
80% had a clinically meaningful response (ie, reduction >10 mmHg) based on office systolic blood pressure at 18 months.
18 month f/u results
24H ABPM

Mean BP Change from Baseline (mmHg)

<table>
<thead>
<tr>
<th>Time Point</th>
<th>N</th>
<th>Change in Systolic ABP</th>
<th>Change in Diastolic ABP</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months (N=70)</td>
<td></td>
<td>-8.0</td>
<td>-5.7</td>
</tr>
<tr>
<td>12 Months (N=66)</td>
<td></td>
<td>-8.5</td>
<td>-5.5</td>
</tr>
</tbody>
</table>

P < .0001 for each time point vs baseline. Error bars represent 95% confidence bounds.

153/88 mmHg (N=103)
18 month f/u results
24H ABPM

6 Months (n=70)
8,0
-5,9
-16,5

12 Months (n=66)
3,4
-6,7
-15,1

Mean Systolic BP Change from Baseline (mmHg)

- BSBP <135 mmHg (n=15)
- BSBP 135-159 mmHg (n=58)
- BSBP ≥160 mmHg (n=30)
REDUCE-HTN Study
Anatomic Consideration

- Flow limiting stenosis
- Artery Diameter
  - Standard is $\geq 4\text{mm}$
  - Vessix is $\geq 3\text{mm}$
- Artery Length
  - Standard is $\geq 20\text{mm}$
  - Vessix is $\geq 15\text{mm}$
- Absence of Stent(s)
REDUCE-HTN Study

Anatomic Consideration: areas to avoid

Avoid treating areas of visible disease

Mahfoud, F. ESC 2012
### Recommended Catheter Sizing Table

<table>
<thead>
<tr>
<th>Artery Size</th>
<th>3.0 – 4.0mm</th>
<th>3.8 – 5.0mm</th>
<th>4.7 – 6.0mm</th>
<th>5.6 – 7.0mm</th>
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<tbody>
<tr>
<td>4mm balloon</td>
<td>Yes</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>5mm balloon</td>
<td>X</td>
<td>Yes</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>6mm balloon</td>
<td>X</td>
<td>X</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>7mm balloon</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Yes</td>
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</tbody>
</table>

The Vessix catheter can treat arteries as small as 3mm.
Preliminary Ambulatory BP 12 month data in 12 patients with treated accessory renal arteries show a mean reduction of 5.7/4.0 mmHg.
Office-based blood pressure measurements over long-term follow-up in the REDUCE-HTN study continue to show significant reductions

- Preliminary 18-month results (N=51) show a mean office blood pressure reduction of 30.2/12.7 mmHg

- Preliminary 12-month data for the subgroup of patients with treated accessory renal arteries (N=21) show a mean reduction of 23.2/14.4 mmHg
REDUCE-HTN Study

Conclusion-2

24-hour ambulatory blood pressure measurements through 12 months in the REDUCE-HTN study support sustained efficacy of the Vessix System in treating resistant hypertension

- Preliminary 1-year results (N=66) show a mean pressure reduction of 8.5/5.5 mmHg

- Preliminary 12-month data for the subgroup of patients with treated accessory renal arteries show a mean reduction of 5.7/4.0 mmHg
Case # 1

- 57 yom
- Family history of HTN and premature CAD
- HTN, HyperCh, previous smoker, obesity
- Type 2, NIDDM
- 2001 Hemispheric TIA → first detection of severe HTN
- 2007 AAA (<4 cm) in f/u with ultrasound
- 2013 Normal renal anatomy and ultrasound Doppler assessment
- **Refractory HTN despite:** metoprolol 100 mg x 2, Amlodipine 10 mg x 2, Telmisartan/hydrochlorothiazide 80/12.5 x 2, Spironolattone 50 mg/day

- 175 cm x 108 Kg, BMI >35
- BP on admission: 160/100 mmHg
- Blood chemistry: glucose 135 mg%, renal 35/0.86/3.88/94 ml/’, cholesterol 169/41/91, Trygliceride 186, TSH 2.5
- **Rest ECG:** aspecific ST-T abnormality.
- **Echocardiogram:** mild LVH. LA dilation (51/24). Normal EF: 62% Absence of diastolic dysfunction
Ambulatory BP monitoring data

Baseline 11/6/2013

Office BP: 200/120 mmHg (S)
180/120 mmHg (U)

SAP: 187±15 mmHg
DAP: 107±17 mmHg
HR: 77±9 bpm
Renal arteries angiography

Right renal artery

Left renal artery

* ISA: inferior suprarenal artery
Renal artery denervation procedure

Right RDN, 3 amt inflation. (Test for occlusion)

Post-RDN (x2 inflations)
Device inflation (8 atm) and test for occlusion

LRA ostium
Left renal artery denervation

**Angiographic and OCT findings**

4.5x5.1 mm

4.9x5.8 mm

**OCT catheter: C7 Dragonfly™ LightLab Imaging Inc., Westford, MA, USA**
Follow-up CT-Angiography

1/23/2014
Office & Ambulatory BP monitoring data in the F/u

Baseline
Office BP: 210/120 mmHg
SAP: 187±15 mmHg
DAP: 107±17 mmHg
HR: 77±9 bpm

30 days post-RDN
Office BP: 140/85 mmHg
SAP: 142±13 mmHg
DAP: 81±9.1 mmHg
HR: 70±6 bpm

90 days post-RDN
Office BP: 130/85 mmHg
SAP: 147±13 mmHg
DAP: 84±13 mmHg
HR: 80±17 bpm

Medical treatment unchanged
Case # 2
Moderate Resistant Hypertension

Definition: Office BP >140/90 mmHg and <160/100 mmHg
ABPM ≥ 130/80 mmHg (Ott C et al. JACC 2013)

- 69 yom
- Family history of HTN and diabetes
- HyperCh, previous smoker, obesity
- Type 2, NIDDM
- 2011 Hypertension
- Refractory HTN despite: olmesartan 40 mg/day, Amlodipina 10 mg/day, Atenolol 100 mg/day, Amiloride+Triamterene ½ cp, Metformin 500 mg x 2

- 100 cm x 163 Kg, BMI >35
- Office BP: 170/90 mmHg
- Blood chemistry: glucose 148 mg%/7.8% HbA1c, renal 63/1.09/>60 GFR, cholesterol 215/48/101, Trygliceride 332
- Rest ECG: within normal limits.
- Echocardiogram: Mild LVH (17/12 mm). LA dilation. EF: 73%
Ambulatory BP monitoring data

Baseline, 10/23/2013

Office BP:
185/90 mmHg (S)
180/80 mmHg (U)

SAP: 144±15 mmHg
DAP: 68±9 mmHg
HR: 57±4 bpm
RDN Procedure: Right renal artery
RDN Procedure: Left renal artery
RDN Procedure: Right renal artery

RDN at the right renal artery ostium (second site of energy erogation)
Office & Ambulatory BP monitoring data in the F/u

Baseline
OBP: 170/90

SAP: 144±15 mmHg
DAP: 68±9 mmHg
HR: 57±4 bpm

30 days post-RDN
OBP: 140/80

SAP: 134±11 mmHg
DAP: 64±8 mmHg
HR: 51±12 bpm

90 days post-RDN
OBP: 135/80

SAP: 125±18 mmHg
DAP: 63±10 mmHg
HR: 51±5 bpm

Medical treatment unchanged
Take home messages

- Both patients with true resistant hypertension & moderate resistant hypertension may be candidates for RDN.

- The Vessix technology appears to be safe and effective. Non-flow limiting dissections of renal arteries may be found, likely due to balloon inflation distal to major artery bifurcation. Spontaneous sealing of this dissections occurs as shown in the CTA after 1 month w/o clinical complications.

- Sustained BP reduction was observed up to 3 month-F/U.